E.V.A. BOUWSMA

ENHANCING POSTOPERATIVE

RECOVERY & PARTICIPATION

in GYNAECOLOGICAL PATIENTS

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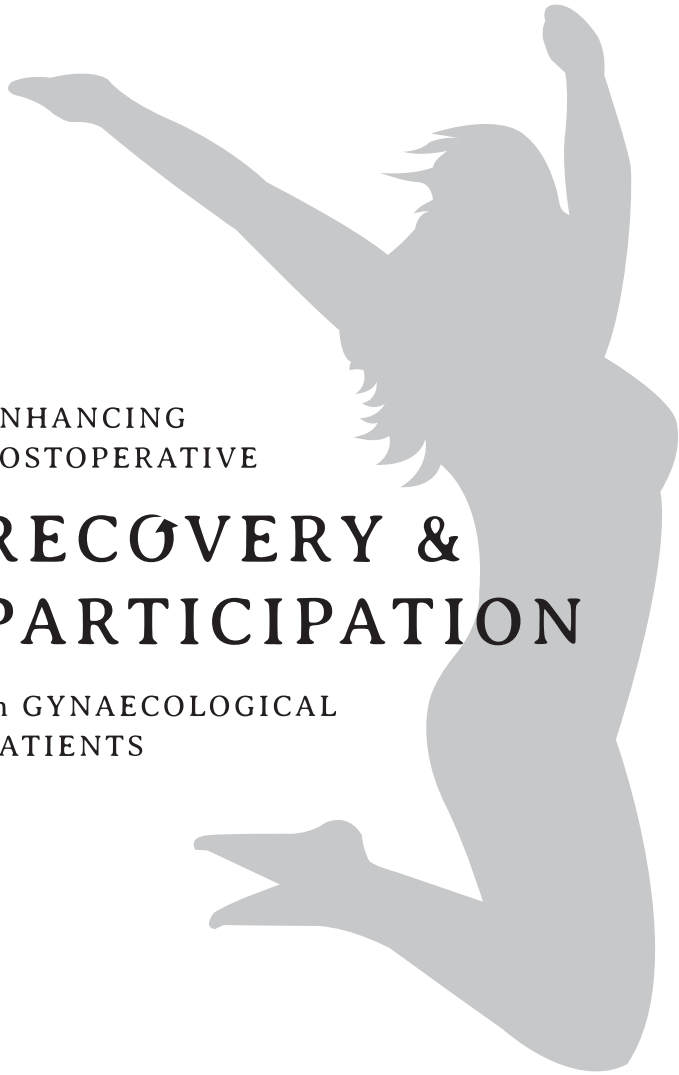

ENHANCING POSTOPERATIVE RECOVERY & PARTICIPATION in GYNAECOLOGICAL PATIENTS

Enhancing postoperative recovery & participation in gynaecological patients
Esther Vivienne Angelique Bouwsma

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CHAPTER 1

General introduction

In 1960, Dr. F. C. Dohan and his colleagues published an article in the journal 'Surgery, Gynecology and Obstetrics' about convalescence following common surgical procedures.[1] In their 'Surgical Convalescence Study' the authors prospectively enrolled employees from an industrial firm who underwent a surgical procedure during the years 1957 and 1958. Sickness disability claim forms were collected and interviews with the patients in the postoperative period were held. The surgeons' forecast duration of convalescence, i.e. the duration between the operation and the day of return to work the doctor had advised or recommended, was compared with the actual duration of convalescence. The results of this study led to the conclusion that prolonged convalescence was caused by the surgeon rather than the patient, due to convalescence advise being unnecessary long, leading towards iatrogenic illness resulting in considerable inconvenience and economic loss to both the patient and society (figure 1).[1]

The total duration of uncomplicated surgical convalescence is usually determined not by the patient's psychologic or psychologic needs, but by the surgeon's opinion. This conclusion is supported by:

1. the high correlation of the surgeon's forecast duration of convalescence with the actual duration of uncomplicated convalescence in this study;
2. the statement of most patients in this study that their surgeons determined the duration of their convalescence period;
3. evidence that patients who follow their surgeons' recommendation for a short convalescence feel as well at the time they return to work as those who follow the surgeons' recommendations for a long convalescence;
4. the wide range of opinion among surgeons concerning the proper duration of in complicated convalescence in the same hypothetic postoperative case;
5. the wide range of actual duration of convalescence within the same age group after the same type of operation;
6. the demonstrated safety of considerable shorter convalescence periods than those usually recommended.

These facts demonstrate that the majority of individuals are advised to undergo far longer convalescence after common surgical procedures than is necessary, and, as a result of this advice, do so. This results in unnecessary "iatrogenic" illness, considerable inconvenience, and economic loss to the individual and the nation.

Figure 1. Abstract from "The role of the surgeon in the prolongation of uncomplicated surgical convalescence" by F.C. Dohan *et al* in Surgery, Gynecology and Obstetrics. 1960;111:49-57.

Since the publication of this article about six decades ago, much has been achieved in the surgical field and many innovations have led to substantial improvements in healthcare delivery and patient outcomes.[2] Examples of such innovations include, but are definitely not limited to: improved anaesthetic practices and the use of short acting and regional anaesthesia, optimal intra-operative guidance of vitals, body temperature and blood glucose, appropriate use of antibiotics to reduce surgical-site infection, advanced postoperative critical care, and proper prophylaxis for deep vein thrombosis. In addition, changes in the processes of care such as the introduction of safety checklists, led to a significant reduction in postoperative complications and deaths.[3, 4] However, the innovation that revolutionized general surgery in the last half century was the introduction of minimally invasive surgery.[5] Compared with open surgery, the use of smaller incisions results in less tissue trauma and inflammation, less blood loss and reduced risk of infection as well as better cosmetic results. Furthermore, patients experience less pain during the postoperative period and mobilize faster, leading to shorter hospital stays. As a result, many (complex) surgeries are now being performed in an ambulatory setting.[6-9]

At present, there is considerable evidence that the length of recovery time after (gynaecological) surgery systematically exceeds the recovery time considered as appropriate by specialists.[6, 10-16] In a national health survey performed in 1960-1961 in the United States among 231,000 women who underwent a hysterectomy, the average duration of convalescence (from surgery to resumption of usual full-time activity) was 52 days.[17] The convalescence period was longer for working women (61 days) compared to women who did not work (46 days).[17] In more recent literature, return to normal activities after abdominal hysterectomy varied between 36 and 59 days (seven studies performed between 1996 and 2003).[18] Return to work (RTW) was not assessed, however, like in other studies, duration until RTW was probably longer than the duration until the resumption of normal activities. In addition, in a prospective study performed by our own study group among 148 patients undergoing gynaecological surgery for benign disease between 2008 and 2010 convalescence turned out to take even longer than six decades ago as the median time to RTW was 69 days in the group undergoing major surgery (including abdominal hysterectomy).[10]

These data suggest that, despite all revolutionary progress in surgical care, unnecessary prolonged recovery after surgery is still a problem in current practice. Furthermore, it brings forth the question why we are not able to fully benefit from the advanced medical and surgical innovations that have been introduced in the last decades and why convalescence duration did not decline accordingly.

In the following paragraphs we will explain:

1. the underlying factors that contribute to unnecessary prolonged convalescence;
2. the relevance of preventing unnecessary prolonged convalescence;
3. the intervention that was developed to prevent unnecessary prolonged convalescence following four types of gynaecological surgery.

UNDERLYING FACTORS CONTRIBUTING TO UNNECESSARY PROLONGED CONVALESCENCE

In 1960, the duration of hospitalization after a hysterectomy generally exceeded one week.[17] Nowadays, outpatient hysterectomy has been demonstrated to be both safe and feasible and same-day discharge protocols are being implemented in various settings.[19, 20] Thus, at present there is a significant transition of care from the hospital setting towards the home environment, leaving much of the recovery phase to occur outside the monitored hospital setting.[12] This transition of care is advantageous, as it leads to containment of healthcare costs. However, it also causes challenges in the way postoperative care is organized in order to take care of postoperative patients at home. Despite this transition, healthcare providers have not shifted their focus of care away from the hospital setting.[21] Moreover, the focus of much research has been on safe discharge from the ambulatory surgical suite[6], leaving efficient strategies to guide outpatient, postoperative patients unexplored. Hence, the combination of current fragmented perioperative care and the lack of coordination of care after discharge, is the first factor we identify that puts patients at risk for unnecessary prolonged recovery.

The second factor contributing to unnecessary prolonged postoperative recovery is the fact that perioperative education has not found its way into routine surgical care, while it has been demonstrated to be beneficial in terms of increasing patient satisfaction, reducing pain and psychological distress and optimizing patients expectations.[14, 22-25] Especially patients' own recovery expectations are considered to be a significant predictor of recovery.[26, 27] Therefore, by not facilitating perioperative education, the opportunity to optimize patient expectations remains neglected, leaving patients unprepared for their recovery at home. Mainly two reasons can be identified for the lack of structured perioperative education. First, there is only little evidence on the duration needed to resume various daily activities following different surgeries.[28-33] This leads to convalescence advise being based on tradition and anecdote from health care providers.[13, 28, 31, 34-39] Second, due to the current trend towards day care and short stay surgery, patient contact is very brief and time available for patient education has practically evaporated.[6, 40-43]

THE IMPORTANCE OF PREVENTING UNNECESSARY PROLONGED CONVALESCENCE

The World Health Organisation (WHO) defines health as a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity.[44] In accordance with the biopsychosocial model disability can involve dysfunctioning at different levels, which can interact with each other: impairments at the body level can lead to activity limitations which can lead to participation restrictions.[45] In this light, the importance of preventing unnecessary prolonged convalescence becomes clear.

Extensive studies and theoretical analyses of work and of unemployment, and comparisons between work and unemployment, support the basic concept that work is beneficial for health and well-being.[46] The importance of work to the individual is not only demonstrated by a financial reward, but work plays a crucial role in the formation of self-esteem as well, as it provides a sense of personal achievement, helps to build confidence and enables people to socialise, build contacts and find support. In conclusion, work contributes to full participation in society. The opposite is also the case: being out of work has a negative impact on health, demonstrated by higher rates of physical and mental problems and higher use of medical services and medication consumption among unemployed persons.[47] Subsequently, there is strong evidence that returning to work after a period of unemployment results in significant physical and mental health improvements, reversing the harmful effects of sickness absence.[46]

Preventing unnecessary prolonged recovery is not only important for the individual itself, but has also great implications for society as a whole. Surgery represents a considerable proportion of hospital services and is generally a costly procedure, requiring considerable resources intraoperatively as well as costly hospital stays.[48] Traditionally, studies focused on health care expenditures but ignored other measures of benefit and cost, such as the impact of procedures on worker productivity.[46, 49] In more recent years, it has been argued frequently that minimal invasive surgery has a beneficial effect on indirect costs as well, through the mechanism of faster convalescence and faster return to normal activity level (including work).[50-52] However, as long as patients are at risk of prolonged convalescence due the current organization of postoperative care, indirect costs associated with absenteeism and presenteeism following surgery will not decrease. Taking into account the high amount of gynaecological surgeries being performed annually in a relative young and employed population, understanding and managing the economic and social implications of postoperative convalescence should be an important priority of policy makers.

DEVELOPING AN INTERVENTION TO PREVENT UNNECESSARY PROLONGED CONVALESCENCE

Since 2008 our research group has been working on developing an effective intervention in order to optimize perioperative (gynaecological) care in the Netherlands. We hypothesized that unnecessary delayed postoperative recovery could be prevented and costs associated with prolonged sick leave and increased health care utilization after surgery could be minimized, through the mechanisms of:

1. providing personalised guidance throughout the entire surgical pathway from the early preoperative phase, starting from the moment the indication for surgery is set, until the late postoperative phase, ending with full recovery and resumption of all daily activities, including work;
2. promoting appropriate recovery expectations by providing tailored convalescence advice;
3. facilitating self-management.

The first achievement included the development of unified convalescence recommendations following four types of benign gynaecological surgery.[53] Using a structured consensus method, an expert panel of gynaecologists, general practitioners and occupational physicians formulated recommended recovery times for the graded resumption of 38 daily activities (e.g. standing, walking, climbing stairs, performing household chores, and return to work).

Secondly, a multidisciplinary care program was developed applying the principles of intervention mapping systematically.[54] The care programme consisted of an eHealth intervention and, for those patients at risk of prolonged sick leave, an occupational intervention. The e-health intervention included an interactive web portal in which the developed convalescence recommendations were incorporated. The web portal was considered to be an excellent platform to guide patients at home throughout the surgical pathway, modify poor recovery expectations, monitor postoperative recovery, and coordinate different processes of postoperative care.

The feasibility of this Internet-based care programme was then studied in an efficacy randomised trial.[55] The care programme resulted in improved return to work rates in the intervention group compared with the control group. In addition, the care programme had a significant beneficial effect on pain intensity and quality of life in postoperative women compared to the control group.[55]

OBJECTIVE OF THIS THESIS

Before complex interventions can be implemented in practice they should follow a developing, piloting and evaluating phase.[56] This thesis builds on the previous work of Dr. A. Vonk Noordegraaf & colleagues and the thesis "Recovery and return to work after gynaecological surgery" which gave the platform for describing the developing and piloting phase of the Internet-based care programme to enhance postoperative recovery in gynaecological patients. The current thesis focusses on the next two phases: the evaluation and the implementation of this Internet-based care programme.

The aim of the present thesis is to contribute to the development of a sound evidence base on post-operative recovery following gynaecological surgery and interventions to enhance postoperative recovery. This will be done by reviewing current literature, generating new evidence, and developing recommendations for clinical practice and further research.

OUTLINE OF THIS THESIS

Chapter 2 presents the results of a process evaluation of the earlier version of the web-based care programme. Lessons learned from the process evaluation were used to further develop the web-based care programme that was subject to evaluation in the current thesis.

Chapter 3 reports the protocol that was designed to study both the effectiveness and cost-effectiveness of the adapted web-based care programme. Results of the stepped-wedge cluster randomized trial on the effectiveness of the intervention are reported in **chapter 4.** Moreover, it reports on the implementation of the intervention in nine hospitals in the Netherlands**. Chapter 5** describes the results of the cost-effectiveness study that was performed alongside the cluster randomized controlled trial.

Chapter 6 describes how patient data from the cluster randomised trial were used to optimize the earlier developed expert-based guideline on convalescence recommendations.

In **chapter 7** the results from a survey study are presented in which patients' needs and benefits about a perioperative eHealth intervention were explored not only in gynaecologic patients but also in patients undergoing general surgical procedures such as cholecystectomy, inguinal hernia surgery, appendectomy and colectomy.

Chapter 8 describes a systematic review that was conducted to summarize and critically appraise the current literature on all interventions that aim to facilitate patients to return to their pre-operative levels of activity and participation.

The general discussion (**chapter 9**) presents an overview of the main findings of this thesis and critically discusses the theoretical, practical and methodological issues encountered in this thesis. Furthermore, it provided suggestions for practice and future research.

A summary in English and Dutch are given in **chapter 10**.

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CHAPTER 2

Process evaluation of a multidisciplinary care program for patients undergoing gynaecological surgery

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ABSTRACT

Purpose This study describes the process evaluation of an innovative multidisciplinary care program for patients undergoing benign gynaecologic surgery. This care program aims at improving recovery and preventing delayed return to work and consists of two steps: (1) an interactive e-health intervention for all participants, and (2) integrated clinical and occupational care management for those participants whose sick leave exceeds 10 weeks.

Methods Eligible for this study were employed women aged between 18–65 years scheduled for a laparoscopic adnexal surgery and/or hysterectomy. Data were collected from patients, their supervisors and their gynaecologists, by means of electronic questionnaires during a 6 month follow-up period and an automatically generated, detailed weblog of the patient web portal (www.ikherstel.nl). Investigated process measures included: reach, dose delivered, dose received, and fidelity. In addition, attitudes towards the intervention were explored among all stakeholders.

Results 215 patients enrolled in the study and accounted to a reach of 60.2 % (215/357). All intervention group patients used their account at least once and total time spent on the patient web portal was almost 2 h for each patient (median 118 min, IQR 64–173 min). Most patients visited the website several times (median 11 times, IQR 6–16). Perceived effectiveness among patients was high (74 %). In addition, gynaecologists (76 %) and employers (61 %) were satisfied with the web portal as well. Implementation of the second step of the intervention was suboptimal. Motivating patients to consent to additional guidance and developing an accurate return-to-work-prognosis were two important obstacles.

Conclusions The results of this study indicate good feasibility for implementation on a broad scale of the e-health intervention for patients undergoing benign gynaecological surgery. To enhance the implementation of the second step of the perioperative care program, adaptations in the integrated care protocol are needed.

INTRODUCTION

In gynaecology, as in other surgical specialties, there is an increasing interest in accelerating recovery after conventional surgery as well as minimal invasive surgery. Although procedure costs may be higher in minimal invasive surgery than with more conventional approaches, there is a perception that minimal invasive surgery gains in cost-effectiveness through shorter length of hospital stay and quicker and better convalescence.[1–3] Reduction of inpatient stay can easily be measured and directly benefits a hospital financially. Convalescence, on the contrary, is not on top of the agenda of many healthcare policy makers. A reason might be the fact that convalescence is much more difficult to influence and monitor, especially now hospital stay is minimized and post-operative care is transferred to outpatient and primary care, and therefore, fragmented. In addition, there is a lack of recognised evidence-based convalescence recommendations for gynaecological procedures,[4, 5] resulting in a situation in which structural convalescence recommendations regarding the resumption of (work) activities are mostly not provided at discharge, or when given, are based on tradition and anecdote.[6–8]

The current poor organisation of peri-operative care in gynaecology may lead to delayed recovery, prolonged sick leave and higher risk of work disability[7, 9, 10] which is associated with a poorer quality of life.[11, 12] In addition, as women comprise 45 % of the workforce in the Netherlands[13], as well as in many other Western countries[14], the unnecessary absenteeism related to gynaecological procedures causes a considerable economic burden on society.[11]

The ikherstel-study ("I recover-study") is a randomized controlled trial (RCT) in which the effectiveness was evaluated of a multidisciplinary care program aimed at improving recovery and preventing delayed return to work following gynaecological surgery.[15] The intervention program, consisting of two steps, provides guidance to patients from the moment the surgery is planned until full resumption of all (work)-activities after the procedure. The intervention program was developed systematically, based on the intervention mapping protocol, involving all stakeholders in the development process.[16, 17]

Besides developing an intervention systematically, it is of equal importance to evaluate the process of implementation systematically.[18–20] A good understanding of the extent to which the program was applied as intended, helps to interpret the outcome results in an effectiveness study. For example, in case positive effects of the program are not found, this could be attributable to either theory failure (the underlying theory is incorrect) or program failure (the program is potentially effective when implemented better).[21] Moreover, a process evaluation helps to gain insight into the facilitators and barriers to future implementation which may expedite the challenging transition from research into daily practice.

This current paper describes the process evaluation of the intervention program of the 'I recover-study'. The primary goal is to investigate the feasibility of the intervention by describing the process systematically. The second objective is to explore facilitators and barriers to future implementation.

METHODS

This process evaluation was carried out alongside an RCT studying the effectiveness of a multidisciplinary care program aimed at improving recovery and preventing delayed return to work following benign gynaecological surgery. The study design was approved by the Medical Ethics Committees of all participating hospitals and all participants signed informed consent. Details of the study design have been published elsewhere.[15] The effectiveness of the multidisciplinary care program was not evaluated in this feasibility study; these results will become available in the near future.

Participants

All women aged between 18–65 years, employed for at least 8 hours per week (salary-employed, self-employed or voluntary work) and scheduled for a surgery for benign gynaecological disease in one of the participating hospitals were eligible to participate. The types of surgeries that were included were: laparoscopic adnexal surgery (LAS) and/or total laparoscopic hysterectomy (TLH), vaginal hysterectomy (VH) or total abdominal hysterectomy (TAH). Excluded were patients with health problems or psychiatric disorders affecting daily life, as well as patients who were being sick-listed for more than 4 weeks prior to surgery or were involved in a lawsuit against their employer. Not being able to understand or complete the Dutch questionnaires, having no access to internet or internet-illiteracy were also exclusion criteria. This process evaluation was only performed for the participants randomised to the intervention group, because only they were exposed to the intervention care program.

Recruitment

Waiting lists from participating hospitals were used to recruit prospective program participants. Patients were contacted by phone one week after they had received an invitation letter on behalf of their gynaecologist, together with an information package. Patients willing to participate and meeting the inclusion criteria were asked to return a signed informed consent. Patients were randomized to an intervention group (n = 110) or a control group (n = 105). As stated before, the current paper focuses only on the patients randomised to the intervention care program.

Intervention

The intervention care program consists of a stepped care approach and contains two steps. The first step, an interactive e-health intervention, was provided to all participants in the intervention group. The second step, integrated care management, consisted of supplementary care coordinated by a clinical occupational physician and (if relevant) a workplace intervention by an occupational therapist (OT), and was only given to those participants whose sick leave exceeded 10 weeks.

The intervention care program was systematically developed applying the principles of intervention mapping.[16] Both theory and practise were combined and all stakeholders were involved in the process. The attitude, social influence and self-efficacy (ASE) model was used as a theoretical framework for determinants of behaviour regarding return to work (RTW).[22, 23] Below, both steps of the program are summarized.

Step 1: E-Health Intervention

The e-health intervention http://www.ikherstel.nl was accessible to all patients, ideally four weeks prior to surgery. However, this period was shorter if the patient was enrolled closer to the surgery date. The patient web portal consisted of 47 unique pages and provided several tools aimed at empowering its users and improving communication between patients, employers and healthcare professionals during the peri-operative period. The most important tools are:

1. *Tool to compose reintegration plan* This tool enabled patients to generate detailed tailored instructions on the resumption of activities after the surgery. These recommendations were based on a multidisciplinary guideline developed by an expert panel of gynaecologists, general practitioners (GPs) and occupational physicians (OPs), using a structural consensus method prior to the RCT.[24] The tool was accessible before surgery, allowing planning of (work) activities and work reintegration. After surgery, the gynaecologist who had performed the surgery was asked to approve the reintegration plan electronically, allowing making adjustments to the standard advice in case of (surgical) complications.
2. *Video* A film was developed and available to watch on the patient web portal illustrating common pitfalls during the peri-operative and reintegration period.
3. *Tool to invite employer* Patients were stimulated to invite their employer to an (anonymous) section of the web portal, including the video. This tool aimed to improve communication between employee and employer and to stimulate to develop a reintegration plan (before surgery) and discuss potential RTW problems. For both the employee as the employer a list of recommendations was provided.

4. *Recovery monitor* Patients' recovery was closely monitored by the patient web portal after surgery. At 2, 4, 7, 14, 28, 56 and 84 days after surgery, patients were encouraged to fill out the monitor, inventorying which activities they had resumed already and which they had not. If patients were not satisfied with their recovery or reintegration process, an alerting system advised them to contact a specific health professional, depending on the cause of dissatisfaction.
5. *Tools to increase knowledge and forum* Several tools were available to provide additional information, such an extended list with answers to frequently asked questions (FAQ), a glossary, and links to other useful patient web portals. In addition, there was a forum enabling patients to interact (privately or publicly) with other patients.

Step 2: Integrated Care Management

Integrated care management refers to a multidisciplinary approach to assist those patients who exceeded 10 weeks of sick leave. A clinical occupational physician was trained as RTW coordinator and fulfilled an intermediate role between the involved health professionals, including a trained occupational therapist (OT) and the patients' own gynaecologist, general practitioner (GP), and occupational physician (OP). The integrated care protocol consisted of two steps:

1. *Consultation with clinical occupational physician* All patients exceeding 10 weeks of sick leave were offered a consultation with the clinical occupational physician in the 10th or 11th week after surgery. During the first contact the clinical occupational physician assessed the mental and physical condition of the patient and discussed the job profile and demands. Taking all factors into consideration, a treatment and reintegration plan with an RTW prognosis was made. If both the patient and her own OP agreed to the plan, the recommendations were executed by calling in the assistance of the OT (if relevant), the patients' employer and/or appropriate health care provider(s).
2. *If necessary, participatory workplace intervention* When a patient was referred to the OT the workplace intervention procedure would start. The workplace intervention consists of three meetings: (1) OT with patient, (2) OT with supervisor and (3) OT, supervisor and patient together. The three meetings focus on identifying and prioritizing obstacles for RTW, finding solutions and achieving consensus between the patient and their supervisor with regard to work adjustments to facilitate RTW. The protocol was originally developed and proved effective for patients with chronic low back pain[25, 26] and is based on methods used in 'participatory ergonomics'.[27] The protocol was adapted to post-operative gynaecologic patients regarding time schedule and involved care providers.

Data Collection

Data for this process evaluation were collected from the patients using online questionnaires at baseline and during the 6 month follow up (2, 6, 12 and 26 weeks after surgery). Besides data collection from the patients, we collected data from (1) the patients' employers (online questionnaire at 8 weeks after surgery) (2) the patients' gynaecologists (online questionnaire after the trial) and (3) the occupational physician involved in the study (evaluation interview after the trial). In addition, data were also obtained by means of an automatically generated weblog of the web portal.

Process Measures

According to the recommendations of Linnan and Steckler[20] the following process items were assessed: (1) the context of the intervention, (2) reach, (3) dose delivered, (4) dose received, (5) fidelity and (6) participants' attitudes towards the different steps of the intervention program. Table 1 gives an overview of these process measures.

Context of the Intervention

Context refers to the larger physical, social and political environment that can affect an intervention program. In this process evaluation we did not assess contextual influences, however, in order to consider future implementation of the intervention program, an understanding is needed of the Dutch social and political situation. Supplementary file S1 provides a short overview on sickness benefit guidance in the Netherlands. In summary, employers are obliged to continue to pay wages of their employers during the first two years of sickness. During this two year period, both the employer as the sick listed employee share a mutual responsibility to increase the probability of return to work. If the employer fails to pursue an active absenteeism policy, he might be required to continue paying that employee's salary for another year. However, if the employee hinders an early return to work, the payment of his sickness benefit may be suspended or reduced.

Reach

Reach concerns the degree to which an intended audience participated in the intervention.

Step 1

The e-health intervention was intended for all patients allocated to the intervention arm of the RCT. A detailed telephone log and the study database were used to determine what proportion of recruited potential participants did decide to engage in the study and who declined to participate. Reasons for exclusion were registered, as well as the number and reasons for drop-outs.

Step 2

Integrated care management was intended for only those patients whose sick leave exceeded 10 weeks. Return to work data were collected through the patient web portal as well as through monthly self-reported calendars of sickness absence. Retrospectively, the proportion could be determined of the patients actually receiving the second part of the intervention considering the total number of patients who should have received it.

Dose Delivered

Dose delivered refers to the proportion of the intended intervention that is actually delivered to the program participants and is determined by the actions of the intervention provider.

Step 1

Accounts for the patient web portal were provided by the research team. The number of generated accounts divided by the total number of participating patients was defined as dose delivered.

Step 2

According to the protocol, the clinical occupational physician should have offered a consultation to all patients exceeding 10 weeks of sick leave. Dose delivered was determined by the number of invitations divided by the total number of patients with extended sick leave.

Dose Received

Dose received is a measure of the extent to which participants actively engage with the intervention. For this paper dose received was defined as the proportion of patients that used the intervention as recommended by the health care providers, likewise the definition of adherence used by World Health Organization (WHO).[28]

Step 1

Activity on the patient web portal was continuously and automatically registered in a weblog. Because of user authentication (username and password) every participant had a unique ID, which made it possible to analyse website activity for each individual participant. Information stored in the weblog included visited page numbers, time stamps (start and end-time) and number of sessions. To prevent over-estimation of activity time, a timer was built in the system which stopped time registration when participants were not active (scrolling, click or mouse movement) for a period of 8 min. The minimum recommended use of the website was defined as usage of the tool to compose an integration plan at least once, as a tailored schedule with convalescence recommendations enables patients to plan

their daily and work-activities after the surgery and to anticipate on facing problems as well. In addition, possible irrational beliefs about recovery could be rectified with this reliable source of information.

Step 2

For the integrated care management dose received was defined as the proportion of patients that received a consultation with the clinical occupational physician and who consented with the recommendations of the OP regarding follow-up, e.g. a referral for the workplace intervention.

Fidelity

Fidelity refers to the quality of the deliverance of an intervention and the extent to which the intervention was delivered as planned.

Step 1

Each gynaecologist who performed a surgical procedure on a participating patient received an electronic request to approve the reintegration plan that the patient had composed on the patient web portal. This essential step prevented that the standardized convalescence recommendations were given to patients with (surgical) complications. If thought relevant, the gynaecologist could adjust the recommendations, and the patient received a confirmation. If a patient experienced complications after discharge from the hospital, she could notify her gynaecologist through the web portal, and he or she was asked to review the patient's reintegration plan again. Fidelity was defined as the proportion of patients whose reintegration plan was approved and/or adjusted by their gynaecologist.

Step 2

Fidelity for the integrated care management was determined by the number of consultations that took place without violation of the study protocol (e.g. accuracy of scheduled appointments, visits or telephone-consultations). Retrospectively, it was determined in how many cases a good assessment was made of the patient's situation, and if the participatory workplace intervention was indicated correctly (sick leave >12 weeks).

Implementation Score

For each step of the care program an implementation score was calculated using the average of the four process measures.

Participants' Attitude

Participants' attitudes towards the e-health intervention were assessed among patients, gynaecologists and employers. Patients were requested to rate their satisfaction with the

(different tools of the) patient web portal. In addition, perceived effectiveness was scored on a 5-point Likert scale and patients were asked if they would recommend the e-health intervention to a friend (yes/no). Reasons for (non-)compliance were evaluated and patients could give suggestions for improvement.

Among employers satisfaction with the different items on the anonymous section of the web portal was assessed, as well as their satisfaction with the guidance the web portal offered their employee during the peri-operative period (both on 5-point Likert scale). Suggestions for improvement were evaluated.

Gynaecologists' opinion on the feasibility of the e-health intervention was evaluated through named facilitators and barriers to future implementation and their answers to the question if they would offer the intervention to their patients if widely available (yes/no). Again, suggestions for improvement were registered.

The clinical occupational therapist involved in the study was asked about her experience with the integrated care management during an evaluation interview after the trial.

Data Analysis

MATLAB version 7.1 (The MathWorks Inc., Natick, MA, USA) was used to transform the weblog into user and page statistics. SPSS version 20.0 (IBM Corporation, Amonk, NY, USA) and Excel 2003 (Microsoft, Washington, DC, USA) were used for descriptive and statistical analyses. Quantitative data were analysed by means of descriptive statistics such as frequencies, means, medians and interquartile ranges. To compare differences in groups, independent t-tests or Mann–Whitney U tests were used for continuous variables, depending on the distribution. All tests were performed two-sided. Statistical significance was defined as $p < 0.05$.

Table 1. Process-measures, definitions and data-collection methods

Process measure	Step 1: E-Health Intervention	Step 2: Integrated Care Management
Reach proportion of the target population that received the intervention	definition: proportion of recruited potential participants that met all inclusion-criteria and decided to engage in the study	definition: proportion of participants whose sick-leave exceeded 10 weeks that received consultation with OP
	data collection-method: - telephone-log - baseline-questionnaire	data collection-method: - RTW-calendars - study database
Dose delivered proportion of intended intervention that was actually delivered to target population	definition: proportion of study population that received an account for the patient web portal	definition: proportion of patients whose sick leave exceeded 10 weeks that received appointment with OP
	data collection-method: - weblog	data collection-method: - appointment system OP
Dose received extent to which the participants used the intervention as recommended	definition: proportion of patients with an account that used the webportal to compose a reintegration plan at least once	definition: proportion of patients with an appointment that received a consultation and consented with the recommendations of the OP regarding follow-up
	data collection-method: - weblog	data collection-method: - patient records OP
Fidelity extent to which the intervention was delivered as planned	definition: proportion of patients who had their reintegration plan electronically approved by their gynaecologist	definition: proportion of consultations that took place without violation of the study protocol (e.g. referral to participatory workplace intervention if sick leave exceeded 12 weeks)
	data collection-method: - weblog	data collection-method: - RTW-calendars - patient records OP
Participants' attitudes - satisfaction - perceived effectiveness - usage barriers - suggestions for improvement	target: - patients - gynaecologists - employers	target: - clinical occupation physician
	data collection-method: - online questionnaire	data collection-method: - face-to-face interview

OP = clinical occupational physician, RTW = return to work

RESULTS

Step 1 E-Health Intervention

Reach

Between March 2010 and January 2011, a total of 673 patients were scheduled for a hysterectomy and/or laparoscopic adnexal surgery in one of the participating hospitals. Fifty-two patients (7.7 %) returned the reply card which was included in the information package, indicating they were not interested in participation. Of the 621 patients to be contacted by telephone, 49 patients were unreachable and 215 patients were excluded because they did not meet the inclusion criteria of the study. The main reason for exclusion was the lack of employment or working less than 8 h a week (99/215; 46 %). A total of 357 patients were eligible for the study, of which 142 patients declined to participate. The remaining 215 patients enrolled in the study and accounted to a reach of 60.2 % (215/357). Figure 1 shows a flow-diagram of the study participants.

Randomization was performed after informed consent and the baseline measurement. The present paper, only reports on the participants allocated to the intervention group (110 patients). Table 2 shows the baseline characteristics of these participants. These participants did not differ significantly from the patients who were allocated to usual care.

The primary outcome full sustainable return to work was complete for all participants. The questionnaires assessing secondary outcome measures at 2, 6, 12, and 26 weeks were completed by 93.6 to 95.6 % of all participants.

Dose Delivered

All 110 patients were given access to the patient web portal www.ikherstel.nl before their surgery by the principal investigator or research-assistant (dose delivered: 100 %). The median number of days patients accessed the web portal prior to their surgery was 16 days (IQR 9–29 days). In 12.7 % of the cases, patients were given access only a week prior to the surgery. These cases can be explained because surgeries were planned on short notice or patients failed to complete the baseline questionnaire earlier.

Dose Received

Table 3 presents data about the usage of the patient web portal and the different tools. All patients used their account at least once, with the vast majority (98.8 %) doing this before surgery. Total time spent on the patient web portal by each patient was almost 2 hours (median 118 min, IQR 64–173 min) (Table 3). Most patients visited the website several times with a median number of 11 sessions (IQR 6–16).

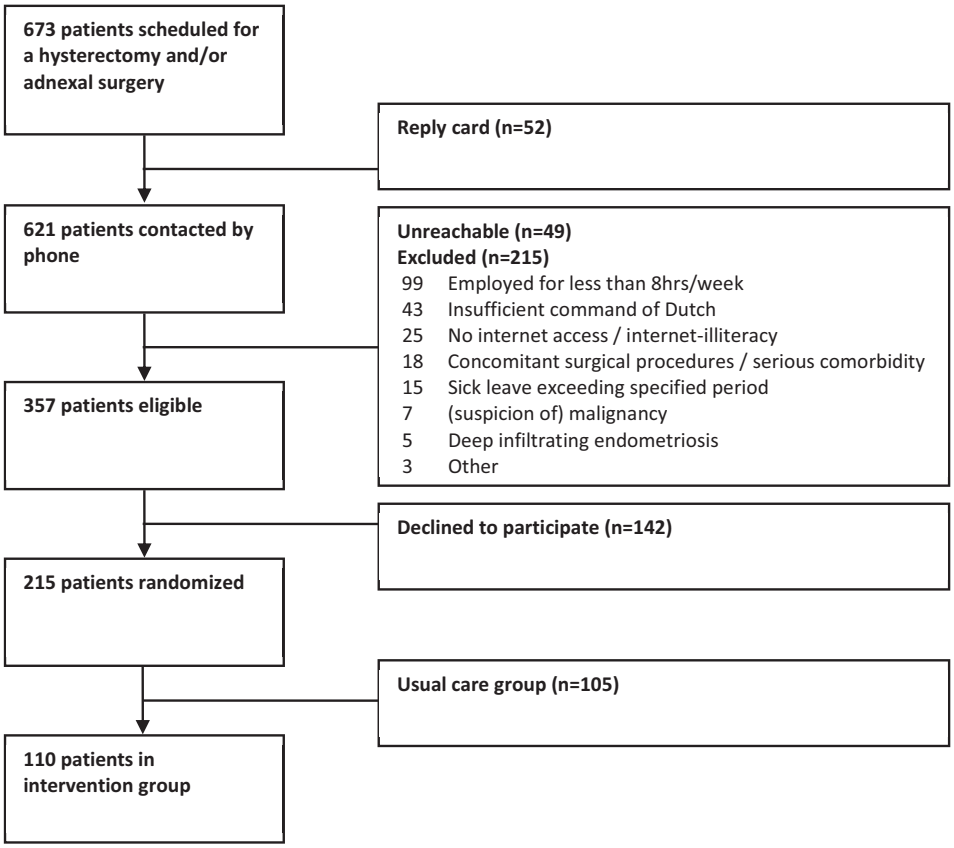

Figure 1. Study flow diagram

Activity on the patient web portal was highest in the week before surgery and the first three weeks after surgery (Figure 2). An average session lasted 12 minutes and 15 pages were viewed per session. There was no significant statistical difference in usage of the patient web portal between patients undergoing different types of surgery.

Before surgery, 63 patients (57.2 %) used the tool to compose a reintegration plan. Taken the total follow up into account, the majority of patients used the tool (dose received: 95/110; 86.4 %).

Table 2. Baseline characteristics

Category	Total n=110
Patient characteristics	
Age (years ± SD)	43.5 ± 7.8
Education level [a]	
low	10 (9.1)
intermediate	50 (45.5)
high	50 (45.5)
Surgery-related characteristics	
Laparoscopic adnexal surgery (LAS)	51 (46.0)
Laparoscopic hysterectomy (TLH)	17 (15.5)
Vaginal hysterectomy (TVH)	25 (23.0)
Abdominal hysterectomy (TAH)	17 (15.5)
Health-related characteristics	
Self-rated health status (mean ± SD) [b]	78.4 ± 15.7
Work-related characteristics	
Type of work	
salaried employed	89 (80.9)
self-employed	19 (17.3)
voluntary work	2 (1.8)
Work hours per week (mean ± SD)	30.3 ± 9.2

Numbers present frequencies and percentages unless otherwise specified.
[a] low = preschool, primary school; intermediate = lower and upper secondary; high = tertiary education, university or postgraduate
[b] EuroQol VAS-scale ranging from 0 (= worst imaginable health) to 100 (= best imaginable health)

Fidelity

Reintegration plans were electronically approved in 3 out of every 4 patients accounting to a fidelity score of 74.5 % of all cases (82/110). In 25 remaining cases (22.7 %), the principal investigator approved the schedules after having had contact with the surgeon. Reasons given by surgeons for not approving the schedule themselves were: lack of time, loss of the electronic invitation or sudden change of surgeon. In seven cases the surgeon adjusted the standard reintegration schedule because of complications during or after the surgery.

Table 3. Patient use of web portal

Category	Total n=110
General data	
Total visit duration per patient (minutes)	118 (64 – 173)
Number of sessions	10.5 (6 – 16)
first login before surgery	108 (98.2%)
first login after surgery	2 (1.8%)
≤ 2 sessions	7 (6.4%)
> 2 sessions	103 (93.6%)
Specific website tools	
Reintegration plan	
composition before surgery	63 (57.3%)
composition after surgery	32 (29.1%)
no composition	15 (13.6%)
Video	
number of unique visitors	77 (70.0%)
total visit duration per patient (minutes)	8.9 (3.9 – 11.4)
Interaction with employer	
number of invitations [a]	41 (46.1%)
number of unique visitors to page with recommendations for employee	73 (66.4%)
number of unique visitors to page with recommendations for employer	55 (50.0%)
Recovery monitor	
number of unique visitors	106 (96.4%)
total visit duration per patient (minutes)	46.2 (28.5 – 69.8)
number of visits per patient	13 (10 – 16)
Frequently Asked Questions	
number of unique visitors	58 (52.7%)
total visit duration per patient (minutes)	9.3 (2.1 – 17.6)
Forum	
number of unique visitors	61 (55.5%)
total visit duration per patient (minutes)	2.2 (0.9 – 6.5)
number of visits per patient	6 (3 – 15)

Numbers present frequencies (%) or medians (IQR).
[a] Only relevant for patients with an employer (N = 89)

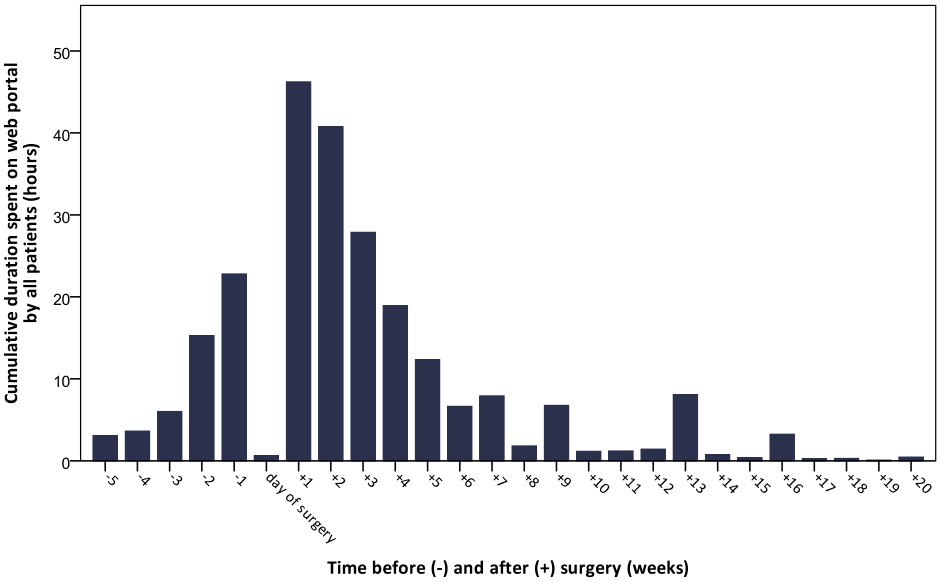

Figure 2. Use of patient web portal related to date of surgery

Implementation Score

Using the average of the four process-measures, the implementation score of the first step of the intervention was 80.3 % ((60.2 + 100 + 86.4 + 74.5 %)/4).

Participants' Attitudes Towards the Intervention

Patients

Satisfaction-scores with the different tools of the website are presented in Table 4. The vast majority of patients (75/102; 73.5 %) were (very) satisfied with the tool to compose a reintegration plan and found it (very) useful to plan normal activities (67.6 %) and work-activities (56.8 %). The majority of patients (87/105; 82, 9 %) followed most convalescence recommendations. Twelve patients explained they did not need a schedule because they rather resumed activities when their body felt ready for it. Another reason for non-compliance was finding the reintegration schedule too optimistic (23 times), while others stated the recommendations were too conservative (12 times).

Perceived effectiveness of the e-health intervention was high. At 12 weeks, 73.5 % (75/102) of all participants felt usage of the web portal contributed positively to their recovery. People who did not perceive an additional effect explained they did not need the web portal (8 times), they felt pushed by the convalescence advice (5 times) or they felt the

e-health intervention did not apply to their personal situation (4 times). Eighty-seven patients (87/102; 85.3 %) would recommend the web portal to a friend. Suggestions for improvement included an extra section with experiences of other women (3 times).

Table 4. Satisfaction with different tools of patient web portal

	Degree of satisfaction 1= totally dissatisfied <-> 5= very satisfied					
	1	2	3	4	5	NA
Patients (n=102)						
Graded activity schedule for general well-being [a]	2.0	5.9	18.6	32.4	41.2	-
Graded activity schedule for planning normal activities [a]	3.9	6.9	21.6	39.2	28.4	-
Graded activity schedule for planning work activities [a]	5.9	11.8	25.5	33.3	23.5	-
Links to other websites	1.0	1.0	28.4	33.3	6.9	29.4
Forum	5.9	4.9	26.5	16.7	3.9	42.2
FAQ	1.0	1.0	25.5	40.2	9.8	22.5
Film	2.9	3.9	32.4	29.4	2.9	28.4
Employers (n=26)						
Film	7.7	0.0	19.2	30.8	11.5	30.8
Recommendations for patients	0.0	0.0	23.1	42.3	7.7	26.9
Recommendations for employers	0.0	7.7	30.8	42.3	7.7	11.5

Numbers present percentages.
[a] Obligatory choice of score 1 to 5.

Employers

Almost half of the salary-employed participants invited their employer to visit an anonymous section of the website (42/89; 47.2 %). Reasons given for not using this tool included: finding it unnecessary because of a fast recovery or good relationship with employer (16 times), not wanting to be a burden or anticipating the employer not to be interested (8 times) or not wanting to share private information with their employer (5 times). Satisfaction about guidance provided by their employer did not differ statistically between patients who did and patients who did not invite their employer. Twenty-six employers (63.4 %) completed the digital questionnaire 8 weeks after the surgery of their employee. Satisfaction-scores with the different tools offered by the web portal are presented in Table 4. In total, 61.1 % of the employers (11/18) were (very) satisfied with the guidance the web portal offered to their employee. One employer suggested including extra information about reintegration-schedules.

Gynaecologists

In total, 40 gynaecologists were involved in the study, with a median number of 2 patients each (range 1–9). Thirty-one gynaecologists (77.5 %) finished (part of) an electronic questionnaire at the end of the trial. Of the 28 gynaecologists answering the questions about usefulness of the intervention, seven gynaecologists found themselves unable to give an answer because of too little experience with the intervention. Of the remaining 21 gynaecologists, 76.2 % rated the e-health-intervention as (very) useful (16/21). The vast majority would offer it to their patients, would it be widely available (20/21; 95.2 %). Possible future usage barriers for patients included: required access to internet (3 times) and the inflexibility of the e-health intervention in case of complications (2 times).

Possible usage barriers for gynaecologists were an increased time-investment (7 times). However, only 2 gynaecologists (2/28; 7.1 %) were unsatisfied with their own actual time-investment in delivering the intervention.

Step 2 Integrated Care Management

Reach

At 10 weeks after surgery 25 patients (25/110; 22.7 %) had not fully returned to work and represented the target audience for the second part of the intervention program, the integrated care management. In total, 12 consultations with the clinical occupational physician took place, accounting for a reach of 48 % (12/25).

As expected, patients with less invasive surgeries were more likely to have resumed their work-activities than those with more invasive surgeries. For the different types of surgeries the proportion of patients eligible for a consultation with the clinical occupational physician (OP) was as follows: TAH: 53 % (9 out of 17), VH: 28 % (7 out of 25), TLH: 29 % (5 out of 17), and LAS: 8 % (4 out of 51). In this group of delayed recovery, five patients (5/25, 20 %) suffered from a complication during or related to the surgery. Complications were defined as an enlargement of the wound with >8 centimetre or re-surgery within two weeks after initial surgery.

Dose Delivered

When patients had not resumed their work-activities 8 weeks after surgery, information about the integrated care management appeared on the patient web portal. Simultaneously, the clinical occupational therapist received the contact information of these patients and approached them by telephone to schedule an appointment in the 10^{th} or 11^{th} week after surgery.

In total, 17 appointments were scheduled, resulting in a dose delivered of 68 % (17/25). In two cases patients were not considered eligible for a consultation, due to medical reasons (severe complications related to the gynaecologic surgery) or personal reasons (recent death of partner). Six patients declined a consultation because they had already partly resumed their work activities and expected to fully return to work shortly. Four of them did resume completely within 12 weeks after surgery. Return to work of the last two patients took much longer than expected (16 weeks).

Dose Received

Of the 17 scheduled appointments, 12 consultations took place. Two patients cancelled because they had fully returned to work before the appointment and three patients cancelled because they did not feel the need for a consultation anymore. Given reason were: (1) the patient had partially resumed, (2) the patient had already consulted her own occupational physician, and (3) the patient did not wish to re-schedule the appointment when the clinical occupational therapist was forced to cancel the appointment.

Of the 12 consultations, two patients turned out to be sick-listed for other reasons than the gynaecologic surgery at time of the appointment (personal problems due to broken relationship and longer existing shoulder complaints). Two patients decided to decline further guidance from the OP during the first consultation. They did not disclose their reasons; however, they stayed sick-listed for 17 and 24 weeks respectively. Lastly, two patients declined a referral for the workplace intervention after discussing this treatment option with their supervisor and/or own occupational physician. One patient expected no additional benefit because she was satisfied with the guidance offered by her own occupational physician. The last patient experienced the consultation as unpleasant, because she felt pushed to return to work, while she felt she was not ready yet and therefore declined follow-up. Both patients stayed sick-listed during the complete follow up of 6 months.

In six cases follow up or referral to the occupational therapist was not indicated by the clinical occupational therapist because of a good RTW-prognosis. In these cases, the patients were already partially resuming their work-activities and did receive sufficient guidance from their own occupational physician and employer. Considering all consultations that were scheduled, the dose received calculated was 24 % (6/25) because in six consultations care was delivered according to the protocol.

Fidelity

The fidelity of the six remaining consultations was very poor (0 %). In all cases in which follow-up or a referral to the occupational therapist was not considered relevant, the good RTW

prognosis was incorrect retrospectively. Average time to full RTW after the consultation with the clinical occupational physician was still more than two months (mean 66 days; range 40–78) with one participant not reaching full RTW at all. Further guidance of the clinical occupational therapist in these cases would probably have been beneficial. Moreover, only three patients visited the clinical occupational physician, the other nine consultations took place by telephone. Telephone consults were offered because patients were not willing to pay an actual visit because of the investment of time and money. In addition, only three cases were scheduled in the 10th or 11th week after surgery as indicated by the protocol, with four appointments scheduled too early (week 9) and five appointments too late (week 13–15).

Implementation Score

The implementation score of the second step of the intervention program was calculated to be 35 % ((48 + 68 + 24 + 0 %)/4).

Experiences of Clinical Occupational Physician

At the end of the trial the clinical occupational physician involved in the study was interviewed to evaluate the integrated care management. The most important topics discussed included the high number of patients that declined additional care and the difficulty to estimate RTW-prognosis. Moreover, possible solutions to these barriers were reviewed.

The clinical occupational physician explained she experienced most difficulties persuading participants to schedule an appointment with her. Because she met patients relatively late after the surgery, most patients were already partly resuming their work-activities and had already made a reintegration-plan often with help of their supervisors or own OPs. It was then very difficult to explain the additional value of a consultation, and in case of an appointment, make alterations in the plans already made. Secondly, most consultations took place by telephone, because patients were not willing to make a visit, making it very hard to develop an accurate RTW-prognosis.

In order to enhance the impact of a consultation, the clinical occupational physician advised to incorporate the consultation in standard care, e.g. women who are planned for a surgery should automatically receive an invitation for the clinical occupational physician. In addition, the moment of contact should be at a much earlier stage, even maybe before surgery, to be able to support the development of a solid RTW-plan and to influence irrelevant cognitions about their recovery. In the current format, the occupational physician was doubtful about the effectiveness of this part of the intervention.

DISCUSSION

Main Findings

The aim of this paper was to evaluate the implementation process and experiences with an innovative care program for women undergoing benign gynaecological surgery. As the care program consisted of two different steps: an e-health intervention and integrated care management. Both steps were evaluated separately, using the criteria outlined by Linnan and Steckler.[20] Overall, the e-health intervention was implemented fairly well with an implementation score of 80 %. Patients, gynaecologists and employers were all highly satisfied with the web portal www.ikherstel.nl. The implementation of the integrated care management protocol was less successful with a final implementation score of 35 %. Convincing patients about the additional value of a consultation with the occupational physician and developing an accurate RTW-prognosis were the two most important obstacles for the second step of the intervention program.

Interpretation of the Findings

Step 1 E-Health Intervention

The use of e-health technologies is considered to be an important key to improving efficiency and quality of health care.[29, 30] Possible benefits include enhancing (self-) monitoring activities, increasing delivery of care based on guidelines, and decreasing utilization of health services. However, there remains a gap between the postulated and empirically demonstrated benefits.[29] The current process evaluation is an essential step towards improving implementation of evidence-based e-health interventions. To the best of our knowledge, our patient web portal is the first evaluated e-health intervention in both fields of postoperative care and gynaecology.

The reach of the e-health intervention was moderately high (60 %). In total, only 25 women were excluded because of having no access to the internet or internet-illiteracy (25/376; 3.7 %). In the Netherlands, the general internet-access rate is 96 %.[31] Compared to national numbers under working females, highly educated women were overrepresented in our study: 50 versus 35 %.[32] Partly, this might be explained by regional differences and the location of some hospitals in and near the capital of the Netherlands. However, selection bias might have played a role as well, when highly educated women might be more interested in the e-health intervention (and fast recovery) and decided to participate more often.

Compliance towards web-based interventions varies among different studies and target populations.[33] For depression and anxiety disorders adherence rates to online treatments

are generally found between 50 and 70 %.[34] In our study we were able to objectively measure usage of the e-health intervention and 86 % of all participants used the web portal as intended. This is relatively high, but in concordance with the high satisfaction scores and an overall high perceived effectiveness of the e-health intervention.

Step 2 Integrated Care Management

Unfortunately, the second part of the intervention did not unfold and reasons might be found in the characteristics of the target population. Participatory workplace programs have been shown to be effective in patients sick-listed due to musculoskeletal disorders and distress.[25, 35–37] Generally, targeted patients were characterized by a history of chronic disease and complaints, whereas the target population in the current study consisted of patients working at the time of recruitment and facing only a temporary period of sick leave during the recovery of their surgery. This temporary nature of the sick leave is probably the most important barrier to full implementation, demonstrated by a number of issues. Firstly, more than half of the patients (13 out of 25) declined additional care at some time during the integrated care management, indicating a general lack of perceived value of additional guidance. This could be related to Dutch legislation which ensures salary income at least during the first 24 months of sick leave (see supplementary file S1). In absence of financial consequences, people might not be urged to return to work as soon as possible, and therefore less interested in initiatives to facilitate return to work. Moreover, a commonly given reason for rejecting a consultation was that the patient had already partly resumed and expected full return to work shortly. However, perception of the own situation turned out to be problematic as it took these patients still 3.5 months to resume all work activities after starting partly. Finally, developing an accurate RTW prognosis was challenging for the occupational physician as well (poor score on fidelity). Up to date, not much is known about prognostic factors for RTW in this specific population.

Strengths and Limitations of this Study

A strength of this study is that data collection was performed systematically using an established theoretical framework to assess the process outcomes. Moreover, multiple sources were employed such as online questionnaires and the weblog generated from the patient web portal. The latter allowed a detailed and objective evaluation of patient compliance to the e-health intervention. Finally, all stakeholders of the intervention program (patients, employers, gynaecologists and the clinical occupational physician) were included in this process evaluation.

This study also has limitations. For example, we failed to measure contextual factors that might have influenced implementation. Moreover, we should be aware that a research setting can be advantageous towards an intervention, due to highly involved health

professionals, motivated patients (selection bias) and interference of the research team. In the current study this can be illustrated by the artificial score of 100 % for dose delivered. Earlier research showed that adherence rates to open access websites can be much lower compared to a research environment (up to 50 % less)[33], so this needs to receive special attention when implementing the intervention program into daily practice. Some procedures that were carried out by the research team should be automated, such as generating accounts. Other procedures will have to be transferred to the health care providers. However, we presume the intervention to receive enough support, as 9 out of 10 gynaecologists indicated they would offer the intervention to their patients would it be widely available.

Practical and Research Implications

A considerable large number of patients reported that the reintegration plan they had composed on the web portal was too optimistic for their own situation (23/110; 21 %). Some participants said this increased insecurities and anxiety, as they fell behind the schedule, which is a negative outcome of the intervention. Before broader implementation, it is essential to take measures to prevent this, as it will influence compliance negatively. The solution should not necessarily mean to loosen the convalescence recommendations, but could also be providing more information and targeting coping mechanisms.

Moreover, this process evaluation showed important directions to improve the second step of the intervention program and these lessons should be taken into account when implementing the intervention program on a wider scale. First of all, the importance of a prosperous recovery in means of improving quality of life and preventing long term sickness should be emphasized to patients. The patient web portal provides an excellent platform for this. In addition, possibilities to incorporate a consultation with a clinical occupational physician in standard care should be explored with all involved stakeholders. Possibly, patient's own occupational physicians can perform this part of the intervention themselves in the future, as this would also increase support in the direct environment of the patient. Contact with the patient in an early stage seems to be crucial to influence patients' attitudes and (irrational) beliefs about their recovery.

CONCLUSIONS

This current paper describes the process evaluation of a new intervention program to provide additional guidance during the perioperative period to gynaecological patients. The results of this study indicate good feasibility for implementation on a broad scale of the e-health intervention. Compliance, perceived effectiveness and satisfaction were high among patients. In addition, other stakeholders such as gynaecologists and employers,

assessed the intervention as potentially very useful. To enhance the implementation of the second step of the perioperative care program, adaptations in the integrated care protocol are needed.

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Supplementary file S1

Sickness benefit guidance in the Netherlands

In the Netherlands, employers are obliged to continue to pay – at least 70% of – the salaries of sick employees during the first two years of sickness. According to the Gatekeeper Improvement Act (April 2002) during this two year period, both the employer as the sick-listed employee share a mutual responsibility to increase the probability of return to work. Both the employer as the employee may be sanctioned in case of noncompliance.

When an employee is sick listed for six weeks a reintegration report should be opened, which starts with a consultation with a company doctor (occupational physician - OP) of the official Health and Safety Executive Organisation ('arbodienst'). The OP assesses the situation and makes a problem analysis, containing all the information relevant to the recovery, return to work and reintegration of the employee. Within two weeks, the employer and employee will then draw up a plan of action based on the concrete recommendations provided by the OP, which will be evaluated regularly, at least once every six weeks. Further consultations with the OP find place regularly as well.

The UWV (Institute for Employee Benefit Schemes) is the body commissioned by the Dutch Ministry of Social Affairs and Employment (SZW) to implement employee insurance schemes and acts as gatekeeper. When an employer did not reintegrate into the employment process within the two year period the UWV assesses if both parties have done everything possible to improve the chances of returning to work, by studying the total reintegration file. When both parties did make enough efforts, the employee can apply for a sickness benefit under the Work and Income according to Labour Capacity Act (WIA). However, if the employer failed to pursue an active absenteeism policy, sanctions may follow such as continuation of payment of the employee's salary. On the other side, if the employee hindered an early return to work, the payment of his sickness benefit may be suspended or reduced.

Workers without an employer are granted a benefit for two years under the Sickness Benefit Act, also provided by UWV. In these cases, UWV is responsible for sickness absence counselling and reintegration as well.

CHAPTER 3

The cost effectiveness of a tailored, web-based care program to enhance postoperative recovery in gynaecological patients in comparison with usual care; protocol of a stepped-wedge cluster randomized controlled trial

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ABSTRACT

Background The length of recovery after benign gynecological surgery and return to work frequently exceeds the period that is recommended or expected by specialists. A prolonged recovery is associated with a poorer quality of life. In addition, costs due to prolonged sick leave following gynecological surgery cause a significant financial burden on society.

Objective The objective of our study was to present the protocol of a stepped-wedge cluster randomized controlled trial to evaluate the cost effectiveness of a new care program for patients undergoing hysterectomy and/or adnexal surgery for benign disease, compared to the usual care.

Methods The care program under study, designed to improve convalescence and to prevent delayed return to work, targets two levels. At the hospital level, guidelines will be distributed among clinical staff in order to stimulate evidence-based patient education. At the patient level, additional perioperative guidance is provided by means of an eHealth intervention, equipping patients with tailored convalescence advice, and an occupational intervention is available for those patients at risk of prolonged sick leave. Due to the stepped wedge design of the trial, the care program will be sequentially rolled out among the 9 participating hospitals, from which the patients are recruited. Eligible for this study are employed women, 18-65 years of age, who are scheduled for hysterectomy and/or laparoscopic adnexal surgery. The primary outcome is full sustainable return to work. The secondary outcomes include general recovery, quality of life, self-efficacy, coping, and pain. The data will be collected by means of self-reported electronic questionnaires before surgery and at 2, 6, 12, 26, and 52 weeks after surgery. Sick leave and cost data are measured by monthly sick leave calendars, and cost diaries during the 12 month follow-up period. The economic evaluation will be performed from the societal perspective. All statistical analyses will be conducted according to the intention-to-treat principle.

Results The enrollment of the patients started October 2011. The follow-up period will be completed in August 2014. Data cleaning or analysis has not begun as of this article's submission.

Conclusions We hypothesize the care program to be effective by means of improving convalescence and reducing costs associated with productivity losses following gynecological surgery. The results of this study will enable health care policy makers to decide about future implementation of this care program on a broad scale.

INTRODUCTION

In the last two decades, the hospital stay following surgical procedures has been shortened drastically, due to recovery-enhancing strategies such as the use of minimally invasive techniques and the implementation of fast-track programs.[1-4] The advantages of early postoperative discharge include increased patient satisfaction, low hospital-acquired infection rates, and reduced hospitalization costs.[5] However, a major disadvantage of minimizing the length of a hospitalization is that patient contact becomes very brief, which is often at the expense of time spent on patient education. Ironically, the lack of detailed convalescence instructions at the time of discharge increases the risk of an unnecessary prolonged recovery.[6-11] Therefore, as long as the organization of perioperative care has not fully anticipated the transition of postoperative recovery to the home setting, early discharge does not necessarily translate into accelerated recovery and earlier resumption of (work) activities.[12-14]

In gynecology, the postoperative convalescence after discharge from the hospital has not received much attention in research and practice. Yet, there is considerable evidence that the length of recovery time after a gynecological surgery systematically exceeds the period considered as appropriate by specialists.[5,10,12-17] In a prospective study performed by our own study group among 148 patients receiving gynecological surgery for a benign disease, median time to return to work (RTW) exceeded the recommended sick leave of 6 weeks by approximately 3 weeks. The median time to RTW following an intermediate surgery (e.g., laparoscopic or vaginal hysterectomy) was 60 days (interquartile range, IQR 28-101) and following a major surgery (e.g., abdominal hysterectomy) 69 days (IQR 56-135).[10]

An unnecessary prolonged recovery is associated with poorer quality of life.[18,19] In addition, work related problems have also been associated with an increase in health care consumption.[20] Furthermore, taken into account that about 14,000 hysterectomies are performed annually in the Netherlands alone[21], the financial burden on society due to delayed convalescence after a gynecological surgery is substantial.

In order to reduce unnecessary delayed recovery, and concurrently decrease costs associated with prolonged sick leave and increased health care utilization following gynecological surgery, our research group started working on an innovative strategy to optimize perioperative care in 2008. Since the beginning of the project several goals were achieved, starting with the development of detailed convalescence recommendations following four types of benign gynecological surgery, using a modified Delphi method.[22] Simultaneously, a multidisciplinary care program was developed[23,24] consisting of an interactive eHealth intervention and – for those patients at risk of prolonged sick leave – an occupational intervention. The care program provides guidance to patients from the

moment the surgery is planned, until the full resumption of all activities, including return to work, and encourages patients to take an active role in their own recovery. The care program was subject to an effect evaluation as well as a process evaluation in 2010.[25] While the effectiveness study among 215 patients showed a positive effect on the outcomes: (1) RTW, (2) quality of life, and (3) perceived pain[26], the process evaluation showed some room for improvement.[27]

Besides evaluating the effectiveness of a study, it is of equal importance to conduct an economic evaluation, especially considering the high economic burden of extended time to convalescence after a gynecologic surgery. The economic evaluations are necessary to gain insight into the costs of an intervention in relation to its effects. Health care policy makers can use these results to decide how resources should optimally be allocated to maximize health or welfare.[28]

Therefore, the primary objective of the current study is to conduct an economic evaluation of the care program compared to the usual care. This economic evaluation will be conducted alongside a randomized trial, as the intervention concerns a further developed version of the care program, which has not yet been subject to an effect evaluation. In addition, this construction enables the systematic collection of relevant effect and cost data under "real-life" conditions. As the intervention care program targets two levels (the hospital level and the patient level), a cluster design was chosen in order to prevent contamination between the study arms. The primary outcome duration until full sustainable RTW will be assessed on the level of the individual participant. On the level of the participating hospitals, we will investigate to what extent the guidelines on convalescence recommendations are adopted, and how future implementation of the guidelines and care program can be facilitated.

METHODS

The Standard Protocol Items, Recommendations for Interventional Trials statement[29], and CONsolidated Standards Of Reporting Trials (CONSORT) statement[30,31], were used in order to describe the design of this study. In addition, we used the extension to cluster randomized trials[32] and the CONSORT eHealth checklist.[33]

Ethical Issues

The Institutional Review Boards of all participating hospitals approved this study protocol. Informed consent was obtained from all of the patients.

Trial Design

This trial is designed as a cluster, randomized controlled, stepped wedge trial, which involves a sequential rollout of the intervention in the participating clusters over several

time periods. In our study, clusters are the departments of obstetrics and gynecology in nine different hospitals in the Netherlands. Each time period (TP) takes 2 months. At the start of the trial (TP1), all of the patients scheduled for a surgery in all of the participating hospitals receive usual care (control phase). After two months (TP2), the intervention is implemented in the first cluster, and from now on the patients scheduled for a surgery in this hospital will receive the intervention program, while in all of the other hospitals the patients still receive usual care. The patients in cluster 2 who underwent surgery during TP1 remain in the control group until they finish the 12 month follow-up. During TP3, the intervention program continues in cluster 1, and the intervention is implemented in cluster 2 as well, resulting in the deliverance of the intervention program to the patients in clusters 1 and 2 that will undergo surgery from this point onward, while patients in clusters 3 to 9 serve as the control group. At the beginning of TP4, cluster 3 starts with the intervention, etc. This is repeated until the intervention is implemented in all clusters (TP10). Figure 1 illustrates the study design.

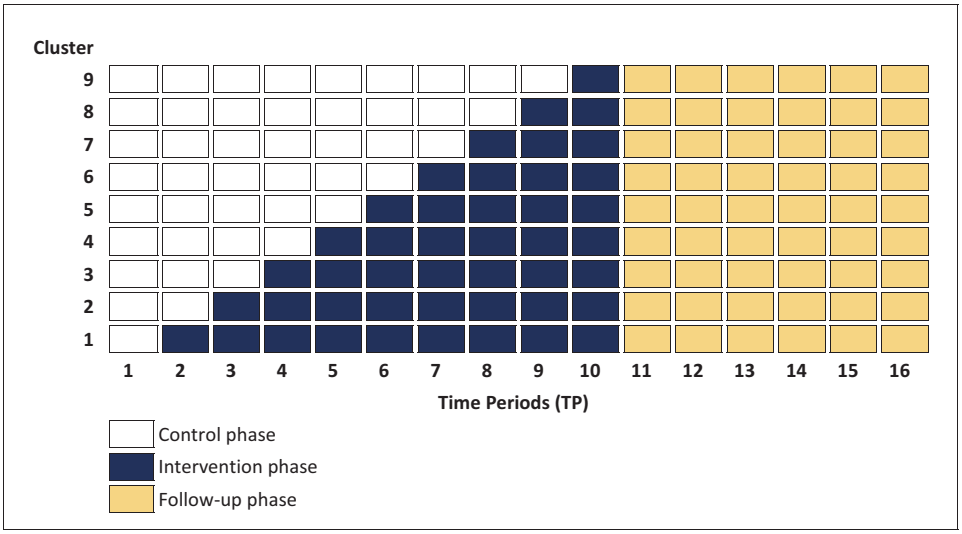

Figure 1. Trial design

A cluster design was chosen to minimize the risk of contamination, as our intervention targets both health care providers and patients. A stepped wedge approach was employed because of the unique feature of a unidirectional crossover, preventing the intervention to be withdrawn from the hospital during the trial.[34-36] Because there is substantial evidence from our previous trial that the care program under study will be effective, this is particularly

convenient, as hospitals will be able to keep using the intervention after the trial. Moreover, it enables us to study the implementation process carefully, giving valuable insight into barriers and facilitators for future broader implementation.

Selection of Clusters

The clusters in this trial consist of nine hospitals in the surroundings of Amsterdam, the capital of the Netherlands. The hospitals were eligible if they performed at least 100 hysterectomies or laparoscopic adnexal surgeries yearly, and were located within 50 km of the Vrije Universiteit Medical Center (VUmc). The research team enrolled the clusters before the start of the trial. In an attempt to select a heterogeneous sample of hospitals, we included 1 university hospital, 7 teaching hospitals, and 1 nonteaching hospital.

Study Population

The eligible participants for this study are women 18-65 years of age, employed for at least 8 hours per week (salary employed, self-employed, or voluntary work), and scheduled for a surgery for a benign gynecological disease in one of the nine participating hospitals. The types of surgeries that are included are: (1) total abdominal hysterectomy (TAH), (2) vaginal hysterectomy (VH), (3) total laparoscopic hysterectomy or laparoscopic assisted vaginal hysterectomy (TLH), or (4) laparoscopic adnexal surgery (LAS). The factors that are possibly complicating the postoperative course (e.g., severe comorbidity, malignancy, pregnancy), the factors that are interfering with the eHealth intervention (computer- or Internet illiteracy), or with the occupational intervention (conflict with employer, prolonged sick leave, or disability) serve as the exclusion criteria. Table 1 lists an overview of all eligibility criteria.

Recruitment of Patients

The recruitment of patients will take place in all participating hospitals. When the patients are scheduled for a hysterectomy or laparoscopic adnexal surgery, they will receive a letter about the study on behalf of their gynecologist. The letter includes detailed information about the trial. In addition, it is explained that someone from the research team will make contact by telephone after one week to evaluate the patients' willingness to participate and answer questions if necessary. If the patient does not wish to be contacted, she can return an included reply card, or send an email to a specified email address.

When contact is made and the patient is willing to participate, eligibility is assessed. The eligible patients are then requested to return a signed informed consent, which is also attached to the information letter. The participants will not receive any financial or nonfinancial incentives.

Table 1. Eligibility criteria

Inclusion criteria	Exclusion criteria
Women scheduled for:	(Suspicion of) malignancy
Laparoscopic adnexal surgery	(Ectopic) pregnancy
Total laparoscopic hysterectomy	Deep infiltrating endometriosis
Vaginal hysterectomy	Concomitant health problems affecting daily activities
Total abdominal hysterectomy	Psychiatric disorders affecting daily activities
18 - 65 years of age	Legal conflict with employer
Employed ≥ 8 hours/week	Being sick listed >4 weeks, or when reason of sick leave is related to gynecological surgery > 2 months
	Inability to understand or complete Dutch questionnaires
	Computer- or Internet illiteracy

Randomization

The randomization takes place at the level of the clusters and determines the order in which the intervention program is implemented in the participating hospitals. The randomization will be performed by a statistician using a computer-generated list of random numbers.

The patients are informed about the allocation of treatment by the research team after the patient's informed consent and the completion of the first questionnaire before surgery. As the treatment allocation depends on the scheduled date of the surgery, and the implementation phase of the hospital in which they are being operated, it is predetermined for each participant, potentially causing selection bias. To minimize the risk of selection bias, the participants will not be informed about the study design, and will be counselled as if they have equal chances between receiving the usual care or the intervention program. For this reason, counselling will be done by the research team, rather than by their own physician, who might be, for example, more willing to include patients during the intervention phase than during the control phase. Moreover, physicians will be blinded to the randomization schedule, and will only be informed about the start of the intervention phase approximately one month before the actual implementation. Once the intervention phase has started, the importance of not communicating this information with the potential patients will be emphasized.

Interventions

Usual Care

Before the implementation of the intervention program, the participants receive the usual perioperative care as provided in the hospital in which they are scheduled for surgery.

Although considerable variation exists in the Netherlands, in most cases patients get verbal (general) instructions at discharge by a nurse and/or physician, often followed – but not necessarily – by a letter or brochure. In general, an outpatient postoperative consultation is scheduled 4 to 6 weeks following the surgery. Between discharge and the postoperative consultation, medical care is only initiated by the patient, who can consult her general physician (GP) or gynecologist, if necessary. Employed workers who have not resumed work within 6 weeks after the surgical procedure will be invited for a consultation with their occupational physician (OP), as required by law in the Netherlands.

Intervention

The systematic development of the care program using the principles of Intervention Mapping is described in more detail elsewhere.[23] Both theory and practice were combined, and all stakeholders were involved in the process. The engagement of the patients was prompted through focus groups.[24] The Attitude, Social influence, and Self-efficacy model was used as a theoretical framework for determinants of behavior regarding return to work.[37,38] The care program targets two levels, which are described below. Figure 2 shows an overview of the intervention care program.

Cluster Level

At the cluster level, the intervention care program aims to structure and stimulate evidence-based perioperative care. Approximately two months before a cluster shifts from the control to the intervention phase, the principle researcher will approach the head of the department to arrange logistics. A minimum of two meetings is planned one or two weeks before the actual implementation with physicians and nurses to provide and explain the new convalescence recommendations that should be communicated to the patients. In addition, all health professionals involved in the clinical care receive a pocket card on which these recommendations are summarized for quick reference. The residents involved in the discharge communication are instructed to explain the convalescence recommendations to their patients before they are discharged. Visual reminders in the patient records will help the residents do so. With the secretary of the department, a strategy is developed to prompt the standard postoperative consultation at 4 weeks following a hysterectomy, and 2 weeks following adnexal surgery. During the trial, newsletters will be spread regularly to reinforce the different aspects of the intervention care program.

Patient Level

At the patient level, the care program aims to provide individual tailored guidance to patients from the moment the surgery is planned until the full resumption of all activities. It consists of two steps: (1) access to an interactive eHealth intervention for all patients, and (2) an additional occupational intervention for those patients at risk for prolonged sick leave.

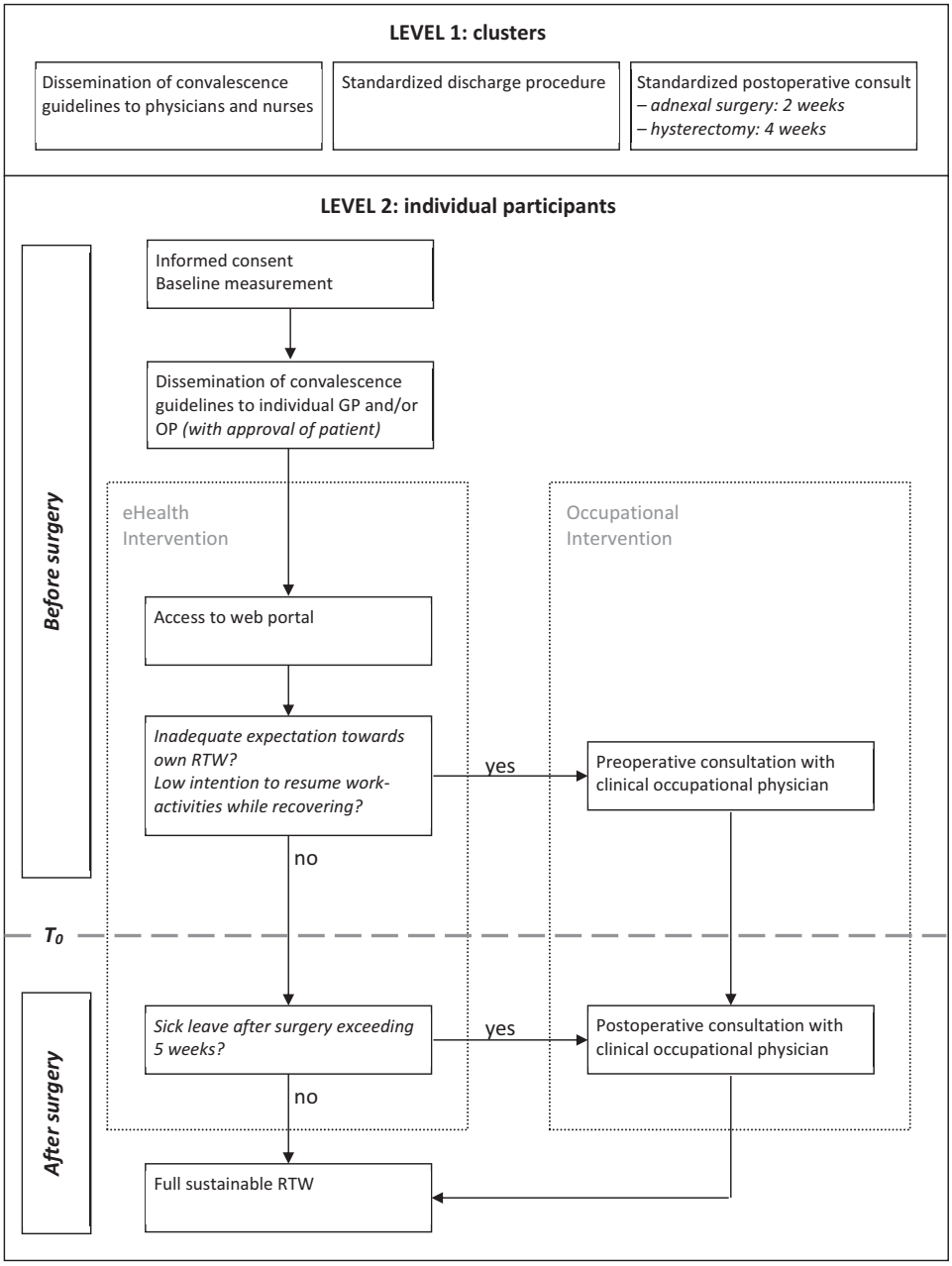

Figure 2. Overview of the care program.
GP = general physician, OP = occupational physician, RTW = return to work

eHealth Intervention

The patient webportal[39] aims at empowering its users and improving communication between patients and their employers, as well as improving the communication between the involved health care professionals during the perioperative period. Access to the webportal will be given to the patients approximately 2 to 4 weeks prior to surgery by the research team, by providing a username and temporary password. The instructions are given by email, and it is explained that if patients require assistance, they can contact the research team by phone or email. If patients fail to log in, an automatic reminder is sent to them one week before their surgery to remind them about the webportal and its functionalities. User authentication will make it possible to analyze website activity for each individual participant (visit duration, number of sessions, number and details of pages visited).

The most important tool of the webportal is the possibility to generate a tailored convalescence plan. In the instruction email, patients are encouraged to generate such a plan at least once, preferably before surgery. Having access to detailed convalescence advice will enable the patients to develop realistic expectations about their own recovery, and plan the resumption of their activities and work reintegration accordingly. Moreover, a tailored convalescence plan will help the patients gain insight into potential recovery problems and find solutions at an early stage, preferably before surgery. Because the convalescence plan is composed before surgery, gynecologists are asked to approve the plan electronically on the first postoperative day. In the case of an uncomplicated procedure, the plan is turned into a definite convalescence plan, and the patients are instructed to follow the recommendations in it. In the case of a converted procedure, the plan is adjusted to the type of surgery that was actually performed. In the event of severe complications, the gynecologist can choose not to approve the convalescence plan, and the patients then receive a message that the convalescence plan is not valid anymore, and that they should follow up with the specific instructions given to them at discharge. With the consent of the patient, the approved convalescence plan is also disclosed to the GP and/or OP of the patient. This last feature was added since the prior evaluation of the webportal, and was developed to facilitate the involvement of other health care professionals during the perioperative period in order to stimulate a multidisciplinary approach. In addition, the webportal was equipped with a tool that enables the patients to generate a recovery report, a graphic presentation of their own recovery, allowing them to track their progress.

During the trial, the content of the website will be frozen, except from the dynamic component (forum). Table 2 summarizes the most important tools of the eHealth intervention. Screenshots of the webportal are included in supplementary file S1.

Table 2. Content of the eHealth intervention

Tool	Description
Personalized convalescence plan [a]	The tool allows patients to generate detailed tailored instructions on the resumption of activities after the surgery, allowing preoperative planning of (work) activities. The convalescence plan is approved electronically by the surgeon who performed the surgery on the first postoperative day, resulting in a definitive convalescence plan. With the consent of the patient, the approved convalescence plan is shared with GP and/or OP.[a]
Recovery monitor + recovery report [a]	The tool makes an inventory of the resumption of activities at 2, 4, 7, 14, 28, 56, and 84 days after surgery. Results are graphically displayed in a recovery report, allowing the patient to track their progress.[a] In case the patients fall behind, an alerting system advises them to contact a specific health care professional, depending on the underlying problem.
Invitation of employer	The tool allows patients to invite an employer to an anonymous section of the webportal to stimulate a dialogue. The development of a reintegration plan preoperatively will help them gain insight into potential RTW problems.
Video	A 9-minute film illustrating the common pitfalls during the postoperative period.
Knowledge	Several tools to find additional information, such as an extended list with answers to frequently asked questions, a glossary, and links to other useful websites.
Forum	The tool allows the patients to interact (privately or publicly) with other patients.

GP = general physician, OP = occupational physician, RTW = return to work
[a] Tools that were modified since the last evaluation of the webportal.

Occupational Intervention

The occupational intervention is developed to provide additional guidance to those patients at risk for prolonged sick leave. The occupational intervention will be delivered by a group of six independent OPs, who will be trained as RTW coordinators before the start of the trial. There are two types of consultations: (1) a preoperative, and (2) a postoperative consultation. All consultations will be delivered by telephone, unless the OP and the patient decide together otherwise.

The patients who have an inadequate expectation about their own recovery (longer than 3 weeks for LAS, longer than 6 weeks for VH/TLH, or longer than 8 weeks for TAH), or have a low intention to resume work activities while still recovering, are offered a preoperative consultation, as expectations about RTW and intention to resume work have been identified as two predictors for RTW in recent studies.[10,40,41] During the preoperative consultation, the OP explains the importance of a prosperous recovery in terms of improving quality of life and preventing long term sickness. In addition, the OP tries to identify and – if necessary – alter attitudes and (irrational) beliefs about recovery.

The patients who exceed 5 weeks of sick leave receive a postoperative consultation, during which, the OP assesses the underlying mechanism for the delayed recovery. The OP gives advice to improve the reintegration process. Moreover, as a RTW coordinator, the OP has an excellent position to communicate with the patient's gynecologist, GP, OP, and employer, if necessary, and of course, with the consent of the patient, stimulating an integrated care approach. In addition, the OP has the possibility to initiate a participatory workplace intervention, aimed at finding consensus between the patient and her employer concerning solutions for identified obstacles for RTW with the help of an occupational therapist (OT).[42,43]

The occupational intervention described above differs from the intervention as delivered during the first trial, due to the insight gained during the process evaluation. Originally, contact with the clinical OP took place in the 10th or 11th week, however, this turned out to be too late in order to be able to alter attitudes and beliefs, and influence the development of a solid RTW plan. Therefore, in the current trial, contact will be made much earlier, at 5 weeks, and on indication already before surgery. In addition, the patients will receive the details of the postoperative appointments before surgery in order to prepare them that the occupational intervention is part of the care program they receive, as in the prior trial, almost half of the patients declined additional occupational care. In the case of full RTW, the postoperative appointment will be cancelled.

OUTCOMES

Effect Measures

The effects of the intervention will be assessed on the level of the patient. The primary outcome of the study is the sick leave duration until full sustainable RTW, defined as the duration of the sick leave in calendar days from the day of surgery until full RTW, in their own work or other work with equal earnings, for at least 4 weeks without (partial or full) recurrence.[44] The recurrence of sick leave due to the gynecologic surgery within the four week period after initial full RTW will be added to the preceding period of the sick leave. The RTW will be assessed by a monthly electronic sick leave calendar.

Secondary outcomes that will be assessed are:

1. Recovery, measured by the Recovery Index-10 (RI-10) a validated recovery-specific questionnaire[45];
2. Self-reported quality of life, assessed by the Dutch versions of the EuroQol-5D (EQ-5D)[46] and the Short-Form Health Survey (SF-36)[47,48];

3. Duration of sick leave until first RTW, and total duration of sick leave due to the gynecological surgery for the entire follow-up period, both measured by the monthly sick leave calendars;
4. Self-efficacy, assessed by the Dutch adaptation of the General Self-Efficacy Scale (GSES)[49];
5. Coping, assessed by the Pearlin Mastery Scale (PMS)[50];
6. Pain intensity, measured by the Von Korff questionnaire (VAS)[51]; and
7. (Post) operative complications both assessed through self-report and by the review of surgical reports. Complications include: (1) enlargement of the wound (≥ 8cm), (2) unintended injury to other structures (e.g., bowel, bladder, ureter), (3) unexpected blood loss requiring transfusion, (4) prolonged hospital stay, (5) readmission within 72 hours (overnight), (6) repeat surgery within 2 weeks, and (7) postoperative infection requiring antibiotics.

Prognostic Factors

Before surgery, data about potential prognostic factors will be collected. In case of coincidental and meaningful differences, analyses will be adjusted for the following characteristics: (1) sociodemographic data such as age, education level, and ethnicity; (2) personal factors such as expectation, motivation, and intention toward RTW, duration of sick leave in the past 3 months; and (3) work-related factors such as physical workload and potential work-related psychosocial factors, assessed by the Dutch Musculoskeletal Questionnaire (DMQ)[52] and the Job Content Questionnaire (JCQ).[53]

In case of an unequal distribution of severe complications (defined as: wound enlargement with more than 8cm or repeat surgery within 2 weeks), between the two study arms, the analyses will be adjusted for these surgery-related characteristics as well.

Cost Measures

The costs will be measured from a societal perspective and consist of: (1) costs of the intervention, (2) health care utilization, and (3) costs associated with lost productivity. All of the costs will be converted to the year 2014 using consumer price indices.[54] The discounting of costs will not be necessary because the follow-up period is limited to one year.

The intervention costs are those that are related to implementing and operating the new care program, and will be estimated using a bottom-up approach. The detailed information regarding the quantity and unit prices of the following resources will be collected: (1) training of involved health care professionals (clinical staff, OP, OT), (2) the eHealth intervention (hosting of webportal, administrator time), and (3) the occupational intervention (number and duration of consultations).

The health care utilization will be assessed on a monthly basis using a retrospective electronic questionnaire. Only the healthcare costs related to the gynecological surgery will be collected and include: (1) surgery and hospitalization; (2) visits to healthcare professionals in primary or secondary care and visits to alternative medicine therapists; (3) medication; and (4) home care and informal help. If available, Dutch guideline prices will be used to value health care utilization. If cost guidelines are not available, costs will be estimated using real prices or population-based estimates if available in the literature. The prices of the Royal Dutch Society for Pharmacy will be used to value medication.[55]

The costs associated with productivity loss consist of absenteeism and presenteeism costs. The absenteeism will be assessed by monthly sick leave calendars. The human capital approach will be used to calculate the costs of losses to production as a result of sick leave due to the gynecologic surgery (net number of days on sick leave during follow-up, multiplied by the estimated prices of production loss of a worker per day of sick leave). The presenteeism (reduced productivity while at work) will be assessed with two items of the Productivity and Disease Questionnaire.[56] A decline in the amount or quality of work performed due to the gynecologic surgery compared to the level at which the patient normally performs, will be considered as presenteeism. The costs associated with presenteeism will be calculated by multiplying the presenteeism score during follow-up by the estimated price of production loss per day.

Process Measures

A process evaluation will be conducted to evaluate the implementation process of the intervention.[57] The assessment of the extent to which the intervention program was applied as intended will provide valuable insight into the facilitators and barriers for future implementation. The process evaluation will take place both on the level of the cluster as well as the patient, and both quantitative and qualitative methods will be used. An automatically generated weblog will enable the analysis of the website activity for each individual participant, giving more insight into which patients used the eHealth intervention, and how it is being used. The appointment system and patient records of the OP will enable us to analyze the number of consultations that have taken place, as well as the reasons for cancellations, and the occurrence of any protocol deviations. By means of an Internet questionnaire at the end of the follow-up period, patient satisfaction, perceived effectiveness, and any usage barriers will be assessed. The principle investigator will continuously collect reasons for exclusion and dropout during the trial. In accordance to the prior process evaluation conducted[27], the following process measures are included: (1) reach, extent to which the intervention reaches the target population; (2) dose delivered, extent to which the intervention is delivered to the target population; (3) dose received,

extent to which the participants used the intervention; (4) fidelity, extent to which the intervention was delivered as planned; and (5) attitudes, satisfaction, perceived effectiveness, and usage barriers.

Cointerventions and Contamination

Cointerventions during the intervention period cannot always be avoided. However, we will be able to determine whether patients received cointerventions by means of the monthly cost diaries. The risk of contamination is reduced by the cluster design of the trial. To assess whether contamination occurred, the patients in both groups are asked about the instructions they received at discharge, which will then be compared to the convalescence recommendations implemented during the intervention phase of the study.

Data Collection

The surgery is considered T0. The data will be collected by means of self-reported electronic questionnaires[58] before surgery and 2 weeks (T1), 6 weeks (T2), 12 weeks (T3), 26 weeks (T4), and 52 weeks (T5) after surgery. In addition, all of the participants will be requested to fill out a monthly electronic sick leave calendar and cost diary. The patients that are not sick listed, and do not have medical costs during 3 consecutive months, receive a shortened version of the monthly questionnaire. In the case of no response, the patients receive an electronic reminder after 1 and, if necessary, 2 weeks. Every 3 months an attempt will be made to complete missing data regarding RTW, sick leave, and health care usage per email, post, and/or telephone. Table 3 provides an overview of all outcome measures and assessment instruments used in this trial. Not all of the instruments have been validated for Internet use.

Blinding

The participants, care providers, and researchers cannot be blinded for the allocated treatment. However, analysis of the data by the researcher will be blind, as all of the patients receive their own study code, under which their data is stored in the database. The assessment of the outcomes is measured through self-reported questionnaires.

Table 3. Assessment of study outcomes

Outcome measures		– ± 4 weeks	Surgery (T_0)	+ 2 weeks (T_1)	+ 6 weeks (T_2)	+ 3 months (T_3)	+ 6 months (T_4)	+ 12 months (T_5)
Primary measures	Duration of sick leave until full sustainable RTW	Monthly sick leave calendar [a]						
Secondary measures	Duration of sick leave until first RTW	Monthly sick leave calendar [a]						
	Total duration of sick leave	Monthly sick leave calendar [a]						
	Recovery (RI-10)	x		x	x	x	x	x
	Quality of life (EQ-5D)	x		x	x	x	x	x
	Quality of life (SF-36)	x				x	x	x
	Self-efficacy (GSES)			x		x		x
	Coping (PMS)			x		x		x
	Pain intensity (VAS)			x	x	x	x	x
	(Post) operative complications			x	x			x [b]
Prognostic factors	Social demographic variables	x						
	Personal factors	x						
	Work-related factors (DMQ, JCQ)	x						
	Type of surgery/complications		x					
Cost measures	Care program	Bottom-up approach [c]						
	Health care utilization	Monthly cost diary [a]						
	Productivity loss	Monthly sick leave calendar [a]						
Process measures [d]	Compliance (dose received)	Continuously by weblog						
	Attitudes (satisfaction, perceived effectiveness, usage barriers)					x		x
	Patient Satisfaction with Occupational Health Services Questionnaire					x		x

[a] short version after 3 consecutive months without sick leave or health care usage
[b] review of surgical reports
[c] calculated by research team
[d] only intervention group

Sample Size

We calculated the sample size needed with the method described by Hussey and Hughes.[35] Based on the previous study, we expect a hazard ratio of 1.5 on the primary outcome full sustainable RTW. To achieve a power of 0.8 with a two-tailed alpha of .05, and taking into account a dropout rate of 10%, a total of 212 patients will be needed when using the log-rank test. With an intracluster correlation of 0.05, 9 clusters, and 10 time periods, the design effect is calculated to be 2.14.[35] By multiplying the design effect by the sample size without a correction for a stepped wedge design, a sample size of 454 women is needed. Assuming that all of the hospitals will include the same amount of participants, each hospital should include approximately 50 patients (5 patients per time period per hospital).

Statistical Analyses

Effect Evaluation

All further described analyses will be performed at the patient level, according to the intention-to-treat principle. In addition, for all tests, a two-tailed significance level of $P \leq 0.05$ will be considered statistically significant. The statistical software packages that will be used include SPSS (version 16.0) and STATA (version 11.2).

The baseline characteristics will be summarized using descriptive statistics, and compared between the experimental and control group to verify prognostic comparability. In case of coincidental and meaningful differences, these variables will be used as covariates in the further described models.

For the primary outcome, the duration of sick leave until full sustainable RTW, Cox regression analyses will be used to investigate the intervention effect. Both the crude and adjusted analyses will be performed. In the adjusted analyses, the following variables will be used as covariates: (1) hospital, to adjust for clustering (random gamma effect); (2) type of surgery performed; (3) time period, to adjust for naturally occurring changes over time irrespective of the intervention; and (4) optionally, (time period) x (intervention) interaction term, to adjust for time effects (the longer the care program is implemented, the more effective it might be).

The differences in secondary outcomes will be assessed using generalized linear longitudinal mixed models. All of the available measurements (2 weeks, 6 weeks, 12 weeks, 26 weeks, and 52 weeks) will be used, and the baseline scores will be used as covariates, as well as the hospital and the type of surgery (random effect).

To assess whether protocol deviations caused bias, a per protocol analysis will be performed, and the results will be compared to the intention-to-treat analyses. In addition, several

subgroup analyses will be performed. The predefined subgroups will be: (1) hysterectomy (TAH, VH, TLH); (2) minimally invasive hysterectomy (VH, TLH); (3) abdominal hysterectomy only; and (4) laparoscopic adnexal surgery only.

Economic Evaluation

Both a cost-effectiveness analysis and a cost-utility analysis will be performed from the societal perspective. The analyses will be performed according to the intention-to-treat principle. The missing cost and effect data will be imputed using multiple imputation.[59] The imputation will include variables that are related to the missing data or the outcome measure, and variables that differ at baseline between the groups. To account for the skewed distribution of costs, predictive mean matching will be used in the multiple imputation. The number of imputed datasets to be created will be determined based on the fraction of missing information.[60] All of the datasets will be analyzed separately, and the results of these analyses will be pooled using Rubin's rules.[61] The incremental cost effectiveness ratios (ICERs) will be calculated by dividing the differences in mean total costs between both treatment groups, by the differences in mean effects between both treatment groups. To avoid double counting, the productivity costs due to sick leave will be excluded in the ICER, with sick leave as the effect measure. The incremental cost utility ratio will be calculated by dividing the incremental costs by the difference in the quality adjusted life years between both treatment groups. To account for the typically skewed distribution of costs, bias corrected and accelerated bootstrapping (5000 replications) will be used to estimate the 95% confidence intervals around the mean cost differences, and the uncertainty surrounding the ICERs. The bootstrapped ICERs will be graphically presented in cost effectiveness planes.[62] The cost effectiveness acceptability curves will be estimated to show the probability of the intervention program to be cost effective in comparison with the usual care for a range of different ceiling ratios, thereby showing decision uncertainty.[63] To assess the robustness of results, several secondary economic analyses will be performed: (1) complete case analysis, (2) per protocol analysis, (3) analysis with costs calculated according to the friction cost approach, and (4) analysis from the health care perspective.

RESULTS

The enrolment of the patients started October 2011. The follow-up period will be completed in August 2014. Data cleaning or analysis has not begun as of this article's submission.

DISCUSSION

This paper outlines the methodology of a stepped wedge cluster randomized trial to evaluate the cost effectiveness of a care program designed to improve postoperative

recovery compared to the usual care. The intervention care program targets two levels: (1) the level of the hospital, and (2) the level of the patient. At the level of the hospital, the newly developed guidelines will be distributed among the clinical staff in order to stimulate evidence-based patient education at the time of discharge. At the patient level, access to an eHealth intervention is provided with tailored convalescence recommendations, and an occupational intervention is available, for those patients at risk of prolonged sick leave, for additional guidance.

What This Study Will Add

The combination of increasing demands on the health care system and the limited health care budget designates a need to enhance the cost effectiveness of our health care system. The introduction of minimally invasive techniques in the last two decades has led to savings in in-hospital care due to shorter lengths of hospital stay, despite higher operative costs, longer operation time, and more expensive equipment.[64-66] However, early discharge does not necessarily lead to enhanced recovery, as postoperative recovery at home requires a different organization of perioperative care as well, such as preoperative patient education, including the deliverance of evidence-based standardized convalescence recommendations.[6,8,9,12,67-70] As far as we know, our care program is the first intervention developed, and being thoroughly evaluated, that anticipates this transition of perioperative care to the home setting. Second, the utilization of innovative eHealth technologies will limit the workload of involved health care professionals, anticipating a personnel shortage in the health care sector due to a shrinkage of the working population in the near future.[71] Finally, our trial will be one of few that conducted an economic evaluation from a societal perspective, not only taking into account solely direct medical costs—which are important for the hospital perspective—but also including costs associated with postoperative health care utilization and productivity losses due to absenteeism and presenteeism after discharge.

Strengths and Limitations

The main strength of the present study is the choice for a stepped wedge cluster randomized trial. The contamination between study arms is prevented by the cluster design. In addition, the stepped wedge approach enables us to study the implementation process carefully, and gain valuable insight into the facilitators and barriers toward future implementation of the intervention program.[72] Because the crossover of the design is unidirectional, the intervention is not withdrawn from the hospitals during the trial. This is particularly convenient, as our previous trial supports our hypothesis that the care program will lead to enhanced postoperative recovery.[73] Finally, there is a statistical advantage to the stepped

wedge approach because the intervention effect is estimated not only by between cluster comparisons, as in a parallel group design, but also by within cluster comparisons, limiting the risk of confounding and increasing statistical power.[36,74]

This study also has limitations. First of all, randomized studies without blinding have higher risks of (selection) bias. A second limitation of this study might be the fact that some of the hospitals have already participated in the earlier trial in 2010. The existing knowledge about the convalescence recommendations could be a source of contamination for the current study, and could lead to an under estimation of the care program effect.

Generalizability

The generalizability of this study will be high, due to the pragmatic study design. In order for procedures to be similar to clinical practice, interference of the research team will be minimized during the trial. The wide diversity of participating (7 teaching, 1 academic, and 1 nonteaching) hospitals, will also contribute to a heterogeneous sample of patients being enrolled in this study, enhancing generalizability. However, we should also be aware of factors that could possibly limit the external validity. A typical feature of eHealth interventions is the risk of selection bias toward the higher educated participants as compared to the general population. Moreover, as the care program was developed in the Dutch setting, and especially tailored to Dutch patients, generalizability of the results of this trial to other countries will be unknown, due to differences in social and healthcare systems.

Policy Implications

The results of this cost effectiveness study will enable health care policy makers to decide about future implementation of the care program on a broad scale in the Netherlands. In the case that the care program under study is proven to be cost effective, this will have considerable impact. Most importantly, the financial burden on society due to prolonged sick leave following benign gynecological surgery will be substantially reduced. Also, the individual patients will benefit through increased quality of life, and employers will profit because of a decline in absenteeism rates. Moreover, for health care professionals, the care program will be an asset, as it will lead to better organized and more efficient care. Finally, the care program has the potential to maximize the beneficial effects of other recovery enhancing strategies, such as the use of minimally invasive surgery.

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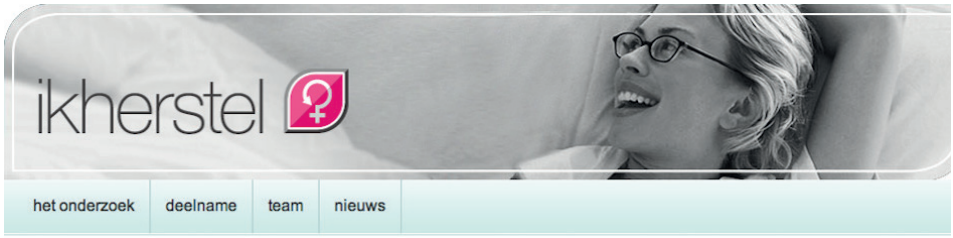
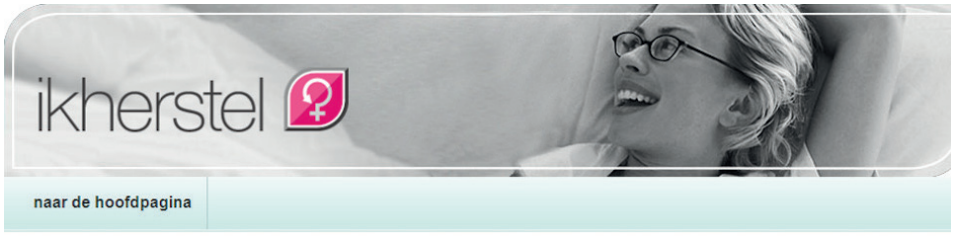
Supplementary file S1. Screenshots of the webportal www.ikherstel.nl





hoofdpagina | richtlijnen | actielijst | film | werknemer | leidinggevende | FAQ | woordenlijst | forum | links

Herstelrapport op 19-02-2012

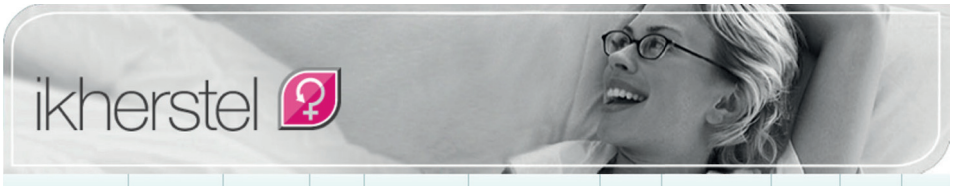
Hieronder ziet u twee wijzerplaten die uw herstel weergeven voor uw persoonlijk functioneren (zoals concentreren, etc.) en uw lichamelijk functioneren.

Als de wijzer omhoog wijst, verloopt uw herstel precies zoals medisch gezien verwacht wordt. Indien de pijl iets naar links wijst, betekent dit dat uw herstel iets achterloopt ten op zichte van de norm. Wijst de pijl naar rechts, dan verloopt uw herstel sneller dan verwacht.

Het is belangrijk om te beseffen dat dit rapport uitgaat van een ongecompliceerde situatie voor een gezond individu. Het houdt dus geen rekening met persoonlijke beperkingen. Het kan daardoor voorkomen, dat de wijzers onterecht aangeven dat uw herstel achterloopt.

Persoonlijk functioneren

Lichamelijk functioneren



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Informatie over de film

Deze film is gemaakt om u inzicht te geven in de valkuilen en tips aan te dragen voor het hervatten van (werk)activiteiten na een gynaecologische operatie. De inhoud is gebaseerd op ervaringen van patiënten die reeds een gynaecologische operatie hebben ondergaan. In de film spelen twee verhaallijnen. Eén lijn waarin het herstel en terugkeer naar werk goed verloopt en één lijn waarin dit niet goed verloopt. De nadruk wordt steeds gelegd op factoren die het herstel en de terugkeer naar werk positief of negatief kunnen beïnvloeden. Deze factoren zijn soms uitvergroot om het contrast te scheppen, maar komen in de realiteit wel voor en zijn hierdoor zinvol om bij stil te staan.

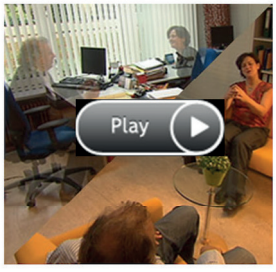
De gehele film duurt ongeveer 9 minuten. Voor het gemak is de film opgedeeld in drie hoofdstukken: 'Voor de operatie', 'Na de operatie' en '5 maanden later' zodat u niet genoodzaakt bent de gehele film in één keer te bekijken.

Trailer
Samenvatting

Deel 1
Voor de operatie

Deel 2
Na de operatie

Deel 3
Vijf maanden later



CHAPTER 4

Effectiveness of an Internet-based perioperative care programme to enhance postoperative recovery in gynaecological patients; cluster controlled trial with randomised stepped-wedge implementation

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BMJ Open. 2018;8(1):e017781

ABSTRACT

Objective To evaluate the implementation and effectiveness of an internet-based perioperative care programme for patients following gynaecological surgery for benign disease.

Design Stepped-wedge cluster randomised controlled trial.

Setting Secondary care, nine hospitals in the Netherlands, 2011–2014.

Participants 433 employed women aged 18–65 years scheduled for hysterectomy and/or laparoscopic adnexal surgery.

Interventions An internet-based care programme was sequentially rolled out using a multifaceted implementation strategy. Depending on the implementation phase of their hospital, patients were allocated to usual care (n=206) or the care programme (n=227). The care programme included an e-health intervention equipping patients with tailored personalised convalescence advice.

Main outcome measures The primary outcome was duration until full sustainable return to work (RTW). The degree of implementation of the care programme was evaluated at the level of the patient, healthcare provider and organisation by indicators measuring internet-based actions by patients and providers.

Results Median time until RTW was 49 days (IQR 27–76) in the intervention group and 62 days (42–85) in the control group. A piecewise Cox model was fitted to take into account non-proportionality of hazards. In the first 85 days after surgery, patients receiving the intervention returned to work faster than patients in the control group (HR 2.66, 95% CI 1.88 to 3.77), but this effect was reversed in the small group of patients that did not reach RTW within this period (0.28, 0.17 to 0.46). Indicators showed that the implementation of the care programme was most successful at the level of the patient (82.8%) and professional (81.7%).

Conclusions Implementation of an internet-based care programme has a large potential to lead to accelerated recovery and improved RTW rates following different types of gynaecological surgeries.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This study provides evidence that implementation of an internet-based care programme targeting the patient's self-management throughout the entire surgical pathway can lead to accelerated postoperative recovery following benign gynaecological surgery.
- The key strength of the study is its stepped-wedge cluster randomised design, minimising the risk of contamination between study groups and allowing assessment of both the implementation process and the effectiveness on patient level.
- Due to a non-proportionality of hazards of the treatment effect, a piecewise Cox model was fitted with a time-dependent covariate.
- The study only included employed women of which the majority was highly educated, thus caution is needed when generalising the findings.
- Further research should focus on the identification of patients who might benefit the most from the care programme.

INTRODUCTION

At present, perioperative care is fragmented due to short hospitalisations and limited coordination of care among involved healthcare professionals following discharge.[1–3] In addition, a lack of knowledge on appropriate postoperative recovery times and an absence of guidelines on convalescence advice hamper healthcare professionals to provide profound patient education and manage their patients' expectancies adequately.[4–6] As a consequence, patients are insufficiently prepared to engage in self-management and retreat to inappropriate recovery behaviour.[7–9] Thus, several barriers at the levels of the patient, the healthcare professional and the organisation lead to suboptimal perioperative care.[10] The current situation puts patients at risk for unnecessary prolonged postoperative recovery, which can lead to personal disease burden[11, 12] and high societal costs.[13–15]

We previously studied the feasibility of an internet-based care programme as an alternative to conventional management of postoperative gynaecological patients. Proof of concept was demonstrated in an efficacy randomised controlled trial (RCT), and the care programme resulted in improved return to work (RTW) rates in the intervention group compared with the control group.[16] However, external validity was low due to strict guidance of patients and professionals by the research team in order to avoid protocol deviations.[17] Following a process evaluation, several improvements were made to the care programme to facilitate implementation in real practice.[17 18]

The aim of the present study was to study the implementation of the care programme in daily practice in nine hospitals in the Netherlands. A multifaceted implementation strategy

was employed, targeting the three identified levels of barriers. Due to a stepped-wedge design, effectiveness of the care programme could be assessed at patient level. The findings on the cost-effectiveness are reported in a separate paper.[19]

METHODS

Study design and participants

Between April 2011 and July 2014, we did a multicentre, stepped-wedge cluster randomised trial. In this unidirectional crossover design, the care programme was sequentially rolled out among the nine participating hospitals (figure 1). Hospitals served as the control group until the care programme was implemented. Outcomes were assessed at patient level. The trial protocol has been published previously in accordance to the Consolidated Standards of Reporting Trials extended guidelines.[18]

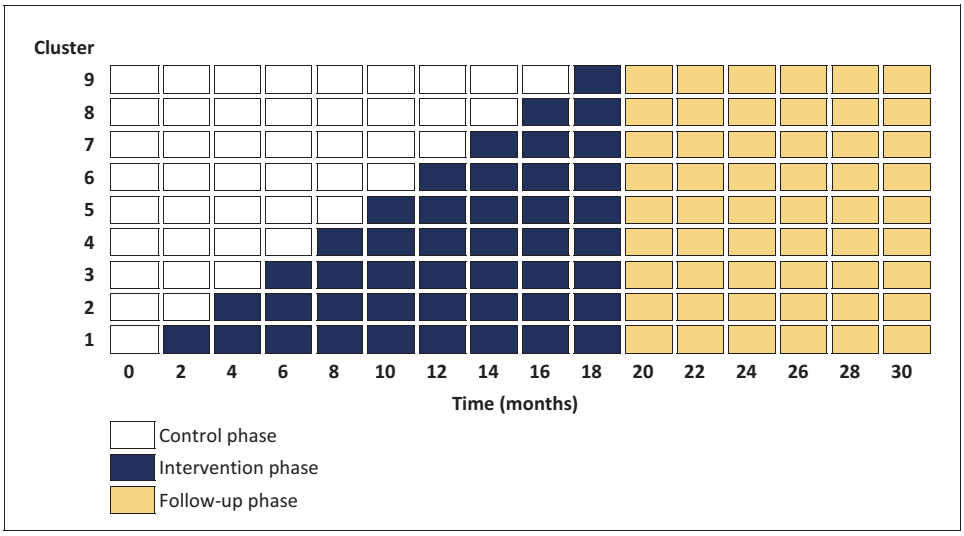

Figure 1. Stepped-wedge design with nine clusters
At baseline, all clusters provide usual care. At 2-month intervals, the clusters cross over to the intervention. How long the care programme is implemented in a cluster at 20 months varies from 2months (cluster 9) to 18 months (cluster 1).

Nine hospitals were selected before the start of the trial. Hospitals were eligible if they performed at least 100 hysterectomies or laparoscopic adnexal surgeries annually, and were located within 50 km of the VU University Medical Centre in Amsterdam, the Netherlands.

Patients scheduled for hysterectomy (abdominal, vaginal or laparoscopic) and/or laparoscopic adnexal surgery in one of the participating hospitals were recruited from the waiting lists and were given verbal and written information about the study. Patients were eligible if they were between 18 and 65 years of age and were employed for at least 8 hours a week. We excluded patients who had severe benign comorbidity or a malignancy, were pregnant, were computer or internet illiterate, were involved in a lawsuit against their employer, were on disability sick leave before surgery or had insufficient command of Dutch.

Randomisation and blinding

Randomisation took place at the level of the clusters and determined the order in which the intervention was implemented in the nine participating hospitals. The sequence was delivered by a statistician using a computer-generated list of nine random numbers. A stepped-wedge approach was employed as it enabled us to study the implementation process as well.

Patients, clinicians and researchers could not be masked to intervention implementation. However, group allocation was concealed to patients until they had agreed to participate and had provided written informed consent. Data analysts (EVAB, PMvdV) were masked to group allocation.

Intervention care programme and implementation strategy

The development and content of the intervention care programme have been described before.[18, 20] In summary, the care programme was developed systematically applying the principles of intervention mapping, involving all stakeholders, including patients, gynaecologists, general physicians (GPs) and occupational physicians (OPs).[21] The theory of planned behaviour was used as a theoretical framework for determinants of behaviour regarding recovery and RTW.[22]

The care programme targeted both the patient level and the cluster level. At the patient level, an interactive web portal facilitated self-management through the entire surgical pathway, by providing individual tailored convalescence advice preoperatively. These convalescence recommendations were developed previously through a Delphi method using an expert panel consisting of gynaecologists, GPs and OPs and are (therefore) in line with current typical beliefs on the resumption of activities following surgery in the Netherlands.[23] Patients were not able to change the length of the recommended recovery times themselves. To illustrate, regarding full RTW, patients were advised to resume their work activities gradually in order to reach full RTW by 2 weeks after laparoscopic adnexal surgery, 4 weeks after a vaginal or laparoscopic hysterectomy and 6 weeks after an abdominal hysterectomy.

An example of a personalised convalescence plan generated by the patient is presented in supplementary file S1. Postoperatively, the web portal contained an interactive self-assessment tool to monitor recovery. Behaviours of healthcare professionals and the general organisation of care were targeted by a multifaceted implementation strategy, developed to achieve maximal adoption of the care programme. An overview of the care programme and the employed implementation strategies is presented in supplementary file S2.

Usual care

Before the care programme was implemented in the hospitals, participating patients received usual care. Although considerable variation in usual care exists in the Netherlands, in general, postoperative patients receive verbal instructions at discharge by a nurse and/or physician, sometimes accompanied by a letter or brochure. Usually, a postoperative consultation is planned 6 weeks following surgery. Due to Dutch legislation, employed patients who do not resume work within 6 weeks after the surgery are invited for a consultation with their OP.

Outcomes

The effectiveness of the intervention care programme was assessed at patient level. As our intervention focused on recovery after discharge, sick leave duration until full sustainable RTW was the primary outcome of this trial. Full sustainable RTW was defined as the resumption of own work or other work with equal earnings, for at least 4 weeks without (partial or full) recurrence of sick leave.[24]

Sick leave data were collected by monthly, self-reported, electronic calendars.

Secondary outcomes were functional health status, assessed by 36-Item Short-Form Health Survey[25, 26]; recovery, assessed by the Recovery Index-10[27]; self-efficacy, assessed by the General Self-Efficacy Scale[28]; coping, assessed by the Pearlin Mastery Scale[29] and pain, assessed by the Von Korff questionnaire.[30] Data on these secondary outcomes were collected by means of self-reported electronic questionnaires 2, 6, 12, 26 and 52 weeks after surgery.

Sociodemographic data, personal factors and work-related factors were collected before surgery to compare baseline characteristics between both study arms. Data on the surgical procedures and operative/postoperative complications were collected by review of surgical reports.

The degree to which the intervention care programme was successfully implemented was measured by three different indicators. Patient compliance was analysed by measuring patient activity on the web portal and by determining the proportion of patients that used

the web portal as intended.[17] To evaluate professional compliance, the number of electronic authorisations that were performed by gynaecologists at the web portal were recorded. The number of consultations that took place with the clinical OPs provided information about the impact of the programme on the organisational level.

Statistical analysis

We calculated the sample size with the method described by Hussey and Hughes.[31] Based on our efficacy study, we assumed a hazard ratio (HR) of 1.5 on the primary outcome full sustainable RTW.[16] To achieve a power of 0.8 with a two-tailed alpha of 0.05 with nine clusters, assuming an intraclass correlation coefficient of 0.05 and a dropout rate of 10%, the sample size was set at 454 patients.

The analyses were done at patient level, according to the intention-to-treat principle. To compare the baseline measurements of both groups, we used descriptive statistics. The primary outcome variable was the duration of sick leave until full sustainable RTW. The independent variable of interest was group allocation. Duration of sick leave in each of the two groups was depicted graphically using the Kaplan-Meier method. Duration of sick leave was compared between the two groups in Cox regression analyses. Here we corrected for possible confounders as indicated in our predefined analysis plan and the characteristics of the stepped-wedge cluster randomised trial design. The adjusted Cox regression model included the fixed effect for group together with (1) a random effect for hospital, (2) a fixed effect for type of surgery performed, (3) a fixed effect for time since start of the trial, (4) a fixed effect for time since implementation of the new intervention in the hospital which we set to zero for all observations in the control condition and (5) if necessary, clinically relevant dissimilarities between both study groups at baseline. HRs for RTW were calculated together with their 95% CIs. The proportional hazard assumption was checked visually and corrected for by including a time-varying covariate for group in the models. Crude analyses were performed in addition to these adjusted analyses.

Linear mixed models were used to assess differences in the longitudinal course of the secondary outcomes over the 52 weeks of follow-up. All of the available outcome measurements (2, 6, 12, 26 and 52 weeks) were used. Models included fixed effects for group, type of surgery, time since surgery, an interaction between group allocation and time since surgery and, if available, the baseline value for the outcome measure. Random effects were included for hospital and patients nested within hospitals. Post hoc tests with Bonferroni correction were used to compare the means between groups separately at each time of follow-up. To assess whether protocol deviations caused bias, a per-protocol analysis was performed. In addition, several subgroup analyses were performed. The predefined

subgroups were: (1) hysterectomy (abdominal, vaginal, laparoscopic), (2) minimally invasive hysterectomy (vaginal, laparoscopic), (3) abdominal hysterectomy only and (4) laparoscopic adnexal surgery only.

All statistical analyses followed a predefined analysis plan and were done in SPSS V.16.0 and STATA V.12.0.

RESULTS

Nine hospitals participated in this trial. Between October 2011 and July 2013, 1591 patients were scheduled for a hysterectomy and/or laparoscopic adnexal surgery in these hospitals. In total, 433 patients were enrolled in the study, 206 patients during the control phase and 227 patients during the intervention phase (figure 2). The timing of crossover from usual care to the intervention of the eighth cluster was delayed by 2 months as the number of inclusions in the control group lagged behind, compared with the number of inclusions in the intervention group at that time. Although lengthening the total inclusion period would have led to reaching the number of patients calculated in the power analysis, this was decided against, as this would only have led to a greater misbalance between the number of patients in the control and intervention groups.

Patient characteristics

Most patient characteristics were well balanced between groups at baseline (table 1). However, baseline dissimilarities were present with type of surgery (P=0.038) and intention to RTW despite physical complaints (P=0.003). Because these variables are potentially associated with the outcome measures, they were added to the adjusted models.

Lost to follow-up

Data for the primary outcome were obtained from self-reported sick leave calendars and were available for 401 participants (92.6%). Twenty-nine patients were lost to follow-up and three patients were censored for the primary endpoint because of the occurrence of an unforeseen independent incident before reaching full RTW (cerebral vascular accident, severe exacerbation of sarcoidosis and diagnosis of post-traumatic dystrophy shoulder). For the secondary outcomes, complete follow-up data were available for 334 patients (77.1%). Lost to follow-up rates did differ between both groups; patients in the intervention group were more likely to get lost to follow-up than patients in the usual care group (P=0.022).

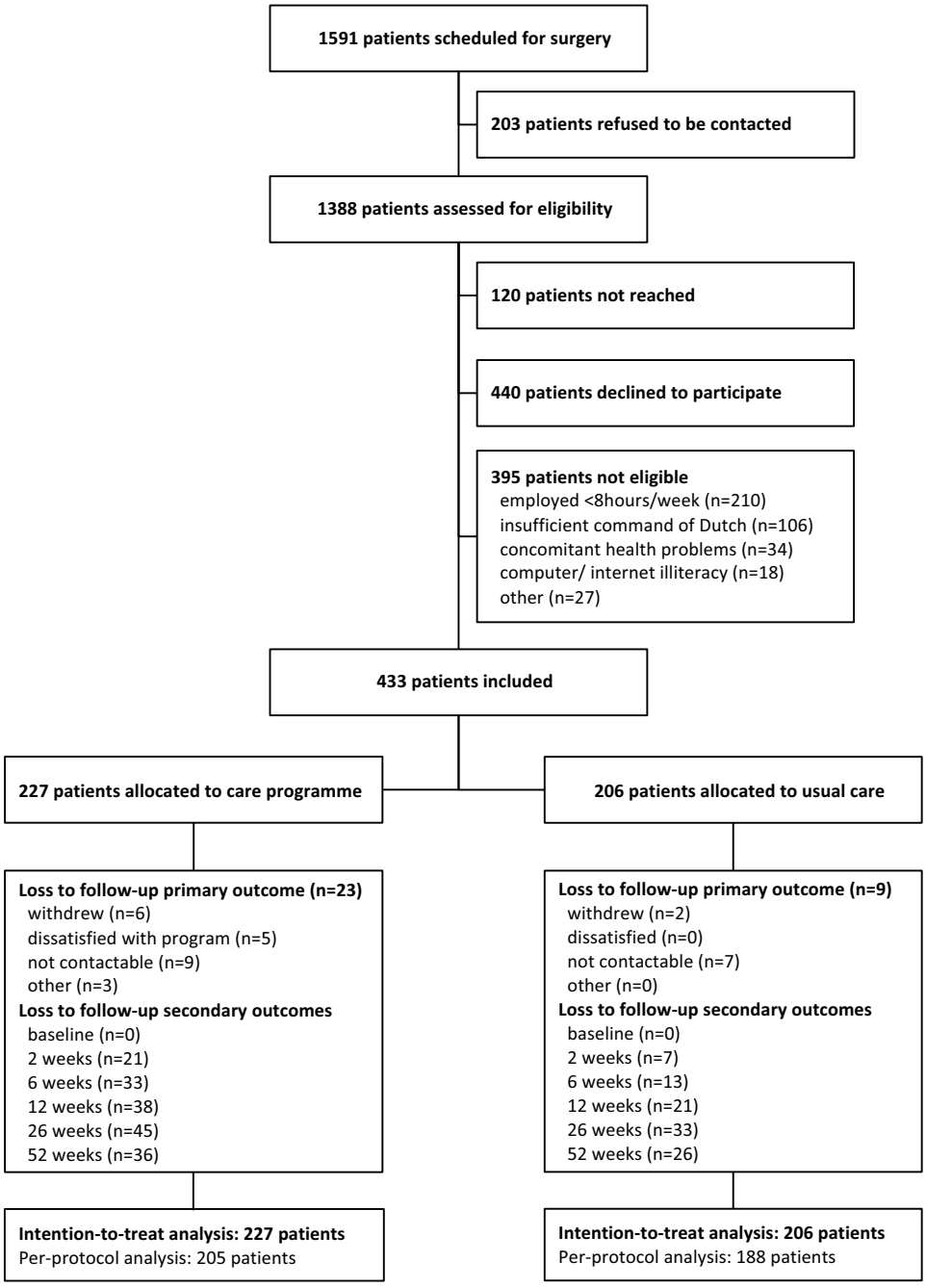

Figure 2. Trial profile

Table 1. Baseline characteristics of individual patients at baseline

	Care Programme (n=227)	Usual Care (n=206)
Patient characteristics		
Age (years ± SD)	46.1 ± 7.3	45.6 ± 6.7
Dutch nationality	220 (96.9%)	202 (98.1%)
Internet use (days/week)		
< 1	2 (0.9%)	3 (1.5%)
1 – 2	9 (4.0%)	10 (4.9%)
3 – 5	45 (19.8%)	42 (20.4%)
> 5	171 (75.3%)	151 (73.3%)
Education level *		
Low	25 (11.0%)	17 (8.3%)
Intermediate	88 (38.8%)	100 (48.5%)
High	114 (50.2%)	89 (43.2%)
Surgery-related characteristics		
Type of surgery		
Adnexal surgery	74 (32.6%)	51 (24.8%)
Laparoscopic hysterectomy	65 (28.6%)	50 (24.3%)
Vaginal hysterectomy	36 (15.9%)	53 (25.7%)
Abdominal hysterectomy	52 (22.9%)	52 (25.2%)
Health-related characteristics		
Perceived health status (mean ± SD)	75.8 ± 16.5	76.9 ± 16.7
Work-related characteristics		
Type of work		
Salary employed	194 (85.5%)	175 (85.0%)
Self-employed	28 (12.3%)	28 (13.6%)
Voluntary work	5 (2.2%)	3 (1.5%)
Work hours per week (mean ± SD)	29.7 ± 9.3	28.7 ± 8.2
Sick leave (3 months before surgery)		
Absence from work §	88 (38.8%)	66 (32.0%)
Number of sick leave days (median (IQR))	4.0 (2-10)	4.5 (2-11)
RTW expectation (long) †	42 (18.5%)	38 (18.4%)
RTW intention (low) ‡	45 (19.8%)	67 (32.5%)

Data are number of patients (%), unless otherwise indicated.
* Low = preschool, primary school; intermediate = secondary school; high = tertiary school, university, or postgraduate.
§ Defined as at least 1 day of absence.
† Defined as expectation longer than 3 weeks for adnexal surgery, longer than 6 weeks for laparoscopic or vaginal hysterectomy, or longer than 8 weeks for abdominal hysterectomy.
‡ Higher scores indicate a higher intention to return to work, despite symptoms (range 1–5). A low intention was defined as score 1 or 2.
IQR = Interquartile range, RTW = return to work, SD = standard deviation

Indicators of implementation

In the intervention group, the vast majority of patients logged in to the web portal at least once (215/227; 94.7%). A total of 188 patients (82.8%) used the website as intended and generated a personal convalescence plan online. Median time spent on the website was 97 min (IQR 55–167). Participants gave the web portal an overall score of 7.3 on a 10-point scale.

Gynaecologists electronically authorised 81.7% of all generated convalescence plans (170/208).

In total, 68 patients were eligible for a telephone consultation with a clinical OP before surgery due to a high risk for delayed recovery; however, only 23 patients (33.8%) received care by the OP as planned. Postoperatively, 126 patients were eligible for a telephone consultation with a clinical OP, of which 84 appointments took place (66.7%). In total, 65.7% of the patients (130/198) received clinical occupational care according to the protocol.

Primary outcome measure

The median duration until full sustainable RTW was 49 days (IQR 27–76) in the intervention group and 62 days (IQR 42–85) in the usual care group (log-rank test P=0.153). Survival curves for duration until RTW diverged directly after surgery but converged again with time (figure 3). The proportional hazard hypothesis was tested and rejected as the time-dependent covariate for group was highly significant (P=0.001). Therefore, a piecewise Cox model was fitted taking into account the non-proportionality of hazards by creating two different time intervals. The cut-off for the time-dependent covariate was determined by plotting the HR over time and calculating the time period the HR was greater than one and smaller than one (supplementary file S3). Duration to RTW was effectively reduced in the first 85 days after surgery: HR 2.66; 95% CI 1.88 to 3.77; P<0.001 (349 patients (191 in intervention group, 158 in control group); table 2). The effect was reversed if patients did not RTW within this period: HR 0.28, 95% CI 0.17 to 0.46; P<0.001 (84 patients (36 in intervention group, 48 in control group); table 2).

In the per-protocol analysis, a total of 40 patients were excluded because they, retrospectively, did not meet the inclusion criteria (n=3), had a significant larger surgery than planned (n=25) or needed a repeat surgery during follow-up (n=12). Findings from the per-protocol analysis were similar to those of the main analysis (table 2).

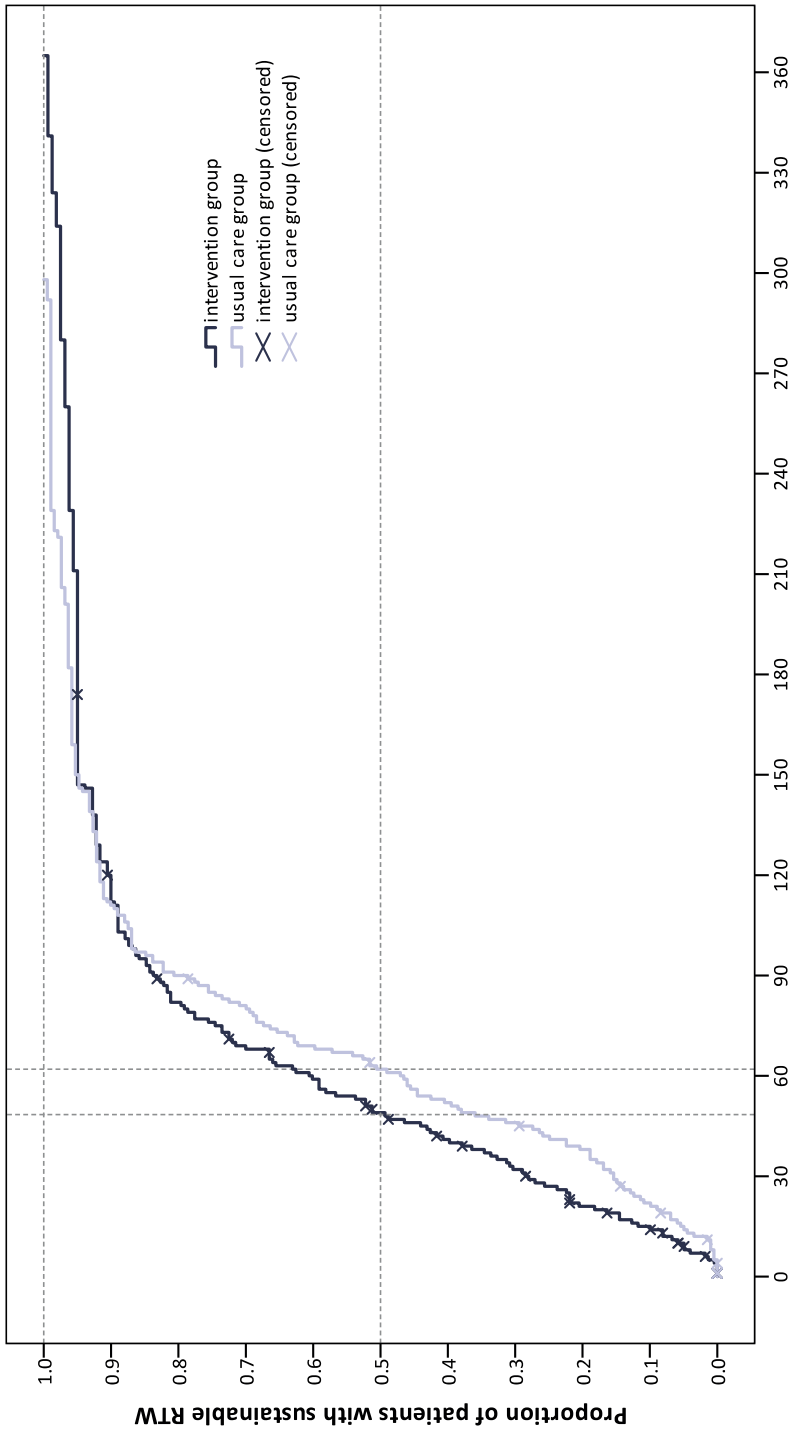

Figure 3. Survival curves for duration until full sustainable return to work
Median time to full sustainable RTW in the control group was 62 days (95% CI 54.9 to 69.1) and in the intervention group 49 days (95% CI 44.2 to 53.8); log-rank test P=0.153.
RTW = return to work.

Table 2. Differences in duration until return to work between the intervention group and the usual care group

	Events/ subjects	Cut off	# Subjects		Hazard ratio	95% CI	
			UC	IC		Lower	Upper
Unadjusted model							
Intention to treat	401/433	T ≤ 85 days	158	191	2.55	2.02	3.21
		T > 85 days	48	36	0.26	0.18	0.39
Per protocol	368/393	T ≤ 85 days	147	175	2.48	1.95	3.15
		T > 85 days	41	30	0.28	0.18	0.43
Adjusted model 1*							
Intention to treat	401/433	T ≤ 85 days	158	191	2.79	1.97	3.94
		T > 85 days	48	36	0.29	0.18	0.47
Per protocol	368/393	T ≤ 85 days	147	175	2.79	1.95	3.97
		T > 85 days	41	30	0.31	0.19	0.52
Adjusted model 2§							
Intention to treat	401/433	T ≤ 85 days	158	191	2.66	1.88	3.77
		T > 85 days	48	36	0.28	0.17	0.46
Per protocol	368/393	T ≤ 85 days	147	175	2.63	1.84	3.75
		T > 85 days	41	30	0.30	0.18	0.50

Results of the crude Cox regression models are not presented, due to violation of the proportional hazard assumption.
Due to violation of the proportional hazard assumption, a time dependent covariate was introduced, and therefore two hazard ratios are presented. The cut off was calculated by determining at what time the hazard ratio equalled value 1.
* adjusted for hospital (random effect), type of surgery performed (fixed effect), time since start of trial (fixed effect), time since implementation (fixed effect).
§ as adjusted model 1, including RTW intention (fixed effect).
UC = usual care, IC = intervention care, 95% CI = 95% confidence interval, RTW = return to work

Subgroup analyses

Results of the prespecified subgroup analyses were also in concordance with the main analysis (supplementary file S4). However, it is important to note that power was lost in some subgroups, due to the reduced sample sizes.

Secondary outcome measures

The results of the secondary outcome measures are presented in supplementary file S5. For the outcome recovery-specific quality of life, a significant interaction between group allocation and time since surgery was found, indicating that there was a difference in the course of mean outcome over time in the two groups (P=0.003). Post hoc analyses showed a difference to be present at 2 weeks following surgery with patients in the intervention

group having a higher score corresponding with a better recovery than patients in the control group (mean score of 30.07 in the intervention group vs 28.61 in the control group; P=0.046). However this difference disappeared with longer follow-up.

Similar findings were established for the outcome pain: 2 weeks following surgery, patients in the intervention group reported a lower pain intensity score than patients in the control group (mean score of 9.20 in the intervention group vs 10.55 in the control group; P=0.014), as well as a lower pain disability score (mean score of 11.83 in the intervention group vs 14.23 in the control group; P=0.000). Again, this difference disappeared with longer follow-up.

For the secondary outcomes functional health status, self-efficacy and coping, there were no differences in the course of mean outcomes over time in the two groups.

DISCUSSION

In this study, an internet-based care programme was implemented in nine Dutch hospitals following a stepped-wedge design. Our results show that implementation was successful and that the internet-based care programme has a large potential to lead to accelerated recovery and improved RTW rates following different types of gynaecological surgeries.

Interpretation of the findings

The majority of patients benefited greatly from the care programme. Duration until full RTW was effectively reduced in the first 85 days after surgery in the intervention group compared with the control group. The reversed effect after 85 days of follow-up is an interesting finding of the study which accounted for a minority of the patients. We hypothesise that this shift may be caused by a statistical limitation, due to the application of a Cox regression model in a population with an overall good prognosis of RTW (99.8% of the population achieved full RTW within the year). In addition, we were confronted with non-proportional hazards of the treatment effect, for which we were forced to take into account the time-dependency of the HR. In case of non-proportional hazards, the power of the log-rank test may be low, and therefore, the outcome of a trial can be declared 'negative' when in fact a clinically relevant difference between groups was present.[32] In our trial, the difference between median durations until full sustainable RTW between treatment groups was 13 days; however, this difference was not statistically significant using the log-rank test.

Patients in the intervention group scored slightly better on the outcomes recovery-specific quality of life and pain (both intensity score and disability score) at 2 weeks following surgery. The differences disappeared with longer follow-up. In addition, it is unknown if the small differences are of any clinical relevance.

Despite a restricted involvement of the research team following the initial instructions and training sessions, implementation at the patient level was quite successful. Due to user authentication, we were able to objectively measure usage of the e-health intervention by participants. The vast majority of the patients (82.8%) used the web portal as intended and generated a convalescence plan online. Compared with other internet-based interventions, this compliance rate is relatively high.[33, 34] However, these results are in concordance with our previous efficacy RCT.[17]

Participating gynaecologists electronically approved the convalescence plans of their patients in 81.7% of the cases. This implementation rate increased in comparison with the efficacy study, which might be attributable to the measures taken to increase the user-friendliness of the electronic procedures. In a survey among all involved gynaecologists, none agreed with the statement that the web portal was too time-consuming, and 94.7% of the responders thought the web portal was (very) easy to use.

At the level of the organisation of care processes, 65.7% of the patients received care according to the protocol. Taking into account the very poor implementation score at this level of 24.0% in the previous trial, adaptations made to the protocol and implementation strategies were highly rewarding. The most important change was to integrate occupational healthcare in clinical care, and therefore, postoperative appointments with a clinical OP were already planned at enrolment, which were to be cancelled in case full resumption of work was reached before the appointment.

Strengths and weaknesses of the study

A strength of our study is that the internet-based programme was developed with all involved stakeholders, including focus groups with patients. In addition, it was rigorously evaluated and adapted through different phases of research, including both an efficacy trial demonstrating proof of concept and a process evaluation. The current implementation study with a stepped-wedge approach provided not only important data on healthcare outcomes and adherence to the programme by its end users, but also valuable information about the organisational context. The latter has been identified as a striking absent outcome in studies reporting on electronic patient portals.[35]

In addition, we believe that our study is unique as the primary endpoint was sick leave duration until full sustainable RTW. WHO uses the International Classification of Functioning, Disability and Health which is a framework for the description of health and classifies functioning and disability associated with health conditions.[36] By assessing participation

restrictions on a social level, in our case sick leave following surgery, we integrated a biopsychosocial model and looked further than the illness and its treatment but also assessed the impact on the community.

Our study also has limitations. Regarding methodology, the cluster design of the study might have led to recruitment bias. This can be a threat to validity, when professionals recruit differently depending on the trial arm to which they are allocated. To minimise this, recruitment took place through the use of waiting lists and was performed independently from the professional invitation. Allocation was concealed to patients until informed consent was received. We believe that recruitment bias was minimised, as the proportion of patients included during the control phase, was broadly similar to the proportion of inclusions during the intervention phase, across all participating hospitals. In addition, the subgroup analyses show that our data are robust and confirmed in all subgroups.

Second, external validity of the result might have been compromised. Only one of every three patients approached, ended up in the trial (31.2%). The other patients either declined to participate (31.7%), did not meet the inclusion criteria (28.5%) or were missed (8.6%). Therefore, as this study only included employed women who had access to internet and of which the majority was highly educated, caution is needed when generalising the findings. Possibly, clinical effectiveness is reduced when the intervention is accessible to the general audience. The most important reason for exclusion was not being employed for at least 8 hours a week. This criterion was put in place because of the primary outcome, sustainable RTW. It should be noted that the benefits of the care programme under study are probably not limited to work outcomes alone, but can also impact the resumption of other daily activities.

Finally, lost to follow-up rates differed significantly between both study groups with more participants withdrawing from the study in the intervention group than in the control group. Some participants judged the intervention programme in combination with the monthly trial questionnaires to be too time-consuming during their recovery. Also, there were a few participants in the intervention group who withdrew because they felt the focus of the care programme was too much on the resumption of work. Differences in lost to follow-up rates between study groups can lead to both overestimation and underestimation of the intervention effect. Since the results from the subgroup analysis with only complete cases were similar to those in the main analysis, we believe the effect in our trial to be minimal.

Comparison to other studies

In the last decade, e-health, defined by WHO as 'the transfer of health-related resources and healthcare by electronic means, including information, support resources, assessments,

interventions, and healthcare records', has known an enormous growth.[37] For patients with chronic disease such as diabetes or hypertension, and for patients with mental disorders such as depression, e-health programmes are numerous and already widespread.[35] Currently, e-health solutions are also being developed for the care of surgical patients.[38, 39]

Besides our own intervention, we are aware of two other internet-based interventions aimed at patients undergoing gynaecological surgery, both in an early stage of evaluation. Dukeshire *et al* developed the Studying Adverse Events From Elective Surgery Research self-care web application, designed to improve recovery after hysterectomy by providing patients timely, accurate information tailored to the patient's stage of recovery.[40] It also contained a screening tool to identify adverse symptoms. Feasibility was tested among 31 patients, of which 11 patients experienced an adverse event. Interviewed women (six) indicated that they used the provided information to guide themselves in seeking care for their complications.[41] Andikyan *et al* evaluated the feasibility of an internet-based patient-reported outcome system in patients recovering from major gynaecological cancer surgery.[42] They used a Symptom Tracking And Reporting for patients (STAR) system to identify adverse events postoperatively. The intervention was tested among 96 patients, of which the majority of patients found it helpful and would recommend it to other patients. Despite positive feedback from patients, clinical personnel found that STAR system increased their current workload without enhancing patient care.[43] Although the results of those two feasibility studies are promising, we want to emphasise the importance of targeting the entire surgical pathway from the early preoperative phase, starting when the indication for surgery is set, until the late postoperative phase, ending with full recovery and resumption of all daily activities, in which our own internet-based care programme is unique.

Policy implications and recommendations

Affronted with increased pressure on current healthcare systems worldwide due to a combination of an ageing population, limited healthcare budgets and a shortage of the workforce, internet-based technology is widely accepted to play an essential role in revolutionising healthcare.

In the surgical field, there is an urgency to reorganise perioperative care as well, considering the escalation of the number of surgical procedures being performed and the transition of care from the hospital setting towards the home setting. In addition, there is considerable evidence that the length of recovery time after (gynaecological) surgery systematically exceeds the period considered as appropriate by specialists.[3,8,44–46] Also in our study, the median time until RTW in the intervention group of 49 days can be considered as quite long. Policy-makers faced with the task to optimise perioperative care should consider the encouraging outcomes of this study demonstrating that our internet-based perioperative

care programme provides an excellent platform to target all phases of the surgical pathway and is effective in facilitating self-management postoperatively, leading to accelerated recovery.

In addition, we showed that implementation was quite successful by employing a multifaceted implementation strategy, targeting both patients and healthcare professionals, as well as the organisation of healthcare. Key learnings from the current implementation study can be applied across other fields of surgical care; however, cost-effectiveness data will be essential to convince policy-makers that implementation of the care programme is worthwhile.

As there was a small group in our study population that did not benefit from the care programme, future research should focus on ways to discriminate between patients who might benefit most from the care programme, and patients who would need a more intensive form of postoperative guidance. In addition, in view of enhancing technologies, the web portal should evolve concurrently, with access to a mobile application being the first priority.

CONCLUSIONS

Our trial provides meaningful evidence that the internet- based intervention care programme can be highly beneficial for a majority of gynaecological patients, resulting in accelerated RTW rates following surgery. Key learnings from the current implementation study can be applied across all other fields of surgical care. Further research should focus on the identification of patients who might benefit most from the internet-based care programme.

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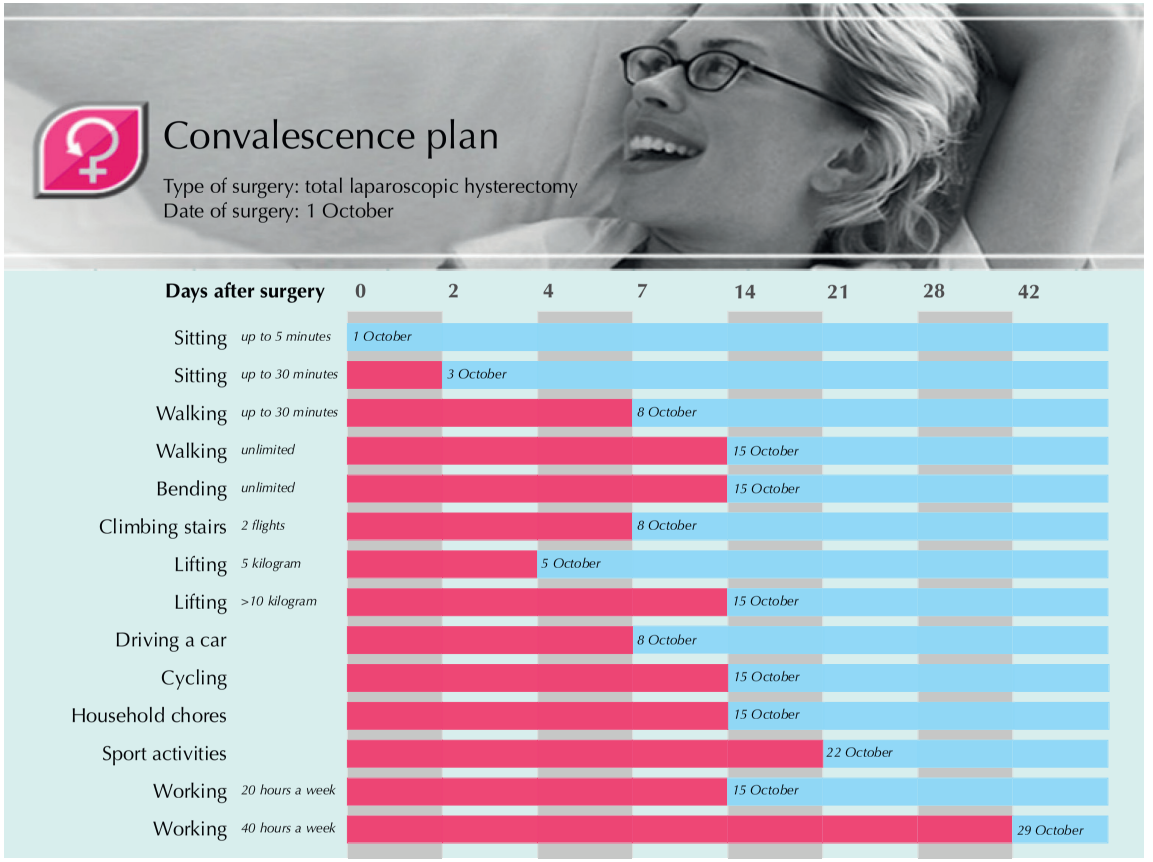
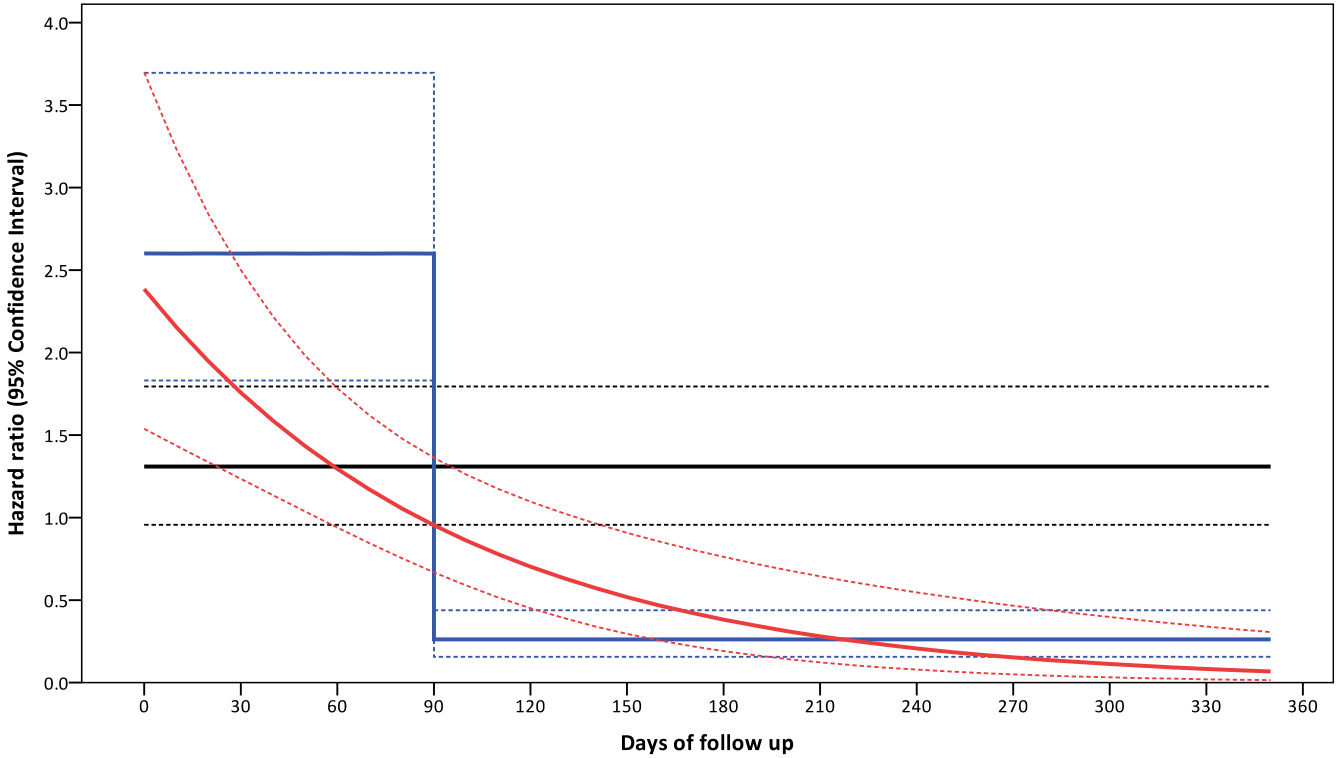


Supplementary file S1. Example of a tailored convalescence plan generated at the patient web portal
In the left column activities are listed that were selected by the patient. The pink boxes present the amount of time the patient is recommended to avoid the specific activity. The blue boxes present the duration after surgery (and the specific date) after which the patient is recommended to resume the specific activity.

Supplementary file S2. Overview of the intervention care programme and multifaceted implementation strategy

Type of strategy	Description of care program
Directed at patients	
Information email	Before surgery, patients received information about the web portal and its functionalities by email. A manual was accessible on the web portal. On request, instructions were given by telephone.
Reminder email	If patients had not activated their account on the web portal, an automatic electronic reminder was sent 1 week before surgery, and if necessary, 1 week after the surgery.
Tailored convalescence plan	The most important functionality on the web portal was a tool to generate a personalized convalescence plan, which included tailored instructions on the resumption of activities (selected by the patient) after surgery, allowing planning of (work-)activities (figure 2).
Interactive self-assessment tool	If recovery fell behind, an alerting system advised patients to contact a specific health care professional, depending on the underlying reason
Standardized discharge procedure	At discharge, patients received printed general recommendations on the resumption of their normal activities by one of their care-providers and were verbally instructed to visit the web portal.
Directed at professionals	
Educational training sessions	Before the start of each implementation phase of a cluster, all physicians and nurses involved in patient care were invited for (two separate) 30-minute educational training sessions, in which the new care program was explained and background information was given about the multidisciplinary guideline on convalescence advice.
Reminder pocket card	The summarized guidelines were printed on pocket cards for quick reference during interaction with patients.
Reminder in patient records	Visual reminders in patient records stimulated physicians to follow the standardized discharge routine.
Reminder newsletters	During the intervention-phase of the trial, newsletters were spread every 3 months to reinforce the different aspects of the care program and give feedback on performance.
Directed at the organization of care	
Web portal (eHealth intervention)	For patients, the web portal provided a tool to monitor their recovery, facilitating self-management. For professionals, the web portal gave access to their patients' tailored convalescence plans in order to decrease variation in advice. In addition, inter-professional communication was facilitated.
Care managers (occupational intervention)	Continuity of care services was maintained by eight clinical occupational physicians, who were trained before the start of the trial during two 2½ hour interactive training sessions. Patients at risk for prolonged sick leave (i.e. had an inadequate expectation towards own work resumption or had a low intention to resume work-activities while recovering) were offered consultations by telephone, both before and after surgery to optimize their expectations.



Supplementary file S3. Hazard ratios in adjusted Cox-regression model without and with a time-dependent covariate

Black line: Hazard ratio in adjusted Cox-regression model without time-dependent covariate.

Red line: Hazard ratio in adjusted Cox-regression model with a time-dependent covariate for group. The interaction between group and time since surgery was used as the time-dependent covariate.

Blue line: Hazard ratio in adjusted Cox-regression model with two different hazard ratios (below t=85 days and above t=85 days). The cut-off of t=85 days was chosen as the time where the red line crosses the hazard ratio of value=1.

Supplementary file S4. Subgroup analyses

			# Subjects			95% CI	
Adjusted model 2*	**Events/ subjects**	**Cut off**	**UC**	**IC**	**Hazard ratio**	**Lower**	**Upper**
Hysterectomy_all *(TAH, VH, LH)*	283/308	T ≤ 94 days	128	128	3.31	2.03	5.40
		T > 94 days	27	25	0.28	0.15	0.52
Hysterectomy_MIS *(VH, LH)*	190/204	-	103	101	1.37 §	0.76	2.47
Abdominal hysterectomy only	93/104	T ≤ 70 days	24	34	8.69	3.24	23.3
		T > 70 days	28	18	0.36	0.15	0.90
Adnexal surgery only	118/125	-	51	74	1.24 §	0.65	2.37
Complete cases	282/282	T ≤ 93 days	113	122	2.32	1.79	4.53
		T > 93 days	29	18	0.21	0.10	0.42

Due to violation of the proportional hazard assumption, a time dependent covariate was introduced, and therefore two hazard ratios are presented. The cut off was calculated by determining at what time the hazard ratio equalled value 1.

* Adjusted for hospital (random effect), type of surgery performed (fixed effect), time since start of trial (fixed effect), time since implementation (fixed effect) and RTW intention (fixed effect).

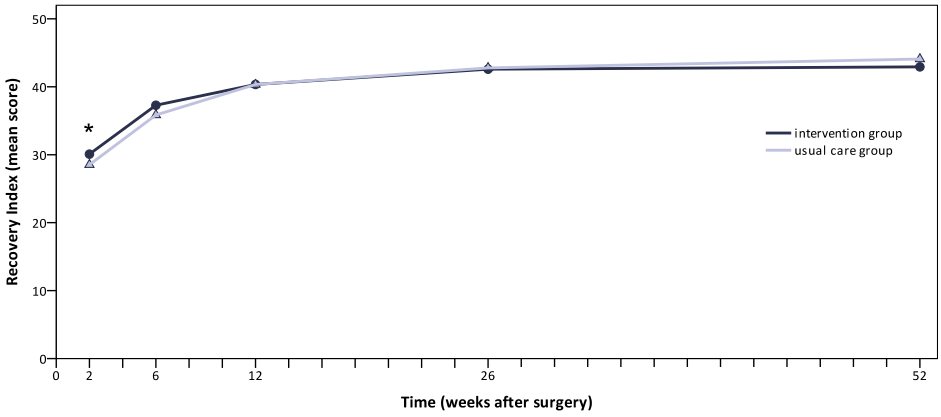
§ An overall hazard ratio is presented as the proportional hazard assumption was not violated.

UC = usual care, IC = intervention care, 95% CI = 95% confidence interval, TAH = total abdominal hysterectomy, VH = vaginal hysterectomy, LH = laparoscopic hysterectomy, MIS = minimal invasive surgery

Supplementary file S5. Secondary outcomes

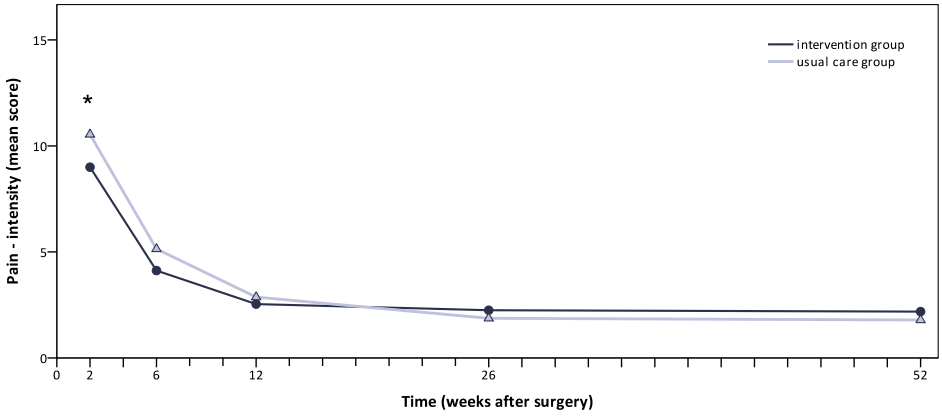
	Mean score			
Recovery	UC	IC	Mean difference	P-value
2 weeks	28.61	30.07	1.46	0.046 *
6 weeks	35.95	37.25	1.30	0.079
12 weeks	40.42	40.47	0.05	0.951
26 weeks	42.86	42.97	0.11	0.889
52 weeks	44.16	43.33	-0.83	0.267

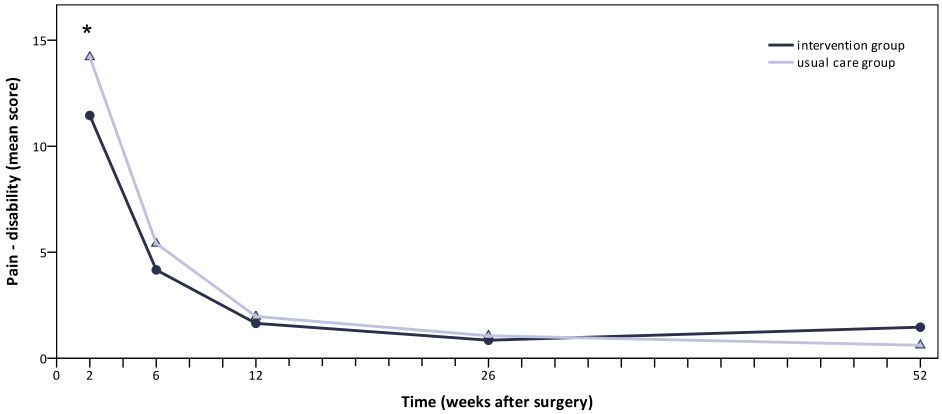
Recovery measured by the Recovery Index, range 10 – 50, with a score of 50 indicating perfect recovery.
Linear mixed model including fixed effects for group allocation, type of surgery, time since surgery, an interaction between group allocation and time since surgery and baseline value, as well as random effects for hospital and patients nested within hospitals.
UC = usual care, IC = intervention care



Pain	Mean score		Mean difference	P-value
	UC	IC		
Intensity score				
2 weeks	10.55	9.20	-1.35	0.014 *
6 weeks	5.14	4.35	-0.79	0.158
12 weeks	2.88	2.72	-0.16	0.777
26 weeks	1.87	2.27	0.40	0.483
52 weeks	1.79	2.14	0.35	0.531
Disability score				
2 weeks	14.23	11.83	-2.40	0.000 *
6 weeks	5.41	4.46	-0.95	0.139
12 weeks	1.98	1.77	-0.21	0.751
26 weeks	1.05	0.93	-0.12	0.851
52 weeks	0.61	1.39	0.78	0.235

Pain measured by the Von Korff questionnaire, range 10 – 100, with higher scores indicating higher levels of pain intensity / disability.
Linear mixed model including fixed effects for group allocation, type of surgery, time since surgery, an interaction between group allocation and time since surgery, as well as random effects for hospital and patients nested within hospitals.
UC = usual care, IC = intervention care





Health Status	Mean score UC	Mean score IC	Mean difference	P-value
Physical Component Scale				
12 weeks	52.25	53.26	1,01	0.111
26 weeks	56.41	55.52	-0.89	0.169
52 weeks	57.06	56.16	-0.90	0.159
Mental Component Scale				
12 weeks	51.31	50.12	-1.19	0.146
26 weeks	52.02	50.89	-1.13	0.179
52 weeks	51.48	50.69	-0.79	0.339

Health status measured by the Short-Form Health Survey, range 0 – 100, with higher scores indicating a better health state.
Linear mixed model including fixed effects for group allocation, type of surgery, time since surgery, an interaction between group allocation and time since surgery and baseline value, as well as random effects for hospital and patients nested within hospitals.
UC = usual care, IC = intervention care

	Mean score			
Coping	UC	IC	Mean difference	P-value
2 weeks	27.38	26.88	-0.50	0.243
12 weeks	28.32	27.72	-0.60	0.181
52 weeks	28.85	27.76	-1.09	0.015

Coping measured by the Pearlin Mastery Scale, range 7 – 28, with higher scores indicating greater levels of mastery.
Linear mixed model including fixed effects for group allocation, type of surgery, time since surgery, an interaction between group allocation and time since surgery, as well as random effects for hospital and patients nested within hospitals.
UC = usual care, IC = intervention care

	Mean score			
Self-efficacy	UC	IC	Mean difference	P-value
2 weeks	32.54	32.42	-0.12	0.811
12 weeks	33.75	33.52	-0.23	0.656
26 weeks	33.89	34.07	0.18	0.717
52 weeks	34.34	34.54	0.20	0.687

Self-efficacy measured by the General Self-Efficacy Scale, range 10 – 40, with higher scores indicating higher perceived self-efficacy.
Linear mixed model including fixed effects for group allocation, type of surgery, time since surgery, an interaction between group allocation and time since surgery, as well as random effects for hospital and patients nested within hospitals.
UC = usual care, IC = intervention care

CHAPTER 5

Cost-effectiveness of an Internet-based perioperative care programme to enhance postoperative recovery in gynaecological patients; economic evaluation alongside a stepped-wedge cluster randomized trial

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ABSTRACT

Objectives To evaluate the cost-effectiveness and cost-utility of an internet-based perioperative care programme compared with usual care for gynaecological patients.

Design Economic evaluation from a societal perspective alongside a stepped-wedge cluster-randomised controlled trial with 12 months of follow-up.

Setting Secondary care, nine hospitals in the Netherlands, 2011–2014.

Participants 433 employed women aged 18–65 years scheduled for a hysterectomy and/or laparoscopic adnexal surgery.

Intervention The intervention comprised an internet-based care programme aimed at improving convalescence and preventing delayed return to work (RTW) following gynaecological surgery and was sequentially rolled out. Depending on the implementation phase of their hospital, patients were allocated to usual care (n=206) or to the intervention (n=227).

Main outcome measures The primary outcome was duration until full sustainable RTW. Secondary outcomes were quality-adjusted life years (QALYs), health-related quality of life and recovery.

Results At 12 months, there were no statistically significant differences in total societal costs (€−647; 95% CI €−2116 to €753) and duration until RTW (−4.1; 95% CI −10.8 to 2.6) between groups. The incremental cost-effectiveness ratio (ICER) for RTW was 56; each day earlier RTW in the intervention group was associated with cost savings of €56 compared with usual care. The probability of the intervention being cost-effective was 0.79 at a willingness-to-pay (WTP) of €0 per day earlier RTW, which increased to 0.97 at a WTP of €76 per day earlier RTW. The difference in QALYs gained over 12 months between the groups was clinically irrelevant resulting in a low probability of cost-effectiveness for QALYs.

Conclusions Considering that on average the costs of a day of sickness absence are €230, the care programme is considered cost-effective in comparison with usual care for duration until sustainable RTW after gynaecological surgery for benign disease. Future research should indicate whether widespread implementation of this care programme has the potential to reduce societal costs associated with gynaecological surgery.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This is the first economic evaluation on an internet-based care programme aimed at improving convalescence and preventing delayed return to work following gynaecological surgery.
- The study was conducted alongside a cluster-randomised controlled trial allowing prospective collection of relevant cost and effect data.
- The study was performed from a societal perspective, and costs associated with lost productivity included both absenteeism and presenteeism costs.
- A latent barrier to future acceptance and implementation of the care programme lies in the fact that the costs and benefits of the care programme are separated between different types of stakeholders.

INTRODUCTION

At present, there is a transition of perioperative care from the hospital setting towards the home environment.[1–4] The introduction of advanced surgical techniques in combination with the implementation of 'fast-track' clinical pathways has considerably reduced the length of postoperative hospital stays, and many (complex) surgeries are now being performed in an ambulatory setting.[5–7] This is beneficial from the perspective of the healthcare system, as it leads to the containment of healthcare costs.[1, 8]

However, costs associated with lost productivity following surgery contribute to the total societal costs of surgical procedures as well, and are mostly not taken into account. Moreover, there is considerable evidence that the duration of sick leave following gynaecological surgery generally exceeds the period considered appropriate by specialists.[9] Therefore, preventing unnecessary prolonged recovery following gynaecological surgery may translate into considerable savings for society.

We developed an internet-based care programme for patients undergoing gynaecological surgery for benign disease, aimed at facilitating recovery after discharge and preventing delayed return to work (RTW).[10, 11] In this paper, we report on the cost-effectiveness and cost-utility of the internet-based care programme compared with usual care. The findings on clinical effectiveness were reported in a separate paper.[12]

METHODS

Study design and participants

This economic evaluation was performed from a societal perspective and was carried out alongside a stepped-wedge cluster-randomised controlled trial comparing an internet-based care programme with usual care for patients undergoing benign gynaecological surgery. The study was done in the Netherlands between October 2011 and July 2014. The follow-up period was 12 months. The trial protocol has been published previously in accordance to Consolidated Standards of Reporting Trials extended guidelines.[9]

The clusters in this trial were formed by separate hospitals. A total of nine hospitals participated, which were selected before the start of the trial. Hospitals were eligible if they performed at least 100 hysterectomies or laparoscopic adnexal surgeries annually and were located within 50 km of the VU medical centre, Amsterdam, the Netherlands.

Patients were recruited from the waiting lists for hysterectomy (abdominal, vaginal or laparoscopic) and laparoscopic adnexal surgery. Eligible participants were women aged 18–65 years who were employed for at least 8 hours a week (unpaid or paid employment or self-employed). We excluded patients who had severe benign comorbidity, had a malignancy, were pregnant, were computer or internet illiterate, were involved in a lawsuit against their employer, were on disability sick leave before surgery or had insufficient command of Dutch.

Randomisation and blinding

Randomisation took place at the level of the clusters and determined the order in which the intervention was implemented in the participating hospitals. The sequence was generated by a statistician using a computer-generated list of random numbers. A stepped-wedge approach was employed as it enabled us to study both the cost-effectiveness of the intervention and the implementation process.[9]

Patients, clinicians and researchers could not be blinded for the intervention. However, group allocation was concealed until patients had agreed to participate and provided written informed consent. Data analysts (EVAB and JEB) were masked to group allocation.

Intervention care programme and implementation strategy

The development and content of the intervention care programme have been described elsewhere in more detail.[9, 11] A multifaceted implementation strategy was employed to achieve maximal adoption of the care programme, targeting three different levels.

At the level of the organisation, the structure of healthcare was changed by the introduction of the interactive web portal that was accessible for patients as well as their healthcare professionals. In addition, care managers were trained to help patients identify possible barriers to resuming work activities and could assist, if necessary, in the planning and execution of work resumption, before and after surgery.

At the level of the healthcare professional, educational training sessions were organised to introduce an earlier developed guideline on postoperative convalescence recommendations to stimulate evidence-based patient education.[10]

At the patient level, the care programme consisted of two steps. First, all participants allocated to the intervention group received access to the web portal several weeks prior to their surgery (eHealth intervention). The interactive web portal facilitated self-management by providing patients with individual tailored convalescence recommendations throughout the entire surgical pathway as well as monitoring recovery postoperatively through an interactive self-assessment tool. Second, for those patients at risk of prolonged sick leave, a care manager was available to provide additional guidance in the process of resuming work activities (occupational intervention).

Usual care

Before the care programme was implemented in the hospitals, participating patients received usual care. Although considerable variation in usual care exists in the Netherlands, postoperative patients generally receive verbal instructions at discharge by a nurse and/or physician, sometimes accompanied by a letter or brochure. Usually, a postoperative consultation is planned 6 weeks after surgery. Due to Dutch legislation, employed patients who do not resume work within 6 weeks after the surgery are invited for a consultation with their occupational physician.

Main outcome measures

The primary outcome was duration until sustainable RTW defined as the resumption of own work or other work with equal earnings, for at least 4 weeks without (partial or full) recurrence of sick leave. This definition was adopted as interventions aimed at expediting RTW of sick-listed employees should also aim at reducing recurrence of sickness absence in order to sustain employees at work after initial RTW. Data on RTW were collected by means of monthly electronic sick leave calendars.

Quality-adjusted life year (QALY) was one of the secondary outcomes and was measured using the Dutch version of the European Quality of Life five-dimensional three-level questionnaire (EQ-5D-3L).[13] The Dutch tariff was used to estimate the utility of EQ-5D-3L

health states.[14] QALYs were calculated by multiplying the utility with the amount of time a patient spent in a particular health state. Transitions between health states were linearly interpolated. Other secondary outcomes included health-related quality of life assessed by Short-Form Health Survey[15] and recovery assessed by the Recovery Index.[16] All secondary outcomes were assessed at baseline and at 2, 6, 12, 26 and 52 weeks follow-up.

Service use and costs

The intervention and implementation strategy costs consisted of costs related to implementing the new care programme. A bottom-up microcosting approach was used for estimating intervention costs, using detailed data regarding the quantity and unit prices of: (1) the training sessions of involved healthcare professionals (clinical staff, occupational physicians and occupational therapist), (2) the eHealth intervention (hosting of web portal and administrator time) and (3) the occupational intervention (number and duration of consultations).[17]

Data on healthcare services used and support received by the participants were collected using electronic questionnaires during 1 year. Each month, the patient was asked to report service use over the previous month. Patients who were not sick listed and did not have any healthcare costs during three consecutive months received a shortened version of the questionnaire. In case of no response, electronic reminders were sent after 1 and 2 weeks. If participants did not respond to the electronic reminders either, an additional attempt was made to complete the missing data per email, mail or telephone every 3 months.

Only healthcare utilisation and support related to the gynaecological surgery were collected and included the following categories: surgery and initial hospitalisation, primary and secondary care including complementary medicine, medication and medical aids, home care and informal help.

Service utilisation was valued using Dutch standard costs.[18] If these were unavailable, prices according to professional organisations were used. The prices of prescribed drugs were estimated using the prices of the Royal Dutch Society for Pharmacy.[19]

Productivity loss

Absenteeism costs were calculated using the human capital approach. The net number of sick leave days during follow-up was multiplied by the estimated costs of 1 day of sick leave for females, stratified for age.[18] In case of partial sick leave, we assumed that participants were 100% productive during the hours of partial work resumption.

Presenteeism (i.e., reduced productivity while at work) was assessed monthly after full resumption of work using two items of the 'Productivity and Disease Questionnaire'.[20]

Patients were asked to report the quantity (q1) and quality (q2) of the work performed during the latest day at work on an 11-point scale, ranging from 'nothing/very bad quality' (0) to 'same as normal' (10).

The level of presenteeism ($Pres_{day}$) on the latest day at work was calculated using the following formula: $Pres_{day}=(1-((q1*q2)/100))$.[20, 21] Assuming linearity, the level of presenteeism on the latest day at work was then extrapolated over the total month. The total number of workdays lost due to presenteeism was calculated ($Pres_{month}$) by multiplying the participants' presenteeism level by their number of days worked during that month. Subsequently, presenteeism costs per month were calculated by multiplying $Pres_{month}$ by the estimated costs of 1 day of lost productivity.

The index year of the study was 2014. Discounting of costs was not necessary because the follow-up was 1 year.[22]

Statistical analysis

The sample size of the study (n=454) was calculated for detecting a relevant difference in RTW (HR 1.5) in the main outcome study.[9] The economic evaluation was done according to the intention to treat principle. Missing cost and effect data during follow-up were imputed using multiple imputation by chained equations. Multiple imputation was done using SPSS V.16.0 with predictive mean matching. An imputation model containing demographic and prognostic variables was used to create five complete datasets after which the loss of efficiency was smaller than 5%.[23] Rubin's rules were used to pool effects and costs from the five imputed datasets.[24]

Differences in costs and effects were estimated using linear multilevel regression analyses, while adjusting for type of surgery. Clustering at the hospital-level and patient-level was accounted for in these multilevel models. For the cost-effectiveness and cost-utility analyses, we calculated incremental cost-effectiveness ratios (ICERs) by dividing the incremental costs by the incremental effects. The ICER indicates the additional investments needed for the intervention to gain one extra unit of effect compared with usual care. In the ICER for duration until RTW, productivity costs due to sick leave were excluded from the cost estimates to avoid double counting.

We used non-parametric bootstrapping with 5000 replications to estimate 95% CIs around cost differences and the uncertainty surrounding the ICERs.[25] To account for the clustering of data, bootstrap replications were stratified for hospital.[26] Bootstrapped cost-effect pairs were plotted on cost-effectiveness planes (CE planes) and used to estimate

cost-effectiveness acceptability curves (CEA curves). CEA curves show the probability that a treatment is cost effective in comparison with the control treatment at a specific ceiling ratio, which is the amount of money society is willing to pay to gain one extra unit of effect.

Sensitivity analyses

To assess whether protocol deviations influenced the treatment effect, a per-protocol analysis was performed. In addition, to assess the robustness of the results, we carried out three sensitivity analyses. First, we did a complete-case analysis to assess the cost-effectiveness of the interventions excluding patients who were lost to follow-up. Second, we replicated the cost-effectiveness analysis using the friction cost approach (FCA). The FCA assumes that costs are limited to the friction period (i.e., the period needed to replace a sick worker). A friction period of 23 weeks and an elasticity of 0.8 were used. Third, an analysis from the healthcare perspective was performed including only healthcare costs.

All statistical analyses followed a predefined analysis plan and were done in SPSS (V.16.0) and STATA (V.12SE).

RESULTS

Participants

During the study period, 1591 patients were scheduled for a hysterectomy and/or laparoscopic adnexal surgery in the participating hospitals. In total, 433 patients enrolled in the study, 206 patients during the control phase and 227 patients during intervention phase (figure 1).

Participants' demographic and prognostic variables are presented in table 1. Complete follow-up data were obtained from 92.6% of the participants on the primary outcome RTW, from 71.8% on the secondary outcomes and 70.0% on healthcare utilisation. Baseline characteristics did not differ between participants with and without complete cost data, except that patients with complete data on healthcare utilisation used the internet more frequently than women with incomplete data.

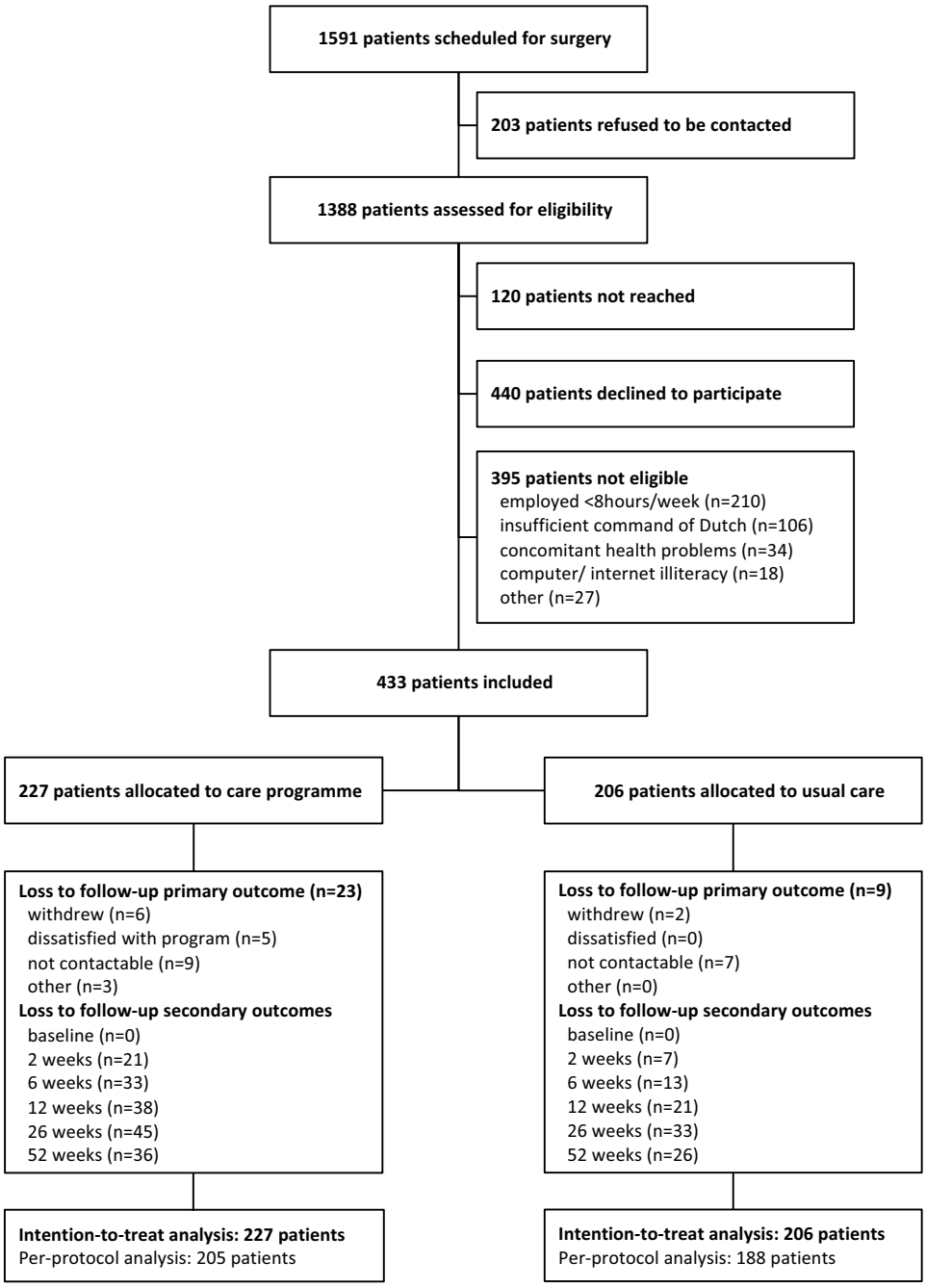

Figure 1. Trial profile

Table 1. Baseline characteristics of individual patients at baseline

	Care Programme (n=227)	Usual Care (n=206)
Patient characteristics		
Age (years ± SD)	46.1 ± 7.3	45.6 ± 6.7
Dutch nationality	220 (96.9%)	202 (98.1%)
Internet use (days/week)		
< 1	2 (0.9%)	3 (1.5%)
1 – 2	9 (4.0%)	10 (4.9%)
3 – 5	45 (19.8%)	42 (20.4%)
> 5	171 (75.3%)	151 (73.3%)
Education level *		
Low	25 (11.0%)	17 (8.3%)
Intermediate	88 (38.8%)	100 (48.5%)
High	114 (50.2%)	89 (43.2%)
Surgery-related characteristics		
Type of surgery		
Adnexal surgery	74 (32.6%)	51 (24.8%)
Laparoscopic hysterectomy	65 (28.6%)	50 (24.3%)
Vaginal hysterectomy	36 (15.9%)	53 (25.7%)
Abdominal hysterectomy	52 (22.9%)	52 (25.2%)
Health-related characteristics		
Perceived health status (mean ± SD)	75.8 ± 16.5	76.9 ± 16.7
Work-related characteristics		
Type of work		
Salary employed	194 (85.5%)	175 (85.0%)
Self-employed	28 (12.3%)	28 (13.6%)
Voluntary work	5 (2.2%)	3 (1.5%)
Work hours per week (mean ± SD)	29.7 ± 9.3	28.7 ± 8.2
Sick leave (3 months before surgery)		
Absence from work [§]	88 (38.8%)	66 (32.0%)
Number of sick leave days (median (IQR))	4.0 (2-10)	4.5 (2-11)
RTW expectation (long) [†]	42 (18.5%)	38 (18.4%)
RTW intention (low) [‡]	45 (19.8%)	67 (32.5%)

Data are number of patients (%), unless otherwise indicated. * Low = preschool, primary school; intermediate = secondary school; high = tertiary school, university, or postgraduate. [§] Defined as at least 1 day of absence. [†] Defined as expectation longer than 3 weeks for adnexal surgery, longer than 6 weeks for laparoscopic or vaginal hysterectomy, or longer than 8 weeks for abdominal hysterectomy. [‡] Higher scores indicate a higher intention to return to work, despite symptoms (range 1–5). A low intention was defined as score 1 or 2. SD = standard deviation, IQR = Interquartile range, RTW = return to work

Table 2. Costs associated with self-reported service used across treatment groups at 12 months follow-up

Cost category	Intervention mean (SEM) n=227	Usual care mean (SEM) n=206	Mean cost difference (95% CI)*
Healthcare costs	**3823 (99)**	**4142 (134)**	**-61 (-361 to 218)**
Surgery costs	3236 (64)	3413 (58)	34 (-118 to 174)
Primary care costs	179 (24)	167 (30)	14 (-58 to 95)
Secondary care costs	242 (42)	458 (98)	-178 (-400 to -31)
Costs of medication and aids	13 (4)	10 (4)	3 (-6 to 11)
Home help costs	72 (24)	94 (26)	-19 (-85 to 45)
Intervention	80 (0)	NA	80 (NA)
Lost productivity costs	**8443 (543)**	**9653 (528)**	**-570 (-1909 to 692)**
Costs of absenteeism from unpaid work	1845 (224)	2124 (299)	-144 (-756 to 282)
Costs of absenteeism from paid work	6499 (425)	7281 (344)	-424 (-1469 to 578)
Presenteeism costs	99 (78)	248 (127)	-154 (-458 to 82)
Total societal costs	**12266 (596)**	**13795 (602)**	**-647 (-2116 to 735)**

* Uncertainty estimated using bootstrapping and corrected for clustering by hospital and type of surgery
Costs are expressed in 2014 Euros (€1.00 = £0.85; $1.06).
Mean values summarize the costs derived after the imputation process.
SEM =standard error, CI = confidence interval, NA = not applicable

Service use and costs

Table 2 presents the costs of self-reported service use per category over the 12 months of follow-up stratified by treatment group and the mean cost differences between both groups.

Intervention costs were €80 per participant (online supplementary file S1). Total societal costs per patient were €12,266 in the intervention group and €13,795 in the usual care group. After correction for clustering by hospital and adjustment for surgery type, total societal costs in the intervention group were €647 lower compared with the usual care group, but this difference was not statistically significant (95% CI €–2116 to €753). In both groups, costs related to productivity losses were about two times higher than total healthcare costs. There were no statistically significant differences in healthcare costs between the intervention group and usual care group (€–61; 95% CI €–361 to €218) and lost productivity costs (€–570; 95% CI €–1909 to €692). Only costs for secondary care were significantly lower in the intervention group compared with the usual care group (€–178; 95% CI €–400 to €–31).

Effectiveness

The mean duration until RTW in the intervention group was 49.6 days versus 56.2 days in the usual care group. The adjusted difference in duration until RTW between the intervention and usual care was −4.1 days, but this difference was not statistically significant (95% CI −10.8 to 2.6) (table 3). For the other outcomes, no statistically differences were found between both groups at 12 months either.

Cost-effectiveness

The results of the cost-effectiveness analysis for duration until RTW are presented in table 4. The ICER for sustainable RTW was 56 indicating that each day earlier RTW in the intervention group is associated with cost savings of €56 in comparison with the usual care group. In the CE plane, 69% of the incremental cost effect pairs were located in the south-east quadrant indicating that the intervention is more effective and less costly than usual care (figure 2A). The CEA curve presented in figure 2B shows that if the societal willingness-to-pay (WTP) for one earlier day of RTW is €0, the probability that the intervention is cost-effective in comparison with usual care is 0.79. This probability increases to 0.97 at maximum if the WTP is €76 per day earlier RTW.

Cost-utility and other secondary outcomes

The difference in QALYs gained over 12 months between the two study groups was small and not statistically significant or clinically relevant (table 4). Therefore, the ICER for QALYs became extraordinarily large (half million Euros). In the CE plane, the majority of cost-effect pairs were located in the southern quadrants, indicating that the intervention was less expensive than usual care. However, the cost-effect pairs were roughly divided between the eastern and the western quadrant, indicating that the intervention can lead to both better and worse outcomes compared to usual care (figure 2C). As a result, the probability that the intervention was cost-effective for QALYs in comparison with usual care was considerably lower than for the primary outcome (0.77 at WTP is €0 per QALY gained and decreasing at higher WTP values) (figure 2D).

The differences observed for the secondary outcomes health-related quality of life and recovery at 12 months were also small and not significant, leading to a low probability of cost-effectiveness for these outcomes as well.

Table 3. Effects across treatment groups at 12 months follow-up

Outcomes	Intervention Mean (SEM) n=227	Usual care Mean (SEM) n=206	Mean effect difference (95% CI) *
Duration until RTW (days)	49.6 (2.7)	56.2 (2.2)	-4.1 (-10.8 to 2.6)
QALY's gained	0.96 (0.008)	0.96 (0.007)	-0.001 (-0.023 to 0.020)
HR-QoL (SF-36)			
PCS	5.7§ (0.7)	6.7§ (0.6)	-0.7 (-2.6 to 1.1)
MCS	3.3§ (0.7)	3.7§ (0.8)	-0.4 (-2.5 to 1.7)
Recovery (RI-10)	24.3§ (0.4)	25.0§ (0.5)	-0.6 (-2.0 to 0.9)

* Uncertainty estimated using bootstrapping and corrected for clustering by hospital and type of surgery.
§ Difference between baseline score and score at 12 months follow-up.
SEM =standard error, CI = confidence interval, RT =, return to work, QALY= Quality Adjusted Life Year, HR-QoL = health-related quality of life, SF = Short Form, PSC = physical component scale, MSC = mental component scale, RI = recovery index

Table 4. Differences in pooled means costs and effects, incremental cost-effectiveness ratios and the distribution of incremental cost-effectiveness pairs around the quadrants of the cost-effectiveness planes (main analysis)

Outcome	Δ Cost* (€) mean (95% CI)	Δ Effect* (days) mean (95% CI)	ICER €/day	Distribution CE-plane			
				NE[1]	SE[2]	SW[3]	NW[4]
RTW	-228 (-708 to 136)	4.1§ (-2.6 to 10.8)	-56	15%	69%	10%	6%
QALY's gained	-647 (-2116 to 735)	-0.001 (-0.023 to 0.020)	501187	4%	42%	35%	19%
HR-QoL (SF36)							
PCS	-647 (-2116 to 735)	-0.7 (-2.6 to 1.1)	870	6%	19%	58%	17%
MCS	-647 (-2116 to 735)	-0.4 (-2.5 to 1.7)	1573	10%	33%	44%	13%
Recovery (RI-10)	-647 (-2116 to 735)	-0.6 (-2.0 to 0.9)	1127	5%	22%	55%	18%

* Uncertainty estimated using bootstrapping and corrected for clustering by hospital and type of surgery
§ Note that a positive value indicates faster RTW in the intervention group compared to the control group.
[1] Refers to the northeast quadrant of the CE-plane, indicating that the intervention care programme is more effective and more costly than usual care.
[2] Refers to the southeast quadrant of the CE-plane, indicating that the intervention care programme is more effective and less costly than usual care.
[3] Refers to the southwest quadrant of the CE-plane, indicating that the intervention care programme is less effective and less costly than usual care.
[4] Refers to the northeast quadrant of the CE-plane, indicating that the intervention care programme is less effective and more costly than usual care.
ICER = Incremental Cost-Effectiveness Ratio, CE plane = cost-effectiveness plane, RTW = return to work, QALY = Quality Adjusted Life Year, HR-QoL = health-related quality of life, SF = Short Form, PSC = physical component scale, MSC = mental component scale, RI = recovery index

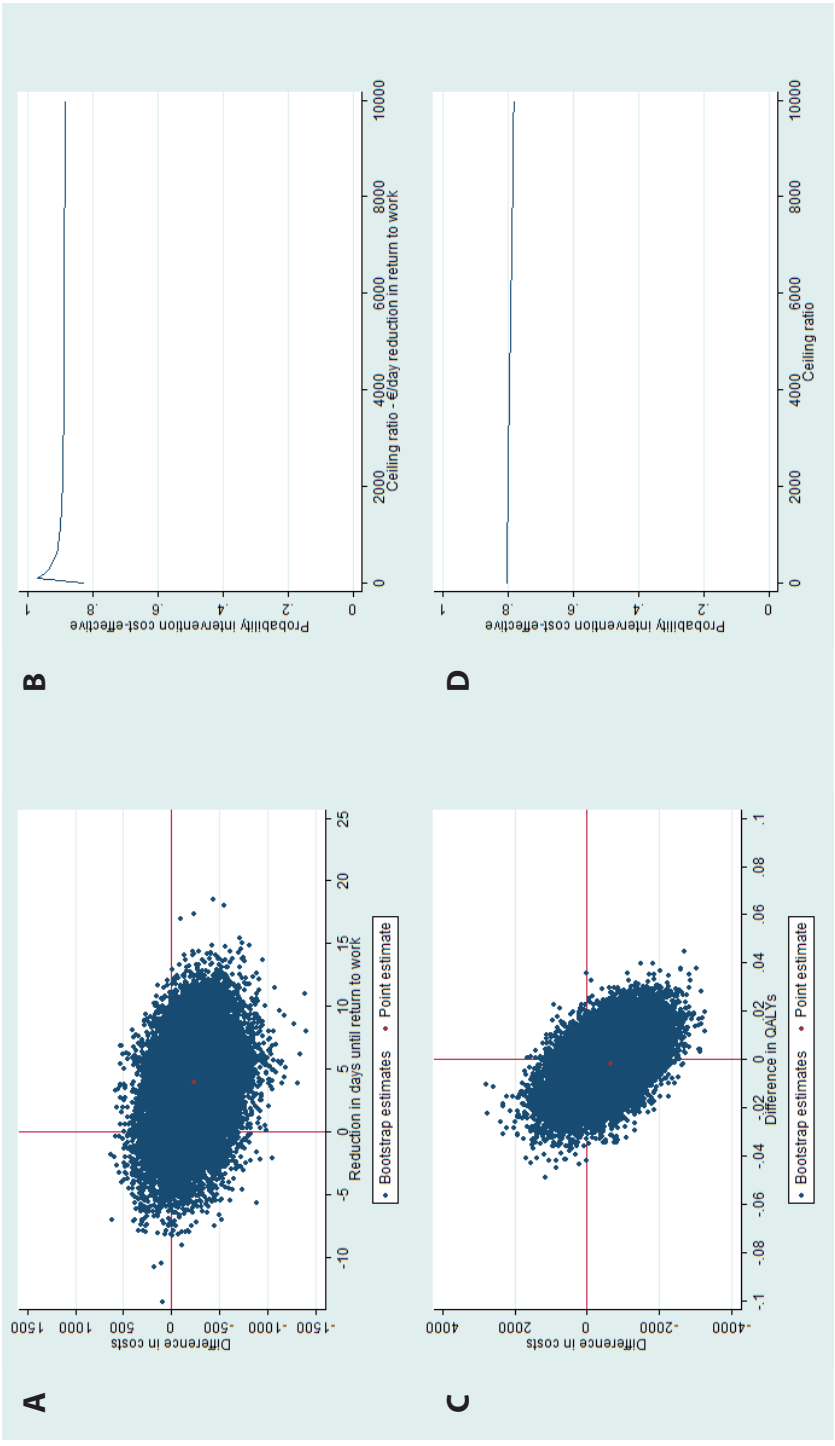

Figure 2. CE planes and CEA curves for RTW and QALYs

The CE planes indicate the uncertainty around the incremental cost-effectiveness ratio for RTW (A) and QALYs (C). The CEA curves indicate the probability of cost-effectiveness for different values (€) of willingness-to-pay per unit of effect gained for RTW (B) and QALYs (D).

CE = cost-effectiveness, CEA = cost-effectiveness acceptability, QALY = quality-adjusted life year, RTW = return to work

Per-protocol analysis

In the per-protocol analysis, 40 patients were excluded because they did not receive the care according to protocol due to several reasons: did not fit the inclusion criteria (n=3), had a more severe surgery than planned (n=25) or had a complicated postoperative course and needed a repeat surgery during follow-up (n=12). By excluding those patients, the difference in effect became larger, but was still not significant (−6.4 days, 95% CI −12.9 to 0.20), and the cost differences became statistically significant in favour of the intervention (mean difference €−359, 95% CI −866 to −11) (table 5). Hence, compared with the main analysis, the probability of cost-effectiveness increased considerably at a WTP of €0 per 1 day earlier RTW (from 0.79 to 0.92).

Sensitivity analyses

The results of the primary outcome in the sensitivity analyses differed in some aspects from the main analysis (table 5). First, in the complete-case analysis, the effect difference between study groups became larger in favour of the intervention group, but the cost savings in the intervention group as compared with usual care became smaller. The probability of cost-effectiveness compared with the main analysis therefore decreased (from 0.79 to 0.55). Second, the results from the friction cost analysis were identical to the intention to treat analysis, indicating that the majority of patients returned to their work before the end of the friction period of 23 weeks. Finally, in the analyses performed from the healthcare perspective, cost savings became much smaller, as costs associated with lost productivity were not taken into account. As a result, the probability of cost-effectiveness reduced (from 0.79 to 0.61).

The results of the per-protocol analyses and sensitivity analyses for the secondary outcomes QALYs, health-related quality of life and recovery are presented in online supplementary table 2. In the per-protocol analyses, cost differences became larger in favour of the intervention group, however, they did not reach statistical significance. The probability of cost-effectiveness at a WTP of €0 per unit of effect increased from 0.77 to 0.93. In contrast to the complete-case analysis for the primary outcome, the complete-case analyses for the secondary outcomes showed a statistically significant increase in cost savings in the intervention group. The probability of cost-effectiveness at a WTP of €0 per unit of effect increased from 0.77 to 0.98.

Table 5. Results from the per-protocol and sensitivity analyses (Return to Work)

	Sample size		Δ Cost* (€)	Δ Effect* (days)	ICER	Distribution CE-plane			
Analysis	IC	UC	mean (95% CI)	mean (95% CI)	€/day	NE[1]	SE[2]	SW[3]	NW[4]
Per-protocol analysis	205	188	-359 (-866 to -11)	6.4[§] (-0.2 to 12.9)	-56	8%	87%	5%	1%
Complete-case analysis	154	150	-45 (-466 to 362)	11.6[§] (-5.4 to 19.3)	-4	45%	55%	0%	0%
Friction cost approach	227	206	-228 (-708 to 136)	4.1[§] (-2.6 to 10.8)	-56	15%	69%	10%	6%
Healthcare perspective	227	206	-61 (-361 to 218)	4.1[§] (-2.6 to 10.8)	-15	28%	56%	5%	10%

* uncertainty estimated using bootstrapping and corrected for clustering by hospital and type of surgery
[§] Note that a positive value indicates faster RTW in the intervention group compared to the control group.
[1] Refers to the northeast quadrant of the CE-plane, indicating that the intervention care programme is more effective and more costly than usual care.
[2] Refers to the southeast quadrant of the CE-plane, indicating that the intervention care programme is more effective and less costly than usual care.
[3] Refers to the southwest quadrant of the CE-plane, indicating that the intervention care programme is less effective and less costly than usual care.
[4] Refers to the northwest quadrant of the CE-plane, indicating that the intervention care programme is less effective and more costly than usual care.
IC, intervention care; UC, usual care; ICER, Incremental Cost-Effectiveness Ratio; CE plane, cost-effectiveness plane.

DISCUSSION

In this study, we evaluated the cost-effectiveness and cost-utility of a rigorously designed internet-based perioperative care programme compared with usual care for gynaecological patients. Our results show that for the primary outcome duration until full resumption of work, the probability that the care programme is cost-effective as compared with usual care is 0.97 at a WTP of €76 per day earlier RTW. Taking into account that the average costs per sick leave day are €230, we conclude that the intervention is cost-effective as compared with usual care.

Interpretation of the findings

In the current economic evaluation, the adjusted mean difference until RTW between study groups was not statistically significant (–4.1 days, 95% CI –10.8 to 2.6). In the accompanying paper on the clinical effectiveness of the intervention, median days until RTW were compared between study arms using Cox regression analyses.[12] However, a survival analysis results in difficulties in interpreting the ICER. Therefore, we chose to compare mean days until RTW in the current cost-effectiveness study and used bootstrapping to account for the skewed distribution of this variable.

In addition, the cost-difference between the intervention group and the control group was not statistically significant either, although total societal costs were lower in the intervention group than in the control group. A possible explanation might be that the sample size of this study was based on the primary outcome full sustainable RTW and, therefore, underpowered to detect relevant cost differences, as cost data are right skewed and require relatively large samples.[27]

Secondary care costs in the intervention group were lower compared with the usual care group. Future research should investigate if the care programme truly leads to different health-seeking behaviour. Possibly, patients receiving additional perioperative care were more confident in their own self-management skills preventing them from visiting a healthcare professional. In addition, costs associated with primary care were similar in both groups, demonstrating that the care programme did not cause a shift from secondary care to primary care in the intervention group compared with the usual care group. Concerns of increased workload in the primary care setting due to changes in perioperative care have been reported before, however, seem to be ungrounded based on our results.[28, 29]

We did not find any clinically relevant differences in the secondary outcomes. Thus, despite the possible difference in the RTW rates between study groups, this did not have an effect on patients' perceptions about their quality of life and recovery. Possibly, the surgery itself has a much larger impact on these outcomes than the method of postoperative guidance.

The results of the per-protocol analyses were slightly more favourable towards the intervention programme than those of the main analyses. Thus, by presenting the intervention to the ideal target population, the probability of cost-effectiveness of the intervention in comparison with usual care increases. This is in concordance with our initial objective to develop an internet-based care programme for women undergoing an uncomplicated surgical procedure.[10] It may be challenging to identify future patients who will benefit most from the care programme, as complications, generally, cannot be predicted preoperatively. In addition, it should be investigated further what the needs are of patients with a complicated course and how they should best be guided and monitored during their recovery.

Strengths and weaknesses of the study

Several strengths of the present study are noteworthy. First of all, we are not aware of other current perioperative interventions that aim at preventing unnecessary prolonged recovery and reducing sick leave in order to contain societal costs associated with gynaecological surgical care. Second, analyses were performed alongside a pragmatic trial, allowing prospective collection of relevant cost and effect data and enabling the evaluation of

the intervention's cost-effectiveness under real-world conditions.[27] The third strength concerns the use of linear multilevel analyses to account for possible clustering of data as a result of the chosen study design. Randomisation at cluster level was chosen to prevent contamination between the study arms. Moreover, the employment of a stepped-wedge design allowed the sequential implementation of the care programme in the participating hospitals, providing the possibility to study the implementation process as well.

Our study also has limitations. The first limitation is the collection of cost data through self-reported retrospective questionnaires. However, since administrative data on service use are very hard to obtain in the Netherlands, societal cost data can only be collected by means of self-report. In order to prevent recall-bias, we minimised the recall period to only 1 month. In addition, if there was recall bias, it seems unlikely that this systematically differed between the study groups. Therefore, we expect that this does not affect our estimations. A second limitation concerns the amount of incomplete data. Despite our efforts to obtain full data from the patients in the trial, only 70.4% of the study population had complete cost data. Although this is an acceptable rate of missing data, complete-case analyses may be biased and have less precision.[30, 31] We tried to account for this by applying multiple imputation for missing data.[32] Comparison of participants with complete and incomplete data resulted in a number of variables that predicted the presence of missing data. Therefore, we concluded that the data was missing at random, making multiple imputation the appropriate method to deal with the missing data. Finally, it should be noted that a typical feature of internet-based interventions is the risk of selection bias towards the higher educated participant. Also in our study, included participants were employed women of which the majority was highly educated, and patients that were computer or internet illiterate were excluded. Therefore, caution is needed when generalising the findings, as clinical and cost-effectiveness may be reduced when the intervention is accessible for the general audience. Moreover, due to (cultural) differences in attitudes towards health and work as well as differences in the organisation of social and healthcare systems, generalisability of the results across countries might be hampered as well.

Comparison with other studies

We showed that costs associated with productivity loss following gynaecological surgery were about two times higher than healthcare costs. We are not aware of previously published literature in the gynaecological field in which this was demonstrated before. As a matter of fact, outcomes such as long-term convalescence, return to normal activities and absenteeism following gynaecological surgery are under-reported in clinical trials. In a review of Roumm *et al* assessing the clinical and economic benefits of minimal invasive surgery compared with open alternatives, only 5 of the 19 eligible studies reported data on RTW or return to normal activities, whereas 15 studies reported on hospital costs and

all studies reported on length of stay.[33] Similarly, in a recent Cochrane systematic review assessing the effectiveness and safety of different surgical approaches to hysterectomy in women with benign gynaecological disease, 45 of the 47 included studies reported on the length of postoperative hospital stay, and only 19 studies reported data on return to normal activities.[34]

Cost-effectiveness is one of the most frequently cited reasons for developing internet interventions because of the relative low delivery costs and the potential high impact.[35] However, economic evaluations are mainly lacking. A recent systematic review that evaluated the effect of perioperative eHealth interventions on the postoperative course concluded that only 6 of 19 included studies reported on costs, and in only one study, a full economic evaluation was performed.[36] Thus, the current study addresses this literature gap as well.

Policy implications and recommendations

Whether the perioperative internet-based care programme under study is considered cost-effective in comparison with usual care in accelerating RTW following gynaecological surgery depends on society's WTP for a reduced sick leave day, as well as the probability of cost-effectiveness that is considered acceptable. Our results show that the probability of cost-effectiveness is 0.97 at a WTP of €76 per day earlier RTW. Considering that on average the costs of a day of sickness absence are €230,[18] we expect that this intervention can be considered cost-effective in comparison with usual care.

A latent barrier to future acceptance and implementation of the care programme lies in the fact that the costs and benefits of the care programme are separated between different types of stakeholders. In the Netherlands, medical costs are paid by the government and health insurance companies and sickness benefits are the main responsibility of the employers, which makes the shifting of costs across these sectors hard. As follows, investments are made in the healthcare sector for implementing the care programme and changing care processes, while the largest benefits accrue to employers through reduced lost productivity costs. However, many countries have an employer-provided health insurance (e.g., the USA), and in those countries, this internet-based care programme is much more likely to be adapted as investments in the internet-based care programme may directly lead to savings through improved productivity rates.

CONCLUSIONS

The encouraging outcomes of this trial show that there is an economic case for supporting patients in the perioperative period with an internet-based care programme. The care programme has a potential to lead to societal cost savings as a result of a reduction in the duration until full sustainable RTW. If society is willing to pay €76 per day earlier RTW, the care programme is considered cost-effective in comparison with usual care in women undergoing benign gynaecological surgery. Policy-makers should investigate how these monetary benefits can be distributed across stakeholders.

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Supplementary file S1. Costs of the intervention care programme from the societal perspective, valued using a bottom-up micro-costing approach

Intervention component	Cost category	Staff	Units	Unit Price	Total costs (n=227)	Costs per patient
Implementation costs						
Training sessions (care-managers)	labour costs	principal investigator	5 hours	€ 36.94	€ 184.69	€ 0.81
	labour costs	occupational physicians	18 hours	€ 89.68	€ 1,614.24	€ 7.11
	labour costs	occupational therapist	2 hours	€ 46.32	€ 92.64	€ 0.41
	capital costs		5 hours	€ 6.26	€ 31.29	€ 0.14
Training sessions (hospital staff)	labour costs	principal investigator	38 hours	€ 36.94	€ 1,403.67	€ 6.18
	travel costs	principal investigator	582 km	€ 0.22	€ 127.28	€ 0.56
	labour costs	gynaecologists	18.9 hours	€ 107.30	€ 2,027.90	€ 8.93
	labour costs	residents	18.9 hours	€ 42.58	€ 804.82	€ 3.55
	labour costs	nurses	45 hours	€ 42.64	€ 1,918.58	€ 8.45
	capital costs		9 hours	€ 6.26	€ 56.33	€ 0.25
	printed materials				€ 821.00	€ 3.62
					Subtotal	**€ 40.01**
eHealth intervention						
Electronic approval	labour costs	gynaecologists	14.2 hours	€ 107.30	€ 1,523.60	€ 6.71
	capital costs		14.2 hours	€ 4.17	€ 59.15	€ 0.26
Maintenance	labour costs	computer specialist	12.2 hours	€ 37.82	€ 461.45	€ 2.03
	capital costs		12.2 hours	€ 1.67	€ 20.33	€ 0.09
Administrator time	labour costs	research assistant	37.8 hours	€ 33.42	€ 1,263.23	€ 5.56
	capital costs		37.8 hours	€ 4.17	€ 157.46	€ 0.69
Website hosting	other		40 months	€ 18.84	€ 578.88	€ 2.55
					Subtotal	**€ 17.90**

Supplementary file S1. Continued

Intervention component	Cost category	Staff	Units	Unit Price	Total costs (n=227)	Costs per patient
Occupational intervention						
Pre-operative consultations	labour costs	occupational physicians	7.9 hours	€ 89.68	€ 708.47	€ 3.12
	capital costs		7.9 hours	€ 4.17	€ 32.91	€ 0.14
	phone costs		413 minutes	€ 0.09	€ 38.71	€ 0.17
Post-operative consultations	labour costs	occupational physicians	37.5 hours	€ 89.68	€ 3.363.00	€ 14.81
	capital costs		37.5 hours	€ 4.17	€ 156.21	€ 0.69
	phone costs		2083 minutes	€ 0.09	€ 195.23	€ 0.86
Workplace intervention	labour costs	occupational therapist	4 hours	€ 46.32	€ 185.29	€ 0.82
	capital costs		3 hours	€ 6.26	€ 18.78	€ 0.08
	labour costs	employer	2 hours	€ 83.69	€ 167.37	€ 0.74
	travel costs	occupational therapist	110 km	€ 0.22	€ 24.06	€ 0.11
					Subtotal	**€ 21.54**
Developmental costs					**€ 33,873.55**	**€ 0.56** [§]
					Subtotal	**€ 0.56**
TOTAL intervention costs						**€ 80.02**

Costs are expressed in 2014 Euros (€1.00 = £0.85; $1.06).

[§] € 33,873.55 was paid for the development of the intervention care-programme. For calculating the development costs per participant, these were divided by the expected number of users during the first five years after implementation (60,200). Per year 20,000 gynaecologic surgeries (LAS, TLH, VH, AH) are being performed in the Netherlands and based on the outcomes of an earlier performed process-evaluation we hypothesized a reach of 60.2%.[37]

Supplementary file S2. Differences in pooled means costs and effects, incremental cost-effectiveness ratios and the distribution of incremental cost-effectiveness pairs around the quadrants of the cost-effectiveness plane

Analysis	Sample size		Δ Cost* (€)	Δ Effect* (days)	ICER	Distribution CE-plane			
	IC	UC	mean (95% CI)	mean (95% CI)	€/day	NE[1]	SE[2]	SW[3]	NW[4]
QALYs									
Intention to treat	227	206	-647 (-2116 to 735)	-0.001 (-0.023 to 0.020)	501187	4%	42%	35%	19%
Per-protocol analysis	205	188	-1148 (-2611 to 162)	0.003 (-0.019 to 0.024)	-432881	1%	59%	34%	6%
Complete-case analysis	132	136	-1607 (-3421 to 52)	0.009 (-0.013 to 0.033)	-202816	1%	72%	24%	3%
Friction cost approach	227	206	-825 (-2209 to 470)	-0.001 (-0.023 to 0.020	639131	2%	44%	42%	12%
Healthcare perspective	227	206	-61 (-361 to 218)	-0.001 (-0.023 to 0.020	46942	13%	33%	28%	26%
SF-36 PHYSICAL COMPONENT SCORE									
Intention to treat	227	206	-647 (-2116 to 735)	-0.7 (-2.6 to 1.1)	870	6%	19%	58%	17%
Per-protocol analysis	205	188	-1148 (-2611 to 162)	-0.9 (-2.8 to 1.1)	1350	2%	21%	71%	6%
Complete-case analysis	153	149	-1689 (-3316 to -231)	-1.2 (-3.3 to 0.8)	1389	0%	12%	86%	2%
Friction cost approach	227	206	-825 (-2209 to 470)	-0.7 (-2.6 to 1.1)	1109	4%	21%	64%	11%
Healthcare perspective	227	206	-61 (-361 to 218)	-0.7 (-2.6 to 1.1)	81	8%	17%	44%	31%
SF-36 MENTAL COMPONENT SCALE									
Intention to treat	227	206	-647 (-2116 to 735)	-0.4 (-2.5 to 1.7)	1573	10%	33%	44%	13%
Per-protocol analysis	205	188	-1148 (-2611 to 162)	-0.5 (-2.7 to 1.7)	2198	2%	32%	61%	5%
Complete-case analysis	153	149	-1689 (-3316 to -231)	-0.1 (-2.6 to 1.9)	12598	1%	49%	49%	1%
Friction cost approach	227	206	-825 (-2209 to 470)	-0.4 (-2.5 to 1.7)	2006	6%	37%	49%	8%
Healthcare perspective	227	206	-61 (-361 to 218)	-0.4 (-2.5 to 1.7)	147	17%	26%	35%	22%

Supplementary file S2. Continued

Analysis	Sample size		Δ Cost* (€)	Δ Effect* (days)	ICER	Distribution CE-plane			
	IC	UC	mean (95% CI)	mean (95% CI)	€/day	NE[1]	SE[2]	SW[3]	NW[4]
RECOVERY INDEX									
Intention to treat	227	206	-647 (-2116 to 735)	-0.6 (-2.0 to 0.9)	1127	5%	22%	55%	18%
Per-protocol analysis	205	188	-1148 (-2611 to 162)	-0.7 (-2.1 to 0.8)	1786	1%	23%	70%	6%
Complete-case analysis	153	149	-1689 (-3316 to -231)	-0.7 (-2.2 to 0.7)	2562	1%	20%	78%	1%
Friction cost approach	227	206	-825 (-2209 to 470)	-0.6 (-2.0 to 0.9)	1437	3%	24%	62%	12%
Healthcare perspective	227	206	-61 (-361 to 218)	-0.6 (-2.0 to 0.9)	106	8%	19%	42%	31%

* uncertainty estimated using bootstrapping and corrected for clustering by hospital and type of surgery
[1] Refers to the northeast quadrant of the CE-plane, indicating that the intervention care programme is more effective and more costly than usual care.
[2] Refers to the southeast quadrant of the CE-plane, indicating that the intervention care programme is more effective and less costly than usual care.
[3] Refers to the southwest quadrant of the CE-plane, indicating that the intervention care programme is less effective and less costly than usual care.
[4] Refers to the northwest quadrant of the CE-plane, indicating that the intervention care programme is less effective and more costly than usual care.
IC = intervention care, UC = usual care, ICER = Incremental Cost-effectiveness Ratio, CE plane = cost-effectiveness plane

CHAPTER 6

Using patient data to optimize an expert-based guideline on convalescence recommendations after gynaecological surgery; a prospective cohort study

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ABSTRACT

Background Convalescence advice is often based on tradition and anecdote from health care providers, rather than being based on experiences from patients themselves. The aim of this study was to analyse recovery in terms of resumption of various daily activities including work, following different laparoscopic and abdominal surgery in order to optimize an expert-based guideline on convalescence recommendations.

Methods This is a prospective cohort study conducted in nine general and one university hospital in the Netherlands. Women aged 18–65 years and scheduled for a hysterectomy (laparoscopic, vaginal, abdominal) and/or laparoscopic adnexal surgery ($n = 304$) were eligible to participate. Preoperatively, participants were provided with tailored expert-based convalescence recommendations on the graded resumption of several daily activities including sitting, standing, walking, climbing stairs, bending, lifting, driving, cycling, household chores, sport activities and return to work (RTW). Postoperatively, time until the resumption of these activities was tracked. Convalescence recommendations were considered correct when at least 25% and less than 50% of the women were able to resume an activity before or at the recommended recovery time.

Results There was a wide variation in the duration until the resumption of daily activities within and between groups of patients undergoing different types of surgery. Recovery times lengthened with increasing levels of physical burden as well as with increasing levels of invasiveness of the surgery. For the majority of activities actual recovery times exceeded the recovery time recommended by the expert panel.

Conclusions This study provided insight in the resumption of daily activities after gynecological surgery and the adequacy of an expert-based convalescence guideline in clinical practice. Patient data was used to optimize the convalescence recommendations.

BACKGROUND

The importance of perioperative education to prepare patients for the postoperative period has been topic of research for decades.[1-5] It has been demonstrated that perioperative education can increase patient satisfaction, reduce pain as well as psychological distress and can optimize patients' expectations.[6-10] Notwithstanding, evidence based perioperative education has not yet found its way into routine surgical care.[11-14] Mainly two reasons can be identified for this. First, there is only little evidence on the duration needed to resume various daily activities following different surgeries.[15-20] This leads to convalescence advise being based on tradition and anecdote from health care providers, rather than being based on experiences from patients themselves.[14, 15, 18, 21-24] Second, due to the current trend towards day care and short stay surgery, patient contact is very brief and time available for patient education has practically evaporated.[25-29]

In order to optimize perioperative care in the Netherlands, our research group developed an expert-based multidisciplinary guideline on convalescence recommendations following four types of gynecological surgery. Using a structural consensus method, an expert panel of gynecologists, general practitioners and occupational physicians formulated recommended recovery times for the graded resumption of 38 daily activities (e.g. standing, walking, climbing stairs, performing household chores, and return to work (RTW)).[31, 31] These convalescence recommendations were then incorporated in a web-based care program. The effect of this intervention care program on duration of sick leave was evaluated rigorously.[32-35]

The objective of the current study was twofold. First, we wanted to use the collected patient data in order to describe the resumption of daily activities, including return to work, following four types of gynecological surgery in patients who were exposed to the expert-based convalescence recommendations. Second, we intended to use this patient data to optimize the expert-based convalescence guideline in pursuance of increasing the evidence on convalescence recommendations.

METHODS

This prospective cohort study was carried out with data collected in two consecutive multicenter trials studying the effectiveness of a multidisciplinary care program aimed at improving recovery and preventing delayed return to work following benign gynecological surgery. Details of the study designs, as well as the results of the efficacy, process evaluation, effectiveness and cost-effectiveness studies have been published previously.[32-37]

Study population

All women aged between 18 and 65 years, employed for at least 8 hours per week (salary employed, self-employed, or voluntary work), and scheduled for a surgery for benign disease in one of the participating ten hospitals were eligible to participate. The types of surgeries that were included were: laparoscopic adnexal surgery (LAS) and/or laparoscopic hysterectomy (LH), vaginal hysterectomy (VH) or abdominal hysterectomy (AH). Patients with severe comorbidity – described as major health problems affecting daily activities or recovery – were excluded, as the intervention was developed for *healthy* patients undergoing *uncomplicated* surgical procedures. Patients were also excluded if they were diagnosed with a malignancy, were pregnant, were computer or Internet illiterate, were involved in a lawsuit against their employer, were on disability sick leave before surgery, or had insufficient command of Dutch.

This study was performed with the participants randomized to the intervention group, because only they received structured convalescence recommendations. Participants that filled in the web-based recovery monitor on the web portal at least twice formed the study population, as they were the participants that provided data on the resumption of their daily activities.

Intervention

The intervention program was comparable in both trials. Patients in the intervention group received access to a patient web portal on which they were encouraged to generate a personalized convalescence plan. This convalescence plan included tailored recommendations for the graded resumption of daily activities based on an algorithm of the expert-based guideline on convalescence recommendations. Figure 1 illustrates an example of a tailored convalescence plan generated at the patient web portal.

Outcomes

The expert-based convalescence guideline included recommended recovery times for 38 activities. For the current study the following ten daily activities were selected: sitting, standing, walking, climbing stairs, bending, lifting, driving, cycling, performing household chores, and performing sport activities. These activities were considered as most common and essential for daily living (supplementary file S1). In addition, they showed a wide variation in physical burden as well. The first six activities consisted of different grades of ability, i.e. different recommended recovery times were given for the partial resumption of that activity. To illustrate, the activities sitting, standing, and walking were graded for different durations (e.g. 15 min, 30 min or more than 60 min). The activities climbing stairs, bending and lifting were graded in number of flights, degrees, and weight, respectively.

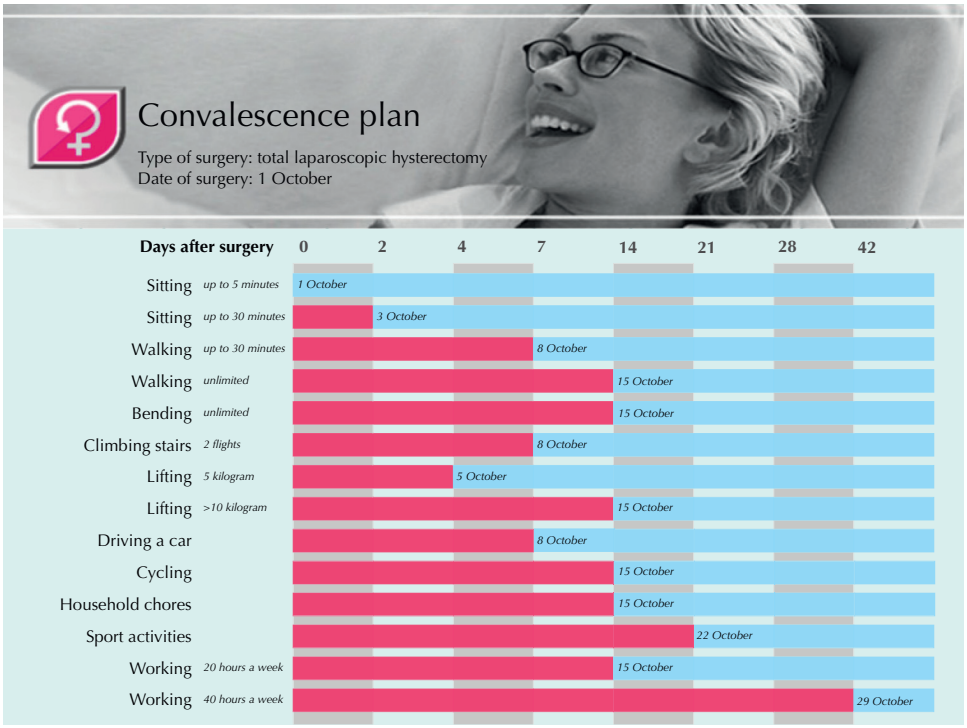

Figure 1. Example of a tailored convalescence plan generated at the patient web portal
In the left column activities are listed that were selected by the patient. The pink boxes present the amount of time the patient is recommended to avoid the specific activity. The blue boxes present the duration after surgery (and the specific date) after which the patient is recommended to resume the specific activity.

Lastly, the outcome time to full sustainable RTW was also included in the current study, defined as the resumption of own work or other work with equal earnings, for at least 4 weeks without (partial or full) recurrence.

Data collection

Socio-demographic data were collected by a baseline questionnaire. A web-based recovery monitor on the patient web portal was used to collect data about the duration until the resumption of daily activities. At 2, 4, 7, 14, 28, 56, and 84 days (=12 weeks) after surgery participants were asked to track the activities that they were able to perform and the activities that were still experiencing problems with (e.g. riding a bike, performing household chores). Graded activities were tracked separately. For example, for the activity lifting, participants were asked whether they were able to lift 5 kg (yes/no), 10 kg (yes/no) and 15 kg (yes/no). Once a certain activity could be performed without problems, this

activity was removed from the recovery monitor. Completion of the recovery monitor was not obligatory, as a result duration of follow-up could vary. Patients were also allowed to complete additional reports between the set time points.

Sick leave data were collected by monthly, self-reported sick leave calendars during the six months after surgery. In addition, duration until RTW was also tracked with the web-based recovery monitor.

Data analysis

Excel 2010 (Microsoft, Washington, DC, USA) was used to transform the weblog into user statistics. SPSS version 22.0 (IBM Corporaton, Amonk, NY, USA) was used for descriptive and statistical analyses.

Due to user authentication (username and password), website activity was logged for each individual participant and it was therefore possible to determine the date at which a recovery monitor was filled in. All data entries were used, except monitors that were filled in retrospectively (later than the next set time point).

To investigate the role of missing data, baseline characteristics and duration until full sustainable RTW were compared between participants that filled in the web-based recovery monitor and the participants that did not, using independent t-test and Pearson's Chi-squared test for continuous and categorical variables respectively. Subgroups were formed by patients that underwent different types of surgery, to analyze the relation between the level of invasiveness of a procedure and the length of recovery.

Time until the resumption of daily activities was determined by calculating the mean between the first time point at which a certain activity could be performed and the last time point at which that activity could not be performed. To illustrate, when a patient reported at 14 days she could not ride a bike and she reported she was able to do this at day 28, the mean recovery time was calculated to be 21 days. For graded activities the resumption of the different gradations was calculated separately in the same manner. Recovery times were truncated to integer numbers. Times until the resumption of normal activities were analyzed by means of descriptive statistics using the median and interquartile range (IQR) for each activity in each procedure. Boxplots were used to present the data graphically.

Duration of sick leave was determined by calculating the time difference between the surgery and the date of full sustainable RTW. Duration of sick leave were depicted graphically for each type of surgery using the Kaplan-Meier method. To analyze differences in RTW between the different surgical types the log rank test was used.

For each activity, the percentage of patients was determined that was able to perform that activity before or at the recommended recovery time. The expert-based convalescence recommendations were considered correct when at least 25% of the population was able to resume an activity before or at the recommended recovery time. The 25th percentile was selected as a cut-off because it was hypothesized that convalescence recommendations should motivate patients to resume their daily activities, yet should not be too challenging resulting in discouragement. In addition, the chosen cut-off also takes into account that there might be some delay between the recommended recovery time and the actual resumption of a certain activity under real life circumstances. To illustrate, we hypothesized that when less than 25% of the participants were able to perform an activity before or at the recommended recovery time, the expert-bases convalescence advise was too strenuous. Similarly, when more than 50% of the participants were able to perform an activity before the recommended recovery time, the expert-based convalescence recommendation was considered as too tolerant.

Patient data were then used to revise the convalescence guideline in case recommended recovery times were too strenuous or too tolerant. This process included two steps. First, the recovery time at the 25th percentile was calculated per (graded) activity for each type of surgery. As the expert panel formulating the original guideline used a fixed schedule of time points (1 – 2 – 4 – 7 – 10 – 14 – 21 – 28 – 42 days following surgery) we used the same mutation moments for the revision of the guidelines. In other words, when the 25th percentile was calculated at 4 days, the revised recommended recovery time would be 4 days. However, when the 25th percentile was calculated at 5 days, the revised recommended recovery time would become 7 days. During the second step, the revised guidelines were compared between the different surgery types. When actual recovery times for the same activity in a more invasive surgery group exceeded the revised recommended recovery times, the revision was undone.

RESULTS

The first randomized study ran from March 2010 until September 2011 and of the 215 patients, 110 patients were allocated to the intervention group. The second trial ran from October 2011 until July 2014 and of the 433 patients, 227 patients were included in the intervention group. Thus, in total 337 patients were exposed to the expert-based convalescence recommendations and were eligible for data analysis for this current study. In total, 304 of these 337 patients (90.2%) completed the recovery monitor at least twice and they formed the study population of this study (Supplementary file S2).

For the resumption of daily activities, the median length of follow-up was 12 weeks (IQR: 6–12 weeks) and on average, participants filled in the recovery monitor seven times (IQR: 4–8). The median number of days between two data registrations was 9 (IQR: 7–12). Length of follow-up for the outcome RTW was 182 days. Table 1 presents the baseline characteristics of the study population. The majority of patients were in their forties, were intermediate or highly educated and were salary-employed. Baseline characteristics did not differ between participants undergoing different types of surgery nor between participants that filled in the web-based recovery monitors and those that did not.

Return to normal activities

The percentage of patients that were able to perform the daily activities before or at the time of the recommended recovery time varied between 4 and 78% depending on the activity as well as the type of surgery (Table 2). The recommendations for VH fitted reality the best (13 correct recommendations and only one too strenuous) followed by the recommendations for AH (ten correct and two too strenuous). The recommendations for LAS were too strenuous for half of the activities.

The activities standing (15 min), walking (15 min) and climbing stairs were performed by more than 50% of the participant across all surgical types before or at the recommended time. The recommended recovery times for the activities sitting, lifting and cycling were determined correctly for the surgery types VH and AH, however, they were too strenuous for patients undergoing LAS and LH. Across all surgical types, participants resumed driving much later than recommended.

Figure 2 shows the difference between actual and recommended recovery times to the (partial) resumption of several daily activities following LH. It also demonstrates how the guideline was revised for the activities for which the recommended recovery times were too strenuous or too tolerant.

Figure 3 shows the actual and recommended recovery times for the graded activity walking across the four types of surgeries. Conform the recommended recovery times formulated by the expert panel, recovery times became longer with each gradation, as well as with higher levels of invasiveness of the surgical procedure. Notably, accuracy decreased with longer recovery times, demonstrated by the increasing interquartile ranges.

Table 1. Baseline characteristics

Category	Total n=304
Patient characteristics	
Age (years ± SD)	45.3 ± 7.5
Dutch nationality	292 (96.1%)
Education level [a]	
Low	33 (10.9%)
Intermediate	124 (40.8%)
High	147 (48.4%)
Smoking status	
None-smoker	176 (57.9%)
Former-smoker	66 (21.7%)
Current-smoker	62 (20.4%)
Surgery-related characteristics	
Type of surgery	
Laparoscopic adnexal surgery	109 (35.9%)
Laparoscopic hysterectomy	79 (26.0%)
Vaginal hysterectomy	58 (19.1%)
Abdominal hysterectomy	58 (19.1%)
Health-related characteristics	
Perceived health status (median (IQR))	80.0 (70.0 – 90.0)
Under treatment by another specialist	130 (42.8%)
History of previous abdominal surgery	110 (36.2%)
Work-related characteristics	
Type of work	
Salary employed	256 (84.2%)
Self-employed	42 (13.8%)
Voluntary work	6 (2.0%)
Work hours per week (mean ± SD)	29.9 ± 9.4
Sick leave prior to surgery [b]	108 (35.5%
RTW expectation (long) [c]	50 (16,4%)
RTW intention (low) [d]	66 (21.7%)

Data present the number of patients (%), unless otherwise indicated.
[a] Low=preschool, primary school; intermediate=secondary school; high=tertiary school, university, or postgraduate.
[b] Defined as at least 1 day of absence.
[c] Defined as expectation longer than 3 weeks for adnexal surgery, longer than 6 weeks for laparoscopic or vaginal hysterectomy, or longer than 8 weeks for abdominal hysterectomy.
[d] Higher score indicate a higher intention to return to work despite physical symptoms (range 1 – 5). A low intention was defined as score 1 or 2.
SD = standard deviation, RTW = return to work

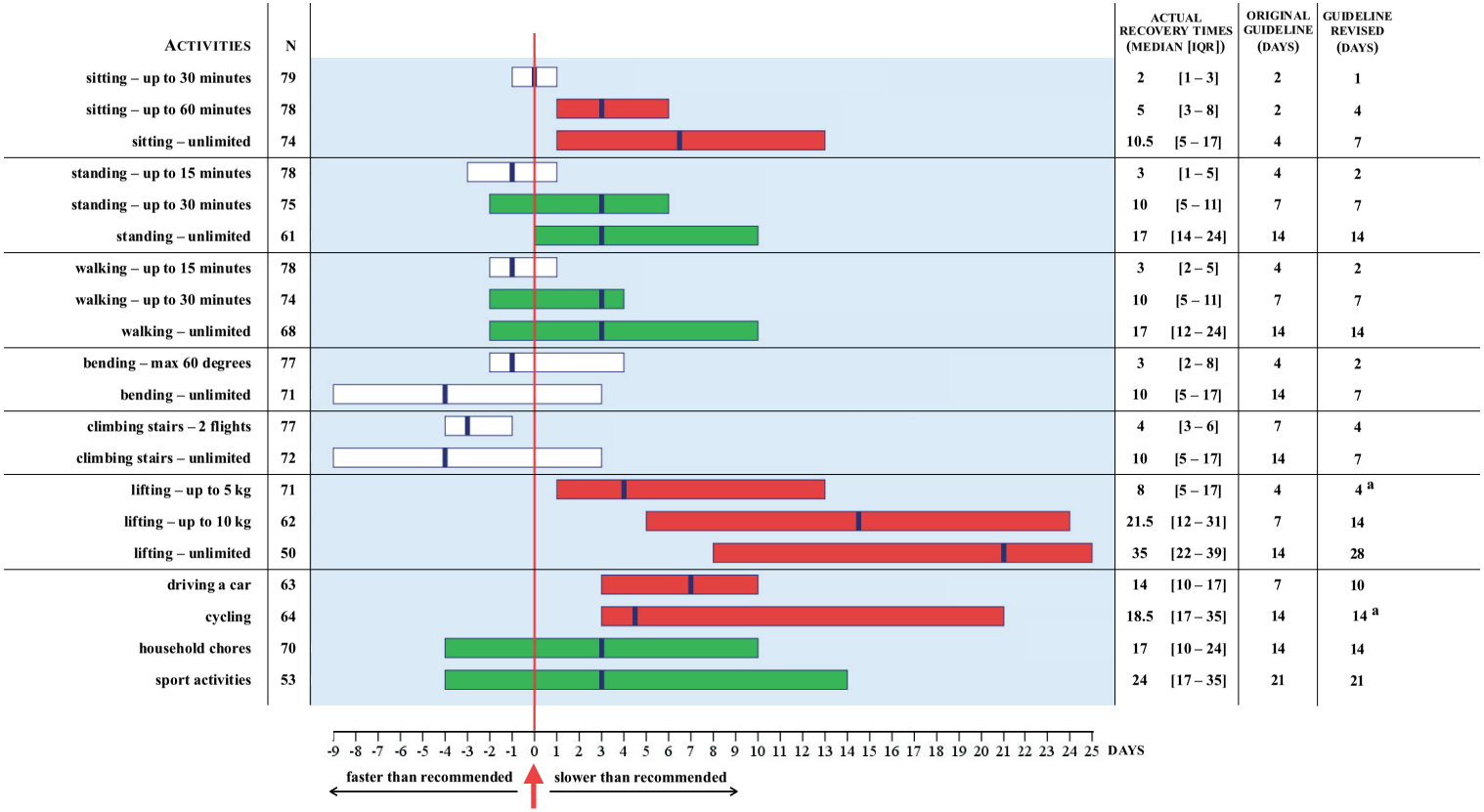

Figure 2. Differences between actual and recommended recovery times after laparoscopic hysterectomy.

The vertical red line presents the convalescence guideline. The boxplots present the 25th percentile, median (thick vertical line) and 75th percentile of the differences between actual recovery times and the recommended recovery times. White boxes present activities that were being performed by more than 50% of the patients before or at the recommended recovery time. Green boxes present activities that were being performed by 25% to 50% of the patients faster than the recommended recovery times. Red boxed present activities that were being performed by less than 25% of the patients faster than the recommended recovery times.

[a] guidelines were not revised due to algorithm taking other surgical types into account (lifting 5 kg, cycling).

N = number of patients that provided data on the activity, IQR = interquartile range

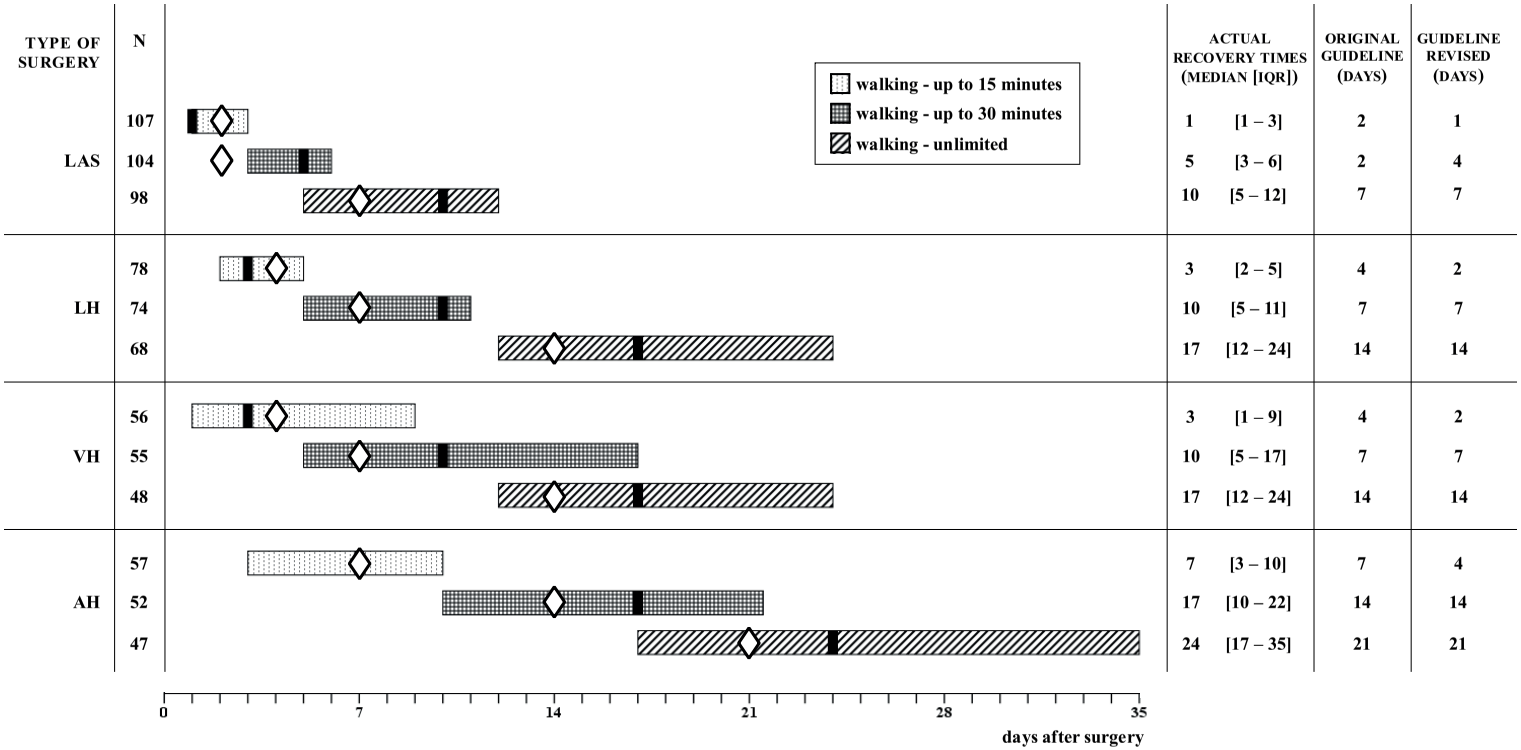

Figure 3. Actual and recommended recovery times for the activity walking per type of surgery.

The boxplots present the 25th percentile, median (thick vertical line) and 75th percentile of the actual recovery times. The diamonds represent the recommended recovery times. LAS = laparoscopic adnexal surgery, LH = laparoscopic hysterectomy, VH = vaginal hysterectomy, AH = abdominal hysterectomy

Table 2. Percentages of patients recovering slower, equal, or faster than recommended

Activity	Gradation	LAS	LH	VH	AH
sitting *continuously*	up to 30 minutes	27	58	48	45
	up to 60 minutes	23	17	35	48
	unlimited	14	18	37	50
standing *continuously*	up to 15 minutes	64	68	57	50
	up to 30 minutes	11	33	37	54
	unlimited	43	26	28	32
walking *continuously*	up to 15 minutes	71	68	54	53
	up to 30 minutes	14	37	38	42
	unlimited	43	34	38	36
bending	no further than 60°	53	58	47	35
	unlimited	30	65	64	74
climbing stairs	2 flights	74	78	68	75
	unlimited	74	72	63	72
lifting / carrying	up to 5 kilograms	21	24	53	31
	up to 10 kilograms	13	3	29	20
	unlimited	14	6	29	32
driving a car		6	14	22	13
cycling		4	23	29	33
household chores		41	37	41	46
sport activities		28	32	36	59

Numbers present the percentages of patients that recovered at the speed of the convalescence guideline (defined as actual recovery time before or equal to recommended recovery time).

Green boxes represent activities that were being performed by 25% to 50% of the patients before or at the recommended time. Recommended recovery time considered to be correct.

Red boxes represent activities that were being performed by less than 25% of the patients before or at the recommended time. Recommended recovery time considered to be too strenuous.

White boxes represent activities that were being performed by more than 50% of the patients before or at the recommended time. Recommended recovery time considered to be too tolerant.

LAS = laparoscopic adnexal surgery, LH laparoscopic hysterectomy, VH = vaginal hysterectomy, AH = abdominal hysterectomy

Return to work

Median times to RTW were 21 days for LAS (95% CI: 17.7–24.3), 56 days for LH (95% CI: 47.4–64.7), 55 days for VH (95% CI: 46.8–63.2), and 68 days for AH (95% CI: 62.1–73.9). Thirteen patients were censored at 182 days because they were still on sick leave. Duration until full sustainable RTW following the four surgical types differed significantly (log rank test: $P < 0.000$) (figure 4).

Actual times to RTW were longer than the recommended times for most of the gradations in the work categories (Table 3). Recommended recovery times for the least invasive surgery group (LAS) and the most invasive group (AH) were closer to the actual recovery times than the recommended recovery times for the intermediate invasive surgery group (LH and VH). There was no difference in duration until RTW between the patients included in this study and those that were excluded because they did not complete the web-based recovery monitor at least twice.

Table 3. Actual recovery times for the (graded) resumption of work

	20 hours per week		30 hours per week		40 hours per week	
Type of surgery (N)	**n**	**Median (IQR)**	**n**	**Median (IQR)**	**n**	**Median (IQR)**
LAS (109)	87	8 (5 – 15)	77	16 (9 – 24)	61	18 (12 – 33)
LH (79)	62	27 (14 – 35)	45	35 (19.5 – 49)	32	39 (24 – 51.3)
VH (58)	37	35 (23.5 – 46)	30	38 (35 – 49)	20	49 (39.8 – 52)
AH (58)	40	35 (24 – 49)	30	40 (32.3 – 60.8)	24	50 (35 – 60.5)

Data present the median number of days after surgery at which the activity could be performed.
N = number of patients per surgery group, n = number of patients that provided data on the activity, IQR = interquartile range

Complicated surgeries

In total, 19 patients experienced a complication, defined as a significant larger surgery than planned or a repeat surgery related to the initial surgery: 5 patients in the LAS group (4.6%), 3 patients in the LH group (3.8%), 3 patients in the VH group (5.2%), and 8 patients in the AH group (13.8%). To investigate if this group influenced the recovery rates, we repeated the analyses excluding those patients with a complicated procedure. Surprisingly, this did not lead to significantly better recovery rates. Instead, for some activities the recovery rates became poorer, indicating that a complicated procedure does not necessarily means prolonged recovery.

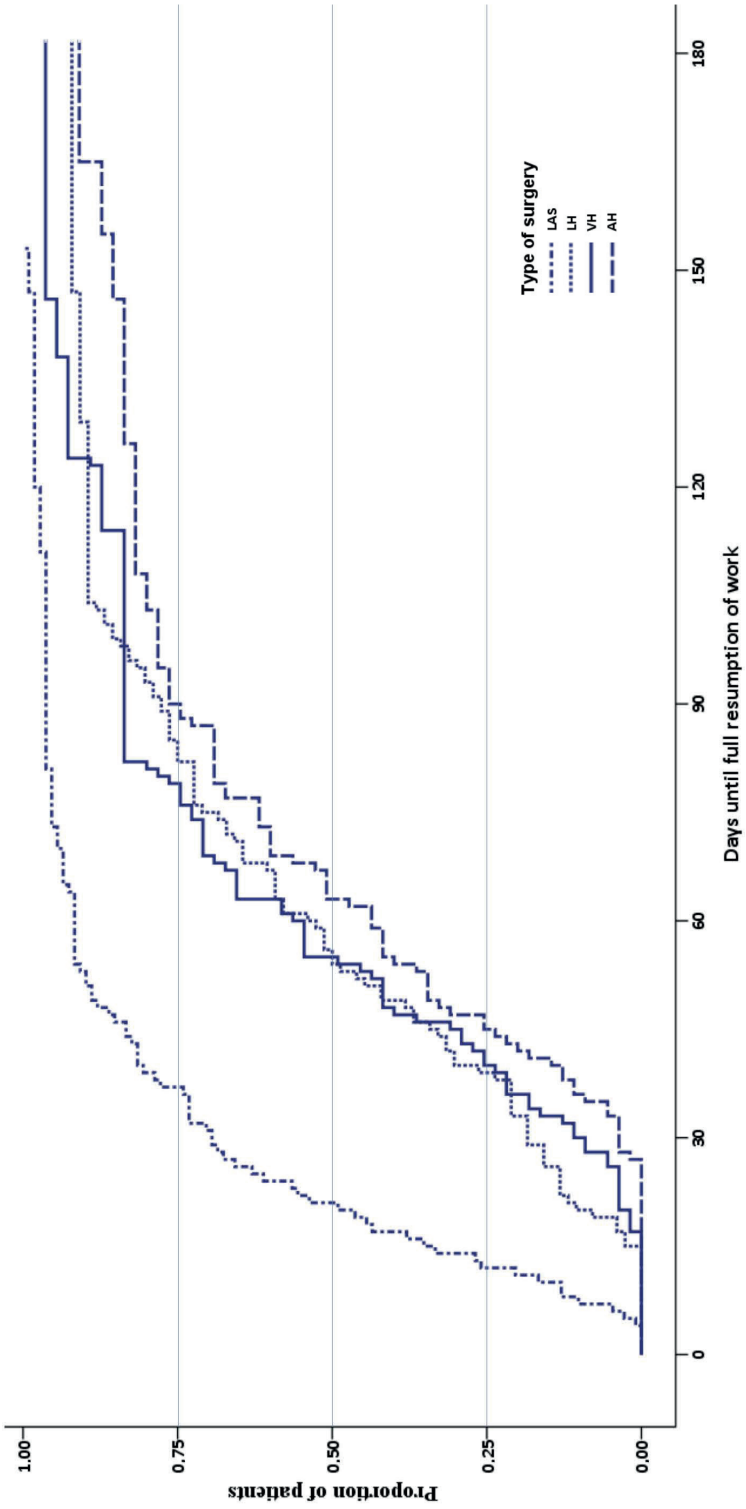

Figure 4. Kaplan-Meier survival curves for time to full sustainable RTW, presented per type of surgery.
Number of days represent days of sick leave after surgery until RTW.
RTW = return to work, LAS = laparoscopic adnexal surgery, LH = laparoscopic hysterectomy, VH = vaginal hysterectomy, AH = abdominal hysterectomy

DISCUSSION

Main findings

In this study we used prospectively collected data about the time until the resumption of ten daily activities as well as the duration until full sustainable work following four types of gynecological surgeries in order to describe median recovery times. In addition, the collected patient data enabled us to optimize an earlier developed expert-based guideline on convalescence recommendations following gynecological surgery for benign disease, and revise recommended recovery times if they turned out to be too strenuous or too tolerant. For the majority of activities actual recovery times exceeded the recovery time recommended by the expert panel. Yet, recovery times lengthened with increasing levels of physical burden of the daily activities as well as with increasing levels of invasiveness of the procedures, conform the algorithm of the expert-based convalescence guideline. The convalescence guideline seemed more accurate for patients undergoing more complex surgery than patients undergoing minimal invasive surgeries, as the recommendations in the latter group were often too strenuous.

Data interpretation

Several survey studies conducted in the last two decades inventorying convalescence recommendations following gynecological procedures demonstrated that there is substantial variation in convalescence advice given by health care providers and emphasized the need for unified convalescence guidelines.[11, 12, 16, 24, 38, 39] However, we are not aware of research similar to our own, in which both input from experts as well as input from patients were used to generate convalescence recommendations. The ultimate goal of our research is to develop a set of general convalescence recommendations that is applicable to the majority of patients undergoing several types of gynecological surgery.

The current study can be used as an example to build the evidence base for convalescence recommendations in the surgical field. Mainly, there are three reasons why this should be on top of the agenda of policy makers. First of all, the availability of evidence-based guidelines will facilitate care providers to provide their patients with more specified and tailored advice.[14] Secondly, it has been previously demonstrated that standardized convalescence recommendations can expedite recovery.[33, 34, 40-43] Thirdly, a more standardized post-operative trajectory would also allow the identification of patients who deviate from the norm and prompt the possibility of intervention.[20, 25]

In our study, we observed a wide variation in the duration until the resumption of daily activities within groups of patients undergoing the same surgical procedure. In a *post-hoc* analysis we investigated a number of potential determining factors for delayed recovery.

The results were not straightforward, and therefore, difficult to interpret. For example, for several activities, we found a significant association between the level of education and the length of recovery (lower education leading to longer recovery). Possibly, education is a proxy for the type of work a patient is performing (sedentary work versus manual labor), however, with the available data we were not able to investigate this relationship any further. The age of the patient did not seem to be an independent factor for delayed recovery. Understanding these mechanisms in the future, would probably help to identify those patients that need more guidance or monitoring during their recovery.

Strengths and limitations

Several strengths of the present study are notable. First of all, data about the resumption of daily activities was collected prospectively, reducing the risk of recall bias. Secondly, we used a relative long follow-up period (12 weeks for daily activities and 26 weeks for RTW) and from a medical point of view it generally may be assumed that the daily activities should have been resumed within this time period. In our study, the vast majority of patients achieved full RTW within 26 weeks (96.1%). In addition, we focused on both the resumption of daily activities as well as RTW. The selected daily activities had a wide variation of physical burden and RTW was considered as the most demanding activity, as it generally requires performing a whole set of single activities. Therefore, RTW is an outcome that is frequently used to define the end of the surgical recovery process.[44] Another strength of the current study is that advice given to patients was standardized as patients were provided with tailored convalescence recommendations based on the expert-based guideline. In this way, other factors that might influence recovery, such as patient expectations and contradictive advise, were reduced.[10, 45]

Our study also has limitations. Regarding methodology, bias may have been introduced because the web-based recovery monitor was not obligatory to complete. This could have led to both over- and underestimations of recovery times, as patients who did not use the web-based recovery monitor could have been the fast recoverees (no need to use the web portal anymore), or the slow recoverees (discouraged by the web portal, and therefore avoiding it). As sick leave duration did not differ significantly between patients who did and who did not use the recovery monitor, we expect the effect of this type of selection bias to be minimal in our study.

Secondly, we collected recovery data by asking patients to track the activities they were able to perform at given set time points prospectively, instead of asking the exact date at which the participant resumed that particular activity. Therefore, we were obliged to estimate at what moment the mutation took place, which we did by calculating the mean between the first time point at which a certain activity could be performed and the last

time point at which that activity could not be performed. As the length between set time points increased (the frequency of data-collection decreased), the estimates became less accurate, demonstrated by the wide IQRs for the activities with relatively high physical burden. Unfortunately, this phenomenon of decreasing accuracy with time was amplified, due to increasing numbers of patients lost to follow-up with time.

Practical and research implications

As stated before, future research should focus on identifying predictors of recovery. Moreover, the relationship between recommended and actual recovery times should be investigated, especially focusing on the question if there is a turning point at which too strenuous recommendations can become preposterous and will lead to delayed recovery. In addition, it should be examined which factors (emotional or physical) determine if a patient will comply to convalescence recommendations given. Future challenges will also involve the dissemination, adaptation and implementation of the convalescence guidelines in daily practice. It should be noted that recovery outcomes may be different across populations due to differences at the level of the health care systems as well as cultural diversity, making external generalization of our guideline uncertain.[44]

Ultimately, convalescence advice should be tailored to the individual patient, also taking into account other patient characteristics such as age and the presence of any co-morbidity, as well as environmental factors such as specific job demands. Hypothesizing, when detailed recovery data were to be centrally registered, advanced data methods (i.e. big data) could be applied to predict personal recovery and generate custom-made convalescence recommendations for surgical patients on a wider scale.[46] In this perspective, smart wearables can be useful for monitoring postoperative physical activity as a proxy of recovery, and simultaneously providing the input for such predictive models.[47-50]

CONCLUSIONS

We described recovery times of various daily activities including work, following four types of gynecological surgeries. Collected patient data were used to revise a previously developed expert-based guideline on convalescence recommendations. This study should be considered as an important step towards the development of evidence-based convalescence advice, leading to the optimization of perioperative gynecological care. Future research should focus on the adaptation of these convalescence recommendations and its implementation into routine surgical care.

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Supplementary file S1.Overview of activities included in the developed convalescence guideline

Dichotomous activities [a]	Graded activities (unit) [b]
Personal functioning	
memory	concentration (duration)
insight	dividing attention (duration)
action tempo	
Static and dynamic movements	
reaching	**continuous sitting (duration)**
handling above shoulder height	total sitting (duration per day)
handling heavy objects	**continuous standing (duration)**
kneeling / squatting	total standing (duration per day)
continuous kneeling / squatting	**continuous walking (duration)**
twisting upper body	total walking (duration per day)
continuous bending / twisting	**bending (angles)**
	bending frequently (duration)
	reaching frequently (duration)
	lifting / carrying (weight)
	pushing / pulling (weight)
	handling light objects (duration)
	climbing stairs (number of flights)
	climbing a ladder (height)
Working	
	hours per day (duration)
	hours per week (duration)
	performing shift work (day, evening, night)
Other activities	
household chores [c]	
sport activities [d]	
bathing	
sexual intercourse	
cycling	
driving	
commuting	

Bold activities were selected for the current paper.

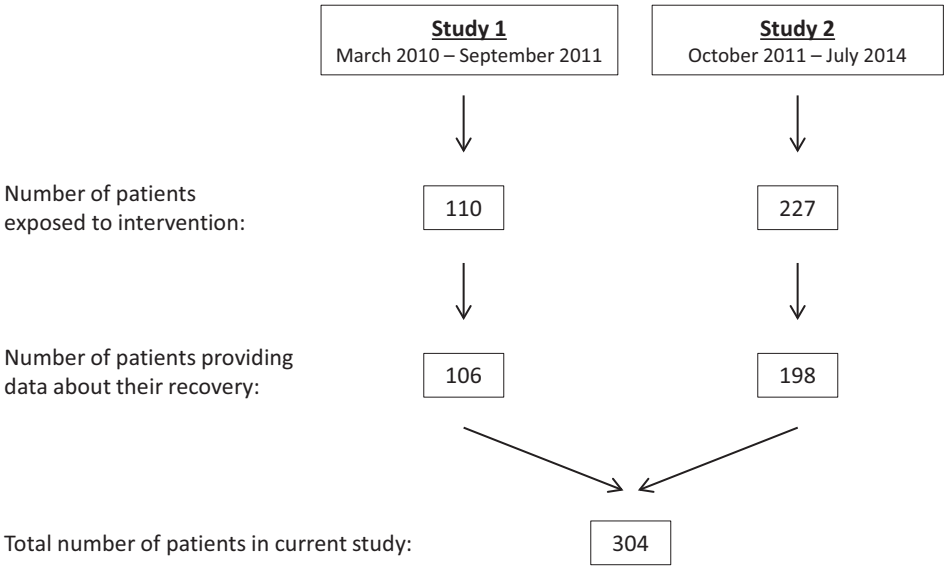
[a] Dichotomous categories have two options: able to perform versus not able to perform (or impaired).

[b] Graded activities are divided in different gradations using different units (e.g. the activity 'lifting' is divided into: up to 5, up to 10, and up to 15 kilograms and the activity "continuous waking" is divided into: up to 15, up to 30, and more than 30 minutes.)

[c] Any activity comparable to vacuum cleaning.

[d] Any activity comparable to jumping.

Supplementary file S2. Organization of the cohort



CHAPTER 7

Using e-health in perioperative care: a survey study investigating shortcomings in current perioperative care and possible future solutions

Using e-health in perioperative care: a survey study investigating shortcomings in current perioperative care and possible future solutions

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ABSTRACT

Background An eHealth care program has previously shown to have a positive effect on return to work, quality of life and pain in patients who underwent gynaecological surgery. Plausibly, providing the care program to a population undergoing other types of surgery will be beneficial as well. The objectives of this study are to evaluate patients' opinions, needs and preferences regarding the information and guidance supplied to patients during the perioperative period, to investigate whether eHealth may be of assistance and to explore if gender specific needs exist.

Methods A questionnaire was sent to all patients between 18 and 75 years (n = 362), who underwent various forms of abdominal surgery between August 2013 to September 2014 in a university hospital in the Netherlands. The questionnaire contained questions about the current situation in perioperative care and questions about patients' preferences in an eHealth care program. Gender differences were evaluated.

Results Two hundred seven participants (57.2%) completed the survey. The majority of the participants were relatively satisfied with the perioperative care they received (68.6%). Most reported shortcomings in perioperative care concerning the supply of information regarding the resumption of activities and guidance during the recovery course. An eHealth care program was expected to be of added value in perioperative care by 78% of the participants; a website was reported as most useful. In particular practical functions on a website focusing on the preparation to surgery and monitoring after surgery were appraised to be highly valuable. Overall, women had slightly more needs for extra information and support during the perioperative course than men.

Conclusions In abdominal surgery, there is a need for an eHealth care program, which should focus mainly on the supply of information about the resumption of activities as well as guidance in the postoperative course.

BACKGROUND

Postoperative recovery often takes much longer than the period considered appropriate by specialists.[1–5] An important predictor for the length of recovery is the level of invasiveness of the surgical procedure. In addition, patient expectations about their recovery influence the length of recovery considerably.[2,5,6] For this reason, a perioperative eHealth intervention focusing on the supply of information with respect to the recovery period after gynecological surgery, was developed in 2011 by a qualitative study using an intervention mapping protocol.[7] Intervention mapping is a systematic description of a logical planning process in several steps, starting with a needs assessment and ending with an evaluation of the developed intervention.[8] The ehealth intervention which was developed included an interactive website containing tailored, structured and detailed instructions concerning the resumption of activities after surgery. The effectivity of this intervention was evaluated by a randomized controlled trial; patients who received the eHealth intervention in addition to usual perioperative care returned to work nine days earlier compared to the patients who received usual perioperative care only.[9] The care program also had a positive influence on quality of life and perception of pain after 26 weeks.

Plausibly, providing the care program to a population undergoing other types of surgery will be beneficial as well. However, it should be investigated whether the intervention should be adjusted to a new patient population. In addition, the care program was developed five years ago and patients' needs and preferences nowadays may have changed. Moreover, the eHealth intervention was originally developed for female patients undergoing gynecological surgery. It has already been proven that, besides disease specific and biochemical differences, women and men differ on various aspects according to their needs and health care use, requiring additional research on this topic taking gender differences into account.[10–16]

In conclusion, patients' views on perioperative care and their preferences regarding eHealth need to be investigated across a broader population, before the earlier developed eHealth intervention for gynaecological patients can be offered to all patients undergoing abdominal surgery. Therefor a survey questionnaire was developed for patients who underwent various forms of abdominal surgery. With this study we aim 1) to evaluate shortcomings in the information and guidance supplied to patients in current perioperative care, and 2) to investigate whether eHealth may be of assistance in this, and finally 3) if gender specific needs exist.

METHODS

Study design

A survey questionnaire study was conducted in accordance with the STROBE statement.[17] The medical ethics committee of the VU medical center approved the protocol in 2014 (registration number 2014.378).

Development of the questionnaire

A questionnaire was developed for this study and was based on the results of a qualitative study which was performed in 2011 to develop the eHealth intervention for patients undergoing gynecological surgery.[7] In this study an intervention mapping protocol was used, including a literature search, focus group discussions with patients and questionnaires for patients, medical doctors and eHealth specialists. The questionnaire of the present study consisted of two parts. First, gaps in current perioperative care were evaluated and patients' needs and preferences were investigated. Topics included patients' mental health state before and after surgery, the information patients received before and after surgery and the guidance and monitoring provided to them during the recovery process. The questions were based on the outcomes of the needs assessment part of the intervention mapping protocol. The second part of the questionnaire consisted of questions about patients' needs regarding various forms of eHealth in perioperative care. These questions were based on the outcomes of the part of the intervention mapping protocol called "the program plan; design of the intervention". In addition, some questions were added based on the comments of patients who had used the earlier developed eHealth intervention in a randomized controlled trial and on additional literature findings.[9,18–21]

Study population

All patients between 18 and 70 years old who underwent a cholecystectomy, inguinal hernia surgery, appendectomy, colectomy, a hysterectomy or adnexal surgery (all laparoscopic or open), between august 2013 and august 2014 in the VU University Medical Center in Amsterdam, the Netherlands, received an invitation to complete the questionnaire. The surgical procedures were selected as these are the most commonly performed general abdominal surgical and gynecological procedures (apart from Caesarean Section) in the Netherlands.[22, 23]

Data collection

In October 2014, the potential participants received an envelope containing information about the study, the questionnaire and a return envelope. In case patients did not wish to participate they could indicate this by returning a return slip. When the researchers had not received the return slip or the completed questionnaire after 3 or 6 weeks respectively,

the participant received a reminder. Questions with five answering options (for example: really useful, useful, neutral, not useful, not useful at all) were recoded to three answering options, by combining 'really useful and useful' and 'not useful and not useful at all', to give a clearer overview of the results. Baseline characteristics such as the American Society of Anesthesiologists (ASA) classification, Body Mass Index (BMI), indication for surgery and complications during or after surgery, were collected by screening the medical records of the participants. The level of invasiveness of the surgical procedure was defined as 'minor surgery' or 'other'. Procedures which were defined as minor surgery were laparoscopic cholecystectomy, hernia inguinal surgery (open and laparoscopic), laparoscopic appendectomy or laparoscopic adnexal surgery. This was based on the fact that these types of procedures are related to more or less the same convalescence recommendations after surgery.[24, 25] The remaining procedures were defined as 'other' because it was not possible to categorize them into groups because of their heterogeneity according to of invasiveness.

Statistical analyses

All statistical analyses were carried out using SPSS version 20.0. Descriptive statistics were used to present the baseline characteristics and responses of the participants. We used cross-tabulations, Chi2-tests and t-tests to compare baseline characteristics between responders and nonresponders. Responses were compared according to gender, only in the group of patients who underwent a general surgical procedure with a minor level of invasiveness (laparoscopic cholecystectomy, laparoscopic or open hernia inguinal surgery, laparoscopic appendectomy). Reason for this was to develop the maximum homogeneous group, to limit the effect of potential confounding factors.

RESULTS

Response

A total of 362 potential participants were identified and received an invitation to participate. The questionnaire was completed by 207 participants (57.2%). Of 6 potential participants, we were sure that we did not reach them, because the questionnaires were returned to us with the notification that the potential participant had moved. Seventeen potential participants indicated that they were not willing to participate by sending back the return slip and four potential participants were excluded because of a language barrier or cognitive impairment. We performed a comparison of the participants and non-participants regarding some important baseline characteristics (Table 1). This analysis only showed significant differences between responders and nonresponders according to age (participants were older than non-participants) and type of surgery (patients who underwent a gynecological procedure were more likely to respond than patients who underwent general surgical

procedures). There were no statistically or clinically relevant differences in the health-related characteristics which we analyzed. Median time between surgery and the moment of sending the questionnaire to the participants was 38 weeks (range 5–62 weeks).

Table 1. Comparison of participants and non-participants

Variable	Participants n=207		Non-participants n=155		P-value
Gender					0.50
Male	56	(27.1)	47	(30.2)	
Female	151	(72.9)	108	(69.7)	
Age (mean ±SD)	46.59	±13.39	39.57	±12.52	**0.00**
SES (mean ±SD)	0.64	±1.05	0.64	±1.18	0.53
BMI [a] (mean ±SD)	27.43	±15.12	27.78	±18.12	0.89
ASA classification					0.53
ASA 1	80	(46.8)	58	(53.7)	
ASA 2	82	(48.0)	39	(36.1)	
ASA 3	7	(4.1)	10	(9.3)	
ASA 4	2	(1.2)	1	(0.9)	
Intoxications [b]					0.26
Yes	105	(54.1)	64	(47.8)	
No	89	(45.9)	70	(52.2)	
Type of surgery					**0.01**
Gynecological	107	(51.7)	60	(38.7)	
Surgical	100	(48.3)	95	(61.3)	
Major complications during or after surgery [c]					0.94
Yes	9	(4.3)	7	(4.5)	
No	198	(95.7)	148	(95.5)	

Data present the number of patients (%), unless otherwise indicated.
[a] Data available for 200 participants and 140 non-participants.
[b] Defined as any current use of alcohol, tobacco and/or drugs. Data available for 194 participants and 128 non-participants.
[c] Defined as conversion to an open procedure, re-surgery within 30 days, injury of the bladder, intestine or liver during surgery, or drainage of an abscess after surgery.
SD = standard deviation, SES = Social Economic Status Scores (based on geographic location), BMI = Body Mass Index, ASA = American Society of Anesthesiologists classification

Baseline characteristics

Table 2 presents the baseline characteristics of the participants who completed the questionnaire. Most participants were female (n = 151, 72.9%) and the indication for surgery was in the majority of the participants benign (n = 181, 87.4%). Mean age was 46.6 years. Of the participants, 95.1% used the Internet on a daily base. The subgroup of participants which was used to compare the results of men and women with each other (i.e. who underwent a general surgical procedure with a minor level of invasiveness), consisted of 71 participants (male n = 42, female n = 29). Men underwent laparoscopic hernia inguinal surgery more often in comparison to women (n = 15, 35% vs n = 2, 6.9%) and women underwent a laparoscopic cholecystectomy more often compared with men (n = 19, 65.5% vs n = 12, 26.6%). In addition, age differed remarkably between men and women in this subgroup (52.67 (SD 13.8) vs 41.66 (SD 13.9)) which is possibly due to the difference in surgical procedures. No other clinically differences were found within this subgroup.

Patients' views on the information and guidance received during perioperative care

Before surgery

Mental health state

About one third of the participants (32.9% (68/207)) answered that they felt nervous before surgery. Compared to men, women were more likely to feel nervous (37.2% (11/29) vs 11.9% (5/42)) (figure 1).

Information supply

The majority of the participants (83.6%, 163/195) received information about the resumption of activities after surgery. The majority felt the information provided was sufficient, however, 26.3% (54/205) patients reported that they would have preferred to receive more information. This percentage was slightly higher in women compared to men (34.5% (10/29) vs 19.0% (8/42)). More than half of the participants (57.5% (115/200)) searched on the Internet for more information about the surgical procedure and recovery process.

Preparations with regard to return to work

Of the employed participants, 23.4% (32/137) reported that they made a plan regarding return to work (re-integration plan). Seventeen of them did this together with their employer and 15 did this on their own. In the subgroup of participants who underwent minor general surgical procedures, the creation of a re-integration plan was less common (0/20 of female participants and 4/24 male participants). All participants who made a reintegration plan except one, reported this to be useful and would do it again.

Table 2. Baseline characteristics

Variable	Total n=207	
Gender		
Male	56	(27.1)
Female	51	(72.9)
Age (mean ±SD)	46.6	±13.4
Nationality		
Dutch	190	(91.8)
Other	17	(8.2)
Level of education		
Low	25	(12.1)
Medium	66	(31.9)
High	116	(56.0)
Employment status		
Employed	142	(68.6)
Non-employed	65	(31.4)
Internet use [a]		
Daily or more times a week	193	(95.1)
Seldom or never	10	(4.9)
Source of Internet use [b]		
Computer/laptop	25	(13.0)
Smartphone/tablet	38	(19.7)
Both	130	(67.4)
BMI [c] (mean ±SD)	26.4	±5.6
ASA classification [d]		
ASA 1	80	(46.8)
ASA 2	82	(48.0)
ASA 3	7	(3.4)
ASA 4	2	(1.2)
Type of surgery		
Gynecological	107	(51.7)
Surgical	100	(48.3)
Indication for surgery		
Malignancy	26	(12.6)
Benign	181	(87.4)
Type of surgery		
Minor [e]	132	(63.8)
Adnexal surgery (LS)	61	
Cholecystectomy (LS)	31	
Hernia inguinal surgery (LS)	17	
Hernia inguinal surgery (O)	3	
Appendectomy (LS)	20	
Other	75	(36.2)
Adnexal surgery (O)	5	
Cholecystectomy (O)	4	
Appendectomy (O)	6	
Colectomy (LS)	9	
Colectomy (O)	10	
Uterus extirpation (LS)	36	
Uterus extirpation (O)	5	
Major complications during or after surgery [f]	9	(4.3)

Data present the number of patients (%), unless otherwise indicated.
[a] Data available for 203 patients.
[b] Data available for 193 patients.
[c] Data available for 200 patients.
[d] Data available for 171 patients.
[e] This subdivision is based on a classification which has been used previously in gynaecologic surgery.[32,33] The general surgical procedures were classified in line with this classification, based on the length of convalescence recommendations for resumption of activities after these general surgical and gynaecological procedures. These convalescence recommendations were developed in a Delphi study.[21,34]
[f] Defined as conversion to an open procedure, re-surgery within 30 days, injury of the bladder, intestine or liver during surgery, or drainage of an abscess after surgery.
SD = standard deviation, BMI = Body Mass Index, ASA = American Society of Anesthesiologists classification, LS = laparoscopic procedure, O = Open procedure

After surgery

Overall, 68.6% (142/203) of the participants reported that they were satisfied with their recovery period.

Mental health state

About one third of the participants (68/199) felt insecure during their recovery process. Women felt insecure more often than men (37.9% (11/29) vs 17.5% (7/40)). Thirty-four patients (16.7%) reported that they would have preferred more emotional or mental support after their surgical procedure. Women had a higher need for this than men (20.7% (6/29) vs 7.5% (3/40)).

Information supply

Confusion about the resumption of daily activities existed in about 35% of the patients (133/205). Recommendations regarding the resumption of activities provided by medical specialists, general practitioners (GP) and occupational physicians (OP), were reported to be inconsistent by 57% of the responders. The majority of patients (79.2%; 164/204) reported that they knew who they had to contact in case of physical complaints or questions. Seventy-six patients reported that they still had questions after discharge. The majority of these patients (76.3%; 58/76) did ask those questions, however only 59.6% (35/58) were satisfied after this contact.

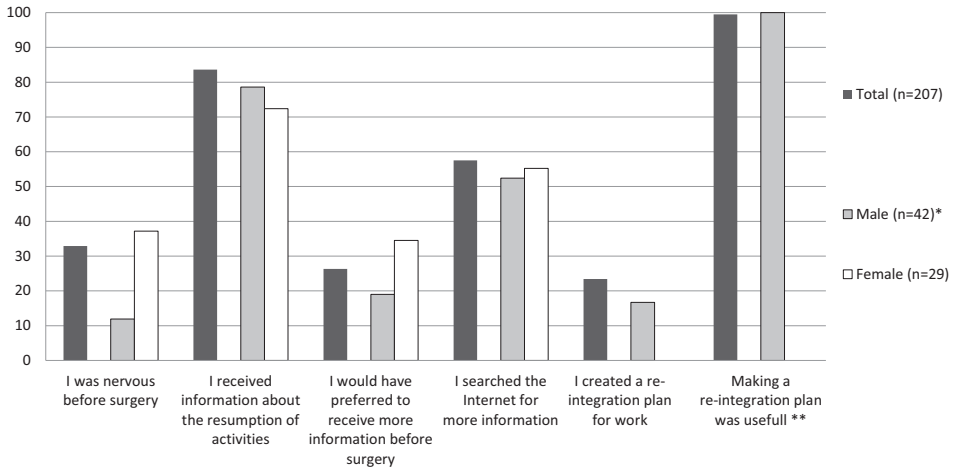
Interaction with occupational physician (OP)

Of the employed participants, 27.0% (38/141) had at least one contact with their OP before or after surgery. Only 39.5% (15/38), designated this contact as useful.

Guidance during the recovery process

Of all participants, 39.0% (78/200) reported that they would have liked to receive more assistance by a health care professional during their recovery process. The mean time between surgery and the appointment in the outpatient clinic was four weeks. The timing of the postoperative appointment was adequate according to 76.2% of the patients. Around one in five patients (22.3%) preferred the appointment to be planned sooner. Only 1.6% preferred the appointment to be later.

A. Patients' statements regarding the PRE-operative period



B. Patients' statements regarding the POST-operative period

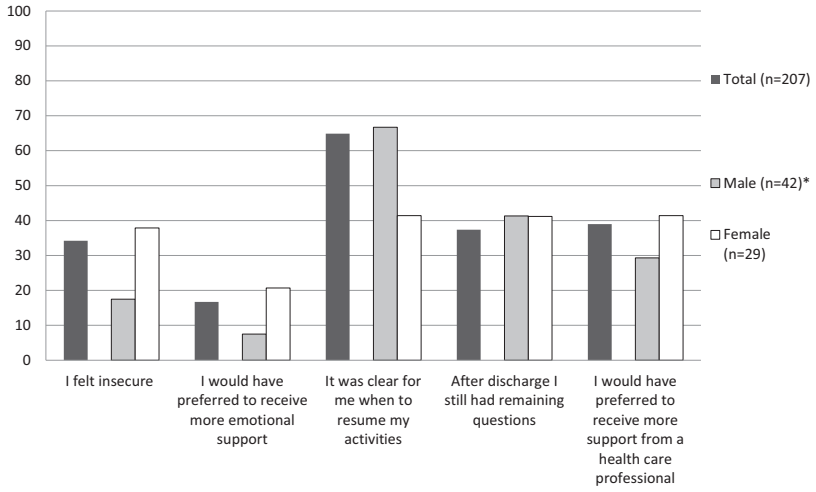


Figure 1. Patients' statements

The bars present the percentage of the participants who agreed with the statement.

* Differences between male and female evaluated in the group of patients who underwent a minor general surgical procedure (n = 71).

** Percentage of the 32 participants who created a re-integration plan.

Patients preferences regarding eHealth

General

A total of 78.7% participants (155/197) agreed with the statement that there is a need for an eHealth care program focusing on the deliverance of information and guidance during the perioperative period. Women were slightly more interested in this than men (88.9% compared to 73.2%). The majority of the patients (82.4%) stated that they were willing to spend about one to two hours of their time on such a program per week during the course of their recovery, while the other 17.6% were willing to spent even more than two hours per week.

Website

The majority of the patients (70.5%; 136/193) reported that if an eHealth intervention (i.e. a specially developed website) had been available before or after their surgical procedure, they would have used it. This was slightly more the case in women compared to men (75.0%; 21/28 versus 62.2%; 23/37). Table 3 presents the functions patients reported to prefer on such a website, in order of popularity. Most items were assessed as useful by the majority of the participants; except two: the ability to give your employer or OP insight into a part of the website and a forum to talk with other patients. Most popular items were a page containing an overview of important telephone numbers, a list with frequently asked questions (FAQ) and the possibility to evaluate symptoms after surgery.

Mobile phone application (app)

Almost half of the participants (48.2%; 95/197) reported that they would prefer to use the eHealth care program by a mobile phone application as well. This was more often the case in men than in women (65.0%; 26/40 vs 48.3%; 14/29). Among the participants who reported that they are using the Internet on a smartphone or tablet in daily life (n = 168), only a slightly higher percentage (51.2%, 86/168) reported that they would prefer to use the eHealth care program on a mobile phone application as well. Less than half of the patients (38.4%; 73/190) reported they would use the possibility to connect an activity tracker to their mobile phone application to track their activity during the recovery process.

E-consultation

Only a minority of the patients (17.6%; 35/199) would have preferred to replace their postoperative appointment in the outpatient clinic by electronic contact with their doctor (e-consult). This percentage increased slightly when only taking the participants into account who underwent minor surgery (27.9%; 19/68). The most reported reason for declining an e-consult was that the participants appreciated to have personal contact with their doctor (n = 153). However, the ability to use an e-consult to ask questions to a doctor

or nurse during the recovery process in case of complaints, was assessed as useful by 57.6% (114/198) of the participants. One in five patients (21.2%; 42/198) assessed e-consultation as not being useful at all.

Table 3. Assessment of different website functions

Function	Useful	Not useful	No opinion	n
Before surgery				
A practical list; what to manage before surgery?	157 (79.7%)	6 (3.0%)	34 (17.3%)	197
Information about the surgical procedure	150 (76.1%)	11 (5.6%)	36 (18.3%)	197
Making a personal convalescence plan	141 (71.6%)	11 (5.6%)	45 (22.8%)	197
A video about the recovery process	132 (67.3%)	25 (12.8%)	39 (19.9%)	196
Making a reintegration plan for work	123 (62.4%)	14 (7.1%)	60 (30.5%)	197
A video about the surgical procedure	104 (52.5%)	39 (19.7%)	55 (27.8%)	198
After discharge				
Evaluation of symptoms	175 (88.8%)	5 (2.5%)	17 (8.6%)	197
Monitoring of recovery	141 (72.3%)	16 (8.2%)	38 (19.5%)	195
Focus on emotional well-being	117 (60.6%)	21 (10.9%)	55 28.6%	193
Inviting your GP to a part of the website	99 (50.8%)	40 (20.5%)	56 (28.7%)	195
Inviting your OP to a part of the website	64 (30.9%)	44 (21.3%)	87 (44.6%)	195
Inviting your employer to a part of the website	53 (27.2%)	62 (31.8%)	80 (41.0%)	195
General				
Contact details of the health care professionals	178 (89.9%)	4 (2.0%)	16 (8.1%)	198
Frequently asked questions	160 (81.6%)	8 (4.1%)	28 (14.3%)	196
A list with frequently used medical terms	142 (72.8%)	9 (4.6%)	44 (22.6%)	195
Links to other websites	119 (64.0%)	15 (8.1%)	52 (28.0%)	186
Forum to chat with other patients	67 (32.4%)	56 (27.1%)	74 (32.6%)	197

DISCUSSION

Principal findings

In this survey study we analyzed the opinions of patients who underwent abdominal surgery about the availability of information and guidance they received before and after their surgical procedure. In addition, we evaluated their views on the use of eHealth in the perioperative period. Although most participants reported that they had received some basic information about the surgical procedure and the recovery process, more than half of

the participants searched the Internet for additional information. Most important reported shortcomings included the absence of detailed information about the resumption of (work) activities as well as the inconsistency between advice received by different healthcare professionals involved in the recovery process. A considerable proportion of patients (39%) reported that they would have liked to receive more assistance from a healthcare professional during their recovery process, and one in eight patients reported that they would have preferred more emotional support. Women had a slightly higher need for additional information and support than men.

A majority of participants expected an eHealth program to be helpful during the recovery trajectory. A website was assessed as most useful. In particular practical functions focusing on the preparation for surgery and monitoring after surgery were expected to be valuable. There was less need for interaction with others (e.g. chat-function or forum, or giving other health care professionals access to the website). Also, the majority of patients opposed the option to replace the standard postoperative consult by an e-consult, since they preferred a personal contact with their surgeon.

Comparison to the literature

When we compare our results to the qualitative study of Vonk Noordegraaf *et al* which was at the base of the development of an eHealth intervention for patients undergoing gynecological surgery, there are many similarities. In concordance to our own findings, Vonk Noordegraaf concluded that important shortcomings in current perioperative care were 1) the lack of instructions regarding the resumption of activities, 2) the inconsistency in the recommendations given by different healthcare providers and 3) the insecurity with respect to postoperative symptoms. However, there was inconsistency between the two studies on one point. In Vonk Noordegraaf 's study, participants reported that they would have preferred to have more contact with other patients during the perioperative course and subsequently suggested this to be one of the three most important tools to incorporate in the eHealth intervention. In our study this option was rated as one of the three most unpopular items of a possible eHealth intervention. Probably, the difference can be explained because of the difference in study population between the two studies. Another possible explanation could be the difference in study design between the two studies. The results from Vonk Noordegraaf's study were derived from focus group discussions and therefor selection bias was highly likely because participants attending in this study were willing to discuss their problems with others. Finally, it could also be that there is indeed not a major need for it, which is in line with the low satisfaction rate with these functions in a previously tested eHealth intervention for peri-operative care in gynecology.[26]

Comparing our results to other recent publications, shows another inconsistency, namely the unpopularity of the postoperative appointment by an e-consult in our study.[18–21,27] This difference might be explained by the fact that those previous studies mainly focused on the feasibility, safety and cost-effectiveness rather than the preferences of patients. Our study suggests, that even it would be feasible and safe from a medical perspective to replace the appointment in the outpatient clinic by an e-consult, from the Dutch patients' perspective there is hardly any foundation for this. However, using e-consultations as an extra means of contact with the hospital in case of complaints, was rated as useful.

Earlier studies described differences in the recovery process after cardiac surgery between men and women.[28–34] These studies conclude that during the recovery process women suffered from more symptoms, showed lower functioning scores and had a higher re-admission rate than men, which could not be explained because of illness severity or other patient characteristics.[29,30,32,33] When specifically focusing on gender differences according to the effectivity of eHealth interventions applied in the recovery process after cardiac surgery, data trends in one study showed that the intervention had greater impact on women than on men in the postoperative course.[34] We only detected some minor differences according to gender: overall women showed a slight higher need to information, extra support or eHealth compared to men. However, the results regarding this topic should be interpreted with caution; although we selected the most homogeneous group possible within the limits set by this study for comparing men and women, the remaining group was small, age differed significantly and the type of minor surgical procedures differed between men and women.

Strengths and limitations

A strength of this study lies in the extensiveness of the questionnaire and the fact that the questionnaire was developed based on the results of a qualitative study. We approached all patients who underwent all types of surgical abdominal procedures over the period of one year, which has led to a good clinical representation.

However, this study has also limitations. First, the recruitment of patients was limited to an academic hospital. This may have influenced the results because, in general, in academic hospitals the more complicated surgical procedures are being performed. Nonetheless, the indication for surgery in our study population was in most cases benign and the complication rate was moderate. In addition, perioperative care provided in the academic and non-academic hospitals in the Netherlands is quite similar; based on the guidelines of the Dutch Society of Obstetrics and Gynecologists (NVOG), patients get verbal instructions by a nurse or physician at discharge and will receive a leaflet with some recovery instructions.[9,35] Moreover, patients receive an appointment at the outpatient clinic between

two and six weeks after surgery. Therefore, we assume that the results are generalizable. Second, because of the retrospective design of this study the time between surgery and the questionnaire varied between 5 weeks and 62 weeks between the study participants. This might have resulted in recall bias as well as in difference between pre-surgery and post-surgery answers. For example, if patients underwent surgery without complications, they would be more likely to answer that they had no need for extra information or support than when they were questioned before surgery. However, since the complication rate was normal in this study, we think that this only could have led to an underestimation regarding the need for information and support. A third limitation might be the relative low response rate (57.2%). However, we were able to compare baseline characteristics between participants and non-responders. Responders were significantly older (46.59 vs 39.51), which may have influenced the results. Possibly, patients' needs and preferences regarding eHealth were underestimated, since older adults generally make less use of new technologies.[36] In addition, the responders underwent gynaecological procedures more frequently in comparison to the non-responders, however, the ratio gynecological procedures versus general surgical procedures was equal in the groups of responders. Although we were able to perform a non-response analysis regarding some important baseline characteristics, we could not rule out that there were other important differences between the two groups which we were not able to compare. For example Internet use: 95.1% of the study participants reported that they are using the Internet several times a week or on a daily basis. We do not have data regarding this topic from the nonparticipants. So, it is therefore possible that the rate of Internet use was much lower in this group, which makes the generalizability of the results, mainly regarding the preferences regarding eHealth, lower. Finally, the heterogeneity in terms of the many types of surgical procedures included in this study, could also be pointed as a limitation. However, we had a good rationale for this since we aimed to evaluate whether the results obtained with a qualitative study in a gynecological population, were also applicable to a broader population.

CONCLUSIONS

The results of this study showed that most important shortcomings in current perioperative care in patients undergoing abdominal surgery are the lack of detailed advice about the resumption of activities following surgery and the limited guidance of professionals during the recovery process. EHealth is expected to be very useful tool to overcome these shortcomings. The results of this study can be used by health care professionals and policymakers when developing these type of eHealth interventions for perioperative care. It provides a broad overview of the different phases of perioperative care and the generalizability of the study is high. Future research should include a cost-effectiveness

evaluation including a process evaluation of such eHealth interventions to evaluate the feasibility. In addition, future research should focus on gender differences in postoperative recovery, since trends of this study suggest that there may be differences.

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CHAPTER 8

Effectiveness of perioperative interventions facilitating the return to preoperative level of activity and participation – a systematic literature review

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ABSTRACT

Background The objective of this literature review is to evaluate current evidence in order to identify characteristics of perioperative strategies that enhance recovery after discharge. A better understanding of measures that help to achieve functional recovery after surgery is highly relevant to patients themselves who are currently made more and more responsible to self-manage their own health, as well as healthcare providers who want to optimize the perioperative period. Policymakers can use this knowledge to stimulate the development and delivery of evidence-based care that has the potential to facilitate long-term recovery outcomes and cut down surgery-related societal costs by reducing costs associated with lost productivity at the same time.

Methods We conducted a systematic literature review and searched for relevant articles in the PUBMED, EMBASE.com, CINAHL and COCHRANE databases. Randomized or quasi-experimental studies assessing the effectiveness of a perioperative intervention using late-phase recovery outcomes in adult patients were included in the review. Data of all included studies were extracted and study quality was assessed by using the Cochrane risk of bias tool.

Findings A total of 41 unique studies were included. Most studies were performed in the field of cardiology (n=11), orthopaedics (n=10) and gynaecology (n=9). To assess the content of the included interventions we identified four different domains which could be targeted: knowledge increase, behaviour modification, psychosocial guidance and organization optimization. Most studies were judged as having a medium risk of bias (16 studies), 13 studies as having a low risk of bias and 12 studies as having a high risk of bias. The majority of interventions targeted more than one domain. Outcomes included return to preoperative levels of activity and participation. In addition, nine studies reported economical outcomes measures such as healthcare usage and costs. Twenty-four studies (58.5%) reported at least a positive effect of the intervention compared to usual care. Due to substantial heterogeneity in perioperative interventions, there were no correlations found between the different types of interventions and the overall outcomes of the studies, therefore is was not possible to determine successful key elements of the interventions.

Conclusions Based on this systematic review we conclude that perioperative interventions have the potential to facilitate return to preoperative levels of activity and participation. However, due to the substantial heterogeneity in perioperative interventions there is insufficient data to identify an optimum programme. Notwithstanding, a multimodal approach is likely to have better impact on functional outcomes compared to single modality.

INTRODUCTION

Despite the fact that the aim of surgery is to treat a disease or injury, each surgery is followed by a period of disability as well. This period, the postoperative recovery period, is complete when the patient returns to their preoperative level of independence in activities of daily living and reaches an optimum level of psychological well-being.[1]

The International Classification of Functioning, Disability and Health (ICF) is a framework of the World Health Organization (WHO) for measuring health and disability.[2] The major components of the ICF are body functions and structures (anatomy and physiology), activity (execution of a task or action by an individual) and participation (involvement in a life situation) and it conceptualises a person's level of functioning as a dynamic interaction between her or his health conditions, and contextual factors which include their unique environmental factors and personal situations. In figure 1 the model is tailored to postoperative recovery. Hence, surgery does not only impact body functions, it also results in limitation of activities and restriction of participation in society.

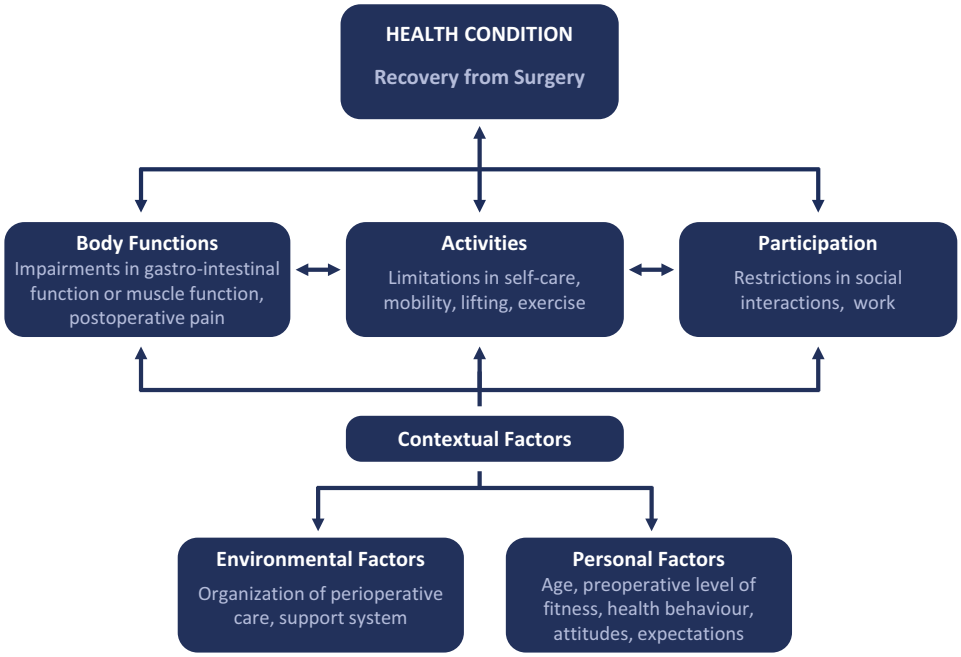


Figure 1. Example of how the ICF model can be tailored to postoperative recovery
ICF = International Classification of Functioning, Disability and Health. Adapted from WHO. Towards a Common Language for Functioning, Disability and Health (ICF Beginner's Guide), 2002. Retrieved from http://www.who.int/classifications/icf/training/icfbeginnersguide.pdf. (Accessed 9 Feb 2019).

Currently, the largest part of the postoperative period occurs after discharge in the patient's own environment. However, the main body of research on interventions targeting the postoperative phase assessed their effectiveness in the domain of body functions and body structures, using short-term recovery outcomes such as perception of pain, anxiety, length of hospital stay, complication rates, and mortality rates.[3] As a result, a clear understanding about the mechanisms of late phase recovery, i.e., recovery to one's pre-operative levels of activity and participation, is lacking. Therefore, it remains unclear how to target postoperative recovery and what type of interventions are effective in supporting the patient in their return to their own level of functioning.

The objective of this literature review is to evaluate current evidence in order to identify characteristics of perioperative strategies that enhance recovery after discharge. The following research-question was formulated: In patients undergoing any kind of surgery what perioperative interventions can be applied in order to facilitate the return to preoperative levels of activity and participation? A better understanding of measures that help to achieve functional recovery after surgery is highly relevant to patient themselves who are currently made more and more responsible to self-manage their own health, as well as healthcare providers who want to optimize the perioperative period. Policymakers can use this knowledge to stimulate the development and delivery of evidence-based care that has the potential to facilitate long-term recovery outcomes and cut down surgery-related societal costs by reducing costs associated with lost productivity at the same time.

METHODS

The PRISMA framework was used to endure accurate and complete conduct and reporting of this systematic review.[4] No protocol was published in advance.

Search strategy

The systematic literature search was performed by RO and EB in the following electronic databases: PUBMED, EMBASE.com, CINAHL (via EBSCO), PsycINFO (via EBSCO) and the Cochrane Collaboration (via Wiley) from inception until the 26th of September 2018. The search contained three sections that were combined with the operand 'AND' including Mesh and free text terms comprising 1) the perioperative period, 2) some type of intervention, and 3) one of the possible outcomes. Although this review was limited to peer-reviewed studies published in English and available as full text, we did not restrict the searches by language or publication status. The reference lists of relevant articles and eligible studies were hand-searched to ensure all eligible studies were ultimately included. The full search strategies for all the databases are summarized in supplementary file S1.

Eligibility criteria

Studies were included in the systematic review if they met the following inclusion criteria:

- Type of studies: We included controlled studies, containing both randomized controlled trials (RCTs) as well as quasi-experimental studies, in which the allocation to the intervention was decided by non-random means such as e.g. the date of the surgery or a specific hospital ward a patient was located to.
- Types of participants: Participants were required to be aged 18 years or over, and undergoing any elective surgical procedure under either regional or general anaesthetic. Excluded were patients undergoing surgeries leading to long-term disability (e.g. amputation) and surgeries that were being followed by adjuvant therapy for cancer treatment (e.g. chemotherapy).
- Types of interventions: Studies were included if they evaluated any type of intervention that aimed at enhancing post-operative recovery. The intervention should be delivered before surgery or in the direct postoperative period, in any case before discharge of the hospital. The patient undergoing the surgery should be the recipient of the intervention. If the intervention was given as part of a multicomponent intervention, such as fast-track or enhanced recovery programs, the study was excluded as in those cases it was not possible to isolate the effect of the different components delivered. Moreover, studies analysing (p)rehabilitation programmes were excluded, which were defined as strategies to optimise a patient's preoperative condition by, e.g. nutritional optimisation, and/or cessation of negative health behaviours. Finally, interventions containing structured physical exercises or monitored physiotherapy were not taken into account.
- Types of control groups: The control group should consist of usual care, placebo, or attention control matching for the amount of time and/or attention received by the treatment group. Studies which did not include a control group drawn from the same population were excluded.
- Types of outcome measure: Studies should evaluate the effect of the intervention with outcomes measuring return to preoperative levels of activity and participation with a minimum duration of follow-up of 2 weeks postoperatively. Eligible outcomes included the ability to complete activities of daily living, physical activity, return to usual (leisure) activities and return to work.[2,5] Studies solely reporting on body function were not considered in this review, for example forced expiratory volume, muscle strength and knee angle. Outcomes should be presented as quantitative data.

Data collection process

Two reviewers (EB and EM) independently screened all titles and abstracts for eligibility. The full texts of potentially relevant titles were reviewed. Disagreements were resolved by

discussion, and if no consensus could be reached a third reviewer (JH) was consulted. If there were more publications on the same study, we only included the study reporting the original research.

Data extraction of the eligible studies was performed by one reviewers (EB) using a standardized data-extraction form which was developed by the authors. A second reviewer (EM) checked the extracted data. If multiple reports were identified from the same study, a composite dataset from these publications were created. Where possible, data selections were used for studies that also included non-eligible patient or treatment groups, in order to select only relevant sub groups. If necessary, the corresponding author was contacted to request additional details.

Data that were extracted, included:

- characteristics of the publication: authors, year of publication, country in which the study was conducted, journal;
- characteristics of the study: study design, availability of a published protocol;
- characteristics of the study population: in- and exclusion criteria, type of surgery, reason for surgery, sample size, demographics (e.g. age, gender, level of education, work status);
- characteristics of the type of intervention: type and content, moment of commencement, intensity, medium through which is was applied, involved healthcare professionals, the use of a theoretical framework;
- type of control group;
- characteristics of the outcome measures of interest: type, method and timing of assessment, follow-up duration.

Assessment of risk of bias in included studies

After data collection, the two reviewers (EB and EM) individually assessed the potential risk of bias of the included studies using the Cochrane risk of bias tool published in the Cochrane Handbook for systematic reviews 5.0.1.[6] This tool estimates potential bias in randomized controlled trials and contains seven domains: sequence generation, allocation concealment, blinding of patients and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other bias. Each item has to be ranked as low risk of bias, high risk of bias or unable to identify information or uncertainty about potential bias. Disagreements between the reviewers were resolved via consensus. If necessary, a third reviewer (JH) was consulted.

Analysis

Due to the heterogeneity in terms of study design, type of surgery, type of intervention, type of outcomes measures it was not possible to conduct a meta-analysis. Instead, we aimed to present a descriptive overview of:

a) the characteristics of the studies in this systematic review;
b) the characteristics of individuals comprising the samples;
c) the characteristics of the interventions being studied;
d) the characteristics of the types of outcomes employed to assess postoperative recovery.

FINDINGS

Results of the search

The literature research yielded 9894 unique citations (figure 2). Screening of the titles resulted in 654 records of which the abstract was reviewed, which resulted in 101 citations of which the full text was examined. This process resulted in 41 unique studies that were included for this systematic review. In addition, eight study protocols were identified of which the results had not been published on the date of the search (supplementary file S2).

Scope of the included studies

The characteristics of the included studies are presented in Table 1. Six studies were published before the year 2000, with the oldest publication originating from 1976. Half of the studies were published in the last 8 years. Most studies were conducted in Europe (n=18), followed by The United States of America and Canada (n=14) and Asia (n=7). Only 9 publications were preceded by a research protocol. Most journals targeted physicians (n=23) or nurses (n=12).

Design

Of the 41 included studies, most studies (n=27) were randomized controlled trials. Five studies employed a cluster-controlled trial of which one had a stepped wedge approach. The remaining nine studies employed a quasi-randomized design. Most studies had two study arms, however there were five studies with three study arms and two studies employed a 2x2 factorial design.

Fourteen studies used inclusion-criteria for age. In 11 studies, patients above a certain age were not eligible for participation (cut-off varying between 59 and 75 years). Four studies[17, 18, 27, 41] focused on the older patient (patients only being eligible if they were older than 40, 50 and 65 respectively). In two studies[7, 50], patients were only eligible if they were employed. In two other studies[9, 20], patients had to have access to a smart phone to be

eligible. Severe comorbidity was an exclusion criterion in half of the studies (21/41). In addition, the occurrence of perioperative complications was an exclusion criterion in two other studies.[7, 50]

Patients

Most studies were performed in the field of cardiology (n=11), orthopaedics (n=11) and gynaecology (n=10), followed by general surgery (n=9) and spine surgery (n=6). Study sizes were relatively large with a median of 100 patients per study (IQR 67-180). The smallest study[16] included 18 patients, the largest study[20] comprised 997 patients.

The median age of participants was 56 years (IQR 50-63). The youngest patients were included in the study by Ginandes *et al*[16], with a population undergoing reduction mammoplasty (median age 39 years). The oldest patients were hip fracture patients in a study by Lin *et al* (median age 79 years).[27]

Most studies included both females and males (31 studies). The studies with cardiac patients comprised of mainly male patients, with the study of MacIntyre *et al*[32] being an exception with a percentage of 77% female patients. The authors state that this conflicts with their average population in which 23% of the patients undergoing coronary artery bypass surgery is female, however, they fail to explain the difference. Possibly, selection bias towards the supportive intervention (healing touch) contributed to this difference and women were more likely to enter the study than men. Moore *et al*[39] made an effort to increase the percentage of women in their cardiac population by approaching every woman and only every fourth man meeting the inclusion criteria.

Data about baseline characteristics varied widely between studies. In 16 studies work status prior to surgery was recorded. In a third of the studies, education level of the patient was presented.

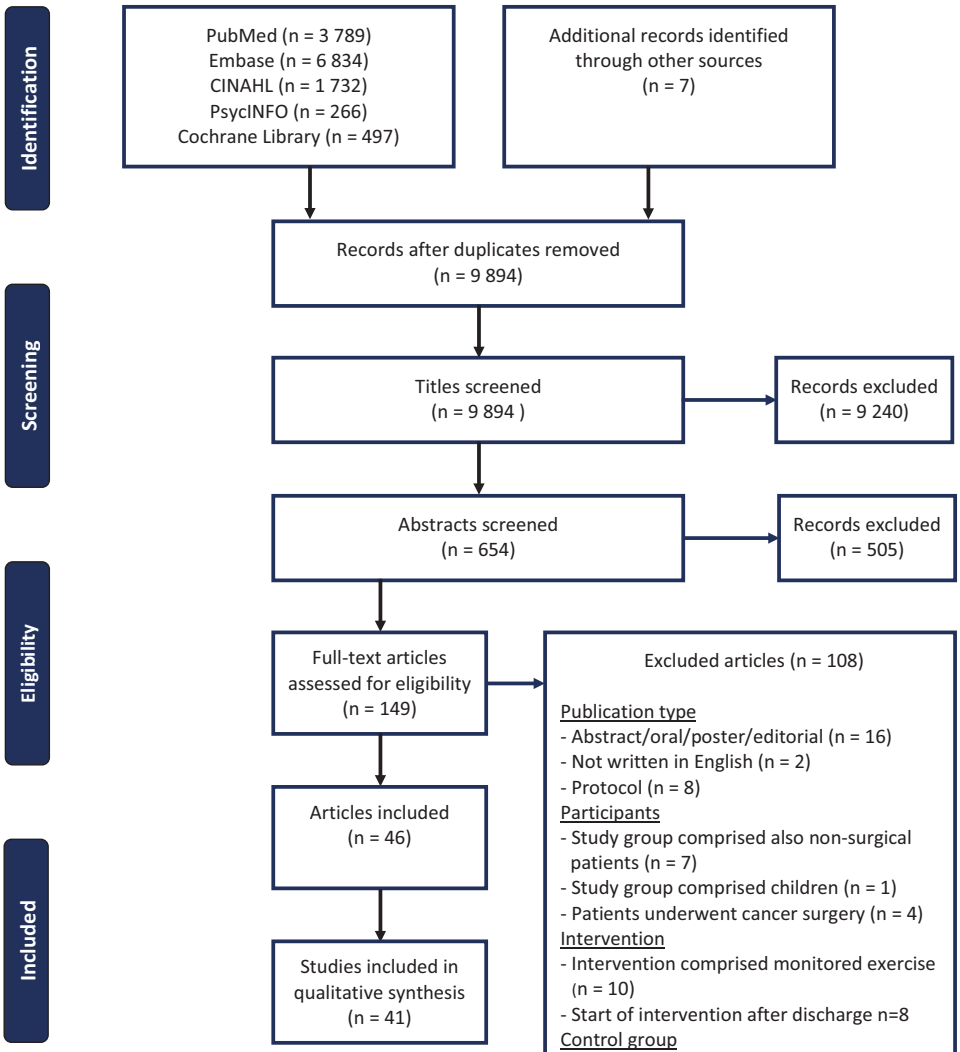


Figure 2. Flow diagram

Table 1. Characteristics of included studies

Author	Study design	Type of surgery	N	Description of the intervention
Bouwsma, 2018[7] §	Cluster RCT	Hysterectomy and/or adnexal surgery	433	**Web-based care program** 1. eHealth intervention for all patients to facilitate self-management by equipping patients with tailored convalescence advice before surgery and monitoring recovery after surgery. 2. guidance by a care manager for those patients at risk for prolonged sick leave through telephone calls before and after surgery to optimize recovery expectations and assess problems with the resumption of work.
Chunta, 2016[9]	Quasi-experimental	CABG surgery, valve replacement or combination	28	**Telephone supportive intervention** Telephone calls in which patients were asked questions about how they were doing in relation to their feelings of anxiety, depression, having positive expectations, and their physical health status.
Claus, 2017[10]	Quasi-experimental	Lumbar discectomy	129	**Evidence based information booklet** Booklet based on a biopsychosocial model which promotes an active approach to patient self-management. Key messages: - there is no good evidence for restricting postoperative activity; restriction may delay recovery and return to work - recovery can be facilitated by knowing what to expect - early activation produces better relief of pain - early return to work may produce faster recovery and better clinical outcomes.
Darwood, 2009[11]	Quasi-experimental	Varicose vein surgery	134	**Booklet with convalescence advice** Revised booklet in which patients were explicitly encouraged to return to all activities as soon as possible.
Dawes, 2007[12]	RCT	Hysterectomy, colposuspension, pelvic floor repair	106	**Specialist nurse supported discharge procedure** Daily assessment following surgery by discharge nurse aiming at early supported discharge on the third postoperative day. Supplementation of advice and information already given in routine care.
Dunbar, 2009[13]	RCT (3arms)	ICD implantation	246	**Psychoeducational intervention** 1. education and information 2. symptom management training 3. coping skill training <u>Support Group</u> group sessions <u>Telephone Group</u> telephone calls
Fortin, 1976[14]	Quasi-experimental	Inguinal herniorrhaphy, cholecystectomy, hysterectomy	69	**PEPCE program (Programme d'enseignement préopératoire dispense a des patients de chirurgie élective).** 1. orientation to surgical experience 2. biological facts 3. effects of smoking 4. importance of early ambulation 5. purpose and techniques of respiratory and muscular exercises 6. techniques of changing position 7. how to anticipate and to cope with postoperative symptoms 8. practical suggestions on self-care.
Gillis, 1993[15]	Cluster RCT	CABG surgery, valve replacement, septal repair	156	**Psychoeducational nursing intervention** 1. In-hospital education (for both patients and partners) including a side-tape presentation as well as a private session with a nurse to allow for individualization of the content (understanding anxiety, anticipating depression, solving problems, and identifying areas of potential conflict with family members). 2. Weekly telephone coaching after discharge to provide support, reinforce the educational content and provide information for formation of self-efficacy expectations.

	Timing	Intensity	Control group	Follow-up (weeks)	Relevant outcomes measures (questionnaire)	Result
	before admission	medium	**Usual care** Verbal instructions and general leaflet. Appointment with a general physician after 12 weeks in case of no return to work.	52	RTW ¥ Functional status (SF36) Recovery (RI) € [8]	+ - * +
	before discharge	medium	**Usual care** No further details provided.	13	Functional status(SF36)	-
	day of admission	low	**Conservative advice** Booklet based on a biomedical approach, promoting self-limitation.	9	Disability (QBPDS) ¥ RTnA RTW	- - -
	before admission	low	**Conservative advice** Standard booklet which suggested 7-10 days before driving and 2-3 days before returning to work.	6	RTnA ¥ RTW	- -
	before discharge	high	**Usual care** routine care was to discharge women on postoperative day 5 or 6.	6	Functional status (SF36) ¥ €	- +
	before discharge	high	**Attention control** Unstructured follow-up telephone calls by the research staff at the same time of the intervention.	52	Functional status (DASI) RTW €	- + +
	before admission	medium	**Usual care** No further details provided.	5	ADL (ordinal scale) RTW	+ *
	before discharge	high	**Usual care** Standard information and a post-hospital visit at 6 weeks to the cardiac surgeon.	24	RTnA RTW	+ -

Table 1. Continued

Author	Study design	Type of surgery	N	Description of the intervention
Ginandes, 2003[16]	RCT (3arm)	Reduction mammoplasty	18	**Medical hypnosis** 1. Pre-operative sessions to provide suggestions for a smooth surgery experience. 2. Postoperative sessions focusing on accelerated healing. 3. Audiotapes after each session for daily practice reinforcement.
Heidarnia, 2005[17]	Quasi-experimental	CABG surgery	75	**Health education program** 1. Initiation of planning the activity 2. Need-assessment 3. Goal setting 4. Planning or programming the activity 5. Implementing the activity 6. evaluating the activity's effectiveness
Huang, 2017[18]	RCT	Total hip arthroplasty	116	**Education empowerment program** Program aimed to empower patients to develop their own self-management program to meet their needs and encourage them to explore needs and worries, their own ability and power to meet their needs, use their social support and resources and to control their own health issues, carry out self-care strategies. A self-care diary was used to assess achievements on pain, wound situation and physical rehabilitation activity per day.
Jacobson, 2016[19]	RCT	Total knee arthroplasty	82	**Guided imagery treatment** audio recordings designed to promote functional outcomes after surgery.
Jaensson, 2017[20]	RCT	Any day surgery	997	**RAPP (Recovery Assessment by Phone Points)** Access to a mobile application assessing postoperative recovery daily and enabling patients to initiate contact with the day surgery unit.
Kahokehr, 2012[22]	RCT	Cholecystectomy	60	**Perioperative psychological intervention** Instruction of deep-breathing techniques followed by reading a script that included: guided breathing, progressive muscle relaxation, and guided imagery of the body being prepared for surgery. Patients received a CD with relaxing background music to listen to prior to surgery and a postsurgical script to listen to after surgery.
Kesänen, 2017[23]	RCT	Lumbar decompression, spinal fusion, or combination	100	**Knowledge Test Feedback Intervention (KTFI)** Intervention aiming at increasing the patients' knowledge on preparation for and recovery from surgery. Patients filled in a test pre-operatively and received the corrected test before an empowering telephone discourse. During the telephone discourse the patients were encouraged to take an active role and reflect on their answers to the knowledge test, as well as provided with feedback on their existing knowledge.
Klaiber, 2018[24]	Cluster RCT	Visceral surgery (oesophagus, stomach, small intestine, colon, rectum, pancreas, liver, kidney)	244	**Preoperative patient education** Standardized event to teach patients measures to prevent postoperative complications, instruct them about the principles of acute pain therapy and various coping strategies. Patients were introduced to breathing exercises, careful post-operative out-of-bed mobilization, and practical exercises to prevent thrombosis and burst abdomen.
Krouse, 2001[25]	RCT	Nasal and/or sinus surgery	52	**Preoperative education including video-modelling** Nursing-based videotape demonstrating specific postoperative care measures with the objective that viewers would see people similar to themselves as capable of performing their own postoperative care.

Timing	Intensity	Control group		Follow-up (weeks)	Relevant outcomes measures (questionnaire)	Result
before admission	high	**Attention control** Open-ended questions to elicit verbalization of thoughts and feelings about the procedure.	**Usual care** No further details provided.	7	Functional status (SF36)	*
before admission	high	**Usual care** No further details provided.		4	Functional status (SF36) ¥ Functional status (NHP)	+ +
day of admission	high	**Usual care** Verbal instruction by a nurse at admission followed by a brochure.		12	ADL (BI) Functional status (SF36)	- -
before admission	low	**Attention control** Commercially available audio recordings (poetry, short stories, essays).		26	Functional status (SF36) Functional status (WOMAC)	- -
day of admission	low	**Usual care** Standard information regarding the postoperative period and who to call in case of concerns or questions.		2	Recovery (SwQoR) €[21]	+ +
before admission	medium	**Usual care** No further details provided.		4	RTW	-
before admission	medium	**Attention control** General telephone discussion about health history.		26	Functional status (SF36) Disability (ODI)	- -
day of admission	medium	**Usual care** Information brochure and standard communications with surgeon and ward nurses.		4	Functional status (SF12)	-
before admission	low	**Usual care** Standard pre-operative teaching by a nurse, including verbal and written instruction in office prior to surgery.		4	Disability (RSDI)	-

Table 1. Continued

Author	Study design	Type of surgery	N	Description of the intervention
Lewin, 2009[26]	Cluster RCT	ICD implantation	192	**Cognitive behavioural preimplantation and rehabilitation programme** 1. Patient-held booklet dealing with common fears before surgery, and introducing relaxation and breathing to help patients cope with the stress of surgery. 2. Patient-held booklet including a cognitive behavioural rehabilitation programme in self-help form. 3. Booklet for relatives 4. Goal-setting diary 5. Relaxation tape/CD 6. Postoperative telephone calls to discuss progress, reinforce success and to set new goals.
Lin, 2009[27]	Cluster RCT	Hip fracture surgery (hemi-arthroplasty or internal fixation)	50	**Discharge-planning program** Comprehensive discharge planning service including - a structured assessment of discharge planning needs - systematic individualized nursing instruction based on the patient's individual needs - monitoring services and coordinated services - arranging of referral placements. Patients received an education booklet and after discharge 2 home visits were conducted to provided necessary support and consultation.
Lin, 2011[28]	Quasi-experimental	Total knee arthroplasty	83	**Care map** Patients were cared for by a nurse based on a care map to provide continuous, including: 1. preoperative calls to provide patients with consultations services, identify concerns and remind them to read the brochures. 2. in hospital visits by the care manager ensured that activities and time frames were coordinated. If patients were not discharged on day 6, the care manager would identify and solve the problem. 3. postoperative calls to follow-up on self-care and any patient difficulties.
Lookinland, 1998[29]	RCT	Gynaecologic, urologic or general surgery procedures	39	**Preoperative education** Structured patient education based on theory, provided to patients in the preoperative phase by trained nurses.
Louw, 2014[30]	RCT	Lumbar decompression	67	**Preoperative pain neuroscience education** Preoperative education accompanied with drawings covering the followings: 1. decision to have surgery 2. physiology 3. Peripheral nerve sensitization 4. surgical experiences and environmental issues effects on nerve sensitivity 5. calming the nervous system 6. recovery after surgery 7. scientific evidence for education booklet content 8. opportunity to reflect and list questions
MacIntyre, 2008[32]	RCT (3arms)	CABG surgery	237	**Healing touch** Preoperative education for healing touch and 3 sessions of healing touch (on the day before surgery, immediately prior to surgery and the day after surgery).

	Timing	Intensity	Control group		Follow-up (weeks)	Relevant outcomes measures (questionnaire)	Result
	before admission	medium	**Attention control** Usual care complemented with a generic information booklet and telephone contact to discuss postoperative progress		26	Functional status (SF12) Functional status (SAQ) €	+ + +
	day of admission	high	**Usual care** Non-structured discharge instruction according to the nurse's own professional judgement without following a standardized procedure		13	Functional status (SF36) Functional status (OMFAQ)	- -
	day of admission	high	**Usual care** No further details provided.		4	ADL (iADL) Functional status (OMFAQ)	+ +
	before admission	medium	**Usual care** Post-admission unstructured education by any nurse that admitted the patient to the surgical unit on the day of surgery.		4	Functional status (FSI)	*
	before admission	medium	**Usual care** Standardized, no further details provided.		52 3years[31]	Disability (ODI) ¥ €	- +
	day of admission	high	**Attention control** General conversations.	**Usual care** No further details provided.	13	Functional status (SF12)	-

Table 1. Continued

Author	Study design	Type of surgery	N	Description of the intervention
McGregor, 2004[33]	RCT	Total hip arthroplasty	39	**Preoperative rehabilitation advice** 1. Information booklet with information about the surgery and all preoperative and postoperative stages, rehabilitation stages, and a series of answers to commonly asked questions. 2. Preoperative class in which the booklet was enforced and it was ensured that all subjects understood the content and could make provisions for any adaptations required to homes for the immediate postoperative phase.
McGregor, 2011[34]	RCT (2x2 factorial design)	Lumbar discectomy, lumbar decompression	338	**Education** Educational booklet which aimed to reduce uncertainty, promote positive beliefs, encourage early reactivation, and provide practical advice on self-management. ***Rehabilitation ‡*** *Rehabilitation classes provided by a physiotherapist to commence 6-8 weeks after surgery*
Meij, 2018[35]	RCT	Adnexal surgery, inguinal herniorrhaphy, cholecystectomy	344	**Personalized perioperative care by e-health** Intervention aiming at preparing the patient for surgery and supporting them during the postoperative period, creating adequate recovery expectations, reducing uncertainties during the recovery period and reducing the workload for healthcare professionals, including: 1. recovery advice based on a personalized convalescence plan 2. information about the perioperative period 3. monitoring and feedback on recovery 4. E-consult
Miro, 1999[37]	RCT (2x2 factorial design)	Hysterectomy with double oophorectomy	92	**Relaxation intervention** 1. verbal instruction of deep-breathing and provision of instructions on how to relax. 2. guided imagery was used so as to help patients deepen their relaxation state. 3. hand-out including detailed suggestions on how to implement advice.
Moore, 1996[38] ¶	Quasi-experimental	CABG surgery	82	**Cardiac Home Information Program (CHIP)** Audiotape describing the typical recovery experiences of patients with particular attention to sensations they may experience and coping behaviours they may find helpful to reduce symptoms, psychological distress and enhance physical functioning.
Moore, 2001[39] ¶	RCT	CABG surgery	180	**Cardiac Home Information Program (CHIP)** Audiotape describing the typical recovery experiences of patients with particular attention to sensations they may experience and coping behaviours they may find helpful to reduce symptoms, psychological distress and enhance physical functioning.
Mueller, 2017[40]	RCT	Surgery for pelvic organ prolapse	95	**Activity recommendations** Liberal activity recommendations encouraging patients to resume postoperative activity at their own pace with no restriction on lifting or high-impact activity (including running, aerobics, sit-ups)
Parent, 2000[41]	RCT	CABG surgery	56	**Peer support intervention** One-on-one support intervention, including supportive sessions of volunteers the patients with "living proof" of a successful surgery and rehabilitation program. Emotional and informational support given during the visit was intended to reassure subjects, coach them towards activity, reinforce risk factor reduction, and strengthen their expectancies concerning their capacities to achieve behavioural change.

Timing	Intensity	Control group	Follow-up (weeks)	Relevant outcomes measures (questionnaire)	Result
before admission	medium	**Usual care** Description of the surgery and its risks and approximations on length of hospital stay.	13	ADL (BI) Functional status (WOMAC) Functional status (HHS) €	- - - +
before discharge	low	**Usual care** No further details provided.	52	Disability (ODI) ¥	-
before admission	low	**Attention control** Placebo website containing a general information leaflet, general recovery advice provided by the hospitals and the contact info of their hospital.	26	RTnA ¥ RTW Physical activity (PROMIS-PF) Physical activity (IPAQ) Social participation (PROMIS-SP) Recovery (RI) € [36]	+ + + - + - +
before admission	medium	**Attention control** Conversation on neutral topics.	2	RTnA	+
before discharge	low	**Attention control** General inquiry regarding the subject's health and well-being.	4	Disability (SIP)	+
before discharge	low	**Usual care** Discharge instructions from a unit nurse including a videotape, pamphlets and one-to-one counselling.	4	Disability (SIP)	+
before admission	low	**Conservative advice** Restricted activity recommendations informing patients to abstain from heavy lifting or high-impact activities for three months.	13	RTnA Physical activity (AAS) Physical activity (PROMIS-PF)	- - -
day of admission	high	**Usual care** Routine information on surgery and recovery by health professionals.	4	RTnA	+

Table 1. Continued

Author	Study design	Type of surgery	N	Description of the intervention
Ridgeway, 1982[42]	RCT (3arms)	Hysterectomy	70	**Psychological preparation** 1. Manual corresponding to the group allocation 2. Reinforcement of manual during a visit prior to surgery. <u>Information group</u> Manual describing the procedures and sensations women were likely to experience before and after the operation. <u>Cognitive group</u> Manual suggesting that people can control how they view the events to some extent by choosing to dwell on the more positive aspects.
Rief, 2017[43]	RCT (3arms)	CABG surgery with or without valve surgery	122	**Expectation Manipulation (EXPECT)** 1. Focus on the development of realistic expectations about the benefits of surgery and the recovery process. 2. Booklet containing all relevant session information. 3. Audio-CD of the session
Rolving, 2015[44]	RCT	Lumbar spinal fusion	90	**Pre-operative cognitive-behavioural intervention** Standardized treatment sessions on the following topics: interaction of cognition and pain perception, coping strategies, pacing principles, ergonomic directions, return to work, and details about the surgical procedure.
Sheard, 2006[46]	RCT	Varicose vein surgery, cholecystectomy, herniorrhaphy, thyroidectomy, haemorrhoidectomy	109	**Commercially produced patient information** Set of three patient booklets at pre-assessment, before surgery, and after surgery: - "About having an operation" - "About anaesthesia" - "Bouncing back from surgery"
Skolasky, 2015[47]	Quasi-experimental	Lumbar decompression, spinal fusion procedures	122	**Health behaviour change counselling (HBCC)** Telephone call before surgery in which motivational interviewing strategies are applied to increase the participant's 1) perception of the importance of physiotherapy or home exercise programs and 2) confidence to follow through on rehabilitation. Two boosters after surgery to discuss the progress and identify engagement barriers and facilitate commitment to engage in adaptive behaviour.
Utriyaprasit, 2010[49] ¶	RCT	CABG surgery	120	**Cardiac Home Information Program (CHIP)** Audiotape describing the typical recovery experiences of patients with particular attention to sensations they may experience and coping behaviours they may find helpful to reduce symptoms, psychological distress and enhance physical functioning.
Vonk Noordegraaf, 2014[50] §	RCT	Hysterectomy and/or adnexal surgery	215	**Personalised e-Health program** 1. Access to an eHealth intervention with detailed tailored convalescence advise and with tools to improve self-empowerment, communication with care providers and employer and to identify recovery problems. 2. Contact with clinical occupational physician in sick leave exceeds 10 weeks after surgery and if necessary, a workplace intervention by an occupational therapist.

	Timing	Intensity	Control group		Follow-up (weeks)	Relevant outcomes measures (questionnaire)	Result
	day of admission	medium	**Attention control** Manual describing the ward and the hospital including the routines, staff roles and the location of various enmities.	***Usual care ‡*** *Patients that did not receive a manual (on request).*	3	RTnA	*
	before admission	high	**Attention control** Encouragement of expressing emotions and anxieties about the anticipated surgery. No audio CD or booklet.	**Usual care** Standardized preoperative counselling session with a cardiac surgeon and anaesthesiologist.	26	Disability (PDI) ¥ Activity level (IPAQ) Functional status (SF12) RTW	+ + + +
	before admission	high	**Usual care** Preoperative information about the surgery, medication and information about postoperative rehabilitation and physical restrictions after surgery.		52	Disability (ODI) ¥ RTW € [45]	* - +
	before admission	low	**Usual care** Standard hospital-supplied information		2	Functional status (SF36)	-
	before admission	high	**Attention control** Standard preoperative education and contact via telephone calls after surgery discussing progress.		52 2&3 years[48]	Disability (ODI) ¥ Functional status (SF12)	+ +
	before discharge	low	**Attention control** Phone calls after discharge in which general questions were asked about health and well-being.		4	Disability (SIP)	+
	before admission	medium	**Attention control** Placebo website containing general leaflet and contact details from hospital.		26	RTW ¥ Functional status (SF36) Recovery (RI)	+ + -

Table 1. Continued

Author	Study design	Type of surgery	N	Description of the intervention
Wang, 2018[51]	RCT	Total hip arthroplasty	389	**Internet-based home care platform ("WeChat")** solving the communication path between nurse specialists and patients after discharge, providing high quality continuous nursing service, solve problems of daily management and clinical care and guide patients to master disease knowledge and the method of rehabilitative exercise with interactive tools as: 'question and answer application', rehabilitation exercises', appointment request', and 'clinical broadcasts'.
Yeh, 2005[52]	Quasi-experimental	Total hip arthroplasty	66	**Patient education through multimedia** Videodisc combining text, pictures, film, animations and sounds. (self-learning) in order to: 1. Understand the structure of hip joint and development of hip disease. 2. Learn about preparation before admission and situations they might encounter during hospitalization 3. To perform rehabilitative and functional activities correctly.
Zieren, 2007[53]	RCT	Inguinal herniorrhaphy	100	**Informative video** Informative video clip performed by an actor demonstrating the following phases of hospitalization: - admission - preoperative measures - information about the surgery - postoperative nutrition, going to toilet, hygiene and analgesic medication. - recommendations concerning patients' behaviour (no limitations on RTW, sport activities or sexual life), advice: resume usual activities in a symptom adapted way.

N: number of patients
+: studies reporting a significant effect favouring the intervention group
*: studies reporting a temporary effect or a trend
-: studies reporting no significant effects
¥: primary outcome
€: economic outcomes being reported
§: based on similar intervention
¶: based on same intervention
‡: this group did decline to participate in study, however, their data were used in the analyses
AAS: Activities Assessment Scale, ADL: Activities of daily living, BI: Barthel Index, CABG: coronary artery bypass grafting, DASI: Duke Activity Status Index, FSI: Functional Status Index, HHS: Harris Hip Score, iADL: instrumental activities of daily living, ICD: implantable cardioverter defibrillators, IPAQ: International Physical Activity Questionnaire, NHP: Nottingham Health Profile, ODI: Oswestry (low back pain) Disability Questionnaire, OMFAQ: OARS Multidimensional Functional Assessment Questionnaire, PDI: Pain Disability Index, PROMIS: Patient-Reported Outcomes Measurement Information System, QBPDS: Quebec Back Pain Disability Scale, RCT: randomized controlled trial, RI-10: Recovery Index, RSDI: Rhinosinusitis Disability Index, RTnA: return to normal activity, RTW: return to work, SAQ: Seattle Angina Questionnaire, SF: Short Form, SIP: Sickness Impact Scale, SwQoR: Swedish Quality of Recovery, WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

	Timing	Intensity	Control group	Follow-up (weeks)	Relevant outcomes measures (questionnaire)	Result
	before discharge	medium	**Usual care** Routine nursing care including a rehabilitations manual, performing telephone follow-up and outpatient review at 3 moments after discharge.	26	Functional status (SF36) Functional status (HHS) ADL (BI)	+ + +
	before discharge	low	**Usual care** One to one patient education with pamphlets during hospitalization.	2	Functional status (FSI)	+
	day of admission	low	**Usual care** Verbal and written information in a standardized way about the planned operations and its potential complications and the expected postoperative course.	52	RTnA RTW Functional status (SF36)	+ + *

Interventions

The degree of detail provided about the interventions varied greatly across studies. In addition, there was a large variation in the content and the intensity of the interventions, but also in the timing and the methods used to deliver the interventions to the patient.

The majority of interventions were delivered in the preoperative period, before admission to the hospital (21/41, 51.2%). In 10 studies the intervention was delivered after admission, but before surgery (24.4%). In the remaining 10 studies the interventions were delivered after surgery, but before discharge (24.4%).

Interventions were delivered through (a combination of) different strategies, including: written materials, multimedia (including audiotape, CD/CD-ROM, video, DVD), e-health (including web portals and smartphone applications), telephone calls, group sessions and individual sessions. The intensity of the interventions was categorized as low, medium and high, according to the amount of time it took the healthcare provider to deliver the intervention. Low intensity interventions (14 studies) included strategies in which patients were able to take up the content of the intervention on their own, e.g. through written materials, listening to audio or watching a video, or visiting a website. Medium intensity interventions (14 studies) were delivered by professionals such as nurses or psychologists through e.g. telephone calls or group sessions. High intensity interventions (13 studies) were delivered by professionals through e.g. multiple individual sessions, in-patient visits and home-visits.

Interventions were most frequently delivered by nurses (15/28 studies) or psychologists (6/28 studies). Other involved professionals were surgeons themselves (3 studies), occupational physicians (2 studies), and a physical therapist (1 study). One intervention was delivered by (trained) former patients.[41]

After reviewing all included interventions, we identified four different domains that were being targeted:

1. Knowledge increase: strategies that focus on providing information about the health disease or surgery, practical information including convalescence advice, sensory information (what to expect), as well as general health and lifestyle information.
2. Behaviour modification: strategies that focus on increasing self-efficacy, facilitating patient participation and self-management, including techniques such as coping mechanisms and goal-setting.
3. Psycho-social guidance: strategies that focus on reducing stress or anxiety, improving confidence and providing emotional support.

4. Organization optimization: strategies that focus on optimizing the organization of care processes.

The vast majority of the interventions contained several elements, and therefore, the interventions could be allocated to more than one domain. Figure 3 presents a full overview of the different types of content and the types of strategies that were being employed.

Control group

In the majority of studies, the intervention under study was compared with usual care (24 studies). In nine of these studies the authors neglected to provide a description of the practices patients in the control group were exposed to. In ten studies the researchers attempted to blind the study participants by providing the patients in the control group with a programme matching for the amount of time and/or attention received by patients in the intervention arm. Types of strategies included unstructured conversations about neutral topics or health history, however, in some cased strategies were employed that were used in other studies as the intervention, such as supportive telephone calls after discharge discussing postoperative progress. In two studies a placebo-website was used on which a general information leaflet and contact information could be found. In four studies with a 3-arm RCT study design an attention control arm as well as a usual care arm were employed.

Types of outcome measures

The overall aim of the current review was to assess outcomes measuring return to preoperative levels of activity and participation. The included studies in this review considered more than 30 different outcomes fitting our predefined definition. We applied the following categorization:

1. Outcomes evaluating the duration until the resumption of normal activities (RTnA)
2. Outcomes evaluating the duration until return to work (RTW)
3. Questionnaires evaluating performance outcomes, including self-care and activities of daily living (ADL), disability, functional status, physical activity, recovery and social participation.

During data collection, we decided to extract all economic outcomes that were being reported as well.

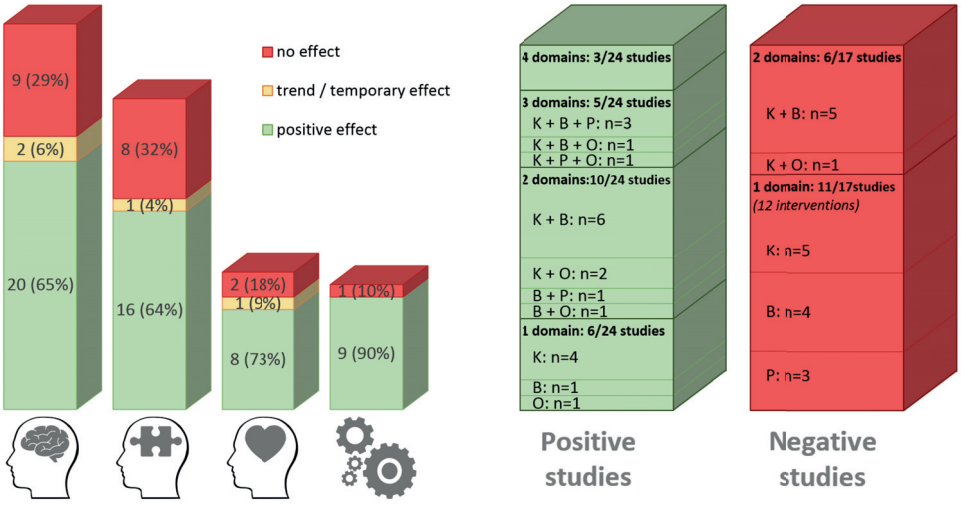
Length of follow-up

Length of follow-up varied between 2 weeks and 12 months (median 12 weeks (IQR 4-26)). There were two studies[31, 48] that published long-term follow-up data after 24 months and 36 months.

Figure 3. Intervention content

Author	 Knowledge increase	 Behaviour modification	 Psychosocial guidance	 Organization optimization	Overall outcome of study
Bouwsma[7]	x	x	x	x	+
Chunta[9]			x		–
Claus[10]	x	x			–
Darwood[11]	x				–
Dawes[12]	x			x	+
Dunbar[13]	x	x	x		+
Fortin[14]	x	x			+
Gillis[15]	x	x	x		+
Ginandes[16]			x		*
Heidarnia[17]	x	x			+
Huang[18]	x	x			–
Jacobson[19]		x			–
Jaensson[20]				x	+
Kahokehr[22]		x			–
Kesänen[23]	x	x			–
Klaiber[24]	x	x			–
Krouse[25]		x			–
Lewin[26]	x	x	x	x	+
Lin, 2009[27]	x			x	–
Lin, 2011[28]	x		x	x	+
Lookinland[29]	x				*
Louw[30, 31]	x				+
MacIntyre[32]			x		–
McGregor, 2004[33]	x				+
McGregor, 2011[34]	x	x			–
Meij[35]	x	x		x	+
Miro[37]		x			+
Moore, 1996[38]	x	x			+
Moore, 2001[39]	x	x			+
Mueller[40]	x				–
Parent[41]		x	x		+
Ridgeway[42] A	x				*
Ridgeway[42] B		x			
Rief[43]	x	x			+
Rolving[44]	x	x	x		+
Sheard[46]	x				-
Skolasky[47]		x		x	+
Utriyaprasit[49]	x	x			+
Vonk Noordegraaf[50]	x	x	x	x	+
Wang[51]	x			x	+
Yeh[52]	x				+
Zieren[53]	x				+

Domain	Type of strategies	Studies in which strategy was employed
Knowledge increase	Information about health condition / surgery	7, 13, 14, 18, 23, 27, 30, 33-35, 42, 43, 46, 50-53
	Practical information: (surgical) procedures / prepatory information	7, 14, 23, 24, 28-30, 33-35, 38, 39, 42, 44, 46, 49, 50, 52, 53
	Sensory information: expected symptoms and sensations	13, 15, 23, 26, 34, 38, 39, 42, 49
	Convalescence advice	40, 43, 50, 52, 53 7, 10, 11, 23, 30, 34, 35, 46
	Health and lifestyle information	12-14, 17, 18, 43, 52
Behavior modification	Goal-setting	41, 43, 44, 50 7, 10, 13, 17, 18, 26, 34, 35
	Cognitive motivation	17, 18, 23, 41, 47
	Guided Imagery / video modelling	19, 22, 25, 37, 43
	Relaxation techniques / breathing techniques	13, 22, 24, 26, 37
	Cognitive reappraisal	18, 34, 42
	Symptom management training	13, 14, 18, 38, 39, 43, 44, 49
	Coping techniques	13, 15, 17, 24, 26, 38, 39, 43, 44, 49
Psychosocial guidance	Peer support	41, 44, 50
	Emotional support	9, 15, 26
	Involvement of family members	13, 15, 26
	Mind-body interventions (healing touch, hypnosis)	16, 32
Organization optimization	Enhanced discharge procedure	7, 12, 27, 28
	Communication with healthcare providers after discharge	35, 51
	Case management	27, 28, 50, 51
	Monitoring recovery after discharge / detect early signs of difficulties	7, 20, 26-28, 35, 47, 51
	Transmural communication between healthcare providers	7, 50



Interpretation of outcomes

Twenty-four studies (58.5%) reported a significant effect in favour of the intervention group regarding at least one of the outcomes measures taken into consideration in this review (Table 1). There were no studies in which a significant effect in favour of the control group was found. Of the 17 remaining studies, three studies[16, 29, 42] demonstrated a trend towards a positive effect or a temporary significant effect. Of the 14 studies in which no positive effect on the relevant outcomes measures of this review were found, still 11 studies demonstrated a significant effect in favour of the intervention on other outcomes (e.g.: improved anxiety, improved fear, improved fatigue, improved knowledge, improved satisfaction, improved perceived control, shorter LOS, lower depression score, less hospital falls). Table 2 shows the overall results of the different types of reported outcomes.

Table 2. Results regarding the different types of outcomes measures

Outcome measure	Number of studies reporting this outcomes measure	Significant effect in favour of the intervention group	No significant difference
Return to normal activities	9	5	4
Return to work	12	6	6
Performance outcomes			
Self-care and ADL	5	3	2
Disability	8	2	6
Functional Status	23	8	15
Physical activity	7	6	1
Recovery	4	1	3
Social Participation	1	1	0
Economical outcomes	9	8	1

There were no studies in which a significant effect in favour of the control group was found.
An overview of all the different questionnaires that were used in each category can be found in S3 Table.
ADL = activities of daily living.

Return to normal activities

Table 3 presents the nine studies[10, 11, 15, 35, 37, 40-42, 53] that reported on return to normal activity (RTnA) as an outcomes measure. In only 2 studies[11, 35] RTnA was a primary outcome. Three studies[11, 35, 53] reported RTnA in duration until resumption of activity. Other outcomes included: activity scores (4 studies)[15, 37, 41, 42], percentage of patients with RTnA at a certain time during follow-up (1 study)[10], a self-reported activity level (1 study)[40] and an activity level

measured by an accelerometer (1 study)[35]. In this last study, participants of the trial selected eight activities from an item bank that were relevant to themselves, creating a personalised primary outcome measure.

Five of the nine studies reported a positive effect of the intervention on RTnA outcomes. Notably, four of these studies had a low intensity approach (patients were able to take up the content of the intervention on their own).

Return to work

Table 4 presents the twelve studies that reported on the resumption of work (RTW). In only two studies[7, 50] this was a primary outcome. Eight studies reported the number of sick leave days.[7, 11, 14, 22, 35, 44, 50, 53] Other RTW outcomes measures included: the percentage of patients with RTW at a certain time during follow-up (2 studies)[10, 13], an activity score (1 study)[15] and the subjective ability to work (1 study)[43].

RTW-data was often collected by means of a prospective calendar or diary (4 studies)[7, 11, 35, 50] or in a retrospective manner (3 studies)[14, 22, 53]. One study[44] used a government registry to analyse the number of sick leave data.

Performance outcomes

In total, 22 different instruments were used to assess some kind of performance outcome (supplementary file S3). Only five instruments were used three times or more. The instruments were grouped into six different categories: self-care and activities of daily living (ADL), disability, functional status, physical activity, recovery and social participation.

In the category ADL, the most frequent used instrument was the Barthel Index of Activities of Daily Living which was used in 3 (orthopaedic) studies.[18, 28, 51] The study by Wang *et al* studying the effectiveness of an Internet-based home care platform "We Chat" was the only study to demonstrate a positive effect on the Barthel Index, remarkably still notable 6 months after total hip arthroplasty, when one expects that patients in the control group should have recovered as well. Fortin *et al* and Lin *et al* also demonstrated positive effects on ADL, but the duration of follow-up in these studies was much shorter (respectively five and four weeks).

Table 3. Return to normal activity outcomes

Study	Outcome	Method	Type of activity	Intervention group	Control group	Overall outcome
Claus[10]	Percentage of patients with RTnA	single question at 2 months follow up	daily activities	29%	36%	NS
Darwood[11]	Time to RTnA (days)	activity diary during 6 weeks	daily activities	21 (14-31)	21 (14-31)	NS
			driving	7 (4-12.25)	7 (5-14)	NS
Gillis[15]	Activity score (calculation not provided)	single question at 4 weeks (and 8, 12, 24 weeks) follow-up (previous 24 hours)	daily activities	13.5	12.6	NS
			walking	10.3	8.8	p = 0.012
			climbing	5.7	4.3	NS
			lifting	5.9	4.7	p = 0.027
Meij[35]	Time to RTnA (days)	prospective monitoring during 6 months	8 personalized daily activities	21 (95% CI 17-25)	26 (95% CI 20-32)	HR = 1.38 95%CI: 1.09 – 1.73
Miro[37]	Activity score (0 – 100) (compared to activity level prior to surgery)	single question at postoperative day 15	home activities	HM: 44.54 ±13.68 * LM: 50.45 ± 10.14	HM: 37.0 ± 20.0 * LM: 38.63 ± 9.51	p < 0.06
			leisure activities	HM: 47.72 ± 20.78 * LM: 52.27 ± 17.08	HM: 11.81 ± 8.44 * LM: 30 ± 13.78	p < 0.001
Mueller[40]	Activity level (min/day)	retrospective question at 2 weeks, 6 weeks and 3 months follow up (previous month)	physical strenuous activity	46.5 min	42.5 min	NS
Parent[41]	Activity score (walking 0-14; stairs 0-7; general 0-100)	single question at 4 weeks follow up	daily activities	84.3 ± 12.8	76.1 ± 14.9	P < 0.05
			walking	12.5 ± 2.8	12.9 ± 1.8	NS
			climbing	6.0 ± 1.3	5.4 ± 1.2	P < 0.10
Ridgeway[42]	Activity score (calculation: # days - # tasks)	activity diary during 3 months	10 (unknown) household chores	intervention 1: 6.6 intervention 2: 6.9	attention-control: 5.9 no intervention: 4.6	NS (however: trend)
Zieren[53]	Time to RTnA (days)	retrospective questions at 3 months follow up (when)	daily activities	3 ± 2	5 ± 2	NS
			sexual activity	5 ± 4	10 ± 7	NS
			sport	7 ± 4	11 ± 5	significantly different (further data not provided)

* patients were divided into 2 groups according to their coping style: HM = high monitors (patients that look for relevant information) and LM = low monitor (patients that avoid information).
95% CI = 95% confidence interval, HR = hazard ratio, IQR = interquartile range, NS = no significant differences between study groups, RTnA = return to normal activities

Table 4. Return to work outcomes

Study	Outcome	Method	Intervention group	Control group	Overall outcome
Bouwsma[7]	Time to RTW (days)	sick leave calendar during 12 months	49 (IQR 27-76)	62 (IQR 42-85)	first 85 days: HR = 2.66 (CI 95%: 1.88 – 3.77) after 85 days: HR = 0.28 (CI 95%: 0.17 – 0.46)
Claus[10]	Percentage of patients with RTW	single question at 2 months follow-up	17%	21%	NS
Darwood[11]	Time to RTW (days)	activity diary during 6 weeks	14 (IQR 7.25-21)	14 (IQR 7.75-16.5)	NS
Dunbar[13]	Percentage of patients who missed work at 12 months follow-up	sick leave calendar during 12months (time to RTW not reported)	intervention 1: 7.8% intervention 2: 46%	56%	P = 0.02
Fortin[14]	Time to RTW (days)	retrospective question (when) at postoperative day 33	23.8	26.0	NS
Gillis[15]	Activity score (higher score means higher activity)	single question at 4 weeks (and 8, 12, 24 weeks) follow-up (previous 24 hours)	12.9	11.0	NS
Kahokehr[22]	Time to RTW (days)	retrospective question (when) at postoperative day 30	13 (IQR 6-20)	13 (IQR 5-27)	NS
Meij[35]	Time to RTW (days)	sick leave calendar during 6 months follow-up	18 (IQR 10-27)	19 (IQR 11-33)	HR = 1.31 95% CI: 1.01 – 1.70
Rief[43]	Ability to work (hours/week)	single question at 6 months	intervention: 25.40 (19.90 - 30.90) attention-control: 17.14 (10.45-23.80)	15.97 (10.50-21.43)	p = 0.041
Rolving[44]	Time to RTW (weeks)	government registry assessed after 12 months	31 (IQR 16-52)	39 (IQR 9-52)	NS
Vonk Noordegraaf[50]	Time to RTW (days)	sick leave calendar during 6 months	39 (IQR 20-67)	48 (IQR 21-69)	HR = 1.43 (1.003 – 2.040)
Zieren[53]	Time to RTW (days)	retrospective question (when) at 3 months follow-up	15 ± 7	18 ± 9	significantly different (further data not provided)

95% CI = 95% confidence interval, HR = hazard ratio, IQR = interquartile range, NS = no significant differences between study groups, RTW = return to work

The Oswestry Disability Index (ODI) is a disease-specific instrument and assesses the degree of disability in patients with low back pain. The ODI was the most frequently used questionnaire to assess disability and was used in five studies[23, 30, 34, 44, 47], all performed in patients undergoing spine surgery. Only in the study performed by Skolasky *et al*[47] a positive effect was demonstrated. In the study by Rolving *et al*[44], the intervention did not produce better outcomes than usual care, however, the reduction in disability was achieved much faster. In the remaining studies in which no group-effects were found in disability outcomes, it was noted that there were significant time-effects, meaning that there was a significant improvement in disability over time following surgery.

Return to functional status was assessed in 23 studies, only in 8 studies a significant effect favouring the intervention group was found. The most frequently used questionnaire was the short-form 12 or short-form 36 (SF12/SF36), which were used in 18 studies. In six studies, positive intervention effects were seen on the physical component scale. In 2 studies there was a trend or a temporary effect. In the remaining studies in which no group differences were seen, it was frequently noted that there was a significant effect in functional status from baseline in both groups, except for the studies of Sheard *et al*[46] and Klaiber *et al*[24] in which the patients had a worse score at respectively 2 weeks and 1 month after surgery compared to their baseline scores.

In total seven different studies[26, 35, 38-40, 43, 49] assessed physical activity, using five different instruments. In six of those studies a positive effect was found in favour of the intervention. In the study by van der Meij *et al*.[35] positive results were found using the physical function short form of the PROMIS questionnaire, but not on the International Physical Activity Questionnaire (IPAQ). However, in the study by Rief *et al*.[43] the IPAQ was able to detect differences in physical activity between groups.

Social participation was only assessed in one study[35] by using the PROMIS Ability to Participate in Social Roles and Activities short form. Patients exposed to personalized perioperative care by e-health scored higher on performing social roles than patients in the control group.

Economic outcomes

Table 5 presents the nine studies that reported on economic outcomes (separate publications: [8, 21, 36, 45]). Types of health care usage typically included: length of hospital stay, emergency visits, readmission costs and visits to healthcare providers after discharge. Only four studies[8, 13, 36, 45] included lost productivity costs. Two studies[8, 36] also included informal home help costs.

In total, seven studies[8, 12, 21, 26, 33, 36, 45] reported on the costs of the intervention applied, which varied between €19 (mobile app)[20] and €630 (cognitive education program with six 3-hour sessions)[45]. The median costs of the intervention were 45 € (IQR €185 – €275)

The majority of studies reported positive economic outcomes through lower health care costs[12, 21, 30, 33] as well as lower societal costs[8, 13]. In the study by Rolving *et al* total costs were neutral from a societal perspective, despite the extra costs related to the intervention of €1356 per person. Van der Meij *et al* reported that each day earlier resumption of daily activities was associated with €13 higher costs compared to the control group. At a willingness to pay €100/day, the probability of cost-effectiveness was 0.97.

Characteristics of successful interventions

The vast majority of interventions targeted knowledge or behaviour, or a combination of the two (37/41 studies). Of the 24 studies with an overall positive outcome, six studies (25%) targeted only one domain. In the 17 studies in which no effect was demonstrated, eleven studies (65%) targeted only one domain (figure 3).

None of the interventions that solely focused on psychosocial guidance were effective. On the contrary, when psychosocial guidance was part of a larger intervention targeting also other domains, the chance of the intervention being effective increased to 73%. Except for one study, all interventions that targeted the organization of care processes in combination with any domain, were effective. All interventions targeting three domain (6 studies) or all four domains (3 studies) demonstrated positive effects.

No differences in effectiveness were found between interventions with different levels of intensity (low, medium, high), nor between interventions that were timed differently (pre-operative, before admission, during hospitalization).

Table 5. Economic outcomes

Study	Type of economic evaluation	Costs of intervention per patient (in €)*	Productivity costs included	Length of follow-up	Overall outcome
Bouwsma[7] Bouwsma[8]	cost effectiveness analysis (societal perspective)	80	yes	12 months	The ICER for RTW was €56; each day earlier RTW in the intervention group was associated with cost savings of €56 compared with usual care. The probability of the intervention being cost-effective was 0.79 at a WTP of €0, which increased to 0.97 at a WTP of €76 per day earlier RTW. The difference in QALYs gained over 12 months between the groups was clinically irrelevant resulting in a low probability of cost-effectiveness for QALYs.
Dawes[12]	cost consequence analysis	473 (£415)	no	6 weeks	The intervention was associated with significantly lower total health care costs than routine care, mainly due to differences in costs of the postoperative length of stay (£4253 versus £4981, p = 0.000)
Dunbar[13]	healthcare usage	NA	yes	12 months	Patients in the control group called their providers more often than patients in the intervention group at 6 months ($p < 0.05$). At 12 months, the patients in the control group had more disability days ($p = 0.12$) than the intervention groups. *Data presented as frequencies and percentages and were not provided as costs.*
Jaensson[20] Dahlberg[21]	cost-minimization analysis	18.89	no	2 weeks	Healthcare costs were lower in the intervention group compared to the usual care group, resulting in a net saving of €4.77 per patient in favour of the intervention. The probability of the intervention being cost-effective was 71%. There was no effect on QALY.
Lewin[26]	cost consequence analysis	31 (£27.53)	no	6 months	Health service resource costs were similar at 6 months in both groups. Large, but no significant differences were seen for outpatient appointments (£302 in the intervention group versus £220 in the usual care group) and inpatient costs (£101 in the intervention group versus £230 in the usual care group). The probability of the intervention being cost-effective was 0.66 at a WTP of 0. This increased to a probability of 0.67 at a WTP of £30.000.

Table 5. Continued

Study	Type of economic evaluation	Costs of intervention per patient (in €)*	Productivity costs included	Length of follow-up	Overall outcome
Louw[30]	healthcare usage	NA	no	12 months	Overall costs of medical treatment were lower in the intervention group than in the usual care group due to fewer medical tests and treatments for their pain and dysfunction ($2678 versus $3135, p = 0.007).
McGregor, 2004[33]	healthcare usage	20 (£14.58)	no	3 months	The intervention led to a cost saving of £587 per patient, mainly through reduced hospital stay by 3 days (£2842 versus 3429, statistics not provided).
Meij[35] Meij[36]	cost effectiveness analysis (societal perspective)	45	yes	6 months	Total health care costs were €202 higher in the intervention group than the control group (not statistically significant). The ICER for return to normal activities was €13; each day of earlier resumption in the intervention group was associated with a cost of €13 compared to the usual care group. The probability of the intervention being cost-effective was 0.38 at a WTP of €0, which increased to a probability of 0.97 at a WTP of €100/day. The cost-effectiveness for QALYs was low at all values of WTP.
Rolving[44] Rolving[45]	cost effectiveness analysis (societal perspective)	1356	yes	12 months	Although there were extra costs related to the intervention in terms of production loss of €610, intervention costs of €630 and travel expenses of €116, the intervention group was cost neutral form a societal perspective. There was a 70% probability of the intervention being cost-effective at a WTP of €40,000 for an additional QALY. For an additional gain of 15 ODI points the probability was 90% at a threshold of €10,000.

* Currencies were being converted to Euros on February 2, 2019.
NA = not available, QALY = quality-adjusted life year; WTP = willingness to pay

Quality of the included studies

The risk of bias assessment of the included trials is represented in table 6 and figure 4. Twenty-two of the 41 studies (54%) used an adequate random sequence generation method, whereas 19 studies did employ an inadequate method or gave insufficient information about the sequence generation method. Allocation concealment was reached in 20 of the trials (49%), but it was not clearly reported in 19 studies (46%). In one study patients were asked to participate after randomization, and that study was therefore scored as having a high risk for selection bias. Blinding of patients and key personnel was the criterion scoring lowest, with only 10/41 studies being assessed as low risk of bias, in six of those studies efforts were being made to provide attention control to patients not receiving the intervention. Blinding of outcome assessment scored significantly better with 27/41 trials (66%) reporting using blinded raters or using only self-report measures. The majority of the studies (21/41, 51%) used an appropriate method for handling incomplete outcome data (i.e. intention-to-treat analyses), however, in eight studies the dropout rate was significantly high and often not equally balanced between study groups, or patients that did not use the intervention as intended were excluded from analyses. Only 12 studies could be checked for selective reporting because the trials were registered in a trial registration and/or the protocol of the study was published separately. Five studies were assessed of having a high risk of bias due to: significant selection bias (n=2), significant contamination between study groups (n=2) or inadequate statistical methods applied (n=1).

Only two studies (5%) met all the quality criteria. Thirteen studies met more than five criteria and were assessed as having a low risk of bias. Sixteen studies met three or four criteria and were assessed as having a moderate risk of bias. Twelve studies met less than three criteria and were assessed as having a high risk of bias.

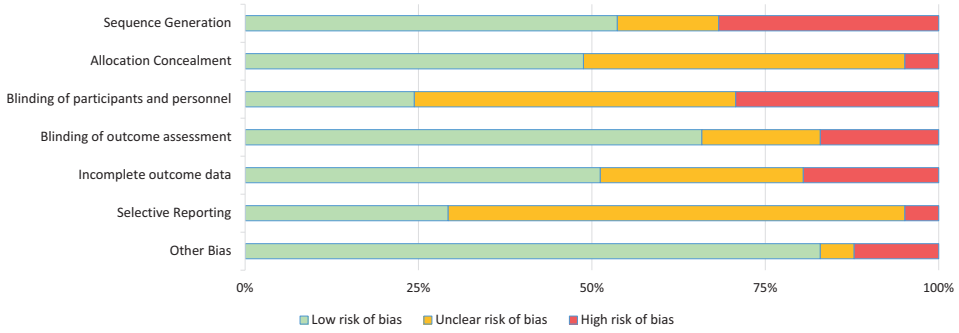


Figure 4. Risk of bias graph: review authors' judgement about each risk of bias item presented as percentages across all included studies

Table 6. Risk of bias summary: review authors' judgement about each risk of bias item for each included study

	Sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Bouwsma[7]	X	√	X	√	√	√	√
Chunta[9]	X	?	?	?	X	?	√
Claus[10]	X	?	√	√	X	?	√
Darwood[11]	X	?	X	√	√	?	√
Dawes[12]	√	√	X	√	√	X	X
Dunbar[13]	√	?	?	√	X	?	√
Fortin[14]	√	?	?	√	√	?	√
Gillis[15]	?	√	?	X	√	X	√
Ginandes[16]	√	√	?	√	√	?	√
Heidarnia[17]	X	?	?	√	?	?	X
Huang[18]	√	?	X	√	√	√	√
Jacobson[19]	√	√	?	√	X	?	√
Jaensson[20]	√	√	X	√	X	√	√
Kahokehr[22]	√	√	X	√	?	√	√
Kesänen[23]	√	√	√	√	?	√	√
Klaiber[24]	X	?	√	?	√	√	√
Krouse[25]	?	?	X	√	√	?	√
Lewin[26]	X	?	√	√	?	?	?
Lin, 2009[27]	X	X	?	X	?	?	√
Lin, 2011[28]	X	?	?	X	√	?	X
Lookinland[29]	√	√	?	√	?	?	√
Louw[30]	√	√	√	√	√	?	√
MacIntyre[32]	√	√	X	?	X	?	X
McGregor, 2004[33]	?	?	?	√	?	?	?
McGregor, 2011[34]	√	√	X	√	√	√	√
Meij[35]	√	√	√	√	√	√	√
Miro[37]	√	?	?	?	√	?	√
Moore, 1996[38]	X	?	√	X	?	?	X

Table 6. Continued

	Sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Moore, 2001[39]	√	√	?	?	√	?	√
Mueller[40]	√	√	√	√	?	?	√
Parent[41]	√	√	X	?	?	?	√
Ridgeway[42]	?	√	√	X	√	?	√
Rief[43]	√	√	?	√	√	√	√
Rolving[44]	√	?	X	√	√	√	√
Sheard[46]	?	X	?	√	X	?	√
Skolasky[47]	X	?	?	√	√	√	√
Utriyaprasit[49]	√	√	?	?	√	?	√
Vonk Noordegraaf[50]	√	√	√	√	√	√	√
Wang[51]	X	?	X	X	X	?	√
Yeh[52]	X	?	?	X	?	?	√
Zieren[53]	?	?	?	√	?	?	√

DISCUSSION

Main findings

The intent of this literature review was to examine the current literature in order to identify characteristics of perioperative strategies that enhance recovery after discharge. We included 41 studies with a large diversity regarding to the type of patients, the interventions as well as the outcome being measured. Twenty-four studies reported at least a positive effect on return to preoperative levels of activity and participation. There were no considerable differences in the effectiveness between the different types of interventions, however, a multimodal approach was more likely to positively impact functional outcomes compared to interventions focusing on a single domain.

Return to preoperative levels of activity and participation was conceptualized in many different outcome measures including return to normal activity, return to work and several performance outcomes. Only a minority of studies reported one of these outcomes as the

primary outcome (four studies reported RTnA or RTW as a primary outcome, six studies reported disability as a primary outcome and two studies reported general health status as a primary outcome). In about half of the cases, studies had a positive impact on RTnA or RTW. Instruments measuring performance outcomes were less responsive, with the exception of instruments measuring physical activity, which demonstrated positive results in six out of seven studies.

Nine studies also evaluated economic outcomes. Remarkably, in all, except one, positive effects were noted due to lower healthcare costs and/or lower societal costs in favour of the intervention.

Comparison with other studies

There are numerous meta-analyses available on the effect of patient education in the surgical field and it has been acknowledged that pre-operative education can reduce the length of stay, fear and anxiety, pain and can increase psychological well-being and satisfaction.[54-59] In the latest systematic review on educational interventions performed by Ronco *et al*[59], 19 additional studies were included besides the 32 studies that were identified in an earlier performed systematic review.[57] Unfortunately, from these 51 studies, it still remained unclear which combination of educational methods, content, timing and duration positively influences patient outcomes. In addition, only two studies reported on functional outcomes after discharge, these two studies were included in the current review.

Another important systematic review was performed by Powell *et al* who evaluated the effect of psychological preparation on postoperative outcomes for adults undergoing surgery under general anaesthesia in 115 studies with 10,302 patients.[60] The authors concluded that the evidence suggested that psychological preparation may be beneficial for the outcomes postoperative pain, behavioural recovery, negative affect and length of stay, and is unlikely to be harmful, however, the strength of evidence is insufficient to reach firm conclusions on the role of psychological preparation for surgery. Fourteen of the included studies also described behavioural recovery outcomes, of which 5 were also included in the current review. The remaining studies either focused on exercise prior to surgery, or the duration of follow-up was too short to be eligible for the current systematic review.

A third relevant systematic review recently performed is the one by van der Meij *et al* on the effect of perioperative eHealth interventions in the postoperative course.[61] Studies included in this review focused on replacing or complementing perioperative usual care with some form of care via eHealth, mostly following cardiac or orthopaedic surgery. Examples of such intervention included educational or supportive websites, telemonitoring, telerehabilitation or teleconsultation. The conclusion from the authors was that in the majority of studies

eHealth led to similar or improved clinical outcomes compared to usual (face-to-face) perioperative care. Again, there was not much overlap between this systematic review and the current one: only one study was included in both.

Strengths and limitations

To the best of our knowledge there are no previous reviews evaluating perioperative interventions regarding long term recovery outcomes. Another strength of our review is that we ensured methodological quality by following the Prisma guidelines for systematic reviews. We conducted a very broad literature search after carefully evaluating the different type of search terms which could be possibly used.

Our study also has limitations. While every effort was made to include all relevant articles, it is possible that articles were missed due to the terms employed in the search strategy. For example, a potential limitation might be the fact that we did not used the term "quality of life" in our search. However, this term yielded another 2285 extra titles in Medline alone, and after screening the first 500 hits, no additional studies were found that were not yet identified through cross-referencing. However, we cannot exclude that we missed some studies because of this procedure.

Secondly, this systematic review included three studies[7, 35, 50] that were conducted and performed by our own research group. Although we tried to achieve objective reporting, it is possible that some risk of bias was introduced because we are too involved in our own work.

Thirdly, due to the heterogeneity of the populations, interventions and outcomes measures, it was not possible to conduct a meta-analysis and therefore, it became very complex to generalize conclusions on the basis of the literature reviewed. Finally, the overall quality of the studies was moderate, therefore the findings of this review need to be interpreted with caution.

Implications for practice and research

Due to technological advances and economic incentives there has been a transfer of postoperative care away from the hospital setting towards the patient's own environment.[62] These considerable changes in the surgical field require changes in perioperative management, facilitating patients in their new role of self-management including their responsibility for self-monitoring and evaluation of signs and symptoms. In this perspective, the need for well-designed perioperative intervention that have the potential to facilitate return to function becomes visible.

Now we established that perioperative interventions can facilitate return to preoperative levels of activity and participation, more research is needed to explore the working mechanisms behind these effective interventions. Ideally, interventions should target knowledge increase, behaviour modification, psychosocial guidance as well as the optimization of care processes. In addition, in these future studies effectiveness should be evaluated on outcomes specifically measuring return to preoperative levels of activity and participation. Return to normal activities or the objective assessment of physical activity is more usable than generic instruments measuring performance outcomes such as disability or health status.

CONCLUSIONS

Based on this systematic review we conclude that perioperative interventions have the potential to facilitate return to preoperative levels of activity and participation. However, due to the substantial heterogeneity in perioperative interventions there is insufficient data to identify an optimum programme. Notwithstanding, a multimodal approach is likely to have better impact on functional outcomes compared to single modality.

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Supplementary file S1. Search strategy

#	Query	Results
Search strategy in PubMed (2018 September 26th)		
#10	#3 AND #6 AND #9	**3789**
#9	#7 OR #8	**1157038**
#8	"counseling"[tw] OR pamphlet*[tw] OR booklet*[tw] OR handout[tw] OR selfcare[tw] OR self care[tw] OR self caring[tw] OR selfmanag*[tw] OR self manag*[tw] OR "Behavior therapy"[tw] OR "Behaviour therapy"[tw] OR "Behavior therapies"[tw] OR "Behaviour therapies"[tw] OR "Conditioning therapy"[tw] OR "Conditioning therapies"[tw] OR Behavior Modification*[tw] OR Behaviour Modification*[tw] OR Cognitive therapy[tw] OR Cognitive therapies[tw] OR Psychotherap*[tw] OR psychoeducation*[tw] OR ehealth[tw] OR e-health[tw] OR web portal[tw] OR internet[tw] OR education intervention*[tw] OR educational intervention*[tw] OR education program*[tw] OR educational program*[tw] OR (("prior to surgery"[tw] OR "before surgery"[tw] OR "preoperative"[tw] OR "pre-operative"[tw] OR "pre-surgery"[tw] OR "presurgical"[tw] OR preadmission*[tw] OR pre-admission*[tw]) AND (education*[tw] OR "advice"[tw] OR "guidance"[tw] OR recommendation*[tw] OR instruction*[tw])) OR mind body[tw] OR mind-body[tw] OR breathing exercise*[tw] OR respiratory muscle training[tw] OR meditation[tw] OR hypnosis[tw] OR yoga[tw] OR relaxation therapy[tw] OR relaxation technique*[tw] OR relaxation technic*[tw] OR music therapy[tw]	**444285**
#7	"Health Education"[Mesh] OR "Patient Education Handout" [Publication Type] OR "Patient Participation"[Mesh] OR "Self Care"[Mesh] OR "Health Promotion"[Mesh] OR "Counseling"[Mesh] OR "Computer Assisted Instruction"[Mesh] OR "Information Dissemination"[Mesh] OR "Instructional Films and Videos" [Publication Type] OR "Pamphlets"[Mesh] OR "Motivation"[Mesh] OR "education"[subheading] OR "audiovisual aids"[Mesh] OR "Self-Help Groups"[Mesh] OR "Imagery (Psychotherapy)"[Mesh] OR "Behavior Therapy"[Mesh] OR "Occupational Therapy"[Mesh] OR "Internet"[Mesh] OR "telemedicine"[Mesh] OR "Mind-Body Therapies"[Mesh]	**964900**
#6	#4 OR #5	**329589**
#5	"Return to Work"[tw] OR "Work disability"[tw] OR "Work incapacity"[tw] OR "Work incapability"[tw] OR "Work inhibition"[tw] OR "Working incapacity"[tw] OR "medical leave"[tw] OR "Sick leave"[tw] OR "disability leave"[tw] OR "work absence"[tw] OR "disability absence"[tw] OR "Recovery of function"[tw] OR "Functional recovery"[tw] OR Absente*[tw] OR Convalescen*[tw] OR Sick day*[tw] OR Illness day*[tw] OR (Evaluation*[tw] AND (disability[tw] OR work capacity[tw])) OR (Recovery[ti] AND function*[ti]) OR "back to work"[tw] OR "work ability"[tw] OR "job resumption"[tw] OR "work resumption"[tw] OR employment outcome*[tw] OR "postoperative recovery"[tw] OR "post-operative recovery"[tw] OR "postoperative rehabilitation"[tw] OR "post-operative rehabilitation"[tw] OR postoperative outcome*[tw] OR post-operative outcome*[tw] OR "enhanced recovery"[tw] OR recovery outcome*[tw] OR "activity ability"[tw] OR functional outcome*[tw] OR functional activity[tw] OR functional activities[tw] OR functional status[tw]	**244307**
#4	"Absenteeism"[Mesh] OR "Convalescence"[Mesh] OR "Recovery of Function"[Mesh] OR "Sick Leave"[Mesh] OR "Disability Evaluation"[Mesh] OR "Work Capacity Evaluation"[Mesh] OR "Rehabilitation, Vocational"[Mesh] OR "Return to Work"[Mesh] OR "Sickness Impact Profile"[Mesh] OR "Activities of Daily Living"[Mesh] OR "Physical Fitness"[Mesh]	**198300**
#3	#1 OR #2	**4102922**
#2	surgery[tw] OR surgical[tw]	**2797319**
#1	"Surgical Procedures, Operative"[Mesh] OR "surgery" [Subheading] OR "perioperative care"[Mesh] OR "perioperative Period"[Mesh]	**3515159**

Supplementary file S1. Continued

#	Query	Results
Search strategy in Embase.com (2018 September 26th)		
#10	#3 AND #6 AND #9	**6834**
#9	#7 OR #8	**1056348**
#8	'counseling':de,ab,ti OR pamphlet*:de,ab,ti OR booklet*:de,ab,ti OR handout:de,ab,ti OR selfcare:de,ab,ti OR 'self care':de,ab,ti OR 'self caring':de,ab,ti OR selfmanag*:de,ab,ti OR ((self NEXT/1 manag*):de,ab,ti) OR 'behavior therapy':de,ab,ti OR 'behaviour therapy':de,ab,ti OR 'behavior therapies':de,ab,ti OR 'behaviour therapies':de,ab,ti OR 'conditioning therapy':de,ab,ti OR 'conditioning therapies':de,ab,ti OR ((behavior NEXT/1 modification*):de,ab,ti) OR ((behaviour NEXT/1 modification*):de,ab,ti) OR 'cognitive therapy':de,ab,ti OR 'cognitive therapies':de,ab,ti OR psychotherap*:de,ab,ti OR psychoeducation*:de,ab,ti OR ehealth:de,ab,ti OR 'e-health':de,ab,ti OR 'web portal':de,ab,ti OR internet:de,ab,ti OR ((education NEXT/1 intervention*):de,ab,ti) OR ((educational NEXT/1 intervention*):de,ab,ti) OR ((education NEXT/1 program*):de,ab,ti) OR ((educational NEXT/1 program*):de,ab,ti) OR (('prior to surgery':de,ab,ti OR 'before surgery':de,ab,ti OR 'preoperative':de,ab,ti OR 'pre-operative':de,ab,ti OR 'pre-surgery':de,ab,ti OR 'presurgical':de,ab,ti OR preadmission*:de,ab,ti OR ((pre NEXT/1 admission*):de,ab,ti)) AND (education*:de,ab,ti OR 'advice':de,ab,ti OR 'guidance':de,ab,ti OR recommendation*:de,ab,ti OR instruction*:de,ab,ti)) OR 'mind body':de,ab,ti OR 'mind-body':de,ab,ti OR ((breathing NEXT/1 exercise*):de,ab,ti) OR 'respiratory muscle training':de,ab,ti OR meditation:de,ab,ti OR hypnosis:de,ab,ti OR yoga:de,ab,ti OR 'relaxation therapy':de,ab,ti OR ((relaxation NEXT/1 technique*):de,ab,ti) OR ((relaxation NEXT/1 technic*):de,ab,ti) OR 'music therapy':de,ab,ti	**665639**
#7	'health education'/exp OR 'patient participation'/exp OR 'self care'/exp OR 'health promotion'/exp OR 'counseling'/exp OR 'information dissemination'/exp OR 'motivation'/exp OR 'audiovisual aid'/exp OR 'self help'/exp OR 'behavior therapy'/exp OR 'occupational therapy education'/exp OR 'occupational therapy'/exp OR 'internet'/exp OR 'telemedicine'/exp	**762277**
#6	#4 OR #5	**392219**
#5	'return to work':de,ab,ti OR 'work disability':de,ab,ti OR 'work incapacity':de,ab,ti OR 'work incapability':de,ab,ti OR 'work inhibition':de,ab,ti OR 'working incapacity':de,ab,ti OR 'medical leave':de,ab,ti OR 'sick leave':de,ab,ti OR 'disability leave':de,ab,ti OR 'work absence':de,ab,ti OR 'disability absence':de,ab,ti OR 'recovery of function':de,ab,ti OR 'functional recovery':de,ab,ti OR absente*:de,ab,ti OR convalescen*:de,ab,ti OR ((sick NEXT/1 day*):de,ab,ti) OR ((illness NEXT/1 day*):de,ab,ti) OR (evaluation*:de,ab,ti AND (disability:de,ab,ti OR ((work NEXT/1 capacity):de,ab,ti))) OR (recovery:ti AND function*:ti) OR 'back to work':de,ab,ti OR 'work ability':de,ab,ti OR 'job resumption':de,ab,ti OR 'work resumption':de,ab,ti OR ((employment NEXT/1 outcome*):de,ab,ti) OR 'postoperative recovery':de,ab,ti OR 'post-operative recovery':de,ab,ti OR 'postoperative rehabilitation':de,ab,ti OR 'post-operative rehabilitation':de,ab,ti OR ((postoperative NEXT/1 outcome*):de,ab,ti) OR (('post operative' NEXT/1 outcome*):de,ab,ti) OR 'enhanced recovery':de,ab,ti OR ((recovery NEXT/1 outcome*):de,ab,ti) OR 'activity ability':de,ab,ti OR ((functional NEXT/1 outcome*):de,ab,ti) OR 'functional activity':de,ab,ti OR 'functional activities':de,ab,ti OR 'functional status':de,ab,ti	**303242**
#4	'absenteeism'/exp OR 'convalescence'/exp OR 'medical leave'/exp OR 'work capacity'/exp OR 'vocational rehabilitation'/exp OR 'return to work'/exp OR 'sickness impact profile'/exp OR 'daily life activity'/exp OR 'adl disability'/exp	**174674**
#3	#1 OR #2	**4893897**
#2	surgery:de,ab,ti OR 'surgery':de,ab,ti	**2266349**
#1	'surgery'/exp OR 'perioperative period'/exp	**4541278**

Supplementary file S1. Continued

#	Query	Results
Search strategy in CINAHL (via EBSCO ; 2018 September 26th)		
S11	S3 AND S7 AND S10	**1,732**
S10	S8 OR S9	**489,351**
S9	TI (("counseling" OR pamphlet* OR booklet* OR handout OR selfcare OR "self care" OR "self caring" OR selfmanag* OR "self manag*" OR "Behavior therapy" OR "Behaviour therapy" OR "Behavior therapies" OR "Behaviour therapies" OR "Conditioning therapy" OR "Conditioning therapies" OR "Behavior Modification*" OR "Behaviour Modification*" OR "Cognitive therapy" OR "Cognitive therapies" OR Psychotherap* OR psychoeducation* OR ehealth OR "e-health" OR "web portal" OR internet OR "education intervention*" OR "educational intervention*" OR "education program*" OR "educational program*" OR (("prior to surgery" OR "before surgery" OR "preoperative" OR "pre-operative" OR "pre-surgery" OR "presurgical" OR preadmission* OR pre-admission*) AND (education* OR "advice" OR "guidance" OR recommendation* OR instruction*)) OR "mind body" OR "mind-body" OR "breathing exercise*" OR "respiratory muscle training" OR meditation OR hypnosis OR yoga OR "relaxation therapy" OR "relaxation technique*" OR "relaxation technic*" OR "music therapy")) OR AB (("counseling" OR pamphlet* OR booklet* OR handout OR selfcare OR "self care" OR "self caring" OR selfmanag* OR "self manag*" OR "Behavior therapy" OR "Behaviour therapy" OR "Behavior therapies" OR "Behaviour therapies" OR "Conditioning therapy" OR "Conditioning therapies" OR "Behavior Modification*" OR "Behaviour Modification*" OR "Cognitive therapy" OR "Cognitive therapies" OR Psychotherap* OR psychoeducation* OR ehealth OR "e-health" OR "web portal" OR internet OR "education intervention*" OR "educational intervention*" OR "education program*" OR "educational program*" OR (("prior to surgery" OR "before surgery" OR "preoperative" OR "pre-operative" OR "pre-surgery" OR "presurgical" OR preadmission* OR pre-admission*) AND (education* OR "advice" OR "guidance" OR recommendation* OR instruction*)) OR "mind body" OR "mind-body" OR "breathing exercise*" OR "respiratory muscle training" OR meditation OR hypnosis OR yoga OR "relaxation therapy" OR "relaxation technique*" OR "relaxation technic*" OR "music therapy"))	**95,136**
S8	(MH "Health Education+") OR (MH "Patient Education+") OR (MH "Consumer Participation") OR (MH "Self Care+") OR (MH "Health Promotion+") OR (MH "Counseling+") OR (MH "Computer Assisted Instruction") OR (MH "Selective Dissemination of Information") OR (MH "Pamphlets") OR (MH "Motivation+") OR (MH "Audiovisuals+") OR (MH "Support Groups+") OR (MH "Behavior Therapy+") OR (MH "Occupational Therapy+") OR (MH "Internet+") OR (MH "Telehealth+") OR (MH "Mind Body Techniques+")	**446,450**
S7	S4 OR S5 OR S6	**111,470**
S6	AB ("Return to Work" OR "Work disability" OR "Work incapacity" OR "Work incapability" OR "Work inhibition" OR "Working incapacity" OR "medical leave" OR "Sick leave" OR "disability leave" OR "work absence" OR "disability absence" OR "Recovery of function" OR "Functional recovery" OR Absente* OR Convalescen* OR "Sick day*" OR "Illness day*" OR (Evaluation* AND (disability OR "work capacity")) OR "back to work" OR "work ability" OR "job resumption" OR "work resumption" OR "employment outcome*" OR "postoperative recovery" OR "post-operative recovery" OR "postoperative rehabilitation" OR "post-operative rehabilitation" OR "postoperative outcome*" OR "post-operative outcome*" OR "enhanced recovery" OR "recovery outcome*" OR "activity ability" OR "functional outcome*" OR "functional activity" OR "functional activities" OR "functional status")	**27,828**

Supplementary file S1. Continued

#	Query	Results
S5	TI ("Return to Work" OR "Work disability" OR "Work incapacity" OR "Work incapability" OR "Work inhibition" OR "Working incapacity" OR "medical leave" OR "Sick leave" OR "disability leave" OR "work absence" OR "disability absence" OR "Recovery of function" OR "Functional recovery" OR Absente* OR Convalescen* OR "Sick day*" OR "Illness day*" OR (Evaluation* AND (disability OR "work capacity")) OR "back to work" OR "work ability" OR "job resumption" OR "work resumption" OR "employment outcome*" OR "postoperative recovery" OR "post-operative recovery" OR "postoperative rehabilitation" OR "post-operative rehabilitation" OR "postoperative outcome*" OR "post-operative outcome*" OR "enhanced recovery" OR "recovery outcome*" OR "activity ability" OR "functional outcome*" OR "functional activity" OR "functional activities" OR "functional status" OR (Recovery AND function*))	**8,677**
S4	(MH "Absenteeism") OR (MH "Sick Leave") OR (MH "Recovery") OR (MH "Disability Evaluation+") OR (MH "Work Capacity Evaluation") OR (MH "Rehabilitation, Vocational+") OR (MH "Job Re-Entry") OR (MH "Sickness Impact Profile") OR (MH "Activities of Daily Living+") OR (MH "Physical Fitness+")	**89,927**
S3	S1 OR S2	**380,908**
S2	TI ((surgery OR surgical)) OR AB ((surgery OR surgical))	**154,392**
S1	(MH "Surgery, Operative+") OR (MH "Perioperative Care+")	**311,961**
Search strategy in PsycINFO (via EBSCO ; 2018 September 26th)		
S11	S3 AND S7 AND S10	**266**
S10	S8 OR S9	**532,332**
S9	TI (("counseling" OR pamphlet* OR booklet* OR handout OR selfcare OR "self care" OR "self caring" OR selfmanag* OR "self manag*" OR "Behavior therapy" OR "Behaviour therapy" OR "Behavior therapies" OR "Behaviour therapies" OR "Conditioning therapy" OR "Conditioning therapies" OR "Behavior Modification*" OR "Behaviour Modification*" OR "Cognitive therapy" OR "Cognitive therapies" OR Psychotherap* OR psychoeducation* OR ehealth OR "e-health" OR "web portal" OR internet OR "education intervention*" OR "educational intervention*" OR "education program*" OR "educational program*" OR (("prior to surgery" OR "before surgery" OR "preoperative" OR "pre-operative" OR "pre-surgery" OR "presurgical" OR preadmission* OR pre-admission*) AND (education* OR "advice" OR "guidance" OR recommendation* OR instruction*)) OR "mind body" OR "mind-body" OR "breathing exercise*" OR "respiratory muscle training" OR meditation OR hypnosis OR yoga OR "relaxation therapy" OR "relaxation technique*" OR "relaxation technic*" OR "music therapy")) OR AB (("counseling" OR pamphlet* OR booklet* OR handout OR selfcare OR "self care" OR "self caring" OR selfmanag* OR "self manag*" OR "Behavior therapy" OR "Behaviour therapy" OR "Behavior therapies" OR "Behaviour therapies" OR "Conditioning therapy" OR "Conditioning therapies" OR "Behavior Modification*" OR "Behaviour Modification*" OR "Cognitive therapy" OR "Cognitive therapies" OR Psychotherap* OR psychoeducation* OR ehealth OR "e-health" OR "web portal" OR internet OR "education intervention*" OR "educational intervention*" OR "education program*" OR "educational program*" OR (("prior to surgery" OR "before surgery" OR "preoperative" OR "pre-operative" OR "pre-surgery" OR "presurgical" OR preadmission* OR pre-admission*) AND (education* OR "advice" OR "guidance" OR recommendation* OR instruction*)) OR "mind body" OR "mind-body" OR "breathing exercise*" OR "respiratory muscle training" OR meditation OR hypnosis OR yoga OR "relaxation therapy" OR "relaxation technique*" OR "relaxation technic*" OR "music therapy"))	**294,252**

Supplementary file S1. Continued

#	Query	Results
S8	((((((((((((((((((((DE "Health Education") OR (DE "Client Education")) OR (DE "Client Participation")) OR (DE "Self Care Skills")) OR (DE "Health Promotion")) OR (DE "Counseling" OR DE "Community Counseling" OR DE "Cross Cultural Counseling" OR DE "Educational Counseling" OR DE "Genetic Counseling" OR DE "Gerontological Counseling" OR DE "Group Counseling" OR DE "Marriage Counseling" OR DE "Microcounseling" OR DE "Multicultural Counseling" OR DE "Occupational Guidance" OR DE "Pastoral Counseling" OR DE "Peer Counseling" OR DE "Premarital Counseling" OR DE "Psychotherapeutic Counseling" OR DE "Rehabilitation Counseling" OR DE "School Counseling")) OR (DE "Computer Assisted Instruction" OR DE "Computer Assisted Language Learning" OR DE "Intelligent Tutoring Systems")) OR (DE "Information Dissemination")) OR (DE "Instructional Media" OR DE "Advance Organizers" OR DE "Educational Audiovisual Aids" OR DE "Reading Materials" OR DE "Teaching Machines" OR DE "Textbooks")) OR (DE "Motivation" OR DE "Achievement Motivation" OR DE "Affiliation Motivation" OR DE "Animal Motivation" OR DE "Drug Seeking" OR DE "Educational Incentives" OR DE "Employee Motivation" OR DE "Extrinsic Motivation" OR DE "Fear of Success" OR DE "Hunger" OR DE "Incentives" OR DE "Intrinsic Motivation" OR DE "Monetary Incentives" OR DE "Procrastination" OR DE "Self Expansion" OR DE "Sex Drive" OR DE "Temptation" OR DE "Thirst" OR DE "Achievement Motivation" OR DE "Academic Achievement Motivation" OR DE "Incentives" OR DE "Educational Incentives" OR DE "Monetary Incentives")) OR (DE "Audiovisual Instruction" OR DE "Televised Instruction" OR DE "Videotape Instruction")) OR (DE "Educational Audiovisual Aids")) OR (DE "Self Help Techniques" OR DE "Self Management")) OR (DE "Behavior Therapy" OR DE "Aversion Therapy" OR DE "Conversion Therapy" OR DE "Dialectical Behavior Therapy" OR DE "Exposure Therapy" OR DE "Implosive Therapy" OR DE "Reciprocal Inhibition Therapy" OR DE "Response Cost" OR DE "Systematic Desensitization Therapy" OR DE "Aversion Therapy" OR DE "Covert Sensitization" OR DE "Exposure Therapy" OR DE "Implosive Therapy" OR DE "Systematic Desensitization Therapy")) OR (DE "Cognitive Behavior Therapy" OR DE "Acceptance and Commitment Therapy")) OR (DE "Cognitive Therapy")) OR (DE "Occupational Therapy")) OR (DE "Internet")) OR (DE "Telemedicine")) OR (DE "Mind Body Therapy" OR DE "Mindfulness")	**330,813**
S7	S4 OR S5 OR S6	**74,862**
S6	AB ("Return to Work" OR "Work disability" OR "Work incapacity" OR "Work incapability" OR "Work inhibition" OR "Working incapacity" OR "medical leave" OR "Sick leave" OR "disability leave" OR "work absence" OR "disability absence" OR "Recovery of function" OR "Functional recovery" OR Absente* OR Convalescen* OR "Sick day*" OR "Illness day*" OR (Evaluation* AND (disability OR "work capacity")) OR "back to work" OR "work ability" OR "job resumption" OR "work resumption" OR "employment outcome*" OR "postoperative recovery" OR "post-operative recovery" OR "postoperative rehabilitation" OR "post-operative rehabilitation" OR "postoperative outcome*" OR "post-operative outcome*" OR "enhanced recovery" OR "recovery outcome*" OR "activity ability" OR "functional outcome*" OR "functional activity" OR "functional activities" OR "functional status")	**29,645**
S5	TI ("Return to Work" OR "Work disability" OR "Work incapacity" OR "Work incapability" OR "Work inhibition" OR "Working incapacity" OR "medical leave" OR "Sick leave" OR "disability leave" OR "work absence" OR "disability absence" OR "Recovery of function" OR "Functional recovery" OR Absente* OR Convalescen* OR "Sick day*" OR "Illness day*" OR (Evaluation* AND (disability OR "work capacity")) OR "back to work" OR "work ability" OR "job resumption" OR "work resumption" OR "employment outcome*" OR "postoperative recovery" OR "post-operative recovery" OR "postoperative rehabilitation" OR "post-operative rehabilitation" OR "postoperative outcome*" OR "post-operative outcome*" OR "enhanced recovery" OR "recovery outcome*" OR "activity ability" OR "functional outcome*" OR "functional activity" OR "functional activities" OR "functional status" OR (Recovery AND function*))	**6,885**

Supplementary file S1. Continued

#	Query	Results
S4	(((((((DE "Employee Absenteeism")) OR (DE "Employee Benefits" OR DE "Bonuses" OR DE "Employee Assistance Programs" OR DE "Employee Health Insurance" OR DE "Employee Leave Benefits" OR DE "Employee Pension Plans" OR DE "Workers' Compensation Insurance" OR DE "Disability Evaluation")) OR (DE "Employee Engagement")) OR (DE "Employee Productivity")) OR (DE "Vocational Rehabilitation")) OR (DE "Reemployment")) OR (DE "Activities of Daily Living")) OR (DE "Physical Fitness")	**49,725**
S3	S1 OR S2	**53,852**
S2	TI ((surgery OR surgical)) OR AB ((surgery OR surgical))	**38,191**
S1	DE "Surgery" OR DE "Amputation" OR DE "Bariatric Surgery" OR DE "Circumcision" OR DE "Cochlear Implants" OR DE "Colostomy" OR DE "Dental Surgery" OR DE "Endocrine Gland Surgery" OR DE "Heart Surgery" OR DE "Hysterectomy" OR DE "Induced Abortion" OR DE "Neurosurgery" OR DE "Organ Transplantation" OR DE "Plastic Surgery" OR DE "Sex Change" OR DE "Stereotaxic Techniques" OR DE "Vasectomy"	**30,132**
Search strategy in The Cochrane Library (2018 September 26th)		
#6	#1 and #4 and #5	**497**
#5	("counseling" or pamphlet* or booklet* or handout or selfcare or "self care" or "self caring" or selfmanag* or "self manag*" or "Behavior therapy" or "Behaviour therapy" or "Behavior therapies" or "Behaviour therapies" or "Conditioning therapy" or "Conditioning therapies" or "Behavior Modification*" or "Behaviour Modification*" or "Cognitive therapy" or "Cognitive therapies" or Psychotherap* or psychoeducation* or ehealth or "e-health" or "web portal" or internet or "education intervention*" or "educational intervention*" or "education program*" or "educational program*" or (("prior to surgery" or "before surgery" or "preoperative" or "pre-operative" or "pre-surgery" or "presurgical" or preadmission* or pre-admission*) and (education* or "advice" or "guidance" or recommendation* or instruction*)) or "mind body" or "mind-body" or "breathing exercise*" or "respiratory muscle training" or meditation or hypnosis or yoga or "relaxation therapy" or "relaxation technique*" or "relaxation technic*" or "music therapy"):ti,ab,kw	**68587**
#4	#2 or #3	**27399**
#3	(Recovery and function*):ti	**1060**
#2	("Return to Work" or "Work disability" or "Work incapacity" or "Work incapability" or "Work inhibition" or "Working incapacity" or "medical leave" or "Sick leave" or "disability leave" or "work absence" or "disability absence" or "Recovery of function" or "Functional recovery" or Absente* or Convalescen* or "Sick day*" or "Illness day*" or (Evaluation* and (disability or "work capacity")) or "back to work" or "work ability" or "job resumption" or "work resumption" or "employment outcome*" or "postoperative recovery" or "post-operative recovery" or "postoperative rehabilitation" or "post-operative rehabilitation" or "postoperative outcome*" or "post-operative outcome*" or "enhanced recovery" or "recovery outcome*" or "activity ability" or "functional outcome*" or "functional activity" or "functional activities" or "functional status"):ti,ab,kw	**26894**
#1	(surgery or surgical):ti,ab,kw	**173682**

Supplementary file S2. Eligible studies not yet published

Author	Patients	Intervention	Control group	Relevant outcome measures for this review	Length of follow-up
Birch[1]	Total knee arthroplasty *in high pain catastrophizing patients*	Cognitive behavioural patient education focusing on pain behaviour and pain coping.	Usual care	Physical function Daily activity Functional limitations	12 months
Culligan[2]	Thoracic surgery	Pre-operative/perioperative interactive patient education program.	Usual care	Functional status Activity	3 weeks
Dowsey[3]	Total joint arthroplasty *in patients with moderate to severe psychological distress*	Mindfulness training program consisting of a personal interview and eight, 2.5hours, weekly group-based classes in mindfulness practice plus a full day (7hours) session prior to surgery.	Usual care	Physical function ¥ Health service utilization	12 months
Ickmans[4]	Lumbar radiculopathy	Brain school: perioperative pain neuroscience education teaching people about the underlying mechanisms of pain, including the pain they will feel following surgery.	Back school: perioperative education that focuses on biomechanics of the lumbar spine and ergonomics	Functional status Return to work Healthcare utilization	24 months
Jepson[5]	Total hip arthroplasty	Pre-surgery home visit by an occupational therapist who discusses expectations, assessed home safety, and provides appropriate adaptive equipment.	Usual care	Functional limitations ¥ Physical function Societal participation Activities of daily living Healthcare utilization	26 weeks
McDonall[6]	Total knee arthroplasty	Multimedia intervention combining text, sound, graphics and animation to provide information to patients in relation to postoperative recovery and goals of care for each day. The 3 main goals are: to manage pain, promote mobility and improve function and to avoid complications	Usual care	Functional limitations Self-management	4 weeks
McGillion[7]	Cardiac and vascular surgery	eHealth-enabled service delivery intervention which combines remote monitoring, education and self-management training to optimize recovery outcomes.	Usual care	Functional status Health care utilization	12 months
Rosal[8]	Total knee arthroplasty	Theory-based telephone-delivered patient self-management support intervention to optimize post-surgical patient function outcomes.	Usual care	Physical function ¥ Performing daily activities Exercise and activity	12 months

¥ Primary outcome of the study

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Supplementary file S3. Overview of different questionnaires

Questionnaire	Description	Studies	Generic	Disease-specific
ADL / self-care				
ADL	Ordinal scale to classify patients in 3 levels of physical function (completely dependent, partially independent, entirely independent)	14	x	
BI[1]	10 item tool to assess functional independence. Information can be obtained from the patient's self-report, from a separate party or from observation.	18, 33, 51	x	
iADL[2]	8 instrumental activities of daily living. A higher score indicated a higher level of independence.	28	x (elderly)	
Disability				
ODI[3]	60 questions divided over 10 domains to assess the degree of disability for patients with low back pain.	23, 30, 34, 44, 47		x
PDI[4]	Assesses the degree to which the aspects of one's life are affected by pain. The activities of life include: family/home responsibilities, recreation, social activity, occupation, sexual behaviour, self-care and life-support activities.	43		x (pain)
QBPDS[5]	20 item condition-specific questionnaire developed to measure the level of functional disability for patients with low back pain. It consists of 20 daily activities that can be categorized into 6 types of activities: bed/rest items - sitting/ standing items - ambulation items - movement items - bending /stooping items - handling of large/heavy objects items. Items are scored from 0 "no disability" to 5 "impossible to do".	10		x
RSDI[6]	30-item tool to assess the physical, functional and emotional impact of sinus disease.	25		x
Functional Status				
DASI[7]	12-item questionnaire containing common daily activities, which can be used to estimate a person's functional capacity in patients with cardiovascular disease.	13		x
FSI[8]	18-item(x3) questionnaire to be used as a functional assessment for patients in primary care. It provides information on the patient's physical, psychological, social and role functions.	29, 52	x	
HHS[9]	Clinician-based outcome measure, including 10 items. The scores range from 0-100 with higher scores representing less dysfunction and better outcomes. The subscales include: pain, function, the absence of deformity, and range of motion.	33, 51		x

Supplementary file S3. Continued

Questionnaire	Description	Studies	Generic	Disease-specific
NHP[10]	38-item questionnaire assessing subjective health status by measuring 6 dimensions: pain, energy, sleep, mobility, emotional reaction and social isolation. The scores range from 0-100 with higher scores representing better functioning.	17	x	
OMFAQ[11]	Assessment of individuals' functioning on five dimensions: social, economic, mental health, physical health and self-care capacity	27, 28	x (elderly)	
SF-36[12]	Survey containing 36 questions addressing 8 health concepts: physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue, and general health perceptions. It also includes a single item that provides an indication of perceived change in health. Two subscales can be derived: the Physical Component Summary (PCS) and the Mental Component Summary (MCS).	7, 9, 12, 16, 18, 19, 23, 27, 50, 51, 53	x	
SF-12[13]	Subset of the larger SF-36. It contains the same 8 domains and the 2 subscales can also be derived from this survey.	24, 26, 32, 43, 47	x	
WOMAC[14] *function score*	Questionnaire used to evaluate the condition of patients with musculoskeletal disease in 3 domains: pain (5 items), stiffness (2 items), and functional limitation (17 items).	19, 33		x
Physical activity				
AAS[15]	13-item postoperative functional activity scale measure for evaluation of physical function	40	x	
IPAQ[16]	Instrument designed to measure physical activity among adults. It includes 4 domains: leisure time physical activity, domestic and gardening (yard) activities, work-related physical activity and transport-related physical activity. It is possible to derive both categorical indicators of physical activity (low, medium, high) and continuous indicators (median minutes/week).	35, 43	x	
PROMIS[17,18] *physical function*	Assessment system for measuring patient-reported health, consisting of Item Response Theory (IRT)-based item banks, which are large sets of questions (items) that all measure the same construct. Questionnaires can be personalized by selecting relevant items for a specific patient (group) from an item bank and administered as short forms, consisting of a fixed set of 4–10 items. The PROMIS Physical Function personalized form measures self-reported capability rather than actual performance of physical activities, including instrumental activities of daily living such as running errands.	35, 40	x	

Supplementary file S3. Continued

Questionnaire	Description	Studies	Generic	Disease-specific
SAQ[19] *physical limitation subscale*	19-item questionnaire measuring five dimensions of coronary artery disease: physical limitation, anginal stability, anginal frequency, treatment satisfaction and disease perception.	26		x
SIP[20] *physical domain*	136-item survey assessing the impact of illness on daily activities and behaviours. It consists of two domains (physical and psychosocial) and twelve categories. The physical category includes: ambulation, mobility, body care/ movement.	38, 39, 49	x	
Recovery				
RI-10[21]	10-item questionnaire measuring postoperative recovery in patients undergoing hysterectomy	7, 35, 50		x
SwQoR[22, 23]	24 items on an 11-point numeric visual analogue scale (from 0 "none of the time" to 10 "all the time") to assess postoperative recovery. The global SwQoR ranges from 0 – 240, with a higher score indicating poorer postoperative recovery.	20	x	
Social Participation				
PROMIS[17,18] *social roles*	Assessment system for measuring patient-reported health, consisting of Item Response Theory (IRT)-based item banks, which are large sets of questions (items) that all measure the same construct. Questionnaires can be personalized by selecting relevant items for a specific patient (group) from an item bank and administered as short forms, consisting of a fixed set of 4–10 items. The PROMIS Ability to Participate in Social Roles and Activities short form assesses the perceived ability to perform one's usual social roles and activities.	35	x	

AAS: Activities Assessment Scale, ADL: Activities of daily living, BI: Barthel Index, DASI: Duke Activity Status Index, FSI: Functional Status Index, HHS: Harris Hip Score, iADL: instrumental activities of daily living, IPAQ: International Physical Activity Questionnaire, NHP: Nottingham Health Profile, ODI: Oswestry (low back pain) Disability Questionnaire, OMFAQ: OARS Multidimensional Functional Assessment Questionnaire, PDI: Pain Disability Index, PROMIS: Patient-Reported Outcomes Measurement Information System, QBPDS: Quebec Back Pain Disability Scale, RI-10: Recovery Index, RSDI: Rhinosinusitis Disability Index, SAQ: Seattle Angina Questionnaire, SF: Short Form, SIP: Sickness Impact Scale, SwQoR: Swedish Quality of Recovery, WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

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CHAPTER 9

General discussion

In a report assessing the global rate of surgery, it was estimated that almost 313 million surgeries took place in the year 2012, which constituted a 33.6% increase over 8 years.[1] The current economic climate and the restricted healthcare budgets necessitate brief hospitalization as a method of minimizing direct healthcare costs.[2] However, indirect costs associated with productivity loss following surgery may contribute to total societal costs associated with surgical care even more. Furthermore, despite all revolutionary progress in surgical care in the last six decades, length of recovery after surgery has not declined accordingly.

This thesis describes the different aspects of an internet-based perioperative care programme aimed at improving perioperative care following gynaecological surgery in order to prevent unnecessary delayed recovery and minimize societal costs associated with prolonged sick leave and increased health care utilization after surgery. The aim of this thesis was to contribute to the development of a sound evidence base on post-operative recovery following gynaecological surgery and interventions to enhance postoperative recovery.

In this final chapter, the main findings of this thesis are presented, followed by an elaboration on methodological considerations. In addition, the results of this thesis are put in broader perspective in the context of the available literature. Moreover, potential implications for clinical practice will be discussed, as well as recommendations for future research.

MAIN FINDINGS

Below, the main findings from this thesis are summarized.

Outline of the problem

- Despite all revolutionary progress in surgical care in the last six decades, length of recovery, i.e., duration until the return to normal activities, after surgery has not declined accordingly. *(Chapter 1)*
- There is a significant transition of care from the hospital setting towards the home environment, leaving much of the postoperative recovery phase to occur outside the monitored hospital setting. *(Chapter 1)*

Working towards a solution

- Patients' own recovery expectations predict their postsurgical outcomes. *(Chapter 1)*
- eHealth can be used to target patients throughout the entire surgical pathway. *(Chapter 1)*

- There is a need for an eHealth care programme, which should focus mainly on the supply of tailored information about the resumption of personal activities as well as guidance in the postoperative course. *(Chapter 7)*
- Perioperative interventions can facilitate return to preoperative level of activity and participation and ideally focus on a combination of knowledge increase, behaviour modification, psychosocial guidance as well as the optimization of care processes. *(Chapter 8)*

Designing the current research

- The feasibility of a prior version of the Internet-based care program was evaluated in a tightly controlled setting with high involvement of the research team, resulting in a low level of external validity. *(Chapter 2)*
- A trial was designed to evaluate the (cost-)effectiveness of a further developed this Internet-based care programme aiming at improving postoperative recovery compared to the usual care in patients undergoing gynaecologic surgery. The primary outcome was duration of sick leave until full sustainable return to work (RTW). *(Chapter 3)*
- A stepped-wedge cluster randomized design was employed to minimize the risk of contamination between study groups and allow assessment of effectiveness on patient level, as well as the entire implementation-process. *(Chapter 3)*

Effectiveness evaluation

- There was a wide variation in duration until the resumption of daily activities between patients. For the majority of activities, actual recovery times exceeded the recovery time recommended by the expert panel. *(Chapter 6)*
- Median time until RTW was 49 days (IQR 27–76) in the intervention group and 62 days (42–85) in the control group. Duration to RTW was effectively reduced in the first 85 days after surgery, but the effect was reversed in the small group of patients that did not reach RTW within this period. *(Chapter 4)*
- Clinically relevant differences in secondary outcome measures (functional health status, recovery-specific quality of life, self-efficacy, coping and pain) between study groups were not found. *(Chapter 4)*

Cost effectiveness evaluation

- Costs associated with productivity loss following gynaecological surgery were about two times higher than healthcare costs. *(Chapter 5)*
- The probability of the care program being cost-effective was 0.79 at a willingness to pay (WTP) of €0 per day earlier RTW, increasing to 0.97 at a WTP of €76 per day earlier RTW. *(Chapter 5)*

Implementation

- This internet-based care programme is an example of an initiative leading to value-based healthcare: by optimizing perioperative care, patients can benefit from innovative minimal invasive surgical approaches and society as a whole can benefit through minimal productivity-loss costs. *(Chapter 9)*
- Implementation of the care programme was quite successful. Implementation of the internet-based care programme on a broader scale has a large potential to lead to accelerated recovery and improved RTW rates. *(Chapter 5)*
- A latent barrier to future acceptance and implementation of the care programme lies in the fact that the costs and benefits of the care programme are separated between different types of stakeholders and payers. *(Chapter 5)*

METHODOLOGICAL CONSIDERATIONS THAT WARRANT FURTHER EXPLORATION

Many of the methodological strengths and limitations have been discussed in the previous chapters. However, a selection of methodological considerations in relation to the study design, selected outcome measures, as well as the generalizability of our results, warrant further exploration.

Study design

Randomised controlled trials (RCTs) are considered the gold standard for establishing a cause-effect relationship between an intervention and an outcome. Therefore, researchers should have valid arguments to employ different (more novel) designs for their research.[3] We decided to employ a stepped-wedge cluster-randomized controlled trial, which involved a sequential rollout of the intervention in the participating clusters over several time periods, until all clusters received the intervention eventually.[4-6] Our most important justification for employing the stepped-wedge design were the results from the previous efficacy trial. Although there was already evidence for support of our intervention, the efficacy trial was performed in a tightly controlled setting and, therefore, it still remained unclear if the intervention would still be effective under 'real-world' circumstances. As it was our intention to implement the intervention once cost-effectiveness was established, the stepped-wedge design was advantageous as the crossover of this design is unidirectional, and it was not obligatory for the participating hospitals to withdraw the intervention after the end of the trial.[7] Our second reason included the possibility to study the implementation process itself, in order to gain valuable insight into the facilitators and barriers toward future implementation of the intervention.[8] At last, the cluster-design prevented contamination between study groups, as it would be very difficult for clinicians to provide 'usual care' once they had participated in the educational training sessions and were made familiar with the multidisciplinary guideline on convalescence advice.

The study design also had a couple of consequences. First of all, the sample size that was required was larger than the sample size for a corresponding individually randomised design (454 versus 212), because it should allow for correlations between individuals in the same cluster, as well as a potential underlying temporal trend.[7] Secondly, as each cluster switched from the control to the intervention phase, we experienced that clusters did not enrol patients at the same pace, leading to an unequal distribution of patients in the control and intervention group (the 'bigger' clusters switched to the intervention phase sooner than the 'smaller' clusters). In order to prevent having too few observations in the control group, we advise researchers who are planning to perform a stepped-wedge trial, to keep all clusters in the control phase for a relatively longer period at the beginning of the trial. Thirdly, our trial was at risk of recruitment bias as individual participants were recruited in the clusters in both the control and intervention-phases of the study. Theoretically, recruitment could differ during the control and the intervention phase of the trial. To minimize the risk, we blinded patients to the exposure status of their cluster, however, it is still possible that participants varied systematically in both phases.[7]

RTW as a primary outcome

Traditionally, surgical outcome studies have been centered on parameters that are easy to collect, commonly gathered from a medical record in a retrospective fashion.[9] An example of such an outcome parameter is length of stay (LOS), which is probably the most commonly reported measure of surgical recovery in the literature. From the perspective of policymakers, LOS is an interesting outcome as well, as hospital services contribute substantially to total medical costs and reducing LOS enhances the efficacy of hospital care.[9] However, it has been argued before that a reduction of LOS might only reflect a transition of postoperative recovery from the hospital towards the home-setting and that LOS may relate to changes in organization of care and not necessarily to a shorter recovery period.[9]

From the patient's perspective, recovery is defined as the absence of symptoms and the ability to perform regular activities including return to work.[10, 11] In this late phase of recovery relevant outcomes include more complex measures of morbidity, patient-reported outcomes, and outcomes measuring return to pre-operative level of activity and particiaption.[12, 13] A recent systematic review that evaluated surgical outcomes after enhanced recovery pathways, demonstrated that follow-up was generally short and that only 17 of 38 included studies reported outcomes measured after discharge (late phase outcomes of recovery) other than complications or readmission.[10]

In our trial the primary outcome was duration until full sustainable return to work (RTW), which was defined as the resumption of own work or other work with equal earnings, for at least 4 weeks without (partial or full) recurrence of sick leave. The motivation for choosing

this endpoint were twofold. First, in our opinion, the focus on short-term outcomes following surgery in current literature gives an incomplete assessment of recovery. As the resumption of work usually requires to perform a whole set of single activities (activities of daily living (ADL), commuting/travelling, concentrating, sitting/standing/walking, lifting, etcetera) we believed that this outcome could be used to define the end of the recovery process. Secondly, in perspective of our economic evaluation, RTW was an excellent outcome as well, because it could be used to calculate absenteeism costs which were necessary to measure the impact of our intervention on society as a whole.

One final remark about the outcome RTW is that it is important to realize that it is not merely a proxy of health, but that it can be influenced by a range of external factors.[9] Examples of such external factors include:

1. patient factors, such as: education level, presence of comorbid conditions, patient expectations;
2. work-related factors, such as: employment type (physical versus sedentary), employment status (salary employed versus self-employed), job satisfaction; and
3. organizational factors, such as: the presence of disability compensation, the presence of uniform physicians' advice.

It has been argued that RTW is therefore unsatisfactory as a method of quantifying health benefits, as the outcome is prone to confounding and difficult to interpret.[9] Notwithstanding, we still believe that RTW was an exemplary outcome in our trial, as our intervention was designed to target different factors related to (unnecessary) delayed recovery, such as irrespective patient expectations and the lack of uniform physicians advice, on the levels of the patient, healthcare professional and the organisation.

How to measure value?

In 2010 Michael Porter published a seminal article in the New England Journal of Medicine called "What is value in health care?".[14] In this article he explained the concept of 'value-based healthcare', which includes all initiatives that aim to increase value for patients. Value is defined as health outcomes attained per 'dollar' expended and can be illustrated as a ratio with quality and patient reported outcome measures (PROMS) in the numerator and costs in the denominator.[15] Therefore, a value-based healthcare model prioritizes patient-centered care.[16] The introduction of value as a goal in healthcare causes a shift towards measuring quality of care instead of merely measuring (and containing) the financial aspects of care.

The care programme in this thesis, is an example of value-based healthcare as the aim of the intervention was to minimize societal costs by optimizing the quality of gynaecological perioperative care. By optimizing guidance throughout the surgical pathway and facilitating

self-management, patient outcomes can improve, which can lead to a higher participation level and lower productivity-loss, through which society can benefit due to lower compensation rates. Therefore: adding value to both the patient and society. However, it might mean switching resources along the whole care pathway.

The current organizational structure of healthcare makes it challenging to measure value.[14] In order to measure the value of our intervention for society, we performed the cost-effectiveness analysis from the societal perspective. In economic evaluations which are performed from the societal perspective, not only costs directly relevant to the healthcare sector are considered, but also costs that fall outside the healthcare budget, in our case: productivity costs. This broad perspective may also conflict with the needs of healthcare decision makers, who generally use a narrower perspective.[17] In the paragraph 'future perspectives' we will discuss how this area of tension can affect the future implementation of our care programme.

Generalizability

Generalization is an act of reasoning that involves drawing broad conclusions from particular observations, that is, making an inference about the unobserved based on the observed.[18] Therefore, drawing conclusions from research is challenging, as the selection of participants for a certain study, results in a non-representative sample with regard to the population of interest.[19]

In the current research, clinical and cost effectiveness could be reduced when the intervention is accessible to the general audience, because our study population comprised only employed women of which the majority was highly educated (unemployment, as well as computer- or Internet illiteracy were exclusion criteria). Selection bias towards to higher educated participant had been described before in different types of studies.[20] In addition, several observational studies and survey studies suggested that the uptake of eHealth interventions may differ by patient-specific factors with lower use by racial and ethnic minorities, lower use with lower education level or literacy, and greater use with increased numbers of medical problems.[21]

In addition, (cultural) differences in attitudes towards health and work and differences in the organization of healthcare and social security systems makes external generalizability of our study towards different countries uncertain.[9, 22] For example, one can imagine that Dutch employees are more inclined to report sick than U.S. employees because Dutch employees generally get paid during sickness absence, while many U.S. employees are not.[23] Also this aspect will be discussed in the paragraph 'future perspectives'.

COMPARISON TO THE LITERATURE

In chapter 8 of this thesis we presented the results of a systematic review in which we assessed the current literature on perioperative interventions that aim to facilitate the return to preoperative level of activity and participation. A total of 41 unique studies were included of which 24 studies reported at least a positive effect of the intervention compared to usual care. No correlations were found between the different types of interventions and the overall outcomes of the studies, therefore is was not possible to determine successful key elements of the interventions. However, it could be concluded that ideally, perioperative interventions should focus on a combination of knowledge increase, behaviour modification, psychosocial guidance as well as the optimization of care processes.

In the following section we will focus on current literature on eHealth. After discussing the trends in eHealth, we will concentrate on the surgical patient as a target of eHealth. At last we will elaborate on how the current work differs from other research conducted by our research group.

Trends in eHealth

In the last two decades, the branch of eHealth is expanding widely and the dissemination of eHealth resources occurs very rapidly.[24] Concurrently, the increasing interest in eHealth is demonstrated by an accumulating number of articles on this topic in the scientific literature (figure 1). However, despite the large volume of work studying the impact of eHealth on the quality and safety of health care, the empirical evidence for the beneficial impact of most eHealth technologies is often absent, or, at best, only modest.[25, 26]

One of the big challenges in conducting research on eHealth technologies, includes the fact that eHealth interventions are often quite complex and studying these interventions takes time. Simultaneously, eHealth interventions appear and change quickly. By the time a RCT of a new intervention is published, technological improvements and clinical discoveries may make the intervention dated and unappealing.[24] In addition, there is a dearth of reporting on organizational context and implementation processes of eHealth interventions, which makes it challenging to distinguish between failure of the intervention versus failure of the implementation in studies reporting no effect. Moreover, for studies that do report beneficial effect, it remains unclear for policymakers how to replicate the success.[21] Finally, current literature on eHealth is characterized by a paucity of cost-benefit data.[21, 25-29]

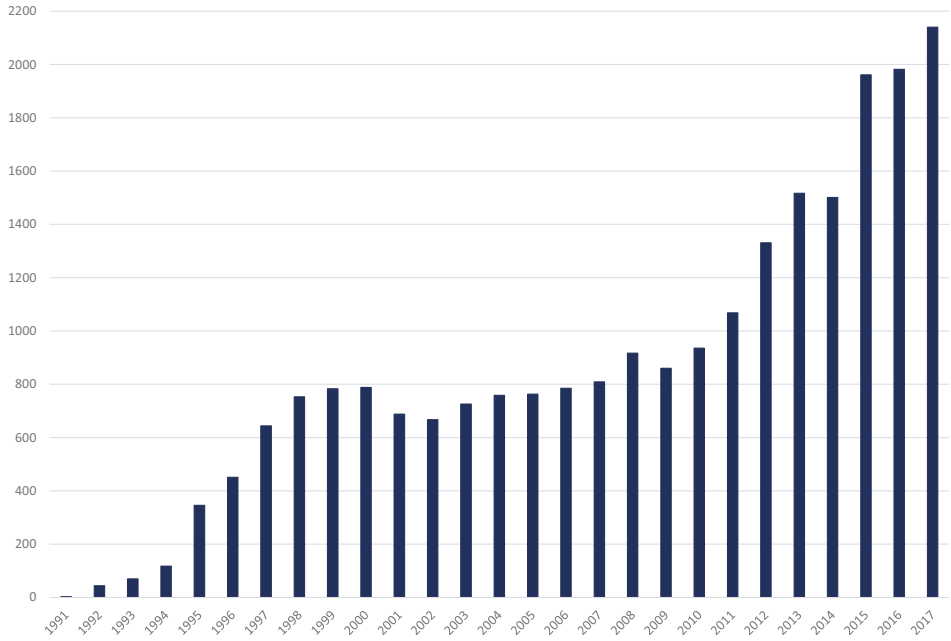

Figure 1. Trend in number of publications on eHealth in MEDLINE

The surgical patient as a target of eHealth

Traditionally, eHealth interventions were employed to manage chronic disease such as diabetes and hypertension, to deliver psychological interventions, for example, for people suffering from depression or anxiety disorders and to engage patients in health promotion activities such as increased physical activity or smoking cessation.[21, 26] More recently, focus has also been directed towards the surgical field in which eHealth has been pointed out to have the potential to improve care and patient outcomes across the entire surgical pathway by facilitating information gathering, information transfer and information exchange.[30, 31]

Conventional care can be replaced or complemented by eHealth solutions.[32] Preoperative preparation of the patient by providing an instruction video on a website instead of meeting the person in an individual session, is an example of an eHealth solution that replaces traditional care. Although it is an exemplary method to ease pressure on care providers, the procedure is highly standardised and can't be easily adapted to meet the personal needs of the patient. More recently, focus has shifted towards care in which digital solutions complement traditional care, in order to obtain optimal benefit from the advantages these two treatment modalities have.[33-35] This last method is also known as blended care and can be illustrated by a mobile application for patients facilitating them to monitor postoperative

symptoms in combination with an automatic notification system towards the healthcare provider who can initiate contact in case of alarming symptoms. Another example would be a tool to make an inventory of unrealistic beliefs and expectation towards recovery using an online survey, and target those specifically in a face-to-face session.

In their discussion paper, Waller *et al* indicated that there are six steps along the surgical pathway that can be targeted by eHealth.[30] Ideally, an eHealth intervention should target all of the following processes, instead of targeting only one or two:

1. enhancing decision-making process and streamlining informed consent
2. collecting medical history data, delivering information and optimizing preoperative preparation
3. streamlining admission procedures
4. delivering individually tailored postoperative care plans
5. promote effective discharge planning
6. optimizing rehabilitation and long-term follow-up.

A selection of the most important eHealth interventions that have some parallels to our own intervention is presented in table 1. This summary is not exhaustive, but is comprised to point out several noteworthy aspects. First of all, the vast majority of surgical eHealth interventions fail to target more than one phase along the surgical pathway: for example, they are only applied during hospitalization[36], or they only start after discharge[37]. Secondly, most interventions focus on only one functionality: for example, solely providing patient education[38, 39], or solely collecting patient reported outcomes[40]. Thirdly, most interventions abide in their early stages of design and evaluation.

When comparing our own intervention to other eHealth interventions in the surgical field, it stands out that our intervention has been evaluated rigorously through a full cycle starting from the development and testing of its feasibility, towards the assessment of both effectiveness and cost-effectiveness, and finally, implementation, which is quite exceptional.[41] In addition, our intervention has been enhanced continuously over the years. For example, gained insights from the process evaluation of our efficacy trial were used to further adapt the intervention.[42] Furthermore, patient data from the effectiveness study were used to optimize the guideline on postoperative convalescence advice.[43] Finally, to the best of our knowledge, we are not aware of other interventions that aim to minimize societal costs associated with surgical procedures by preventing unnecessary prolonged convalescence and facilitating return to preoperative levels of activity and participation.

Table 1. Examples of comparable eHealth interventions in the surgical field

		Type of Intervention			
Author	**Type of surgery**	**Description**	**Strengths**	**Limitations**	**Type of evaluation**
Cook, 2013[36]	cardiac surgery	EHealth platform to support the delivery and the acquisition of patient-reported outcomes.	Collection of patient-reported outcomes, in combination with education and recovery planning (including discharge).	Intervention ended after discharge	Feasibility study
Dukeshire, 2012[44]	gynaecological surgery	Website designed to provide advice specific to the recovery phase and to self-monitor their postoperative symptoms Patients were advised to contact appropriate healthcare providers if they experience abnormal problems.	Provision of tailored information as well as guidance in case of symptoms.	Care provider did not have access to patient reported outcomes	Pilot study (satisfaction, usability)
Heikkinen, 2010[38]	orthopaedic surgery	Website to provide extensive preoperative education to support patient empowerment.	Extensive information, divided into three levels (basic, medium, advanced) using different types of media (text, graphics, video).	Focus on the provision of information only	Pilot study (utility and usability)
Hussain, 2017[45]	orthopaedic surgery	Digital orthopaedic rehabilitation platform that comprises a mobile phone app, wearable activity tracker, and clinical web portal in order to engage patients with self-management tasks for surgical preparation and recovery.	Multimodal approach targeting knowledge, recovery expectations and behaviour coaching (self-management). Exchange of information to clinicians.	Limited focus on return to preoperative levels of activity and participation	RCT currently running. Primary outcome: knee function. Secondary outcomes: quality of life, self-efficacy, cost-effectiveness.
Kummerow Broman, 2015[37]	elective general surgery	Patient portal to provide postoperative care including symptom surveys, wound pictures and electronic correspondence with their surgeons.	Patient-provider communication was automatically documented in the electronic medical record	Focus on the postoperative phase only	Pilot study (patient acceptance)

Table 1. Continued

Author	Type of surgery	Type of Intervention			Type of evaluation
		Description	Strengths	Limitations	
Neary, 2010[39]	parathyreoidectomy	Website with an individualized online pathway with a detailed stepwise description of expected clinical course from initial diagnosis to eventual discharge.	Focus on the entire surgical pathway.	Focus on the provision of information only	RCT, however, only short-term recovery outcomes were used (satisfaction, anxiety, pain) instead of outcomes regarding return to preoperative levels of activity and participation.
Graetz, 2018[40]	gynaecological oncology surgery	Web-based intervention containing discharge instructions and allowed patients to report symptoms in their postoperative course. Self-reported health information is integrated into their electronic health records.	The clinical care team was notified automatically in case of concerning symptoms.	Focus on the collection of patient-reported outcomes only	Feasibility study

Table 2. Overview of studies

	Trial 1 "Efficacy Trial" Vonk Noordegraaf *et al* 2009 - 2010	**Trial 2 "Current work" Bouwsma *et al* 2011 - 2013**	**Trial 3 van der Meij *et al* 2015 - 2016**
Study Characteristics			
Design	RCT, n=215	SWCRT, n=434	RCT, 344
Population	gynaecology	gynaecology	gynaecology & general surgery
Intervention	website and occupational intervention	website and occupational intervention	website, app, activity tracker, e-consult
Control	placebo website and usual care	usual care	placebo website and usual care
Primary outcome	RTW	RTW	RTA
Study Results			
RTW	+ [1]	+ [2]	+ [3]
RTN	n/a	n/a	+ [4]
QoL	+	x	x
Pain intensity	+	+ [5]	x
Cost-effectiveness	n/a	+ [6]	x
Process measures			
reach	60.2%	52.3%	33.5%
dose delivered	100%	94.7%	98.8%
dose received	86.4%	82.6%	79.9%
fidelity	74.5%	65.7%	25.2%

+ positive effect in favour of the intervention group, x = no effect detected, n/a = outcome not measured.
[1] 39 days in intervention group versus 48 days in control group; HR 1.43; 95% CI 1.003 to 2.040; p=0.048 (during the first 49 days after surgery).
[2] 49 days in intervention group versus 62 days in control group; HR 2.66, 95% CI 1.88 to 3.77; p<0.001 (during the first 85 days after surgery).
[3] 18 days in intervention group versus 19 days in control group; HR 1.31; 95% CI 1.01 to 1.70; p=0.045.
[4] 21 days in intervention group versus 26 days in control group; HR 1.38; 95% CI 1.09 to 1.73; p=0.007.
[5] temporary effect in pain intensity score and pain disability score in first 2 weeks after surgery.
[6] probability of cost-effectiveness of 0.79 at a WTP of €0 per day earlier RTW, increasing to 0.97 at a WTP of €76 per day earlier RTW.
RCT = randomized controlled trial, SWCRT = stepped-wedge cluster randomized trial, RTW = return to work, RTA = return to normal activity, QoL = quality of life, CI = confidence interval, HR = hazard ratio, WTP = willingness to pay

Comparative work from our own study group

Within our own research group, we performed two other randomized controlled studies focusing on optimizing perioperative care (table 2). In the following section we describe the most important differences in the interventions that were studied, the differences in study design and differences in the (interpretation of the) results, compared to the current study.

Trial 1. Studying efficacy

The first comparative study that was performed, is already mentioned before as 'the efficacy study' and was conducted by Dr. A. Vonk Noordegraaf between March 2010 and January 2011.[46, 47] The process evaluation of this earlier study can be found in chapter 3 of this thesis.[42] The intervention in this study was quite comparable to the one in the current study, however, some improvements were made to the intervention of the current trial, such as lay-out, work-flow and user-friendliness. Moreover, the tool to make a personalized convalescence plan was refined and another tool to monitor one's recovery was added.

From a methodological perspective, both studies were quite different as the efficacy study was designed as a randomized controlled trial, and the current study was designed as a cluster randomized trial. In the efficacy study, patients in the control group received a placebo website with the telephone numbers of their hospitals and the general patient leaflet from the Dutch Society of Obstetrics and Gynaecology (NVOG). Remarkably, 31% (32/104) of the patients in the control group indicated that this (placebo) website contributed positively to their recovery and 66% (69/104) of them would recommend the website to a friend.[48] To be able to compare the intervention to real "usual care", a cluster randomized design was employed in the current study.

A second difference between these two studies was the degree of involvement of the research team. In the efficacy study, in order to avoid protocol deviations, the research team participated actively in the trial, providing (uninvited) assistance to patients who did not use the intervention and prompting healthcare providers if they did not timely approve the convalescence plans for their patients. In the current study, involvement of the research team was restricted, in order to be able to investigate the implementation of the intervention under 'real-life' conditions. Fortunately, implementation scores did not decline, and implementation could be called quite successful.

The same primary and secondary outcomes measures were used in the first two studies, however, length of follow-up was different (6 months in the first study versus 12 months in the current study). In the efficacy study, duration until sustainable RTW was 39 days (IQR 20-67) in the intervention group and 48 days (IQR 21-69) in the control group. In the current study, duration until RTW was 49 days (IQR 27-76) and 62 days (IQR 42-85), respectively. The

differences in overall duration until RTW in both studies might be explained by a difference in composition of study groups. To illustrate, in the current study relatively more patients underwent more invasive procedures.

In the efficacy study, significant effects were found on the secondary outcomes quality of life as well as pain. In the current study, only a small effect was seen on the outcome pain, but the effects disappeared with longer follow-up and were labelled as clinically irrelevant. In the first study the effects were a little larger, however, one might argue that we did not merely measure the effect of the intervention in the efficacy trial, but we did also measure the impact of the high level of involvement of the research team.

Trial 3. Transition towards general surgery

Following the study described in this thesis, the intervention program was adapted to be applicable for patients undergoing commonly applied general surgical procedures.[49, 50] Secondly, a new aim was to substitute perioperative care with eHealth, instead of only providing extra information and support. This was operationalized by replacing the standard postoperative consultation by *e*-consultation. Moreover, the web portal was redesigned and was enhanced with more advanced features such as animations with a more interactive design. A mobile application was developed to have easy access from a smartphone. An activity tracker was integrated in the mobile app, measuring daily step count, and was used to monitor recovery and give patients feedback about their level of activity postoperatively. Finally, the occupational intervention was discontinued.

The new intervention programme was than subject to evaluation in a multicentre RCT between August 2015 and March 2017 in 344 patients who underwent laparoscopic cholecystectomy, inguinal hernia surgery, or laparoscopic adnexal surgery for a benign indication. The primary outcome of this study was return to normal activities, instead of return to work. A summary of the results is presented in table 2.[51-53]

FUTURE PERSPECTIVES AND RECOMMENDATIONS FOR FUTURE RESEARCH

Now that we have demonstrated that society could benefit from our care programme, implementation on a broader scale should be next on the agenda. Notwithstanding, the implementation of innovations to healthcare concerns a multilevel complexity. An essential number of interventions that are proven to be (cost-)effective, fail to be implemented in daily practise, because of ineffective implementation strategies that do not lead to necessary changes in behaviour of patients and/or health care professionals or to definite changes in the organization of healthcare. [54-56]

In the following paragraphs, we will discuss a number of key features at the level of the patient, the health professional as well as the organisation of healthcare that are associated with the future implementation of our intervention and determine the degree of success of implementation. Furthermore, we will discuss the directions on which future research should focus, in order to address the research gaps in the current evidence base of perioperative care.

Level of the patient

In healthcare, the role of patients is changing. From traditional provider-centered care, there is now a shift towards collaborative care, in which self-management is a key component and patients are encouraged to take charge of their own health and expected to play an active role in managing their own disease.[57, 58] This new concept is also captured in the newly proposed definition of health as 'the ability to adapt and to self-manage in the face of social, physical, and emotional challenges', developed at a conference of international health experts held in the Netherlands.[59] The experts reasoned that the focus on self-management is necessary in an era in which ageing with chronic illnesses has become the norm.

A commonly used definition of self-management is 'an individual's ability to manage the symptoms, treatment, physical and psychosocial consequences and lifestyle changes inherent with living with a chronic condition'.[60] However, the concept of self-management can also be applied to patients without chronic disease, which can be demonstrated by the numerous amount of healthcare apps that are widely available to promote healthy behaviour. In addition, patients with temporary conditions (such as a period of convalescence after surgery) can also be targeted through self-management by teaching them to actively identify challenges and solve problems in their recovery process, and emphasizing their responsibility to regain their health – which is the key element of the current intervention under study.

Focus on self-management can lead to a positive impact on the organization of care. In a literature review on the impact of self-management in chronic disease management, it was concluded that the biggest impact on the organization of care took place through less hospitalization.[57] However, self-management can offer patients significant benefit as well, for example through facilitating shared decision making, improved autonomy and improved quality of life.[57]

Frequently, self-management and eHealth go hand in hand. eHealth applications are well suited to provide patients with the knowledge and equipment required to manage their own health. In addition, it is also a promising tool to engage healthcare professionals to the health-seeking behaviour of their patients in the near future, as current applications are often

solely used by patients themselves.[57] On the other hand, it is of high importance to evaluate how to reach all patients at stake. To illustrate, the results of our trial demonstrated that for a small group of the participants, the intervention was not beneficial. Possibly, certain patients do not possess the crucial skills necessary to manage their own health. Future research should therefor focus on the underlying mechanisms that determine the adaptation of self-management strategies in patients. In fact, healthcare professionals should be able to differentiate (at front) between patients who are eligible for self-management and patients who might need a face-to-face guidance only.

Level of the healthcare professional

Contingent upon the trend towards collaborative care, the role of healthcare professionals will change as well and it will become their responsibility to facilitate self-management. In this process, the healthcare professional will take the role of consultant: a resource person who offers treatments suggestions and facilitates informed decision making. In addition, the future healthcare professional provides support and helpful tools to their patients, promotes healthy behaviour and optimizes patient beliefs. Furthermore, healthcare professionals should confirm that patients are able to find true facts in their search on the Internet for health information, as currently, patients are at risk of accessing information that is wrong, harmful or incomprehensible.[38, 61, 62]

Applying the above recommendations on our own research, the first priority should be to present our prior developed guideline on convalescence advice after hysterectomy (laparoscopic, vaginal, or abdominal) to the Dutch Board of Gynaecology in the Netherlands (NVOG) for authorization. Currently, the patient leaflet of the NVOG is a source of convalescence advise after hysterectomy for patients, however, the leaflet is hopelessly outdated as it does not even differentiate between the different types of surgical approaches for hysterectomy and it fails to provide specific, detailed and unified convalescence advice (figure 2). In addition, the adoption of the convalescence guidelines would also facilitate evidence-based perioperative education by all involved professionals.

In a broader perspective, our research can be used as a blueprint for similar projects ahead. As mentioned before, we already proceeded with the development of a guideline for convalescence advice for the most commonly performed procedures in general surgery. However, there are still many other (surgical) procedures to explore in gynaecology, general surgery and other specialities.

- Your body will let you know what you can handle after surgery and it is important to listen to it.
- In the first weeks after surgery it is advised to restrain from heavy lifting. Lighter activities can be resumed gradually. Stop if you get tired.
- If you don't feel recovered after 6 weeks, you should discuss this with your gynaecologist, general physician, of occupational physician. Sometimes you will be advised to stay at home a little longer to get stronger, or to resume your work partly for a couple of weeks.

Figure 2. Current convalescence advice after hysterectomy in Dutch patient leaflet (2005)

Future research should also focus on identifying predictors of recovery. As we have demonstrated in chapter 6, the majority of patients resumed their daily activities much later than recommended, and it remains unclear which factors determine if a patient will be compliant to the convalescence advice given. As long as these mechanisms are not clear, it is very difficult to optimize this process. Moreover, we also recommend healthcare professionals to collect recovery data from their patients, as detailed knowledge about recovery in the general population can aid future initiatives to develop convalescence advice tailored to the patient, also accounting for various other factors such as, for example, comorbidity or job demands. In addition, the availability of recovery data would allow healthcare professionals to identify the patients who deviate from the norm and prompt the possibility of intervention.[63, 64]

It will be only a matter of time, before most healthcare processes will be organized through digitized web portals. Driven by advancing technological developments web portals like the one we used in the current research, will be adapted further and be expanded with more functionalities. In this perspective, we challenge all healthcare professionals to play an active role in formalizing these developments. For example, decision-support tools that are created by healthcare professionals could be easily integrated in to a web portal and could be beneficial to patients, but also to healthcare professionals themselves.

Level of the organisation of healthcare

At the level of the organization of healthcare there are several important factors that determine the degree of future implementation of our intervention (or other interventions that are similar to ours). In this paragraph, we will discuss two of them. First of all, we address the importance of privacy and security of personal health data and the role of the government in this. Secondly, we elaborate on the fact that costs and benefits of

our intervention programme are separated between different stakeholders and how this segregation could hamper future implementation unless the organisation of health care changes.

Privacy, confidentiality and security of personal health data

Health information privacy is an individual's right to control the acquisition, uses, or disclosures of his or her identifiable health data. Confidentiality, which is closely related, refers to the obligations of those who receive information to respect the privacy interests of those to whom the data relate. Security refers to the physical, technological, or administrative safeguards or tools used to protect identifiable health data from unwarranted access or disclosure.[65]

Privacy, confidentiality and security of personal health data is an important concern for the public. In a recent survey among 800 persons assessing their perceptions of benefits and barriers to the use of mobile health applications after surgery, the most common mentioned barrier was the concern about protecting personal information.[63] Participants said: "I would need to know who is able to access the information", and "I could see people having problems with that". Participants were also concerned about data security and "hackers", as well as about the involvement of third parties. As one participant put it: "I would be worried that they would track me doing things that maybe I shouldn't be doing. Reporting the insurance company that maybe I'm not doing my exercise".[66]

The apprehension of the general public could be a barrier to future implementation of web-based interventions. Healthcare practitioners and researchers have an ethical duty to protect patient privacy in their pursuit of developing and implementing the next innovative health techonology.[67] Simultaneously, sufficient effort should be made to ensure patients that security measures taken are satisfactory.[66]

Until very recently, legislation on this matter was limited and dated, since the European Union Data Protection Directive, the security and privacy law in the European Union (EU), was established in 1995 at a time that many of today's Internet-based interventions and mobile interventions had yet to be invented.[68] As a consequence, current available web-based interventions and mobile applications usually do not have enough security and privacy mechanisms in order to protect their users' data.[69] On May 25, 2018 the EU General Data Protection Regulation (GDPR) came into force. The aim of the GDPR is to protect all EU citizens from privacy and data breaches in an increasingly data-driven world that is vastly different from the time in which the previous law was established. Compliance to the new law is still to be evaluated, however, introduction of this new legislation is an important step forward.

This new legislation also has consequences for our work. The web-based intervention under study in this thesis does not have a CE-marking yet; a certification mark that indicates compliance with all relevant EU legislation ('CE' is an abbreviation of '*Conformité Européenne*', meaning 'European Conformity'). It is inevitable that we have to invest in achieving a CE-marking before we can implement our intervention on a broad scale.

Costs and benefits separated between different stakeholder

The care programme under study is characterised by the fact that costs and benefits are unequally shared between different types of stakeholders. Investments are made in the healthcare sector for implementing the care programme and changing the processes of care, while the largest benefits accrue to employers and social income insurers through reduced lost productivity costs. In countries with an employer-provided health insurance (e.g. the USA) this should not lead to problems, however in the Netherlands, medical costs are paid by the government and health insurance companies and sickness benefits are the main responsibility of the employers. Due to the compartmentalization of finances, shifting costs and benefits across these sectors is almost impossible.

A possible solution for the above-mentioned problem could be the transition from a 'fee for service' payment model towards a novel payment model called 'fee for performance'. The first mentioned is the current (more traditional) payment model, in which providers are reimbursed based on the amount of healthcare services they deliver. Lately, it has become topic of discussion as it is argued that it has a reverse effect as there is no reward for efficient or responsible care or the substitution of care.[14, 70] Moreover, in this model it is difficult to pay attention to the entire care chain: treatment A might be more cost-effective than treatment B for a certain disease, while in fact, investing the available resources in the prevention of that disease would benefit the population most. In the 'fee for performance' model, which is embraced in value-based healthcare, providers are encouraged to consider the quality of care provided and the overall outcomes of that care in relation to cost-efficiency, as they are reimbursed for the quality and efficiency of care they provide. In this way, 'value' becomes the shared goal of all involved stakeholders.[14]

Another model which could be of help overcoming the segregation of costs and benefits between different stakeholders is the 'shared savings model', which is a payment strategy that offers incentives for providers to reduce health care spending by offering them a percentage of net savings realized as a result of their efforts.[71, 72] This strategy finds it origins in the United States, but was launched in the Netherlands on behalf of the Ministry of Health, Welfare and Sport in 2013. The innovation program, called Triple Aim, pursues improving the quality of healthcare, improving population health and decrease healthcare costs, and has provided a platform for numerous projects since.[73]

Practically, in a shared savings program, involved stakeholders agree to work together in order to achieve both quality and cost improvements. It is required to reach agreement on both the performance measures, targets and benchmarks to evaluate quality, and the methods to establish any savings. Only then savings can be distributed between all parties in a pre-arranged way, in which the costs associated with changing infrastructure and redesigning care processes are fully reimbursed. The remaining savings can be allocated between the other stakeholders. For example, insurance companies can invest some money in services of which their members will benefit and hospitals can invest some money in an innovation fund which can be used for new broad-based supported initiatives (e.g. listed in a research agenda).[73]

At the level of the organisation of health care it will take time, patience and adjustment before value-based healthcare becomes the norm and these innovative models are accepted and adopted.[16] However, small steps are already visible. In 2017, The Dutch Council for Health and Society proposed in their report that investments in care should be expressed as value for society as a whole (participation, work force and public health) instead of percentages of the national income.[70] Cost-effectiveness studies like our own, performed from the societal perspective, will challenge healthcare planners in the future to allocate scarce resources in order to maximize the welfare to the entire society.

CONCLUDING REMARKS

This thesis started with citing the work of Dr. F.C. Dohan who published the results of the 'Surgical Convalescence Study' in 1960 and concluded that unnecessary long convalescence advice led to iatrogenic illness resulting in inconvenience and economic loss to both the patient and society as a whole.

About six decade later, a similar conclusion can be drawn from the current thesis. In line with the foregoing idea that convalescence advice plays an important role in determining the length of recovery, we demonstrated that postoperative recovery in gynaecological patients can be enhanced by improving recovery expectations and facilitating self-management through an internet-based perioperative care programme. Patients exposed to the intervention had better RTW-rates compared to patients receiving usual care, and society benefitted through reduced lost productivity costs.

Although great strides have been made in the field of surgical care, at present, postoperative recovery still takes unnecessary long. In this thesis we describe the importance of optimizing perioperative care in order to prevent unnecessary prolonged convalescence. In fact, we

advocate that society will be able to fully benefit from innovative surgical developments, if only effective strategies are employed to equip patients with tools to prepare themselves for surgery and manage their own postoperative course.

Future implementation of such strategies will be challenging, not least because costs and benefits are unequally shared between different types of stakeholders. However, we can only hope that it does not take another half a century before the insights derived from this thesis find their way into routine surgical care.

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CHAPTER 10

- English summary
- Nederlandse samenvatting
- List of co-authors
- List of publications
- Dankwoord
- Curriculum Vitae

ENGLISH SUMMARY

The current economic climate and the restricted healthcare budgets necessitate brief hospitalization as a method of minimizing direct healthcare costs. However, indirect costs associated with productivity loss following surgery may contribute to total societal costs associated with surgical care even more. In addition, despite all revolutionary progress in surgical care in the last decades, length of recovery after surgery has not declined accordingly.

This thesis describes the different aspects of an internet-based perioperative care programme aimed at improving perioperative care following gynaecological surgery, in order to prevent unnecessary delayed postoperative recovery and minimize societal costs associated with prolonged sick leave and increased health care utilization after surgery. The aim of this thesis was to contribute to the development of a sound evidence base on post-operative recovery following gynaecological surgery and interventions facilitating the return to pre-operative levels of activity and participation.

Chapter 1 provides a general introduction and describes the outline of the thesis. First, we illustrated that the two most important underlying factors that contribute to current unnecessary prolonged convalescence include the transition of care from the hospital towards the home environment, leaving much of the recovery phase to occur outside the monitored hospital, as well as the lack of standardized perioperative education, leaving the patient unprepared for their own recovery trajectory. Second, we explained that preventing unnecessary prolonged postoperative recovery is not only beneficial to the individual patient, but has also great implications for society as a whole. At last, we described the work of our research group on which the current thesis was build. Previously, a multidisciplinary care programme was developed, consisting of an eHealth intervention and, for those patients at risk of prolonged sick leave, an occupational intervention. The conceptual framework for this care programme includes the hypothesis that unnecessary delayed postoperative recovery can be prevented through the mechanisms of:

1. providing personalised guidance throughout the entire surgical pathway from the early preoperative phase, starting from the moment the indication for surgery is set, until the late postoperative phase, ending with full recovery and resumption of all daily activities, including work;
2. promoting appropriate recovery expectations by providing tailored convalescence advice;
3. facilitating self-management.

Proof of concept of this previously developed Internet-based care programme was demonstrated in an efficacy randomized controlled trial (RCT). Exposure to the care programme led to improved return to work rates in the intervention group compared with the control group. **Chapter 2** presents the results of a process evaluation which was conducted alongside that RCT. Compliance, perceived effectiveness and satisfaction were high among patients. In addition, other stakeholders such as gynaecologists and employers assessed the intervention as potentially very useful. Notwithstanding, external validity was low due to strict guidance of patients and professionals by the research team in order to avoid protocol deviations. The results of this process evaluation were used in order to make several improvements to the care programme to facilitate implementation in real practice.

Chapter 3 presents the protocol that was designed to evaluate both the effectiveness and cost-effectiveness of the adapted perioperative care programme. A stepped stepped-wedge cluster-randomized controlled trial was employed, which involved a sequential rollout of the intervention in the participating clusters over several time periods, until all clusters received the intervention eventually. This design was advantageous as it was not obligatory for the participating hospitals to withdraw the intervention at the end of the trial. In addition, it enabled us to study the implementation process itself.

Eligible for this study were employed women, 18-65 years of age, who were scheduled for hysterectomy and/or laparoscopic adnexal surgery. The power calculation demonstrated that at least 454 participants had to be included. Depending on the implementation phase of their hospital, patients were allocated to usual care or the Internet-based care programme. The primary outcome was the duration until full sustainable return to work. The secondary outcomes included general recovery, recovery-specific quality of life, self-efficacy, coping, and pain. The data were collected by means of self-reported electronic questionnaires before surgery and at 2, 6, 12, 26, and 52 weeks after surgery. Sick leave and cost data were measured by monthly sick leave calendars, and cost diaries during the 12-month follow-up period. The economic evaluation was performed from the societal perspective.

The results of the stepped stepped-wedge cluster-randomized controlled trial are revealed in **Chapter 4**. In total, 433 women were included of which 206 women received usual care and 227 women were exposed to the Internet-based care programme. Median time until RTW was 49 days (interquartile range (IQR) 27–76) in the intervention group and 62 days (IQR 42–85) in the control group. The proportional hazard hypothesis was tested and rejected as the time-dependent covariate for group was highly significant (P=0.001). Therefore, a piecewise Cox model was fitted taking into account the non-proportionality of hazards by creating two different time intervals. In the first 85 days after surgery, patients receiving the

intervention returned to work faster than patients in the control group (hazard ratio (HR) 2.66, 95% confidence interval (CI) 1.88 to 3.77), but this effect was reversed in the small group of patients that did not reach RTW within this period (0.28, 0.17 to 0.46).

Patients in the intervention group scored slightly better on the secondary outcomes recovery-specific quality of life and pain at two weeks following surgery. The differences disappeared with longer follow-up and are probably not of any clinical relevance. Indicators showed that the implementation of the care programme was most successful at the level of the patient (82.8%) and the professional (81.7%).

Based on the results presented in this chapter we concluded that the implementation of an Internet-based care programme has a large potential to lead to accelerated recovery and improved RTW rates following different types of gynaecological surgery.

Chapter 5 describes the results of the cost-effectiveness study that was performed alongside the stepped-wedge cluster-randomized controlled trial. At 12 months, there were no statistically significant differences in total societal costs (€–647; 95% CI €–2116 to €753). However, the incremental cost-effectiveness ratio (ICER) for RTW was 56, indicating that each day earlier RTW in the intervention group was associated with cost savings of €56 compared with usual care. The probability of the intervention being cost-effective was 0.79 at a willingness-to-pay (WTP) of €0 per day earlier RTW, which increased to 0.97 at a WTP of €76 per day earlier RTW.

Taking into account that on average the costs of a day of sickness absence are €230, we considered the care programme to be cost-effective in comparison with usual care for duration until sustainable RTW after gynaecological surgery for benign disease. A latent barrier to future acceptance and implementation of the care programme lies in the fact that the costs and benefits of the care programme are separated between different types of stakeholders.

In **chapter 6** we investigated if the prospective recovery data collected in the two previous trials could be used to verify the adequacy of an earlier developed expert-based guideline on convalescence recommendations. In order to do so, we calculated median recovery times for ten daily activities (sitting, standing, walking, climbing stairs, bending, lifting, driving, cycling, household chores, sport activities and RTW) and compared these to the recovery times recommended by an expert panel. Convalescence recommendations were considered correct when at least 25% and less than 50% of the women were able to resume an activity before or at the recommended recovery time.

Recovery data were available of 304 patients with a median length of follow-up was 12 weeks (IQR: 6–12 weeks). There was a wide variation in the duration until the resumption of daily activities within and between groups of patients undergoing different types of surgery. For the majority of activities actual recovery times exceeded the recovery time recommended by the expert panel. Yet, recovery times lengthened with increasing levels of physical burden of the daily activities as well as with increasing levels of invasiveness of the procedures, conform the algorithm of the expert-based convalescence guideline. The convalescence guideline seemed more accurate for patients undergoing more complex surgery than patients undergoing minimal invasive surgeries, as the recommendations in the latter group were often too strenuous.

With the data from this study we were then able to optimize the developed expert-based guideline on convalescence recommendations. Ultimately, the collection of detailed recovery data leads to advanced tailored convalescence advice, also taking into account individual patient characteristics such as age and the presence of any co-morbidity, as well as environmental factors such as specific job demands.

Chapter 7 describes the results from a survey study which was conducted in preparation of adapting the eHealth intervention to a different patient population undergoing other types of surgery. The objective of the study was to evaluate patients' opinions, needs and preferences regarding the information and guidance provided to them during the perioperative period and to investigate whether eHealth may be of assistance in this.

Patients who underwent various forms of abdominal surgery in a one-year period were invited to complete a questionnaire about this topic. In total 207 participants completed the questionnaire. Although most participants reported that they had received some basic information about the surgical procedure and the recovery process, more than half of the participants searched the Internet for additional information. Most reported shortcomings included the absence of detailed information about the resumption of (work) activities as well as the inconsistency between advice received by different healthcare professionals involved in the recovery process. A majority (78%) of the participants expected an e-health program to be helpful during the recovery process. A website was assessed as most useful, followed by a mobile phone application. In particular practical functions focusing on the preparation for surgery and monitoring after surgery were expected to be valuable. The majority of patients opposed the option to replace the standard postoperative consult by an eConsult, since they preferred a personal contact with their surgeon.

Chapter 8 presents a systematic review that was conducted to summarize and critically appraise the current evidence on the effectiveness of perioperative strategies that facilitate

the return to preoperative levels of activity and participation. A total of 41 unique studies were included. Most studies were performed in the field of cardiology (n=11), orthopaedics (n=10) and gynaecology (n=9). To assess the content of the included interventions four different domains were identified which could be targeted: knowledge increase, behaviour modification, psychosocial guidance and organization optimization. The majority of interventions targeted more than one domain.

Outcomes included outcome measures assessing the return to preoperative levels of activity and participation. Twenty-four studies (58.5%) reported at least a positive effect of the intervention compared to usual care. Due to the substantial heterogeneity in perioperative interventions there was insufficient data to identify an optimum programme. Notwithstanding, a multimodal approach is likely to have better impact on functional outcomes compared to single modality.

In **chapter 9** the main findings of this thesis are presented, methodological considerations of the studies are discussed and the results of this thesis are put in broader perspective in the context of the available literature. Finally, a number of key features at the level of the patient, the health professional as well as the organisation of healthcare are listed that are associated with the future implementation of our intervention and determine the degree of success of implementation.

In conclusion, the present thesis demonstrated that postoperative recovery in gynaecological patients can be enhanced by improving recovery expectations and facilitating self-management through an internet-based perioperative care programme. This care programme is an example of an initiative leading to value-based healthcare: by optimizing perioperative care, patients can benefit from innovative minimal invasive surgical approaches and society as a whole can benefit through reduced healthcare utilization and minimal productivity-loss costs.

NEDERLANDSE SAMENVATTING

De totale kosten van de gezondheidszorg nemen toe. Met als doel de maatschappelijke kosten welke geassocieerd zijn met postoperatieve zorg enigszins te beperken, wordt gepoogd de lengte van ziekenhuisopnames zo kort mogelijk te houden. Echter, het blijkt dat de indirecte kosten van postoperatieve zorg, de kosten die het gevolg zijn van het verlies van productiviteit tijdens de herstelperiode, mogelijk een nog groter aandeel hebben in de totale maatschappelijke kosten. Bovendien is de duur van herstel na chirurgische ingrepen in de afgelopen decennia nauwelijks afgenomen, zeker als dit wordt afgezet tegen de geboekte vooruitgang in de medische wetenschap.

Dit proefschrift beschrijft de verschillende aspecten van een perioperatief zorgprogramma dat o.a. gebruikmaakt van het Internet ('internet-based') en dat als doel heeft de perioperatieve zorg rondom gynaecologische chirurgie te optimaliseren. De gedachte is dat onnodig langdurig postoperatief herstel door gebruik van het zorgprogramma beperkt kan worden en dat op deze manier de maatschappelijke kosten die gepaard gaan met langdurig werkverzuim en toegenomen zorgconsumptie na (gynaecologische) chirurgische ingrepen, geminimaliseerd kunnen worden. Het doel van dit proefschrift was het leveren van een wetenschappelijke bijdrage aan de kennis rondom postoperatief herstel na gynaecologische chirurgie en interventies die de terugkeer naar het preoperatieve niveau van functioneren en participatie faciliteren.

In **hoofdstuk 1** wordt een algemene introductie van dit proefschrift gegeven. Er wordt uiteengezet welke factoren een bijdrage leveren aan de huidige situatie van onnodig langdurig herstel van postoperatieve patiënten. De transitie van zorg van de ziekenhuisomgeving naar de thuisomgeving leidt ertoe dat een groot deel van het herstelproces buiten het medisch gezichtsveld plaatsvindt, terwijl de afwezigheid van gestandaardiseerde perioperatieve adviezen ertoe leidt dat patiënten zich niet optimaal kunnen voorbereiden op hun eigen hersteltraject. Het voorkomen van een onnodig langdurig postoperatief beloop is niet alleen voordelig voor de patiënt zelf, maar komt ook de maatschappij als geheel ten goede.

Met als doel de perioperatieve zorg te optimaliseren werd in een eerdere fase een multidisciplinair zorgprogramma ontwikkeld, bestaande uit eHealth-interventie en, voor patiënten met een risico op langdurig ziekteverlof, persoonlijke begeleiding door een klinisch arbeidsgeneeskundige. De werking van dit zorgprogramma is gebaseerd op de hypothese dat onnodig vertraagd postoperatief herstel kan worden voorkomen door het:

1. bieden van gepersonaliseerde begeleiding, gedurende het gehele chirurgische traject vanaf het moment van indicatiestelling tot aan het moment van volledig herstel;

2. beïnvloeden van de eigen verwachtingen ten aanzien van het herstel van patiënten, door het aanbieden van op maat gemaakt hersteladviezen;
3. faciliteren van zelfmanagement.

Het eerste bewijs voor de werking van het zorgprogramma werd gedemonstreerd in een pilot onderzoek. **Hoofdstuk 2** geeft de resultaten weer van een procesevaluatie die plaatsvond ten tijde van dit onderzoek. Patiënten die werden blootgesteld aan het zorgprogramma bleken de website daadwerkelijk te gebruiken op de manier waarop het bedoeld was, hadden zelf de indruk dat het zorgprogramma bijdroeg aan hun herstel en waren zeer tevreden. Bovendien waren andere partijen, zoals gynaecologen en werkgevers, positief over de bruikbaarheid van de interventie. De externe validiteit was echter laag. Dit had te maken met het feit dat de patiënten en de zorgprofessionals nauw werden begeleid door het onderzoeksteam om te zorgen dat er zo min mogelijk van het onderzoeksprotocol werd afgeweken. De resultaten van deze procesevaluatie werden vervolgens gebruikt om waar nodig het programma te optimaliseren.

In **hoofdstuk 3** wordt het onderzoeksprotocol gepresenteerd dat ontworpen werd om zowel de effectiviteit als de kosteneffectiviteit van het aangepaste zorgprogramma te onderzoeken. Er werd besloten gebruik te maken van een stepped-wedge, cluster-gerandomiseerd onderzoek, een methode waarbij het zorgprogramma in verschillende fases, stapsgewijs, kon worden uitgerold over de deelnemende centra. Deze methode bood verschillende voordelen, onder andere omdat het zorgprogramma aan het einde van de studie in principe niet meer hoefde te worden stopgezet in de deelnemende klinieken. Verder bood het de mogelijkheid om het implementatie proces zelf te bestuderen.

Vrouwen tussen de 18 en 65 jaar, die tenminste 8 uur per week werkten en op de wachtlijst stonden voor een eierstokoperatie en/of een baarmoederverwijdering, kwamen in aanmerking voor deelname aan de studie. Op basis van een power berekening dienden 454 deelnemers geïncludeerd te worden. Afhankelijk van de implementatie-fase van het ziekenhuis, ontvingen de patiënten de gebruikelijke perioperatieve zorg, of het interventie-zorgprogramma. De primaire uitkomstmaat was de duur tot volledige, duurzame werkhervatting. Secundaire uitkomstmaten bestonden uit een generieke maat voor herstel, kwaliteit van leven, self-efficacy, coping en pijn. Patiënte werden uitgenodigd digitale vragenlijsten in te vullen vóór de operatie en na 2, 6, 12, 26 en 52 weken na de operatie. Tevens werd gedurende 12 maanden het werkverzuim en zorggebruik gemeten met maandelijkse digitale verzuimkalenders en kostendagboekjes. De economische analyses werden verricht vanuit het maatschappelijk perspectief.

De resultaten van het stepped-wedge cluster-gerandomiseerd onderzoek worden uiteengezet in **hoofdstuk 4**. In totaal namen 433 vrouwen deel aan het onderzoek waarvan 206 vrouwen de gebruikelijke zorg ontvingen en 227 vrouwen werden blootgesteld aan de interventie. De mediane duur tot duurzame werkhervatting was 49 dagen in de interventie groep (interkwartielafstand (IQR) 27 tot 76) en 62 dagen in de controle groep (IQR 42 tot 85). Aan de proportionele hazard hypothese werd niet voldaan, aangezien de tijdsafhankelijke covariaat voor groep significant bleek (P=0.001). Dit betekende dat er twee tijdsintervallen dienden te worden gecreëerd om te corrigeren voor deze non-proportionaliteit. In de eerste 85 dagen na de operatie hadden patiënten in de interventiegroep een grotere kans op sneller herstel dan de patiënten in de controle groep (hazard ratio (HR) 2,66, 95% betrouwbaarheidsinterval (95% BI) 1,88 tot 3,77). Dit effect was omgekeerd in de kleine groep patiënten die na 85 dagen nog niet volledig hersteld was (HR 0,28; 95% BI 0,17 tot 0,46).

Twee weken na de ingreep scoorden patiënten in de interventiegroep iets beter op de secundaire uitkomstmaten kwaliteit van leven en pijn. De verschillen verdwenen echter weer met langere duur van de follow-up en zijn meest waarschijnlijk niet klinisch relevant. Verschillende indicatoren lieten zien dat de implementatie het meest effectief was op het niveau van de patiënt (82,8%) en de zorgprofessional (81,7%)

De resultaten van dit hoofdstuk leidden tot de conclusie dat de implementatie van het zorgprogramma in potentie tot versneld herstel en snellere werkhervatting kan leiden na verschillende gynaecologische ingrepen.

Hoofdstuk 5 beschrijft de resultaten van de kosteneffectiviteit-studie die gelijktijdig werd verricht met de bovengenoemde studie van hoofdstuk 4. Na 12 maanden waren er geen statistisch significante verschillen in de totale maatschappelijke kosten (€–647; 95% BI €–2116 tot €753). De incrementele kosteneffectiviteitsratio (IKER) voor werkhervatting was 56, wat betekent dat iedere dag snellere werkhervatting in de interventiegroep gepaard gaat met een kostenbesparing van €56 vergeleken met de controle groep. De kans dat de interventie kosteneffectief was, bleek 79% bij een betalingsbereidheid van €0. De kans op kosteneffectiviteit bleek geleidelijk toe te nemen met een toenemende betalingsbereidheid tot respectievelijk 97% (betalingsbereidheid: €76 per gewonnen verzuimdag).

De gemiddelde kosten voor een dag werkverzuim zijn ongeveer €230, derhalve kan het zorgprogramma in relatie tot de gebruikelijke zorg als kosteneffectief worden beschouwd. Een mogelijke barrière voor toekomstige implementatie van het zorgprogramma wordt veroorzaakt door het feit dat de kosten en de baten van het zorgprogramma gedeeld worden door verschillende belanghebbende partijen.

In **hoofdstuk 6** hebben we de prospectief verzamelde hersteldata uit de voorgaande twee gerandomiseerde onderzoeken bestudeerd. Het doel was om de eerder, door experts ontwikkelde hersteladviezen, met behulp van deze verzamelde gegevens te valideren. Om dit te bewerkstelligen werden de mediane hersteltijden van tien verschillende dagelijkse activiteiten (zitten, staan, lopen, traplopen, buigen, tillen, autorijden, het verrichten van huishoudelijke taken, sporten en werken) vergeleken met de hersteladviezen van het expert team. Hersteladviezen werden als correct beschouwd als ten minste 25% en minder dan 50% van de vrouwen de betreffende activiteit kon uitvoeren vóór het moment waarop dit door de experts werd geadviseerd.

Van 304 patiënten waren hersteldata beschikbaar met een mediane duur van follow-up van 12 weken (IQR 6 tot 12 weken). De duur tot het hervatten van dagelijkse activiteiten varieerde zeer, zowel tussen patiënten die dezelfde soort ingreep ondergingen, als tussen patiënten die verschillende soorten ingrepen ondergingen met een verschillende mate van invasiviteit. Voor het merendeel van de activiteiten gold dat de mediane duur tot het hervatten van de activiteit langer was dan de lengte van de herstelduur zoals deze werd geadviseerd door het expert team. De hersteltijden namen echter toe naarmate de intensiteit van de activiteit toenam en naarmate de invasiviteit van de chirurgische ingreep toenam, conform het algoritme dat door het expert-team was vastgelegd. De hersteladviezen bleken accurater te zijn voor patiënten die zwaardere ingrepen hadden ondergaan dan voor de patiënten die minimaal-invasieve ingrepen hadden ondergaan, omdat de adviezen voor de laatste groep vaak te streng bleken.

De data uit deze studie stelden ons vervolgens in staat de door experts ontwikkelde hersteladviezen aan te passen. In de toekomst zal de analyse van gedetailleerde hersteldata moeten kunnen leiden tot geavanceerde, op de persoon toegespitste adviezen die ook rekening houden met individuele karakteristieken zoals leeftijd of de aanwezigheid van co-morbiditeit, alsook omgevingsfactoren zoals specifieke taakvereisten van iemands baan.

In **hoofdstuk 7** worden de tekortkomingen in de huidige perioperatieve zorg vanuit een patiënten perspectief geïnventariseerd en wordt bekeken hoe eHealth hier een rol in zou kunnen spelen, door middel van een vragenlijstonderzoek. Dit onderzoek werd uitgevoerd als voorbereiding op de uitbreiding van het zorgprogramma naar een andere patiëntenpopulatie en had als doel de meningen, behoeften en voorkeuren van patiënten rondom perioperatieve zorg te evalueren.

Patiënten die verschillende vormen van abdominale chirurgie hadden ondergaan, werden uitgenodigd om een vragenlijst in te vullen over dit onderwerp. In totaal vulden 207

patiënten de vragenlijst in. Alhoewel de meeste patiënten aangaven dat zij basisinformatie hadden ontvangen over de chirurgische ingreep en het herstelproces, gaf meer dan de helft van de deelnemers aan dat zij op het Internet aanvullende informatie hadden opgezocht. Patiënten hadden vooral een gebrek aan gedetailleerde informatie ervaren over de hervatting van dagelijkse en werk-gerelateerde activiteiten. Bovendien bleek dat zij vaak tegenstrijdige adviezen hadden gekregen van verschillende zorgverleners die betrokken waren bij de perioperatieve zorg. Het merendeel van de patiënten (78%) gaf aan dat zij verwachtten dat een eHealth interventie van toegevoegde waarde had kunnen zijn tijdens hun herstel. Een website werd als meest waardevol beoordeeld, gevolgd door een mobiele applicatie (app). In het bijzonder werden functies die zich richten op de voorbereiding naar de operatie toe en de begeleiding direct na de operatie als nuttig beoordeeld. Het grotendeel van de patiënten was niet geïnteresseerd in de mogelijkheid om het postoperatieve consult te vervangen door een eConsult, sinds zij het persoonlijk contact met de operateur erg waardeerden.

Hoofdstuk 8 beschrijft een systematisch uitgevoerd literatuuronderzoek naar de effectiviteit van interventies die de terugkeer naar het preoperatieve niveau van functioneren en participatie trachten te bevorderen. In totaal werden 41 unieke studies geïncludeerd, waarvan de meeste werden uitgevoerd binnen de cardiologie (n=11), orthopedie (n=10) en gynaecologie (n=9). Om de inhoud van de verschillende interventies te beoordelen werden de volgende domeinen geïdentificeerd waarop de interventie kon aangrijpen: kennistoename, gedragsverandering, psychosociale begeleiding en optimalisatie van (zorg)processen. De meeste studies raakten meerdere domeinen aan.

Vierentwintig studies (58,5%) rapporteerden tenminste één positief effect van de interventie vergeleken met gebruikelijke zorg op een van de gebruikte uitkomstmaten die de terugkeer naar preoperatief niveau van functioneren en participatie representeerden. Vanwege de substantiële mate van heterogeniteit was het niet mogelijk om vast te stellen hoe een ideaal zorgprogramma eruit ziet.

In **hoofdstuk 9** worden de belangrijkste bevindingen van dit proefschrift samengevat. We bespreken de methodologische overwegingen van de studies en de resultaten van dit proefschrift worden in de context van de beschikbare literatuur geplaatst. Tot slot wordt een aantal belangrijke aspecten op het niveau van de patiënt, de zorgverlener en de organisatie van de gezondheidszorg benoemd, die verband houden met de toekomstige implementatie van onze interventie en de mate van succes hiervan.

Concluderend heeft dit proefschrift aangetoond dat een internet-based, perioperatief zorgprogramma in staat is het postoperatieve herstel van gynaecologische patiënten

te bevorderen. Dit kan bereikt worden door, onder andere, de verwachtingen van patiënten ten aanzien van het herstel positief te beïnvloeden en door het faciliteren van zelfmanagement. Dit zorgprogramma is een voorbeeld van waardegedreven zorg, waarbij patiënten kunnen profiteren van innovatieve minimaal-invasieve chirurgische ingrepen en bijgevolg de samenleving als geheel zal profiteren door snellere werkhervatting en hierdoor verminderde productiviteitsverliezen in deze populatie.

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CURRICULUM VITAE

Esther Vivienne Angelique (Eva) Bouwsma werd op 22 december 1982 geboren te Ede. Aan het Marnix College te Ede volgde zij tweetalig VWO en haalde haar VWO diploma in 2001. In dat zelfde jaar startte zij met haar studie Geneeskunde aan de Vrije Universiteit van Amsterdam. Zij verrichtte een wetenschappelijke stage in Groote Schuur in Kaapstad in Zuid-Afrika en deed een keuze-coschap kindergeneeskunde in het Kanti Kinderziekenhuis in Kathmandu in Nepal.

In augustus 2008 behaalde Eva haar artsexamen en startte zij als ANIOS verloskunde en gynaecologie in het Spaarne Gasthuis te Hoofddorp (opleider dr. M.H. Emanuel). In 2010 besloot zij voor een jaar af te reizen naar Rochester, Minnesota, in de Verengde Staten, waar zij kennismaakte met wetenschappelijk onderzoek onder begeleiding van prof. dr. E.A. Stewart in de Mayo Clinics.

Tussen 2008 en 2012 was Eva actief lid van vrijwilligersorganisatie Medical Checks for Children en ging zij mee op missie naar Nepal, Tanzania, Bangladesh en India. Ook was zij missieleider en medisch eindverantwoordelijke tijdens een medische missie naar Bolivia.

In 2011 startte Eva onder leiding van prof. dr. J.A.F. Huirne en prof. dr. J.R. Anema haar promotie onderzoek, waarvan dit proefschrift het resultaat is. Van ZonMw ontving zij een AGIKO stipendium wat haar in staat stelde het wetenschappelijk onderzoek met de klinische praktijk te combineren. In deze periode volgde Eva tevens de Masteropleiding Epidemiologie aan de Vrij Universiteit en mag zij zich sinds 2014 epidemioloog noemen.

In 2015 startte Eva met haar opleiding tot gynaecoloog in het Onze Lieve Gasthuis in Amsterdam (opleider dr. E.M. Kaaijk) binnen het cluster VU medisch centrum. Vanaf juni 2017 was zij werkzaam in Amsterdam UMC locatie VUmc (opleider prof. dr. J.I.P. de Vries). In oktober 2019 zal Eva starten met haar differentiatie benigne gynaecologie in het Flevoziekenhuis te Almere (opleider dr. W.M. van Baal).

Eva woont, samen met Lloyd Denswil, in Amsterdam.