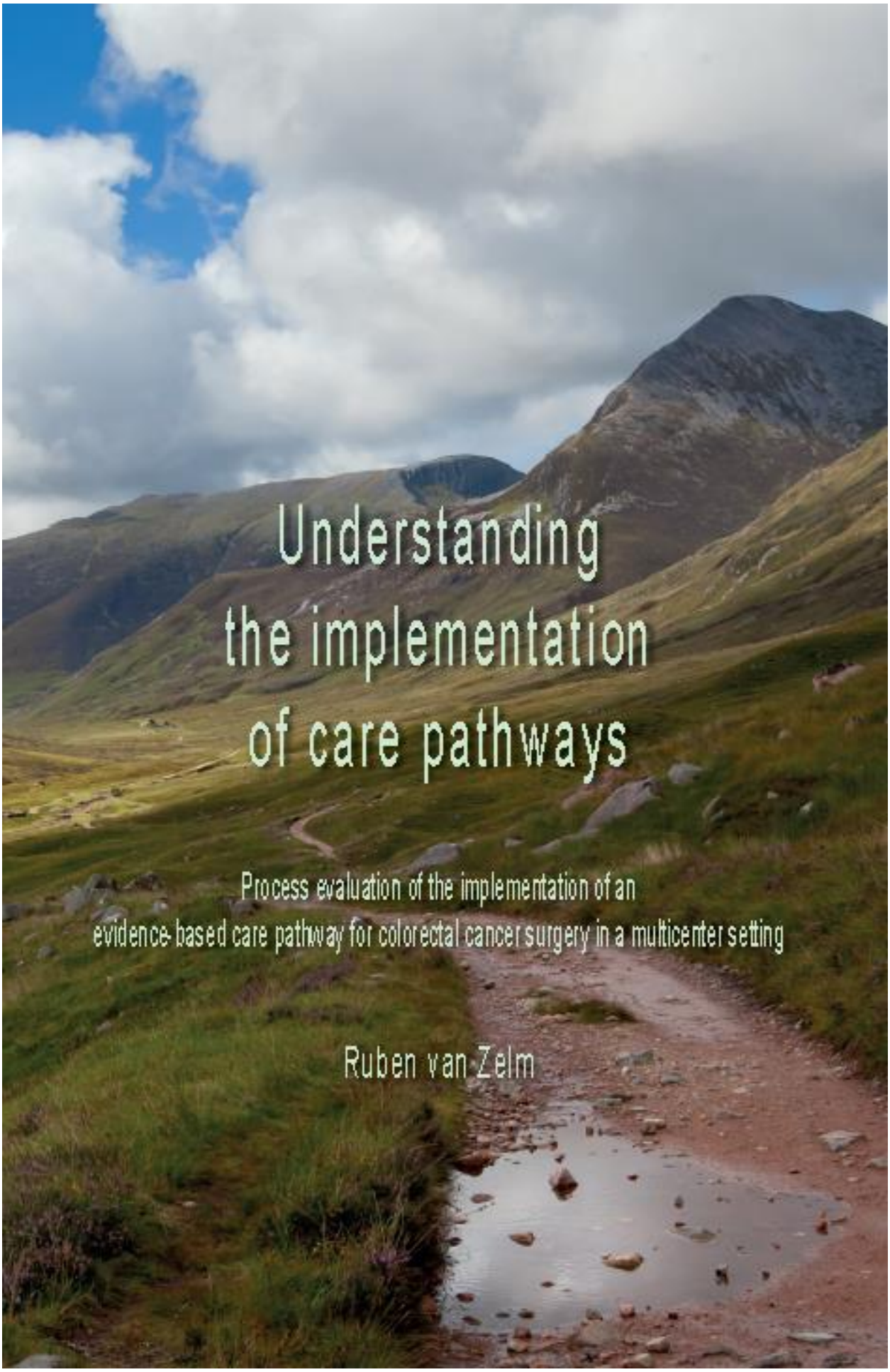
Understanding
the implementation
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Process evaluation of the implementation of an
evidence-based care pathway for colorectal cancer surgery in a multicenter setting
Ruben van Zelm

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KU LEUVEN

DOCTORAL SCHOOL
BIOMEDICAL SCIENCES

DOORGRONDEN VAN DE INVOERING VAN ZORGPADEN

PROCESEVALUATIE VAN DE INVOERING VAN EEN EVIDENCE-BASED ZORGPAD VOOR COLORECTALE KANKER CHIRURGIE IN EEN MULTICENTER SETTING

Ruben VAN ZELM

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Proefschrift voorgedragen tot het behalen van de graad van Doctor in de Biomedische Wetenschappen

18 december 2019

Cover by Arno van den Bergh, Woerden
West Highland Way, Kinlochleven – Fort William (2018)

ISBN: 978 90 903 2618 4
Printed by Acco Drukkerij, Herent – Belgium

KU Leuven
Biomedical Sciences Group
Faculty of Medicine
Department of Public Health and Primary Care

KU LEUVEN

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PROCESS EVALUATION OF THE IMPLEMENTATION OF AN EVIDENCE-BASED CARE PATHWAY FOR COLORECTAL CANCER SURGERY IN A MULTICENTER SETTING

Ruben VAN ZELM

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Dissertation presented in partial fulfilment of the requirements for the degree of Doctor in Biomedical Sciences

December 18, 2019

DANK! DANKE! MERCI! THANKS!

Het is al vaker gezegd en geschreven: een promotieonderzoek uitvoeren is teamwork. Ik ben in de afgelopen jaren door velen ondersteund en geholpen, op vele verschillende manieren. Een aantal personen wil ik hier graag specifiek benoemen.

Allereerst mijn promotor, professor Sermeus. Beste Walter, dank je voor je inzet en tijd, je kennis, je vertrouwen in me, je wijze adviezen en vooral de prettige en humorvolle samenwerking. Opmerkingen als “er is nog wat werk aan” haalden het beste in me naar boven!
Dan mijn copromotor professor Vanhaecht. Kris, vriend, zonder jou was dit doctoraat er niet geweest. Ik waardeer je om je enorme expertise. Ik dank je voor je vriendschap, schouderklopjes, duwtjes in de rug en schop(jes) onder andere lichaamsdelen wanneer nodig.... “That’s what friends are for”.
Copromotor doctor Bruyneel. Luk, dank je voor je expertise en je geduld, je kritische vragen naar zaken die ik zelf al niet meer zag. Je input was oneindig veel meer waard dan de “two cents” zoals je het zelf eens noemde.

De leden van de interne en externe jury. Professoren D’Hoore en Van Achterberg, en professoren Ahaus, Dejong, Hellings, en Milisen, hartelijk dank voor de kritische opvolging van mijn doctoraat en de waardevolle input op mijn manuscript.

Professor Panella, friend and chairman of the E-P-A. Dear Massimiliano, thanks for your support over the past years and your contribution to the conception of the study.

A big thank you to all involved professionals in the 12 hospitals that participated in the study. Without you and your input, this study would have been impossible. I hope sincerely that the implemented care pathway is helpful in providing high quality care to your patients. Thank you, Vielen Dank, Merci Beaucoup, Hartelijk dank!
Dit onderzoek was niet mogelijk geweest zonder de steun van Baxter. Leentje Nonneman en collega’s, bedankt voor de praktische ondersteuning en constructief meedenken in het project.

Klinische experts en coauteurs van verschillende papers, professoren De Buck van Overstraeten, Weimann en Wolthuis. Beste Anthony, Arved en Albert, dank dat jullie mij op het juiste “klinische pad” hielden!

Een deeltijd doctoraat naast twee jobs maakt dat er veel behulpzame collega’s zijn! Ingrid, dank je voor je inzet en steun bij de start van het onderzoek. Collega’s van het LIGB. Ellen, lieve Ellen, dank voor je goede adviezen, praktische hulp en de gezelligheid, vooral tijdens onze road trip langs de ziekenhuizen. Daan, dank voor je onmisbare hulp bij de sessies in de Franstalige ziekenhuizen. Deborah, je adviezen en input op methodologisch en praktisch gebied waren meer dan behulpzaam. Ellen V., dank voor je praktische hulp.
Collega’s van de Hogeschool Utrecht, master innovatie in zorg en welzijn. Dank voor het meedenken en -leven. In het bijzonder wil ik Marlou bedanken. In al je wijsheid heb je me het allerbelangrijkste gegeven wat ik de afgelopen jaren nodig had: tijd!
Collega’s en MT van Q-Consult zorg en speciaal de collega’s uit het team doelmatigheid. Bedankt voor jullie niet aflatende belangstelling, aanmoediging en zorgzaamheid. Sanne, dank je voor het mogelijk maken van de flexibiliteit bij het invullen van mijn droom-mix-van-banen.

Lieve familie, schoonfamilie en vrienden. Dank voor het begrip de afgelopen jaren dat ik soms letterlijk wat afwezig was, en voor jullie support en belangstelling. Mam, wat was je betrokken en wat had je hier graag bij willen zijn. Pap en mam, jullie hebben me de best denkbare start gegeven.

En last but not least, mijn eigen microsystem: Carolien, Job en Oscar. Mannen, ook jullie bedankt voor het begrip, de belangstelling en vooral de ontspanning die jullie brachten met gekkigheid, (gesprekken over) games die ik niet begreep en verhalen over studie, school, werk of theater. Lieve Carolien, terwijl ik doctoreerde, werd jij “even” meester in de rechten. Wat ben ik ontzettend trots op je! Jouw inzet voor jouw studie, elke avond, elk weekend, vier lange jaren. Het was een inspiratie voor mij. Daarnaast slaagde je erin om de beperkte tijd die we samen konden doorbrengen, dubbel waardevol te maken. Lieve Carolien, dank voor je geduld, begrip en liefde.

Ruben van Zelm
December 2019

LIST OF ABBREVIATIONS

ASA	American Society of Anesthesiologists
CFIR	Consolidated Framework for Implementation Research
COM-B	Capability, Opportunity, Motivation – Behavior framework
CP	Care pathway
CPSET	Care Process Self Evaluation Tool
CRC	Colorectal Cancer
CRP	C-Reactive Protein
Dept	Department
DSM	Diagnostic and Statistical Manual of mental disorders
E-P-A	European Pathway Association
eNPT	extended Normalization Process Theory
ERAS	Enhanced Recovery After Surgery
ERP	Enhanced Recovery Protocol
ICU	Intensive Care Unit
I-P-A	Important Performance Analysis
IQR	Inter Quartile Range
KI	Key Intervention
LMWH	Low Molecular Weight Heparin
LOS / ΔLOS	Length Of Stay / difference in Length Of Stay
MRC	Medical Research Council
MUSIQ	Measuring and Understanding Success in Quality improvement
NoMAD	Normalization Measure Development
NSAID	Non Steroid Anti Inflammatory Drug
OR	Odds Ratio
RR	Relative Risk
SD	Standard Deviation
TIDieR	Template for Intervention Description and Replication
TNM	Tumor-Node-Metastasis
TPN	Total Parenteral Nutrition
UCV	Unwarranted Clinical Variation

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CHAPTER 1

GENERAL INTRODUCTION

VARIATION AND INSUFFICIENT ADHERENCE TO EVIDENCE-BASED CARE

Providing healthcare is knowledge intensive. However, there is still a challenge in translating knowledge into clinical practice. This implies that patients potentially do not receive care which is up to date with the latest evidence.[1] As early as 2003, the "Quality of health care study" was published in the New England Journal of Medicine. This paper, regarded as a landmark study, stated that adherence to clinical guidelines is low and highly variable. The authors concluded that patients receive on average 55% of care recommended in guidelines.[2]

Mickan et al. (2011) performed a systematic review on "leakage" in the use of clinical guidelines. In all phases from awareness to adherence to guidelines, there is observed leakage from research knowledge. The authors concluded that leakage increases proportionally in the consecutive phases, and that recommendations may not be adhered to in two thirds of the time. Clinical guidelines are not sufficient to implement research.[3]

In September 2018, the National Academies of Sciences, Engineering and Medicine concluded in their Global Quality Chasm Report, that variation in care and underuse of evidence-based care is still a worldwide problem.[4]

A recent "rapid review" of current evidence by Harrison et al. (2019) focused on unwarranted clinical variation (UCV). This is defined as variation that can only be explained by differences in health system performance. Based on the literature, the authors concluded that there is growing evidence on UCV, but that it is not straightforward to determine the parameters for UCV. There is variation in healthcare, of which some may be problematic, according to the authors.[5]

These findings strongly suggest that there exists two distinct, but related problems regarding evidence-based recommended care: adherence to guidelines is relatively low, and variable. This could lead to underuse or overuse of care.

COLORECTAL CANCER SURGERY AS A CASE

Colorectal cancer surgery is an area that reflects the problems mentioned above. It concerns a high volume patient group. Worldwide, the number of new cases diagnosed yearly, is over 1.8 million, making colorectal cancer the third cancer type (after lung and breast cancer). Europe accounts for 27% of the total volume.[6] A national registry study over a 25 year timeframe in the Netherlands by Brouwer et al. (2018), showed that the incidence of colon cancer increased by 35%, while the mortality decreased. For rectum cancer the same but less pronounced trends were observed. Nearly all patients with a tumor of TNM stage I-III underwent colorectal surgery. Approximately half the patients with a tumor stage IV underwent surgery, while the use of adjuvant radiotherapy and chemo radiotherapy increased over time.[7] These data suggest that resection of the tumor is still the most prevalent treatment. This surgical care process is predictable, making the use of care pathways possible. More importantly, there is a well-established international standard for the perioperative care of colorectal cancer, the so-called “enhanced recovery after surgery” (ERAS) protocol, with a recent update.[8,9] In a review paper ERAS is described as the new revolution in surgery, leading not only to better outcomes, but lower costs as well.[10] Pedziwiatr et al. (2018) concluded that there is growing evidence that ERAS is “safe, feasible and associated with improved outcomes” (p7). The authors also concluded that there are challenges in daily practice in sustaining protocol adherence, and that new implementation strategies are needed.[11] A meta-analysis by Lau et al. (2017) showed that the implementation of the ERAS protocol in surgery programs, including colorectal cancer surgery, leads to significant reduced length of stay (LOS) (difference of means -2.3 days), postoperative complications (RR 0.634) and costs (-$1003.79), and an earlier return of gastrointestinal function. There were no differences in overall mortality and readmission rates between ERAS groups and “usual care” groups.[12]

Despite the availability of the well-established ERAS protocol for almost 15 years, there is still considerable variation in protocol adherence, with reported adherence rates ranging between 45 and 92%.[13-15] Moreover, a “dose-effect” relationship between adherence rate and patient outcomes has been suggested. A prospective cohort study by Gustafsson et al. (2016) in 911 consecutive

patients undergoing major colorectal cancer surgery, showed an adherence rate of ≥70% in 30% of the patients. For these patients, the risk of cancer specific death was reduced by 42%.[15] Li et al. (2017) performed a prospective cohort study in 251 patients. The patients were divided in four groups, based on adherence rate: group I 0-60%, II 60-70%, III 70-80% and IV 80-100%. Their results showed better outcomes with higher adherence rates. The outcomes included complication rate (group I 41.3%, II 33.3%, III 26.4%, and IV 16.7%) and median LOS (group I 12.5, II 10, III 9, and IV 8 days).[16] Recently, Martin et al. published a multicenter prospective study including 4023 patients. Although the focus was on the nutritional aspects of the ERAS protocol, overall protocol adherence was also measured. The authors concluded that low adherence to ERAS (defined as ≤70%) predicted the occurrence of complications (OR 2.69).[17] This research suggests that high adherence rates of 70% and higher are to be pursued.

Several evaluations of the implementation of ERAS for colorectal surgery are published. Gotlib Conn et al. (2015) performed a process evaluation on normalization of ERAS in everyday practice. The Normalization Process Theory is used as framework to describe and explain the implementation. The authors conclude that ERAS implementation is achieved by complex cognitive and social processes in which a “champion”, external and internal relationship building, and strategic management of the project are key.[18] Gramlich et al. (2017) performed a multicenter evaluation of the implementation of an ERAS program, showing similar findings.[19] Qualitative investigation of implementation of ERAS programs in multiple surgical specialisms, including colorectal surgery, by Herbert et al. (2017) and colorectal surgery by Alawadi et al. (2016) identified facilitating factors, including alignment with evidence-based practice, leadership, teamwork and communication, staff and patient education, monitoring and feedback, and adapting the care pathway to fit local circumstances. Barriers identified included resistance to change, standardization affecting personalized care, lack of coordination, stakeholder buy-in, and resources, aligning different cultures, rotating residents, and using a segmented approach.[20,21] In a literature review by Coxon et al. (2017), two theories regarding the implementation of enhanced recovery protocols (ERPs) were presented. The first theory focuses on staff consultation. The second theory focuses on change agency, the availability of a champion. The theories present a complex and delicate combination of

context and mechanisms.[22] Stone et al. (2018) published a systematic review by identifying barriers to and facilitators of implementation of ERAS protocols. They included 53 studies in a variety of surgical specialisms. Main facilitators were adapting the protocol to local circumstances, achieving quick wins, engagement of frontline staff and management, having a strong ERAS team with good communication, and availability of effective supporters and ERAS staff. Barriers were resistance to change, lack of resources and external factors (e.g. patient complexity). The authors conclude that few publications describe implementation in detail, and that more high-quality studies on the implementation process are needed.[23] The studies described above suggest that implementing and sustaining an ERP is not straightforward. It requires multiple facilitators, identification and management of barriers, and complex social and cognitive processes in a multidisciplinary team, within their context.

CARE PATHWAYS AS STRATEGY TO IMPROVE ADHERENCE TO EVIDENCE

Both reviews by Mickan and Harrison provided a number of recommendations to improve guideline adherence. The recommendations by Mickan et al. (2011) include, among others, the use of research evidence to clarify expected outcomes and key points of decision making, and to manage clinical environments to develop specialist clinics and monitor key outcomes.[3] Harrison et al. (2019) identified a number of approaches to tackle UCV, including the development and implementation of care pathways (CPs), patient education, benchmarking, use of opinion leaders and financial incentives.[5]

As suggested by the above papers, one strategy to improve the adherence to guidelines is developing and implementing CPs. Care pathways, also known as clinical or critical pathways, are used worldwide as one of the tools to structure or design care processes around patients' needs and, by doing so, to improve the quality of care. In this study the definition of the European Pathway Association is used. A CP is defined as "a complex intervention for the mutual decision making and organization of predictable care for a well-defined group of patients during a well-defined period". A care pathway combines evidence-based key interventions, feedback on the actual care process,

with a strategy for quality improvement. Defining characteristics of a CP include: (1) An explicit statement of the goals and key elements of care based on evidence, best practice, and patients' expectations and their characteristics, (2) the facilitation of the communication among the team members and with patients and families, (3) the coordination of the care process by coordinating the roles and sequencing the activities of the multidisciplinary care team, patients and their relatives, (4) the documentation, monitoring, and evaluation of variances and outcomes, and (5) the identification of the appropriate resources. [24,25] Despite the worldwide use of CPs, international research on the impact of care pathways is still inconclusive, although a Cochrane review concluded that CPs lead to positive outcomes.[26] A more recent systematic review on interventions to improve safety in surgery, identified adherence to CPs as one of the effective interventions.[27] A study in breast cancer radiation therapy, showed that the use of a care pathway improved compliance to evidence-based recommendations from 4 to 95%. The authors conclude that CPs effectively standardize care to reflect up-to-date evidence.[28]

Previous research at KU Leuven has shown that care pathways have positive effects on team outcomes (team work, level of organization of work and risk of burnout)[29,30], positive effect on adherence to clinical guidelines [31,32], and that synergetic elements of context and intervention mechanisms affect the level of implementation of the CP.[30]

Although evidence on the effect of CPs on outcomes and process (including adherence to guidelines) is still growing, little is known on the implementation process itself. A number of studies have identified barriers and facilitators to CP development and implementation. Evans-Lacko (2010) described the process of implementing CPs in three phases: development, implementation, and evaluation. The authors identify facilitators and barriers in all three phases, including lack of clinician involvement, management support, clarity of the CP, time and resource constraints, and mixed attitudes of staff regarding standardization.[33] A study on implementation of CPs in emergency departments identified implementation influencing factors using the COM-B system (capability, opportunity, motivation – behavior) proposed by Michie et al. (2012) as framework to understand behavior.[34] The barriers and enablers identified in capability include knowledge and skill, and

characteristics of the CP (e.g. user friendly). Factors within opportunity include resources, staffing issues, and “challenging periods”. Motivation included factors such as beliefs about capabilities, commitment to evidence-based practice, and believe in positive patient benefits.[35] A qualitative study on implementation of CPs in Swedish intensive care units (ICU’s), showed that CP implementation is a complex process, characterized by the struggle for a feasible tool, as conceptualized by the authors. A bottom-up implementation strategy is recommended, combined with need for strategic priority, participation of involved professionals and the support of skilled facilitators.[36]

Although this research adds to the understanding of both the effect and the implementation process of CPs, a number of questions remain. The variability in the effect of CPs is substantial. Why do CPs have better effect in one study or organization, compared to others? When studying the implementation of CPs, what exactly has been implemented? Who was involved, what interventions were used, what was the role of audit and feedback? In what context was the CP implemented, and how does this context affect the implementation?

PROCESS EVALUATION TO UNDERSTAND THE IMPLEMENTATION PROCESS

Our rationale for effectiveness of CPs is that a core set of evidence-based key interventions is delivered to an improvement team, together with feedback on their current performance (both patient outcomes and compliance to the key interventions). This feedback will identify the room for improvement. The team then develops its strategy for improvement, including goal-setting and implementation activities, based on the received feedback. CPs are therefore, by definition, “complex interventions”.[25,37] Complex interventions are usually defined as interventions containing several interacting components. Next to this, complex interventions have other characteristics that determine the complexity: the number and difficulty of behaviors required by those using the intervention, the number of groups or organizational levels targeted by the intervention, the degree to which the intervention can be tailored, and the number and variability of outcomes.[38]

Because of the different components and characteristics involved, evaluating the implementation process of complex interventions is challenging. In 2015, the Medical Research Council (MRC) published guidance on process evaluation of complex interventions. The MRC recommends an integral approach, which links the key components of process evaluation of complex interventions. These components are context, implementation, and mechanisms of impact. A description of the intervention which is evaluated, acts as input for the evaluation. The output is the actual outcome achieved with the intervention.[39,40]

The MRC guidance is used for the overall methodology of this PhD thesis. Theoretical guidance on implementation processes is further needed to understand and explain relationships between elements of context, implementation activities, mechanisms, and outcomes. In current implementation literature, a wide range of implementation theory is offered. A scoping review recently identified 159 implementation frameworks, models and theories reported in studies. The majority of these frameworks, models and theories (87%) were found to be used in only five or less studies, and 60% was used only once.[41]

For our purpose, understanding the implementation process and explaining the relationships between factors, selection of a theory is needed. We chose the (extended) Normalization Process Theory (eNPT) as theoretical framework.[42] Normalization Process Theory explains how complex interventions are implemented and integrated in everyday practice (i.e. “normalized”). NPT has developed over the years, and is still developing.[43,44] The first development phase (2006) focused on collective action and interaction of people with the complex intervention. Mechanisms proposed by the theory (then referred to as Normalization Process Model) were workability and integration of the complex intervention.[43,44] The second phase (2009) focused on what people do to implement a complex intervention. The mechanisms coherence, cognitive participation, collective action, and reflexive monitoring were introduced to explain implementation processes.

The third phase (2013) was presented as a step toward a general theory of implementation. This version is an “extended” version of the theory, hence the name eNPT. The previously described mechanisms are embedded in a broader theory, also focusing on context. Four main constructs are

proposed that explain the implementation and normalization process. Two of these constructs deal with the context (potential and capacity), and two constructs explain expressions of agency (capability and contribution).[42] A more recent publication suggests that the role of context in the theory is still developing.[43]

In a systematic review on the use of Normalization Process Theory (all three versions described above) by May et al. (2018) 108 studies published between 2006 and 2017 were identified. The theory was applied in a variety of settings and for a range of different interventions, suggesting broad applicability. Reasons for using NPT mentioned in the included studies were: NPT as conceptual framework to structure study design, the empirical grounding of the theory, and its usefulness in considering implementation design. The majority of the included studies (68%) were process evaluations.[44] However, only three of the included studies used the extended NPT, all three being process evaluations.[45-47]

The rationale for using eNPT, next to the reasons mentioned above, is first that it fits our purpose as an explanatory theory that originates in implementation science, but is built on existing theories of change, structure and action, and social cognitive psychology.[42] Second, the four main constructs of eNPT allow the exploration of context, and both individual and group implementation activities and mechanisms as described in the MRC guidance, providing a conceptual “fit” between our methods and theory. And finally, several other studies have been published on CP implementation using (e)NPT, which can facilitate the comparison and understanding of our results.[18,20,30,48,49]

RESEARCH OBJECTIVES AND OVERALL METHODOLOGY

A distinction can be made between (practical) quality improvement projects and other (scientific) types of studies. The primary goal of quality improvement studies is to secure change, and to learn what works in a local context. This includes the study of the effect of quality improvement, as well as the study of mechanisms of change, and methods and tools for quality improvement. The primary goal of other studies, is evaluation and the advance of knowledge, although the “practical” and

"scientific" are not opposites or in conflict with each other.[50] Both groups of studies have their own designs and strengths. Portela et al. (2015) listed the strength of quality improvement studies as the flexibility in testing change, incorporating local knowledge and experience, and the possibility to gradually move from testing an intervention to more broad application. Weaknesses are that the results are not easily generalizable, and that a structured explanation of mechanism of change usually lacks. Strengths of a process evaluation are that it provides understanding of improvement interventions in practice and the level to which an intervention was implemented as intended.[50]

This PhD study combines the strengths of both quality improvement studies and process evaluation, mitigating the weaknesses of quality improvement studies as mentioned above. The study has two main objectives:

1. To perform an international quality of care improvement initiative for patients undergoing surgery for colorectal cancer, by:
    a. developing a model care pathway including key interventions and indicators;
    b. studying the pre- and post-implementation adherence to and variation in perioperative care;
    c. implementing a care pathway.
2. To evaluate the implementation process of a care pathway for colorectal cancer surgery by performing a process evaluation:
    a. developing a method to perform process evaluation of evidence-based care pathways;
    b. evaluating the context, implementation process, mechanisms of impact of the implementation of the care pathway;
    c. exploring the relationships between context, implementation and mechanisms, in relation to the intervention and outcomes.

A mixed method design is used, as recommended by the MRC, to capture all essential elements of the implementation of the care pathway.[38-40] The core mixed methods design is the convergent design. In this design, both quantitative and qualitative data are collected and analyzed parallel, and are only then combined in an overarching analysis.[51]

Figure 1.1 provides a diagram of this PhD study, showing the sequencing of the phases. The rationale for using mixed methods is to achieve the best insight from both a quantitative as well as narrative perspective, and then combining and integrating both perspectives which leads to a more comprehensive understanding then would have been possible with quantitative or qualitative data alone.[51]

In this mixed methods process evaluation design, five phases have been conducted over time. First, a literature review in three electronic databases was performed. The purpose of this literature review was to identify, summarize, and operationalize the clinical content of both key interventions and clinical indicators. An evidence-based "model pathway" for perioperative care for patients undergoing colorectal cancer surgery was developed (**chapter 2**). The ERAS protocol (2013 version) was used as basis for the model care pathway, supplemented with a number of extra interventions found in literature.

Second, based on the interventions in the model pathway, a pre-implementation quantitative measurement was performed to assess the variation in both process and outcomes of care (**chapter 3**). The purpose of this study was to assess colorectal units' protocol adherence rates in daily practice. Two major objectives have been defined:

1. To describe protocol adherence for perioperative care in colorectal cancer surgery.
2. To study the relationship between adherence to the individual protocol elements ("key interventions") and the importance (strength) of key interventions.

The study was performed in 12 hospitals across four countries. Twenty consecutive patients per hospital who met the inclusion criteria (adults undergoing planned colorectal cancer surgery) were included. Data were collected retrospectively from patient records, focusing on patient outcomes (e.g. length of stay, time to normal diet, readmission rate) and protocol adherence.

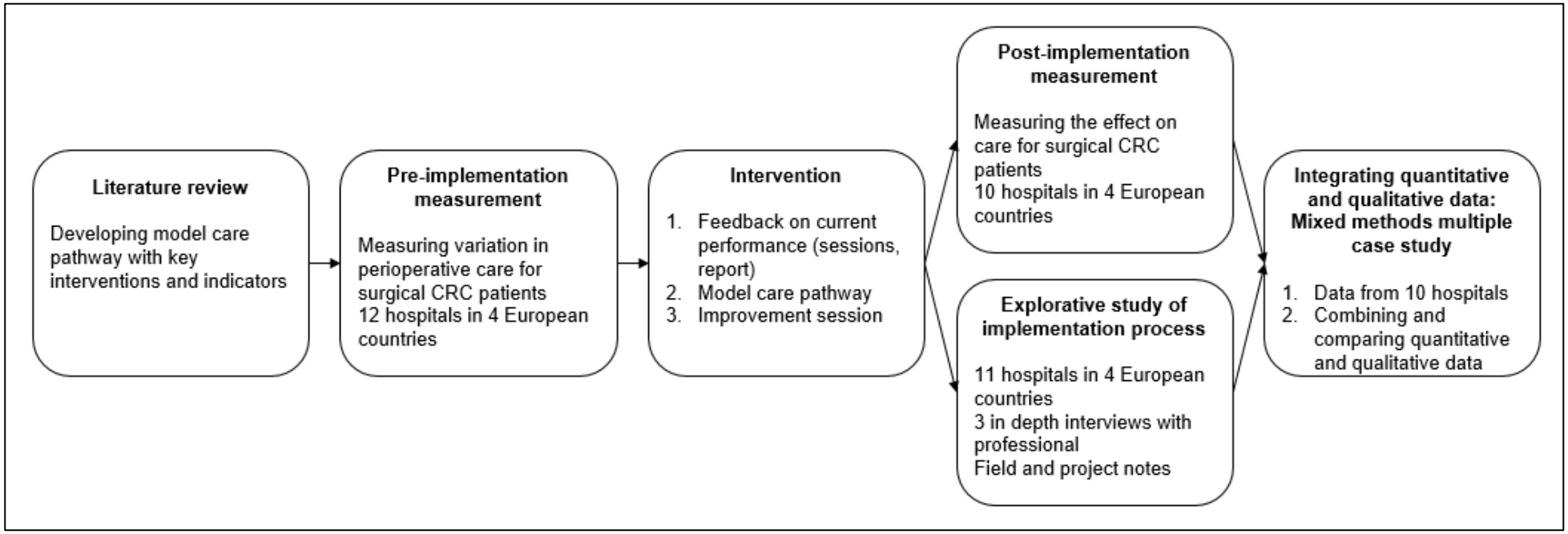

Figure 1.1 Overview of the PhD study

Third, following the pre-implementation measurement, the participating improvement teams in the hospitals received feedback on their current care process in the form of a national feedback session organized within each country, a local feedback session within each hospital, and a detailed feedback report to supplement the sessions. Next, the local quality improvement teams received the model care pathway, including the evidence-based key interventions, as base for the local pathway. It was delivered and explained on-site in all participating centers to the quality improvement teams, as support for their strategy for change.

In the following study phases the actual process evaluation was performed. A protocol for this process evaluation was developed and published (**chapter 4**). The objective of this protocol paper was twofold: first, it proposed a study protocol to evaluate the implementation process of evidence-based care pathways. Second, it provided a worked example of the application of the study protocol to generate results that will help understand and inform future implementation of (colorectal cancer surgery) care pathways.

In the fourth phase, a qualitative exploration of the implementation process took place using the MRC guidance on process evaluations of complex interventions as theoretical framework (**chapter 5**). The overall aim was to explore the experiences of professionals with the implementation process of the CP. Research questions were:

1. What is the context of the CP implementation?
2. How was the CP implemented, who was involved?
3. What mechanisms influenced the implementation of the care pathway?
4. What is the relationship between the outcomes of the formative evaluation and implementation priorities and strategy?
5. What unexpected events or consequences occurred during implementation?

Data were collected using in-depth interviews with three direct involved professionals (colorectal surgeons, (head) nurses, quality officers) in 11 hospitals in four countries, focusing on the interviewee's experience with the implementation process.

Parallel to the qualitative study, a post-implementation quantitative effect study was performed (**chapter 6**). The primary aim of this study was to evaluate the clinical effectiveness of implementing a care pathway for perioperative care in adults undergoing colorectal cancer surgery. The secondary aim was to assess adherence to and documentation of the CP, and describe variation in adherence and improvement rates across and within hospitals.

This study was performed in 10 hospitals across four countries. Data in both pre- and post-implementation phase were collected retrospectively from patient records, focusing on patient outcomes and protocol adherence. Twenty consecutive patients per hospital who met the inclusion criteria were included in both pre- and post-test. Additionally, a questionnaire per hospital was used to collect self-reported adherence rates in the post-implementation phase.

In the fifth and final phase, the quantitative and qualitative data were integrated in an overall interpretation (**chapter 7**). We used a mixed methods multiple case study design to first identify the top- and bottom-improving hospitals based on quantitative data. Next, we used qualitative data to investigate the cases and look for explanations for the differences in improvement and performance. The eNPT was used as theoretical framework. Research questions were:

1. Which factors explain the relationship between pre-and post-implementation performance (LOS and protocol adherence) and improvement rate?
2. What is the relationship between intended and measured adherence rate?

The final chapter in this PhD-thesis (chapter 8) is the general discussion in which the main findings and conclusions are presented.

Ethics approval for this study was obtained from the ethics committee of the University Hospital Leuven, Belgium (S57152 (ML11311). Interview participants were given the opportunity to ask questions about the study and each participant provided written informed consent to participate in the study, including consent for publication. The participants were informed that their participation was voluntary, and that it was possible to withdraw from the study at any time.

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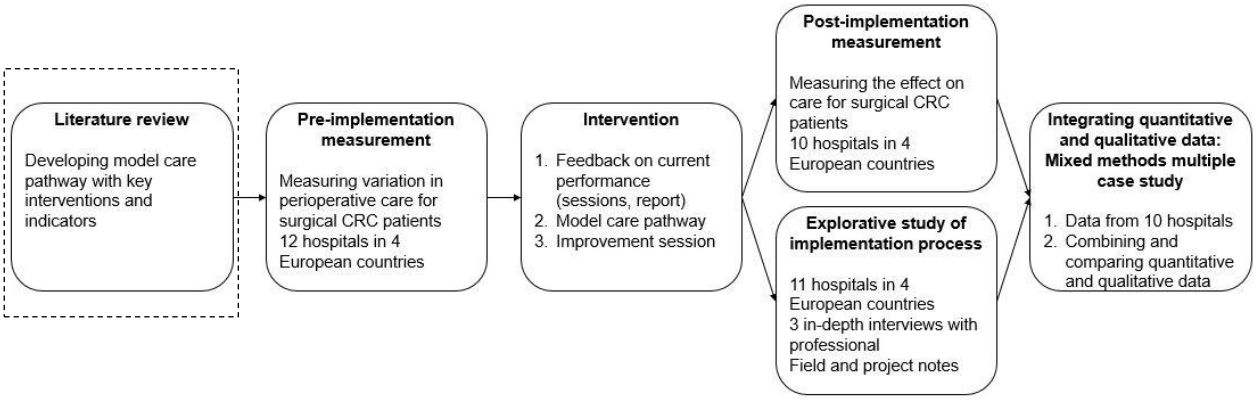
CHAPTER 2

DEVELOPMENT OF A MODEL CARE PATHWAY FOR ADULTS UNDERGOING COLORECTAL CANCER SURGERY: EVIDENCE-BASED KEY INTERVENTIONS AND INDICATORS



Published as:

Van Zelm R, Janssen I, Vanhaecht K, de Buck van Overstraeten A, Panella M, Sermeus W, Coeckelberghs E (2018) Development of a model care pathway for adults undergoing colorectal cancer surgery: Evidence-based key interventions and indicators. Journal of evaluation in clinical practice 24 (1):232-239. doi:10.1111/jep.12700

ABSTRACT

Rationale, aims and objectives

During the last decades, perioperative care for patients with colorectal cancer has shifted towards more standardized care, so-called “enhanced recovery after surgery”. Those programs aim to optimize interventions in perioperative care in order to decrease the rate of postoperative complications, improve patients’ recovery, and shorten hospital stay. The purpose of this literature review is to identify, summarize and operationalize the clinical content of both key interventions and clinical indicators in order to develop an evidence-based model pathway for surgical patients with colorectal cancer.

Methods

A systematic search in three databases was conducted to identify key interventions (KIs) and indicators to measure the effect of implementation of care pathways. The KIs from the enhanced recovery after surgery protocol were listed and used as framework to identify and match KIs used in the included studies. The Clinical Pathway Compass was used to categorize the indicators.

Results

Fifteen studies were included. The number of KIs used in the study protocols ranged from 9 to 20. In total, 33 KIs were identified. Little information was available concerning the implementation of and compliance to the protocol. Length of stay and complication rate are the most common used indicators (used in 15/15 and 14/15 of the studies), followed by 23 other measures. All but one of the included studies reported a reduction in length of stay.

Conclusion

There is considerable variation in both number of KIs and indicators as well as operationalization of key interventions, for surgical patients with colorectal cancer documented in literature. Therefore, we summarized the input from different studies and developed an evidence-based model pathway, which can serve as basis for a local/regional care pathway team to build their own pathway.

INTRODUCTION

During the last decades, perioperative care for patients with colorectal cancer has shifted towards more standardized care, so-called “enhanced recovery after surgery” (ERAS) documented in the ERAS-society protocol.[1] These programs aim to optimize interventions in perioperative care in order to decrease the rate of postoperative complications, improve patients’ recovery, and shorten length of stay (LOS).[2,3] Recent guidelines strongly recommend using the ERAS program.[4] Key interventions (or “care elements” in ERAS terminology) of structured care methodologies like ERAS protocol in colorectal surgery, are based on the best evidence available. They include patient education and preparation, preservation of gut function, minimization of pain and discomfort and promotion of patient autonomy.[1,5] The most common interventions in preoperative and postoperative care are nutritional management, pain management, and early mobilization.[5-7] Others are fluid restriction, use of thoracic epidurals, and preemptive analgesia.[6,7] The ERAS protocol is defined as “a multimodal pathway”. This means that the protocol consists of multiple interventions working interactively to achieve early recovery for patients with major surgery, including colorectal cancer surgery. The interventions in the protocol are divided in three distinct phases: preoperative, intraoperative, and postoperative care.[1,6]

Despite growing evidence for the benefit of implementing such standardized programs, adherence remains difficult in daily practice.[2,5,8,9] One method to successfully implement and follow-up structured care methodologies in practice, is the development and implementation of a clinical pathway, also known as care pathway. A systematic review, published in Annals of Surgery 2014 defines care pathways as one of the proven interventions to reduce adverse events in surgery.[10] A recent meta-analysis by Song et al. on the effects of clinical pathways for patients with gastro-intestinal cancer, shows a reduction in expenditure and higher patient satisfaction, and a significant reduction in average LOS.[11]

The European Pathway Association uses “care pathway” as terminology. Their definition of care pathway is “a complex intervention for the mutual decision making and organization of care processes for a well-defined group of patients during a well-defined period”. The aim of a care

pathway is to enhance the quality of care across the continuum by improving risk-adjusted patient outcomes, promoting patient safety, increasing patient satisfaction and optimizing the use of resources.[12]

A complex intervention is defined as a health service intervention, built up from a number of components, which may act both independently and interdependently.[13] For the development and implementation of care pathways, these components are (1) integration of a set of evidence-based key interventions, (2) objective feedback on the current care process, and (3) systematic approach to change/improve current care process.

The purpose of this literature review is to identify, summarize and operationalize the clinical content of both key interventions and clinical indicators, in order to develop an evidence-based model pathway for surgical patients with colorectal cancer (component 1 of the complex intervention). Therefore, evidence-based key interventions for a care pathway for surgical patients with colorectal cancer in preoperative, intraoperative, and postoperative care (30-day follow-up) were listed and indicators to measure effect were identified.

METHODS

Literature Search

We conducted a systematic literature search in three electronic databases (Medline, Embase and Cinahl) from 2006 (the end date of a previous systematic review on care pathways for patients with colorectal cancer surgery)[5] up to February 2014. The following terms were used: “clinical pathway” combined with “colorectal”; “cancer”, “surgery”, “preoperative”, “perioperative”, “postoperative”, “fast track”, “enhanced recovery program”. All synonyms for these terms were included in the search. From this search, we included papers written in English, Dutch or German. In addition, the reference lists from published original and review articles were searched manually to identify other possible eligible studies.

Study Selection

Inclusion criteria were (1) papers including adults undergoing elective colorectal surgery, (2) studies concerning the implementation and use of clinical/critical/care pathways in an inpatient setting, (3) retro- or prospective comparison with a control group (conventional/usual care), (4) studies reporting at least one of the following clinical relevant outcome measures: LOS, complication rates, re-admission rates or mortality, and (5) published in a peer-reviewed journal between January 2006 and February 2014, as the model pathway was used in a study which started in October 2014. Studies not meeting all five criteria were excluded.

Data extraction

Two independent reviewers read all abstracts and selected eligible studies. In case of disagreement, consensus was obtained on the articles that could be included for full-text analysis. All full-text articles were read by one reviewer to decide whether the article fulfilled the inclusion criteria. In case of any doubt, the second reviewer was consulted and consensus was reached. A specifically developed data extraction sheet was used to collect data on study source, study design, level of evidence, sample size, preoperative, intraoperative and postoperative interventions, and the studies' different outcome parameters and results. Content was divided into preoperative, intraoperative, and postoperative key interventions in accordance with the ERAS-protocol.[1,6] The ERAS protocol was used as framework for the extraction of clinical content. We listed the 22 key interventions of the ERAS protocol and compared the key interventions used in the included studies with this list. Any additional interventions not listed in the ERAS protocol, where added.

For the clinical indicators, we used the Leuven Clinical Pathway Compass as framework.[14] This compass consists of five domains to subdivide indicators: clinical (e.g. complication rate, mortality), financial (e.g. LOS), process (e.g. time between diagnosis and surgery), service (e.g. patient satisfaction), and team indicators (e.g. job satisfaction, team effectivity). The compass serves as conceptual framework specifically developed to measure the effect of care pathways and to follow-up a patient population.[14]

Statistical Analysis

Descriptive statistics were used to summarize our results. Categorical data were presented by their observed frequencies and percentages.

RESULTS

Literature Search

One hundred eighty potentially relevant studies were retrieved from the search in the databases, and two extra studies were found by manual search and cross-referencing. Sixty one papers met all mentioned inclusion criteria, of which three were unavailable/irretrievable, 10 compared open vs. laparoscopic technique, regardless of fast track and seven were non-comparative studies. Papers commenting on other studies, sharing the same population or protocol/pathway, reporting the effect of one single intervention (e.g. early mobilization) were also excluded. Ultimately, 15 studies were included in the analysis (figure 2.1).

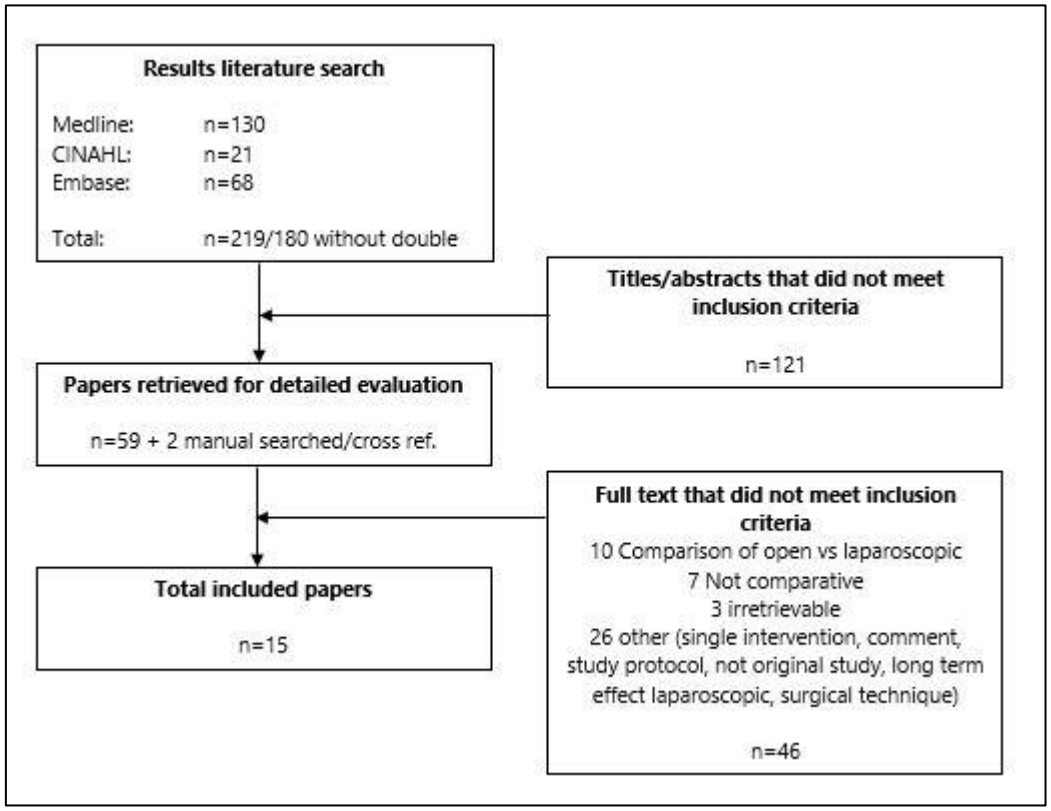


Figure 2.1 Systematic review flow diagram

The study methodologies were very heterogeneous: four papers were prospective comparative studies,[15-18] five were RCT's,[19-23] three were pre-posttest designs,[3,24,25] and three were observational studies.[8,26,27] Three were multicenter studies.[8,16,24] We rated the studies according to the levels of evidence from the Oxford Centre of Evidence-Based Medicine.[28] See Annex 1 for the study characteristics.

Key interventions

Many studies named the interventions or protocols differently. The most common names were ERAS, enhanced recovery protocol, or "fast track". Moreover, the content of the protocols differed. The number of key interventions (or care elements) that are listed in the included studies ranges from nine interventions[24] to 20 interventions.[27] In comparison, the ERAS protocol contains 22 care elements. The reported interventions and their usage are summarized in table 2.1. The description or operationalization of the specific interventions differs between studies. For example the key intervention "No prolonged fasting" is described as "Fluids up till 3h before surgery",[20] but also as "Clear fluids until 2h before initiation of anesthesia and 6h for solid food".[23] A more detailed overview of the descriptions of key interventions is provided in Annex 2.

We identified a number of interventions used in the studies that are not included in the ERAS protocol. In total, 33 key interventions were listed, of which 11 were not included in the ERAS protocol. Because these 11 interventions are studied as part of a protocol, it was impossible to determine a level of evidence for each of them. The level of evidence and grade of recommendation for the ERAS interventions is included in table 2.1.

Table 2.1 Key interventions for patients undergoing colorectal cancer surgery

Phase	Intervention	Eras element	Level of evidence[a]	Used	Reference by first author
Gen	Dedicated ward	N	*	2/15	Christensen; Khoo
Gen	Dedicated team	N	*	2/15	Christensen; Feo
Gen	OR scheduling (Tu or Wed, 1st on program)	N	*	1/15	Christensen
Pre	Fluid and carbohydrate loading	Y	Moderate Strong	10/15	Alcantara-Moral; Gouvas; Huibers; Ionescu; Khoo; King; Polle; Ren; Wang (2012); Wang (2011)
Pre	No/selective bowel preparation	Y	High Strong	9/15	Alcantara-Moral; Christensen; Huibers; Ionescu; Moronczyk; Ren;

Phase	Intervention	Eras element	Level of evidence[a]	Used	Reference by first author
					Schwarzbach; Wang (2012); Wang (2011)
Pre	Preadmissions counseling	Y	Low Strong	8/15	Christensen; Gouvas; Huibers; Ionescu; King; Moronczyk; Polle; Wang (2011)
Pre	No prolonged fasting	Y	Moderate Strong	6/15	Gouvas; Huibers; Khoo; Polle; Wang (2012); Wang (2011)
Pre	No premedication	Y	High Strong	4/15	Alcantara-Moral; Christensen; Polle; Wang (2011)
Pre	Antibiotic prophylaxis	Y	High Strong	1/15	Huibers
Pre	Thromboprophylaxis	Y	High Strong	1/15	Huibers
Intra	Mid-thoracic epidural anesthesia/analgesia	Y	Moderate Strong	12/15	Alcantara-Moral; Christensen; Gouvas; Huibers; Ionescu; Khoo; King; Polle; Ren; Schwarzbach; Wang (2012); Wang (2011)
Intra	Avoidance of salt and water overload	Y	High Strong	8/15	Alcantara-Moral; Christensen; Gouvas; Khoo; King; Polle; Schwarzbach; Wang (2011)
Intra	Short acting anesthetic agents	Y	Low Strong	7/15	Christensen; Feo; Khoo; King; Polle; Wang (2012); Wang (2011)
Intra	No drains	Y	High Strong	7/15	Alcantara-Moral; Khoo; Moronczyk; Polle; Ren; Wang (2012); Wang (2011)
Intra	Laparoscopic technique	N	High Strong	5/15	Gouvas; Huibers; Lloyd; Polle; Wang (2012)
Intra	Maintenance of normothermia (body warmer/warm IV fluids)	Y	High Strong	4/15	Alcantara-Moral; Gouvas; Huibers; Polle
Intra	Incision	N	-	4/15	Christensen; King; Polle; Wang (2011)
Intra	Wound infiltration	N	-	3/15	Moronczyk; Polle; Wang (2011)
Intra	Preemptive analgesia	N	-	2/15	Christensen; Huibers
Intra	Standard ASA monitors	N	-	1/15	Feo
Post	Early mobilization	Y	Low Strong	15/15	Alcantara-Moral; Christensen; Feo; Gouvas; Huibers; Ionescu; Khoo; King; Lloyd; Moronczyk; Polle; Ren; Schwarzbach; Wang (2012); Wang (2011)
Post	Early oral nutrition	Y	Low Strong	14/15	Alcantara-Moral; Christensen; Feo; Gouvas; Huibers; Ionescu; Khoo; King; Lloyd; Moronczyk; Polle; Ren; Schwarzbach; Wang (2011)
Post	Mid-thoracic epidural anesthesia/analgesia	Y	Moderate Strong	13/15	Alcantara-Moral; Christensen; Feo; Gouvas; Huibers; Ionescu; Khoo; King; Moronczyk; Polle; Schwarzbach; Wang (2012); Wang (2011)
Post	No nasogastric tubes	Y	High Strong	13/15	Alcantara-Moral; Feo; Gouvas; Huibers; Ionescu; Khoo; King; Lloyd; Moronczyk; Polle; Ren; Schwarzbach; Wang (2011)
Post	Non-opioid oral analgesia/NSAIDs	Y	Moderate Strong	13/15	Alcantara-Moral; Christensen; Gouvas; Huibers; Ionescu; Khoo; King; Lloyd; Moronczyk; Polle; Ren; Schwarzbach;

Phase	Intervention	Eras element	Level of evidence[a]	Used	Reference by first author
Post	Audit of compliance and outcomes	Y	Moderate Strong	12/15	Feo; Gouvas; Huibers; Ionescu; King Lloyd; Moronczyk; Polle; Ren; Schwarzbach; Wang (2012); Wang (2011)
Post	Early removal of catheter	Y	Low Strong	11/15	Christensen; Guavas; Huibers; Ionescu; Khoo; King; Lloyd; Moronczyk; Schwarzbach; Wang (2012); Wang (2011)
Post	Prevention of nausea and vomiting	Y	Low Strong	10/15	Alcantara-Moral; Christensen; Huibers; Ionescu; Khoo; Lloyd; Polle; Ren; Wang (2012); Wang (2011)
Post	Avoidance of salt and water overload	Y	High Strong	9/15	Christensen; Huibers; Khoo; Lloyd; Moronczyk; Polle; Ren; Schwarzbach; Wang (2011)
Post	Stimulation of gut motility	Y	Moderate Strong[b]	6/15	Alcantara-Moral; Christensen; Huibers; Khoo; Ren; Schwarzbach
Post	Respiratory training	N	-	1/15	Schwarzbach
Post	Routine monitoring at Medium Care Unit	N	-	1/15	Schwarzbach
Post	Body weight	N	-	1/15	Christensen

Abbreviations: ERAS indicates enhanced recovery after surgery; Intra, intraoperative; Gen, General; Post, postoperative; Pre, preoperative.
[a]Level of evidence (low, moderate, and high) and grade of recommendation (weak-strong) based on ERAS protocol.[6]
[b]Oral magnesium: low, weak

Clinical indicators

The indicators used in the studies were identified and allocated to the domains of the Clinical Pathway Compass. Clinical and financial indicators were used in all 15 studies. Two of the studies used process indicators, two studies used a service indicator. Indicators in the team-domain were not used.

The most common used (outcome) indicators are LOS (15/15) and complication rate (14/15). Table 2.2 presents the individual indicators used to measure the effect of using ERAS/fast track, and the observed effect. All but 1 study report reduction in LOS. Other outcome indicators, e.g. complication rate, mortality, readmission rate, show no effect. In none of the studies a negative effect is reported. This implies that LOS can be reduced without causing obvious harm to patients.

Table 2.2 Indicators per domain of Clinical Pathway Compass, and effect per indicator

Domain	# of studies	Positive effect	No effect	Negative effect
Clinical domain				
Complication rate	14/15	**7%** (Gouvas)	**93%** (Alcantara-Moral; Christensen; Feo; Huibers; Ionescu; Khoo; King; Lloyd; Moronczyk; Polle; Ren; Schwarzbach; Wang (2012); Wang (2011))	
Readmission rate (<30d)	11/15		**100%** (Alcantara-Moral; Christensen; Gouvas; Huibers; Ionescu; King; Lloyd; Moronczyk; Polle; Schwarzbach; Wang (2011))	
Time to passage of stool	9/15	**56%** (Gouvas; Huibers; Ionescu; Khoo; Ren)	**44%** (Feo; Lloyd; Moronczyk; Schwarzbach)	
Time to solid diet	7/15	**86%** (Ionescu; Moronczyk; Schwarzbach; Wang (2012))	**14%** (Lloyd)	
Mortality	6/15		**100%** (Gouvas; Huibers; King; Moronczyk; Polle; Schwarzbach)	
Reoperations / re-interventions	6/15	**17%** (Moronczyk)	**83%** (Alcantara-Moral; Huibers; King; Polle; Schwarzbach)	
Time to passage of flatus	4/15	**75%** (Ren; Wang (2012); Wang (2011))	**25%** (Feo)	
Time to independent mobility	5/15	**100%** (Ionescu; Khoo; Schwarzbach; Wang (2012) Wang 2011))		
Postoperative pain	3/15	**100%** (Gouvas; Ionescu; Lloyd[a])	**33%** (Lloyd[a])	
Vomiting	3/15		**100%** (Feo; Ionescu; Moronczyk)	
Time to remove catheter	3/15	**67%** (Moronczyk; Wang (2012))	**33%** (Schwarzbach)	
Time to semi-liquid diet	2/15	**100%** (Ionescu; Wang (2012))		
Time to remove drain	1/15	**100%** (Moronczyk)		
Use of NG tubes	1/15		**100%** (Feo)	
Use of Central Venous Catheter	1/15		**100%** (Schwarzbach)	
Use of epidural catheter	1/15	**100%** (Schwarzbach)		
Use of drains	1/15	**100%** (Wang (2012))		
Nutrition and metabolism index	1/15	**100%** (Ren)		
Stress index	1/15	**100%** (Ren)		
Financial domain				
(Postoperative) length of stay	15/15	**93%** Alcantara-Moral; Christensen; Feo; Gouvas; Huibers; Ionescu; Khoo; King; Lloyd; Moronczyk; Polle; Ren; Wang (2012); Wang (2011)	**7%** (Schwarzbach)	
Cost	2/15	**100%** (King; Ren)		
LOS in HDU/ICU	1/15	**100%** (Ionescu)		
Process domain				
Compliance to protocol	2/15	**100%** (Alcantara-Moral; Polle)		

Domain	# of studies	Positive effect	No effect	Negative effect
Service domain				
Quality of life	1/15		**100%** (King)	
Patient satisfaction	1/15		**100%** (Polle)	
Team domain				
-	-	-		

Indicators used to evaluate the effect of clinical pathway/enhanced recovery after surgery protocol.
Number of studies indicates number of included papers that describe the specific indicator.
Positive effect, no effect, negative effect are proportions of papers that describe the specific indicator and that show improvement, no difference, or deterioration in outcome.
References by first author between brackets.
Abbreviations: ICU indicates intensive care unit; HDU, high dependency unit; LOS, length of stay.
[a]Study reported improvement for laparoscopic group and no difference for open group.

DISCUSSION

Since the publication of "To Err is Human" in 2000 (Institute of Medicine), attention to quality of care is increasing.[29] In order to provide high quality care, we find that overuse and particularly underuse of evidence-based activities should be eliminated.[30,31] Care pathways, also known as critical pathways or clinical pathways, are used worldwide as a tool to structure or design care processes around patients' needs and, by doing so, to improve the quality of delivered care.[32] However, to the best of our knowledge, there is no evidence-based model (clinical) pathway available yet.

The ERAS or fast track pathways are strongly suggested in current clinical guidelines.[4] Nevertheless, most of the included studies incorporated only a limited number of key interventions from the original ERAS protocol. Even routine interventions, such as thromboprophylaxis and antibiotic prophylaxis, are only mentioned in 1 study protocol.[27] The ERAS is a multimodal pathway, suggesting that the different elements are applied together.

Alcantara-Moral et al. found that the more interventions from the protocol are applied, the shorter the LOS, with similar morbidity and without any increase in readmissions or re-interventions.[8] A recent study by Gustafsson et al. suggests that better compliance to the ERAS protocol is associated with higher 5-year survival. In patients with an adherence of ≥70% to ERAS interventions, the risk of cancer specific death was reduced by 42%.[33] We believe that in this matter, "more is better". An enhanced recovery protocol is a complex intervention, built up from a number of components, which

may act both independently and interdependently.[13] Not applying recommended, evidence-based key interventions could mean that patients do not receive optimal care, and in fact are undertreated.

We advise caution in interpreting the effect of the key interventions. First of all, although we present an overview of key interventions used in these pathways, we did not consider the evidence for the rationale behind each specific key intervention. Most of the ERAS care elements are used in studies that provide moderate evidence (level II + level III studies). Exceptions are antibiotic prophylaxis and thromboprophylaxis, and maintenance of normothermia, which are used in lower level studies. From the 11 additional key interventions we identified, type of incision and laparoscopic access are also used in studies that provide moderate evidence. The other nine interventions are used in studies that support weak evidence. However, this does not mean that routine interventions, such as administering antibiotic prophylaxis, or weighing the patient, are to be excluded from the care pathway. There might be other evidence, based on guidelines and studies for these interventions (e.g. guidelines on antibiotic prophylaxis), or clinical expertise (e.g. monitoring body weight as important indicator) supporting the application of the interventions. We listed the interventions in our overview, including references and description, so that teams can consider the appropriateness of including this intervention in their local care pathway.

Secondly, the level of compliance to the protocols is unknown. Polle et al. evaluated compliance to the ERAS interventions and found that patients received on average 7.4 out of 13 key interventions.[3] Alcantara-Moral et al. report a slightly higher compliance: 8.4 out of 13 interventions.[8] This means it is difficult or even impossible to determine the level of implementation fidelity and spread, for both the complete protocols, and the individual key interventions. It is therefore impossible to conclude which intervention is contributing to what effect.

The indicators used in the included studies, suggest that there is primarily attention to clinical and financial outcomes. LOS is predominantly used, followed by complication rate. The other domains receive little (process and service) or no (team) attention. This confirms a previous review by Lemmens et al.[34] The process domain should deserve more attention, especially “compliance to protocol”. The service domain, with indicators, e.g. patient satisfaction, patient experience, is an

important domain to include in studies concerning a patient-centered concept such as care pathways. However, patient satisfaction and quality of life were measured in only one study, making it impossible to draw conclusions. The team domain is completely overlooked. We think this is an omission, because it is people that make care pathways work. Deneckere et al. showed that teams working with care pathways have better team performance (teamwork, higher level of organized care, and lower burnout risk) than teams not working with pathways.[35]

The indicators used in the included studies, show a wide variety in topics. It could be useful to develop an international set of common indicators, so that teams can compare their results internationally.

Strength and limitations

This review comes with its strengths and limitations. We made a strict selection of eligible studies, only peer-reviewed, comparative studies on care pathways were retained, which strengthens this review. On the other hand, there are two limitations. First of all, we only found positive results, which raises questions about publication bias. Second, the included studies use different methodologies, and some of the studies with a stronger design have a small population.

CONCLUSION

We have observed considerable variation in both number of key interventions and indicators as well as operationalization of key interventions, for surgical patients with colorectal cancer documented in literature. Therefore, we summarized the input from the different studies and developed an evidence-based model pathway, which can serve as basis for a local/regional care pathway team to build their own pathway. The model pathway is intended for adult patients, with a scheduled admission for colorectal surgery, and without severe dementia. Next to the model pathway we present input for current and future indicator selection for monitoring and follow-up of surgical patients with colorectal cancer.

Compliance to care pathways or protocols can be difficult, but has to be strived for, in order to deliver the best possible care for patients. Different type of indicators, e.g. clinical (complication rate, time to first bowel movement, mobilization), financial (LOS), and process (compliance) should be monitored to gain insight in performance of the team.

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SUPPLEMENTAL MATERIAL – ANNEX 1. CHARACTERISTICS OF INCLUDED STUDIES

Author, year	Study type	Level of evidence	Population, Intervention (control)	Main outcome measures	Results	Nr KI
Alcantara-Moral, 2014	Observational, cross-sectional, multicenter	4	Colon cancer N= 190 (173)	LOS Morbidity Readmission rate	5.2 vs 6.2 d (p<0.05) 31.1 vs 24.3% (ns) 3 vs 5% (ns)	13
Christensen, 2011	Retrospective observational	4	Malign, benign, open elective colorectal resections N=131 (39)	LOS Complication rates Readmissions	3 vs 7 d (p<0.0001) No differences 15% vs 16% (ns)	19
Feo, 2009	Controlled trial	3	Colorectal resections, elective N=50 (50)	Complication rate Morbidity LOS	28 vs 26% (ns) 22 vs 32% (ns) 5 vs 7 d (p<0.001)	9
Gouvas, 2012	Multicenter, comparative, prospective	3	Open en lap. Sphincter preserving rectal resection N= 156 in 4 groups: Open Fast-track (36), Lap Fast-track (42), Open Usual care (45), Lap Usual care (33)	Mortality Major morbidity / complications Readmission LOS	Lap: 2.4 vs 0 (ns) 21.4 vs 51.5 (p=0.007) ns 4 vs 8 d (p<0.001) Open: 2.8 vs 0 (ns) 38.9 vs 55.6 (p=0.007) ns 7 vs 8 d (p=0.001)	14
Huibers, 2012	Retrospective comparative	4	Laparoscopic TME, Rectal cancer N=43 (33)	Postoperative LOS Complications Readmission (<30d) Mortality (<30d)	7 vs 10 d (p=0.04) ns 11.6 vs 18.2% (ns) 0 vs 0	20
Ionescu, 2009	Randomized Controlled Trial	2	Colorectal cancer, open N=48 (48)	PONV LOS in HDU/ICU LOS Readmissions Complications	34.7 vs 42.8% (p=0.538) 0.9 vs 1.8 d (p=0.001) 6.4 vs 9.2 d (p=0.001) No difference No difference	12
Khoo, 2007	Randomized Controlled Trial	3	Colorectal resections, elective N=35 (35)	Postop LOS	5 vs 7 d (p<0.001)	13
King, 2006	Prospective comparative	3	Colorectal resections N=60 (86)	Postop LOS Readmissions <30d Major complications Mortality <30d	5.8 vs 10.7 d (p<0.001) 12 vs 9% (ns) 18 vs 28% (ns) 3 vs 7% (ns)	15

Author, year	Study type	Level of evidence	Population, Intervention (control)	Main outcome measures	Results		Nr KI
Lloyd, 2010	Interrupted Time Series	4	Open or laparoscopic colorectal resection Open: N=25 (22) Laparoscopic: N=55 (15)	Postop LOS Complication rate	Lap: 6 vs 9.5 d (p=0.01) Ns	Open: 7.5 vs 12 d (p=0.04) ns	8
Moronczyk, 2011	Prospective comparative	4	Colon resection N=15 (18)	Complication rate Mortality Reoperation rate Re-hospitalization LOS	40 vs 22.2% (ns) 6.7 vs 22.2% (ns) 0 vs 11.1% 0 vs 0 8 vs 10.5 d (p<0.05)		12
Polle, 2007	Retrospectively controlled comparative	4	Elective colorectal resection N=55 (52)	Complication rate Reoperation rate LOS Readmission <30d Mortality <30d	27.3 vs 30.8% (ns) 12.7 vs 9.6% (ns) 4 vs 6 d (p= 0.002) 10.9 vs 5.8% (ns) 0 vs 0		19
Ren, 2012	Randomized Controlled Trial	2	Elective colorectal resection N= 299 (298)	Postop LOS Complications	5.7 vs 6.6 d (p<0.001) Ns		16
Schwarzbach, 2011	Interrupted Time Series	4	Colon resections N= 78 (133)	LOS Morbidity Mortality Readmission rate	9 vs 9 d (p=0.84) 28.2 vs 32.3% (p=0.53) 1.3 vs 2.2% (p=1) 2.6 vs 3.8 (p=1)		14
Wang, 2012	Randomized Controlled Trial	2	Lap. Colon resections N=49 (50)	Postop LOS Complication rate	4 vs 5 d (p<0.01) 12 vs 20% (ns)		13
Wang, 2011	Randomized Controlled Trial	2	Colorectal cancer N=104 (106)	Morbidity <30 days Postop LOS Readmission rate	14 vs 28 patients (p=0.016) 5 vs 7 d (p<0.01) 4 vs 9% (ns)		19

Abbreviations: D indicates days; KI, number of key interventions used in study; ns, not significant.

SUPPLEMENTAL MATERIAL – ANNEX 2. COMPONENTS CARE PATHWAY FOR SURGICAL PATIENTS WITH COLORECTAL CANCER

General
***Dedicated ward*[#]** Patients admitted on 1 ward (Christensen; Khoo)
***Dedicated team*[#]** Fast track team: surgeons, nurses, anesthetists (Christensen) and pain management, physical therapy, social work (Feo)
***OR scheduling*[#]** Patients first on operating program and scheduled for surgery on Tuesdays or Wednesdays to avoid discharge on weekends (Christensen)

Pre-operative care
Preadmission counseling *ERAS: patients should routinely receive dedicated preoperative counseling (Gustafsson)* Information on the consecutive steps of postoperative care (Ionescu; Moronczyk; Wang (2011)) and expected length of stay (Christensen); Pre-operative assessment with written information (King); Written and oral information on Fast Track, informed consent (Huibers; Polle); Guided tour on surgical ward (Polle); Written and oral information, explanation epidural pump (Gouvas)
Fluid and carbohydrate loading *ERAS: Preoperative oral carbohydrate treatment (400ml of 12.5% drink of mainly maltodextrins) should be used routinely (Gustafsson)* Liquid protein/calorie supplement from admission, 3 drinks (Khoo; King); Last carbohydrate loaded drink 2h before surgery (Polle); 400ml nutritional supplements before midnight or 6h before surgery, 200ml 2h before surgery (Ren); 100g of glucose in 1000ml of water (glucose injection 10%) orally administered at 10pm on the evening before surgery, a further 50g of carbohydrate in 500ml of water given 3-4h before surgery (Wang (2012)); Oral nutrition with high-calorie carbohydrate drinks until 2h prior to surgery (Gouvas); 4 packages of carbohydrate drinks on day -1 (Wang (2011)); 2 packages of carbohydrate drinks 2h before surgery (Huibers; Wang (2011)); Carbohydrate fluids load 3h before surgery (Alcantara-Moral; Ionescu)
No prolonged fasting *ERAS: Patients should be screened for nutritional status and, if deemed to be at risk of under-nutrition, given active nutritional support. Clear fluids should be allowed up to 2h and solids up to 6h prior to induction of anesthesia (Gustafsson)* Fluids up to 3h before surgery (Khoo); Last meal 6h before surgery (Polle; Wang (2011)); Clear fluids until 2h before initiation of anesthesia and 6h for solid food (Wang (2012)); Oral nutrition with high-calorie carbohydrate drinks until 2h prior to surgery (Gouvas); Normal diet until midnight, fluid intake until 2h before surgery (Huibers)
No / selective bowel preparation *ERAS: Mechanic Bowel Preparation should not be used routinely in colonic surgery (Gustafsson)* No bowel preparation (Alcantara-Moral; Christensen; Ionescu; Ren; Wang (2012); Wang (2011)); No mechanical preoperative bowel preparation (only a small enema allowed) (Moronczyk); Two enemas the evening before surgery (Huibers); Only in the cases of planned intraoperative colonoscopy (Schwarzbach)
Antibiotic prophylaxis *ERAS: Routine prophylaxis with intravenous antibiotics should be given 30–60 min before initiating colorectal surgery. Additional doses should be given during prolonged procedures according to the half-life of the drug used (Gustafsson)* Cefalozine (1000mg) and metronidazole (500mg) IV 30m before first incision, repeated after 3.5h (Huibers)

Thromboprophylaxis
ERAS: Patients should wear well-fitting compression stockings, have intermittent pneumatic compression, and receive pharmacological prophylaxis with LMWH. Extended prophylaxis for 28 days should be given to patients with colorectal cancer (Gustafsson)
0.3ml fraxiparine from day -1 until discharge (Huibers)
No premedication
ERAS: Patients should not routinely receive long- or short-acting sedative medication before surgery because it delays immediate postoperative recovery. If necessary, short-acting intravenous drugs can be titrated carefully by the anesthetist to facilitate the safe administration of epidural or spinal analgesia because these do not significantly affect recovery (Gustafsson)
No premedication (Alcantara-Moral; Christensen; Polle; Wang (2011)); Lorazepam 1mg evening before surgery if necessary (Polle); Haloperidol (1.5 mg) intraoperatively (Huibers)

Intra-operative care
Pre-emptive analgesia[#]
Epidural pain relief by 0.5% ropivacaine Preoperatively (Christensen); 4x1000mg paracetamol from day -1 until discharge (Huibers)
Short acting anesthetic agents
ERAS: A standard anesthetic protocol allowing rapid awakening should be given (Gustafsson)
Propofol or remifentanil (Christensen); Propofol, 1,5-2,5mg/kg or 2-4 mg/kg thiopental or fentanyl 2-3µg/kg and vecuronium 0.1±0.02 mg/Kg (Feo); Propofol (King); Remifentanil 1µg/kg/min, Propofol 2-4mg/kg/h, Cisatracium 0.15mg/kg (Wang (2012); Wang (2011))
Midthoracic epidural anesthesia / analgesia
ERAS: Mid-thoracic epidural blocks using local anesthetics and low-dose opioids should be considered for open surgery. In laparoscopic surgery, spinal analgesia or morphine PCA is an alternative to epidural anesthesia. If intravenous opioids are to be used the dose should be titrated to minimize the risk of unwanted effects (Gustafsson)
Epidural catheter placed between T6 and T9 thoracic vertebrae for right-sided colonic resections, and between T8 and T11 thoracic vertebrae for left-sided resections, by 0.2% ropivacaine containing 50µg morphine per ml (Christensen); Between T10 and T12 (Feo; Ionescu); Between T8-T9, bupivicaine 0.5% <= 10ml, diamorphine 2.5mg in bupivicaine 0.25% at wound closure (King); Placement of thoracic epidural catheter (T6-T10, depending on the surgical resection); test-dose (bupivacaine 0.25% with adrenaline 1:200,000), top-up dose (bupivacaine 0.25% (±10ml) with sufentanil 25µg, (Polle); Continuous epidural anesthesia combined with general endotracheal anesthesia (Ren); Placed between T6 and T12 (Wang (2012)); Placed between T10 and T12 (Wang (2011)) Test: lidocaine 2% 3ml with epinephrine, bupivacaine 0.5% (6+6)ml (Wang (2012); Wang (2011)); Placement of epidural catheter unless contraindicated (Alcantara-Moral; Gouvas); Between T9 and T11, levobupivacaine and sufentanil (15); Epidural catheter placement (Schwarzbach)
No drains
ERAS: Routine drainage is discouraged because it is an unsupported intervention that probably impairs mobilization (Gustafsson)
No drains (Alcantara-Moral; King; Moronczyk; Polle; Wang (2012); Wang (2011)); According to circumstances (Ren)
Avoidance of salt and water overload
ERAS: Balanced crystalloids should be preferred to 0.9 % saline. In open surgery, patients should receive intraoperative fluids (colloids and crystalloids) guided by flow measurements to optimize cardiac output. Flow measurement should also be considered if: the patient is at high risk with comorbidities; if blood loss is >7 ml/kg; or in prolonged procedures. Vasopressors should be considered for intra- and postoperative management of epidural-induced hypotension provided the patient is normovolemic (Gustafsson)
Intraoperative fluids restricted to 1500ml unless bleeding in excess of 500ml (Khoo); 2000ml crystalloid intraoperatively (King); Restricted per-operative fluid infusion regime (Ringers lactate 20ml x kg^{-1} in the 1st h followed by RL 6ml x kg^{-1} x h^{-1}) (Polle); Restrictive protocol (4ml/kg/h) (Ren); Fluid restriction 10ml/kg/h; Limited intravenous administration of colloids (Gouvas); Restrictive fluid therapy (Alcantara-Moral); Goal of perioperative fluid management: achieve normovolemia (Schwarzbach)

Maintenance of normothermia
ERAS: Intraoperative maintenance of normothermia with a suitable warming device and warmed intravenous fluids should be used routinely to keep body temperature >36°C. Temperature monitoring is essential to titrate warming devices and to avoid hyperpyrexia (Gustafsson)
Forced body heating (Bair hugger system/warmer coat and warmed IV fluids) (Polle; Ren); Active warming of patient (Alcantara-Moral; Gouvas); Using warm blankets (Huibers)
***Incision**#*
Right-sided horizontal incision was used for right colectomy and transverse resection, and a curved incision in the left iliac fossa was used for left hemicolectomy and sigmoid resection (Christensen); Transverse／curved incision for open surgery (King); Minimal invasive incisions (Polle); Minimal-access surgery or transverse curved incision used included right-sided hemicolectomy through a right horizontal incision above the umbilicus, sigmoid resection through a curved incision in the left iliac fossa (Wang (2011))
***Laparoscopic technique**#*
Based on clinical assessment of the most appropriate method (Lloyd); Laparoscopic in all patients (Huibers; Wang (2012)); Low anterior rectal resection through a mini-laparotomy in the subumbilicus which was extended toward the curvature if necessary (Wang (2012))
***Wound infiltration**#*
Infiltration of surgical wounds with bupivacaine (Moronczyk; Polle; Wang (2011))
***Standard ASA monitors**#*
EKG, blood pressure, pulse oximetry (Feo)

Post-operative care
Mid-thoracic epidural anesthesia / analgesia
ERAS: Thoracic Epidural Analgesia (TEA) using low-dose local anesthetic and opioids should be used in open surgery. For breakthrough pain, titration to minimize the dose of opioids may be used. In laparoscopic surgery, an alternative to TEA is a carefully administered spinal analgesia with a low-dose, long-acting opioid (Gustafsson)
Epidural catheter placed between T6 and T9 thoracic vertebrae for right-sided colonic resections, and between T8 and T11thoracic vertebrae for left-sided resections, by 0.2% ropivacaine containing 50 µg morphine per milliliter. Second postoperative day: removal of epidural catheter (Christensen)
Between T10 and T12, 30 minutes before end of surgery bolus of ropivacaine 0.75% 10 ml, infusion of ropivacaine 2% 5-10 ml/h, for 48 hrs (Feo); Thoracic epidural, bupivacaine 0.167% and diamorphine, for 48 hrs (Khoo); Continuous epidural analgesia (2 days) 5 mg diamorphine in 60 ml bupivicaine 0.125% at 0–10 ml/h (King); Epidural (bupivacaine with fentanyl (Moronczyk); Continuous infusion (bupivacaine 0.125% with fentanyl 2.5 µg x ml^{-1}) until day 2 postoperatively (Polle); Continuous epidural anesthesia combined with general endotracheal anesthesia (Ren); Bupivacaine 0.125% with fentanyl 2.5$µm^{-1}$ (Wang (2012); Wang (2011)); Day 1 epidural analgesia with continuous infusion of local anesthetics (epidural-PCA) (Gouvas); Remove epidural catheter if pain score (VAS) < 4 (Huibers); Bupivacaine 0.125% + fentanyl 2 µg/ml via epidural catheter (Ionescu); Epidural catheter placement (Schwarzbach)

No nasogastric tubes
ERAS: Postoperative nasogastric tubes should not be used routinely. Nasogastric tubes inserted during surgery should be removed before reversal of anesthesia (Gustafsson)
No NG tube (Alcantara-Moral; Feo; Huibers; King; Moronczyk; Ren); Removal in recovery room (Khoo); remove before leaving Operating Theatre (Lloyd; Schwarzbach); Removal of NG tube before extubation (Gouvas; Polle); no NG tube unless severe PONV (Ionescu; Wang (2011))
Prevention of nausea and vomiting
ERAS: A multimodal approach to PONV prophylaxis should be adopted in all patients with ≥2 risk factors undergoing major colorectal surgery. If PONV is present, treatment should be given using a multimodal approach (Gustafsson)
Treatment of nausea (Christensen); regular Domperidone, magnesium hydroxide 8% (Khoo); Ondansetron (4 mg) (King; Polle; Wang (2012); Wang (2011)); Combination of dexamethasone and tropisetron (Ren); Dexamethasone (5mg) and ondansetrone (4mg) preoperatively (Huibers); Metoclopramide IV 10mg every 8h, ondansetrone only for severe PONV (Ionescu); Using prokinetics (Alcantara-Moral)
Avoidance of salt and water overload
ERAS: The enteral route for fluid postoperatively should be used as early as possible, and intravenous fluids should be discontinued as soon as is practicable (Gustafsson)
Free oral fluids immediately after the operation, discontinue IV fluids when patient is able to tolerate 200 ml of water over 30 minutes (Khoo); Day 0: 1 liter oral intake, 2 protein drinks, day 1: 4 protein drinks (Christensen); 1 high protein/high calorie drink on day 0, 3 high protein/high calorie drinks per day thereafter, Free fluids from day 0 (King; Lloyd); Oral fluid from day 0, limiting IV fluid in favor of oral (Moronczyk); First oral drinks at 2 h post-surgery + IV infusion of RL 1.5 liters x day^{-1}, day 1 oral intake >2l (including 4 units CHL drinks), stop IV fluid administration (leave cannula) (Polle; Wang (2011)); Restrictive protocol, 1500ml/day, 500 ml water starting at 6 h after surgery on day 0 and 500ml nutritional supplements and 1000ml water daily post-operatively (Ren); Day 0, oral fluid intake directly encouraged, IV fluid restricted to 1 liter per 24h (Huibers); High-calorie drinks a few hours after surgery (Gouvas); Goal of perioperative fluid management: achieve normovolemia, remove venous canula as soon as patient is able to drink (Schwarzbach)
Early removal of catheter
ERAS: Routine transurethral bladder drainage for 1–2 days is recommended. The bladder catheter can be removed regardless of the usage or duration of Thoracic Epidural Analgesia (Gustafsson)
Day 1 (colon), day 3 (rectum) (Christensen; Feo; Khoo); Day 1 (laparoscopic), day 2 (open) (Lloyd); Early removal (Moronczyk); Suprapubic urine catheter, close and remove when residue <50ml (Polle); Use for the duration of thoracic epidural analgesia and early removal (Ren); Usually within 24h (Wang (2012); Ionescu; Wang (2011)); Removal if urine output >40 ml/h (Gouvas); Removal on day 2 (Huibers); Directly after operation (Schwarzbach)
Early oral nutrition
ERAS: Patients should be encouraged to take normal food as soon as possible after surgery. Oral nutritional supplements can be used to supplement total intake (Gustafsson)
From day 2: normal diet (Christensen); Liquid diet day 1, soft diet day 2 and regular diet as tolerated (Feo); Normal diet allowed immediately after surgery (Khoo); Normal diet offered and encouraged from day 1 (King); Day 1 light diet, day 2 regular diet (Lloyd); Introduction of diet on day 1 (Moronczyk); First semi-solid food intake in the evening, from day 1 offer solid food (Polle); Clear liquid diet after the first postoperative flatus (Ren); Day 1 solid diet (Gouvas); Day 0 liquid diet in the evening, day 1 restart normal diet at noon (Huibers); Day 0 fluids if tolerated, day 1 semi-solid food, day 2 solid food, regular diet (Ionescu); Day 1 semi-solid food, day 2 normal diet (Wang (2012)); Oral diet within 12h (Alcantara-Moral); Yoghurt on the evening day 0 and normal diet from day 1 (Schwarzbach)
Non-opioid oral analgesia / NSAIDs
ERAS: In connection with TEA withdrawal, NSAIDs and Paracetamol should be used (Gustafsson)
Paracetamol or NSAIDs, nicomorphine as rescue medication (Christensen); Paracetamol (1000mg) and ibuprofen (400mg) 4xd (Khoo); Paracetamol 1g 4 hourly from day 1, Ibuprofen 400mg 8 hourly +200mg PRN (max 1.2g/d) once epidural stopped, morphine as rescue medication (King); From day 1 tramadol and NSAID (Lloyd); Analgesia complemented with parenteral, and then oral NSAIDs, paracetamol or tramadol, opiod as needed (Moronczyk); paracetamol 4x 1 g x d^{-1}, from day 2 add NSAID (Polle); Patient-controlled analgesia and oral NSAIDs (Ren); Analgesia with NSAIDs or paracetamol intramuscularly (Gouvas); diclofenac 50mg 3xd from day 2 (Huibers; Wang (2011)); Ketorolac IV 60mg/8h the first 48h and orally after, and paracetamol 1g/8h orally (or intravenously if PONV) (Ionescu); No opiods (Alcantara-Moral); Additional standardized oral analgesic scheme: ibuprofen 400mg 2x day, metamizol 1g 3x day and, only if required, oxycodone/naloxone 10/5mg 2x day (Schwarzbach)

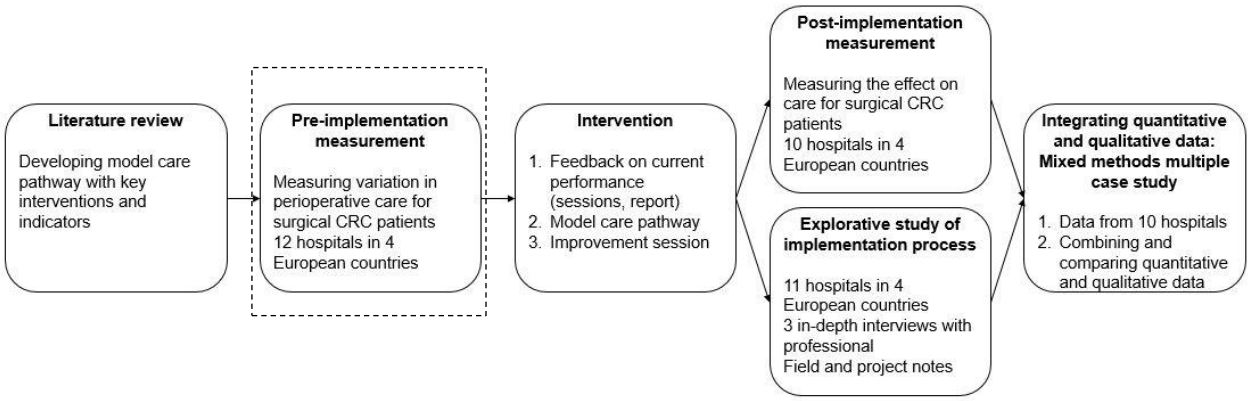
Early mobilization
ERAS: Prolonged immobilization, increases the risk of pneumonia, insulin resistance, and muscle weakness. Patients should therefore be mobilized (Gustafsson)
Day 0: out of bed for >2h, day 1: out of bed for >8h (Christensen, King); Resume physical activities day 1 (Feo; Khoo); 4 x 60m walks from day 1 (King); Mobilize bed-chair evening of surgery, walk 100m by the end of day 1, more than 100m the following day (Lloyd); Attempt at bedside rehabilitation at day 0, rehabilitation from day 1 (Moronczyk); Mobilization in the evening (>2h out of bed); day 1 expand mobilization (>6h out of bed), day 2 expand mobilization (>8h out of bed) (Polle; Wang (2011)); Out of bed for 2h on day 1 and 4–6h each day thereafter (Ren); Encourage patients to ambulate early (Wang (2012)); Mandatory 1h mobilization out of bed on day 0, 4h mobilization out of bed on day 1, fully mobilized on day 2 (Gouvas); Day 1 2–3h of mobilization, day 2 stimulate to fully mobilize (Huibers); Day 0 mobilized in bed (turning, sitting in bed), day 1 mobilized out of bed (Ionescu); Mobilization at 24h (Alcantara-Moral); Ambulation scheduled to start on the evening of day 0 (Schwarzbach)
Stimulation of gut motility
ERAS: Chewing gum can be recommended, whereas oral administration of magnesium and alvimopan (when using opioid based analgesia) can be included (Gustafsson)
Prokinetics (Alcantara-Moral; Christensen); Infusion of raw rhubarb 10g 5x day after surgery, injection of neostigmine 0.5 mg at each Zusanli acupoint daily after surgery (Ren); Start magnesium oxide on day 1 (Huibers); Postoperative bowel activity was stimulated by oral laxatives (magnesium oxide) and enemata if needed (Schwarzbach)
Audit of compliance and outcomes
ERAS: A systematic audit is essential to determine clinical outcome and measure compliance to establish successful implementation of the care protocol. The system should also report patient experience and functional recovery, but validated tools are required for this aspect (Gustafsson)
Evaluating discharge criteria; discharge if fulfilled (Feo; Gouvas; Huibers; Ionescu; Khoo; Lloyd; Moronczyk; Polle; Ren; Schwarzbach; Wang (2012); Wang (2011))
Routine monitoring at Medium Care Unit[#]
Routine postoperative monitoring of patients at the intermediate care unit was done when deemed necessary by the surgeon and/or anesthesiologist (Schwarzbach)
Respiratory training[#]
Every patient was instructed to perform respiratory training with an incentive spirometer (Schwarzbach)
Body weight[#]
At discharge (Christensen)

Abbreviations: Day 0 indicates, day of surgery; day 1, first postoperative day, et cetera

[#]Add on to ERAS protocol

CHAPTER 3

VARIATION IN CARE FOR SURGICAL PATIENTS WITH COLORECTAL CANCER: PROTOCOL ADHERENCE IN 12 EUROPEAN HOSPITALS



Published as:

Van Zelm R, Coeckelberghs E, Sermeus W, De Buck van Overstraeten A, Weimann A, Seys D, Panella M, Vanhaecht K (2017) Variation in care for surgical patients with colorectal cancer: protocol adherence in 12 European hospitals. International journal of colorectal disease 32 (10):1471-1478. doi:10.1007/s00384-017-2863-z

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ABSTRACT

Purpose

Surgical care for patients with colorectal cancer has become increasingly standardized. The Enhanced Recovery After Surgery (ERAS) protocol is a widely accepted structured care method to improve postoperative outcomes of patients after surgery. Despite growing evidence of effectiveness, adherence to the protocol remains challenging in practice. This study was designed to assess the adherence rate in daily practice and examine the relationship between the importance of interventions and adherence rate.

Methods

This international observational, cross-sectional multicenter study was performed in 12 hospitals in four European countries. Patients were included from January 1, 2014. Data was retrospectively collected from the patient record by the local study coordinator.

Results

A total of 230 patients were included in the study. Protocol adherence was analyzed for both the individual interventions and on patient level. The interventions with the highest adherence were antibiotic prophylaxis (95%), thromboprophylaxis (87%), and measuring body weight at admission (87%). Interventions with the lowest adherence were early mobilization – walking and sitting (9% and 6%, respectively). The adherence ranged between 16 and 75%, with an average of 44%.

Conclusion

Our results show that the average protocol adherence in clinical practice is 44%. The variation on patient and hospital level is considerable. Only in one patient the adherence rate was >70%. In total, 30% of patients received 50% or more of the key interventions. A solid implementation strategy seems to be needed to improve the uptake of the ERAS pathway. The importance-performance matrix can help in prioritizing the areas for improvement.

INTRODUCTION

Over the last decade surgical care for patients with colorectal cancer has become increasingly standardized. The use of structured care methods, such as care pathways and protocols, has helped in standardizing (not only) colorectal cancer (CRC) surgery. The Enhanced Recovery After Surgery (ERAS) protocol [1] is a widely accepted structured care method to improve postoperative outcomes of patients after surgery. This protocol aims to optimize interventions in the perioperative care (pre- per- and postoperative phase), to decrease postoperative morbidity, by enhancing patients' recovery, and thus shorten length of stay (LOS) [1-4]. The ERAS protocol has recently been described as a "true revolution in colorectal surgery", highlighting its importance in today's surgical care [3]. Even more, evidence regarding its safety and effectiveness is still published nowadays.

Despite the growing evidence, adherence to the ERAS protocol remains insufficient in daily practice. Adherence rate, or protocol adherence, is defined as the percentage of protocol elements (interventions) delivered to an individual patient. Protocol adherence ranging from 45 to 90% has been reported in the literature, illustrating the difficulty to implement an ERAS protocol [5-8].

Recently, a "dose-effect" relationship between protocol adherence and patient outcomes has been suggested: the more protocol elements are applied, the better the patient outcomes, with an adherence of >70% showing improved outcomes [4,9]. Therefore, it is important to assess the level of adherence, not only in study settings, but in daily practice.

The purpose of this study was to assess colorectal units' adherence rate in daily practice. Two major objectives have been defined: (1) to describe protocol adherence for perioperative care in colorectal cancer surgery, and (2) to study the relationship between adherence to the individual protocol elements ("key interventions") and the importance (strength) of key interventions.

METHODS

Population

This international observational, cross-sectional multicenter study was performed in 12 hospitals in four European countries: Belgium, France, Germany and the Netherlands. The study was supervised by the European Pathway Association (E-P-A, www.e-p-a.org), an international not-for-profit organization aiming to increase and disseminate knowledge of care pathways. Three hospitals in each country were included in the study using purposive sampling. Purposive sampling is a non-probability sampling technique, in which known characteristics of the population are used to construct the sample [10]. The goal was to obtain a sample with a mix of academic/teaching versus non-teaching and small versus large hospitals, to provide a representation of different characteristics of current health care systems.

Within the participating hospitals, consecutive patients were included. Inclusion criteria were: (1) scheduled admission for colorectal cancer surgery (open or laparoscopic), and (2) adults (≥ 18 years) Exclusion criteria were: (1) emergency (not planned) admission for colorectal cancer surgery, and (2) severe dementia (DSM IV) or severe concomitant disease that may affect very short-term outcome (life expectancy less than 3 months).

The local study coordinator was instructed to collect the data from the patient record, for 20 consecutive patients admitted from January 1, 2014, using a standardized data extraction form. If data were not available or retrievable in the patient record, this was marked as “no information available”. The requested data were retrospectively collected by the local study coordinator.

Ethical approval for this study was obtained with the ethical committee of the University Hospital Leuven (S57152 [ML11311]). Based on the study protocol, all hospitals provided written agreement of the local study coordinator and approval of the local ethical committee.

Variables

Demographic data and data on the perioperative care (see table 3.1), as well as data on time intervals and the following outcomes: length of stay (LOS) (total hospital stay and stay on ICU),

morbidity (defined as readmission rate and reintervention rate), and time of first flatus and first stool, and 31-day mortality were recorded. Protocol adherence was measured based on the care elements (or key interventions) from the ERAS protocol. A number of interventions (e.g. measuring C-reactive protein (CRP), albumin) not included in ERAS protocol, but relevant for the patient group, were also studied based on the outcomes of a previous literature review [11]. Where clinically relevant, adherence to specific interventions (e.g. use of drain) was assessed for patients with colon or rectal cancer. In these cases, patients with tumors in the colorectal joint, were analyzed as colon cancer patients.

Statistical analysis

Data were recorded using MS Excel®. Analyses were performed using MS Excel® and visualizations were made in MS Excel® and statistical package R version 3.2.5, using easyGgplot2.

Continuous data are reported as mean and standard deviation (SD) or median and interquartile range (IQR); dichotomous data are presented as count and percentage. The relationship between strength of the key interventions and adherence is presented by using an importance-performance matrix, as used in similar research [12]. The importance dimension is defined by the strength of the key interventions. To determine the strength of each key intervention, the levels of evidence as reported in the ERAS protocol were converted to points. Three levels of evidence are distinguished [1]: low (1 point), moderate (2 points), and high (3 points), and two grades of recommendations: weak (1 point) and strong (2 points). Subsequently, the strength of the key intervention is defined as the sum of the points. A cutoff point was defined as ≥3 points, in order to include key interventions with a strong recommendation, even if the evidence was low. The performance dimension is defined by the adherence rate. This was measured per key intervention as the number of patients that received the intervention (numerator) / the number of patients for whom the intervention was indicated (denominator), resulting in a percentage between 0 and 100%. A cutoff of ≥70% was used, based on thresholds in previous studies showing an effect on outcomes with a compliance of 70% or higher [4,9]. Combining the importance dimension and performance dimension forms a matrix consisting of four quadrants (see figure 3.1). The top two quadrants signify important interventions, with a high adherence rate (top-right) and a low adherence rate (top-left). The bottom two quadrants

signify the less important interventions, with high adherence rate (bottom-right) and low adherence rate (bottom-left). The variation between and within hospitals is visualized by boxplots.

RESULTS

Hospital and patient characteristics

The 12 participating hospitals were divided equally over the countries (see Acknowledgements). One was an academic hospital, six were teaching hospitals, and five were non-teaching hospitals. The number of beds ranged between 145 and 1995. The number of admissions for colorectal cancer (CRC) surgery in 2014 ranged between 65 and 340.

Table 3.1 Patient characteristics (n=230)

Indicator	
Age (in years) (mean ± SD)	69.36 ± 11.96
Male (N, %)	130 (56%)
Female (N, %)	100 (44%)
Comorbidities (N,%)	
Hypertension	119 (52%)
Cardiovascular Disease	46 (20%)
Coronary Disease	44 (19%)
Diabetes	43 (19%)
Pulmonary Disease	33 (14%)
Liver Disease	11 (5%)
Renal Failure	6 (3%)
Location of tumor (N,%)	
Colon	141 (61%)
Rectum	56 (24%
Colorectal joint	27 (12%)
Missing data	6 (3%)
ASA classification[a] (N,%)	
I	29 (13%)
II	132 (58%)
III	56 (25%)
IV	9 (4%)
Type of surgery (N,%)	
Open	75 (33%)
Laparoscopic	103 (45%)
Laparoscopic converted to open	37 (16%)
Missing data	15 (7%)

[a]American Society of Anesthesiologists

The 12 hospitals provided data on 230 patients. One hospital provided data on 12 patients, of which two proved to be duplicates. All other hospitals provided data on 20 consecutive patients as required.

The patient characteristics are summarized in table 3.1. The mean age of the patients was 69.4 years, and 44% was female. The majority of patients had colon cancer (61%), and laparoscopic surgery was performed in 45% of the cases (table 3.1).

Table 3.2 Patient outcomes (n=230)

Indicator	
Length of stay (in days) (mean ± SD)	13.76 ± 12.29
Number of days on ICU (mean ± SD)	1.96 ± 6.19
31-day mortality (N, %)	4 (1.7%)
Re-intervention rate (N, %)	20 (9%)
Readmission rate (N, %)	27 (12%)
Post Op Day of first flatus[a] (mean ± SD)	2.76 ± 2.93
Post Op Day of first stool[b] (mean ± SD)	3.29 ± 2.15

[a]Reported in 67 patients, from 9 hospitals
[b]Reported in 124 patients, from 12 hospitals

Outcomes are reported in table 3.2. The average LOS was 13.8 days. Overall 31-day mortality was 1.7%, reintervention and readmission rate were 9% and 12% respectively (table 3.2).

Adherence to versus strength of the perioperative key interventions

Table 3.3 summarizes all key interventions, with their level of adherence and strength. The table shows the observed variation in adherence, ranging between 95% (antibiotic prophylaxis), and 6% (early mobilization: sitting the evening of surgery). The interventions with the highest adherence rate were widely accepted surgical and anesthesiological practices, such as antibiotic and thromboprophylaxis and no prolonged preoperative fasting. The lowest adherence rates were found in postoperative interventions, e.g. early mobilization, early nutrition, and the use of mid-thoracic analgesia. The adherence to nutritional screening, including measuring body weight, is noteworthy. Adherence to measuring body weight at the start of the care process (normal body weight, day of admission) was 70%. At discharge it was 31%. Nutritional screening was carried out in 59% of patients. However, if patients were at risk, only in one out of four patients a nutritional care plan was implemented.

Figure 3.1 shows the relationship between the strength of the recommendation and the adherence to the key interventions in the importance-performance matrix. There were six interventions in the

top-right quadrant (importance: strength ≥3, and adherence ≥70%): antibiotic prophylaxis, thromboprophylaxis (LMWH), measuring body weight (day of admission and normal), administering paracetamol/novaminsulfon, no prolonged preoperative fasting. In total, there were 29 interventions in the top-left quadrant (importance, strength ≥3, and adherence <70%), (e.g. no use of nasogastric tubes, no use of drains, early oral nutrition). These interventions are strongly recommended, but are used in a relative low percentage of patients, suggesting possible underuse.

The interventions in the bottom-left quadrant, totaling nine interventions, (e.g. no/selective bowel preparation (rectal tumors), measuring body weight at discharge and follow-up), are less-important interventions (strength <3), with a low adherence rate (<70%). The bottom-right quadrant includes only one intervention (measuring body weight at day of surgery). This intervention is weakly recommended (strength <3), and used in a high percentage of patients (70%).

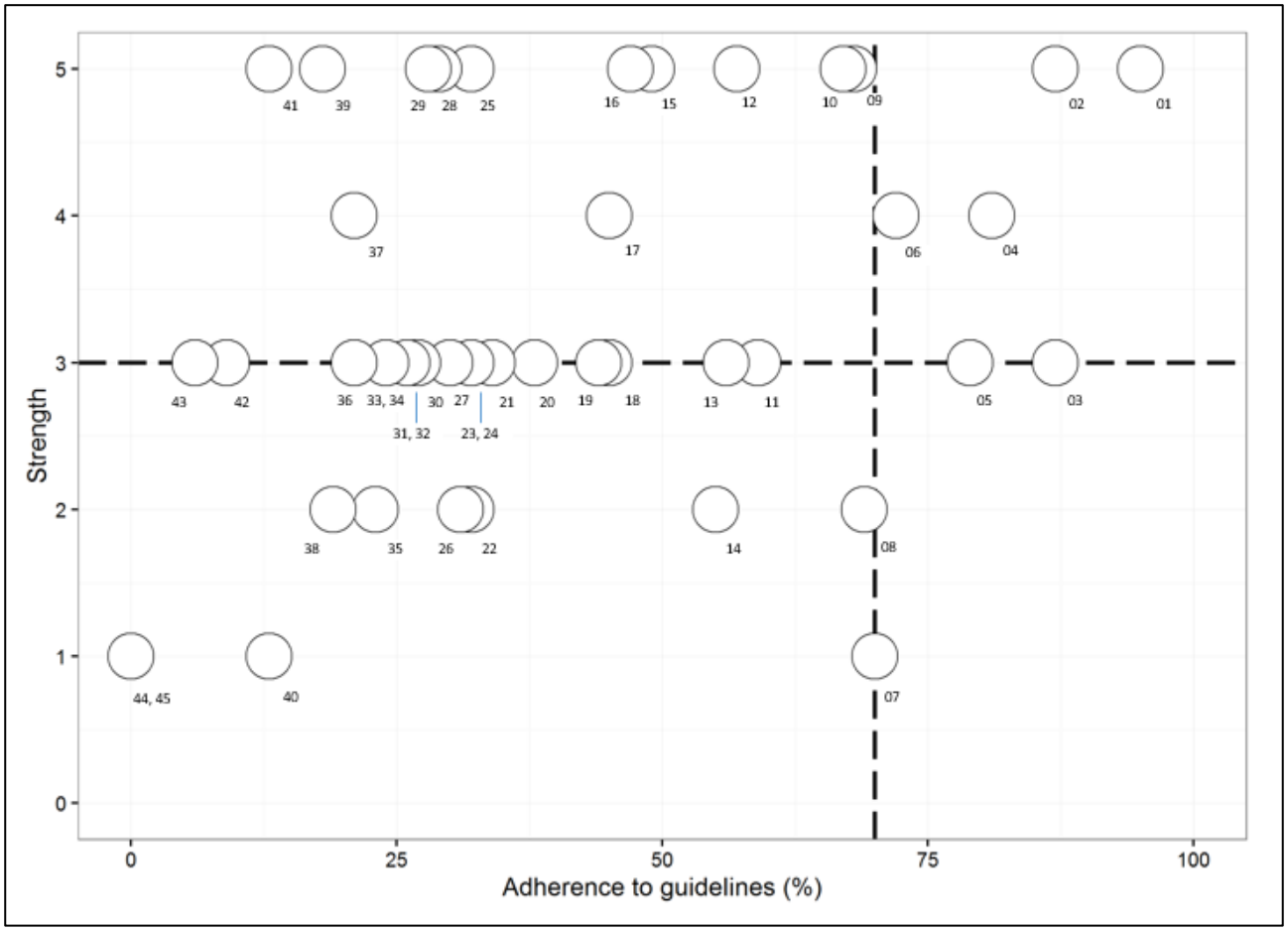

Figure 3.1 Importance-performance matrix for the CRC pathway interventions

The numbers in figure 3.1 correspond to the numbers in table 3.3, identifying the key interventions. Upper right quadrant: correct use; upper left quadrant: under use; lower right quadrant: over use.

Table 3.3 Adherence to the perioperative interventions

Nr	Intervention	Performance n/N (%)	Hospital Median (Q1 – Q3)	Level of evidence	Grade of recomm.[a]	Strength[b]
01	Antibiotic prophylaxis	219/230 (95%)	98% (90-100)	High	Strong	5
02	Thromboprophylaxis – Low Molecular Weight Heparin	200/230 (87%)	90% (84-100)	High	Strong	5
03	Measuring Body weight – day of admission	200/230 (87%)	90% (86-95)	Low	Strong	3
04	Paracetamol / novaminsulfon	187/230 (81%)	90% (79-96)	Moderate	Strong	4
05	Measuring Body weight – pre-surgery	181/230 (79%)	88% (68-96)	Low	Strong	3
06	No prolonged fasting – solid up to 6 hrs. before surgery	166/230 (72%)	88% (65-96)	Moderate	Strong	4
07	Measuring Body weight – day of surgery	161/230 (70%)	70% (64-81)	-	Weak	1
08	Measuring CRP level at discharge	157/226 (69%)	68% (54-90)	-	Strong	2
09	Skin cleansing with chlorhexidine	156/210 (68%)	100% (14-100)	High	Strong	5
10	No/selective bowel preparation colon / colorectal tumor	112/168 (67%)	74% (67-92)	High	Strong	5
11	Screening of nutritional status	135/230 (59%)	75% (21-100)	Low	Strong	3
12	No nasogastric tubes (incl. removal before reversal of anesthesia)	132/230 (57%)	48% (29-86)	High	Strong	5
13	Preadmissions counseling – patient received information leaflet	129/230 (56%)	88% (38-95)	Low	Strong	3
14	Measuring CRP level at admission	126/230 (55%)	70% (23-88)	-	Strong	2
15	No drains colon / colorectal tumor	82/168 (49%)	62% (27-75)	High	Strong	5
16	Thromboprophylaxis – well-fitting stockings	108/230 (47%)	19% (0-86)	High	Strong	5
17	No prolonged fasting – fluid up to 2 – 3 hrs. before surgery	104/230 (45%)	50% (0-86%)	Moderate	Strong	4
18	No opiates (oral, intra muscular or intravenous)	104/230 (45%)	53% (29-96)	Low	Strong	3
19	Preadmissions counseling – leaflet discussed (partly) with team member	102/230 (44%)	45% (0-88)	Low	Strong	3
20	Postoperative counseling – patient received information leaflet	88/230 (38%)	38% (0-66)	Low	Strong	3
21	Early removal of catheter (postop. day 0 - 2)	73/215 (34%)	34% (23-42)	Low	Strong[c]	3 (2)
22	No/selective bowel preparation rectal tumor	18/56 (32%)	37% (22-57)	?[d]	Strong	2
23	Prevention of nausea and vomiting – screening for risk factors	73/230 (32%)	10% (0-54)	Low	Strong	3
24	Prevention of nausea and vomiting – if at risk: prophylaxis	62/192 (32%)	26% (4-69)	Low	Strong	3
25	Antibiotic prophylaxis - repeated dose if surgery prolonged	19/59 (32%)	16% (0-64)	High	Strong	5
26	Measuring Body weight - at discharge	71/226 (31%)	20% (19-46)	-	Strong	2
27	Prevention of nausea and vomiting – if at risk: antiemetics	57/192 (30%)	21% (0-64)	Low	Strong	3
28	No drains rectal tumor	16/56 (29%)	25% (0-36)	High	Strong	5
29	Avoidance of salt and water overload – IV drip (removal postop. day 0 - 3	65/230 (28%)	30% (19-36)	High	Strong	5
30	Early oral nutrition – solid start postop. day 0 or 1	61/230 (27%)	20% (9-51)	Low[e]	Strong	3
31	Screening of nutritional status – if at risk: nutrition assessment	46/180 (26%)	19% 4-68)	Low	Strong	3
32	Fluid and carbohydrate loading	60/229 (26%)	0% (0-32)	Low	Strong	3
33	Screening of nutritional status – if at risk: nutrition care plan	44/180 (24%)	19% (0-73)	Low	Strong	3

Nr	Intervention	Performance n/N (%)	Hospital Median (Q1 – Q3)	Level of evidence	Grade of recomm.[a]	Strength[b]
34	Postoperative counseling – leaflet discussed (partly) with team member	55/230 (24%)	8% (0-22)	Low	Strong	3
35	Measuring albumin level at admission	52/230 (23%)	8% (0-18)	-	Strong	2
36	Early oral nutrition – fluid start day of surgery	51/230 (21%)	28% (5-31)	Low	Strong	3
37	Non-opioid oral analgesia/NSAIDs	49/230 (21%)	13% (4-26)	Moderate	Strong	4
38	Measuring Body weight – 31 day follow up	41/225 (19%)	13% (0-30)	-	Strong	2
39	Mid-thoracic epidural anesthesia/analgesia	41/230 (18%)	0% (0-30)	High	Strong	5
40	Measuring albumin level at discharge	30/230 (13%)	0% (0-13)	-	Weak	1
41	No premedication	30/230 (13%)	3% (0-21)	High	Strong	5
42	Early mobilization – walking postop. day 1	20/230 (9%)	5% (0-16)	Low	Strong	3
43	Early mobilization – sitting evening of surgery	14/230 (6%)	5% (0-10)	Low	Strong	3
44	Calculate CRP/albumin ratio at admission	0/230 (0%)	-	-	Weak	1
45	Calculate CRP/albumin ratio at discharge	0/230 (0%)	-	-	Weak	1

[a]Based on ERAS Protocol
[b]Strength: Level of Evidence 1-3 points, grade of recommendation 1,2 points, strength = sum (e.g. measuring body weight at admission: low evidence (1 point), strong recommendation (2 points), strength is 3)
[c]Weak when epidural is used
[d]ERAS only states high level of evidence for colonic, no level of evidence for rectal
[e]Effect: low; Safety: high

Protocol adherence and variation

In this analysis, only the key interventions with a strength level of at least 3 were included, since these are considered the most important interventions (see figure 3.1). The overall protocol adherence (patient level) ranged between 16% and 75% (median 44%). No patient received all key interventions, only one patient received care with an adherence of more than 70%, the cut-off described by Gustafsson et al. [4]. In total, only 30% of patients received 50% or more of the key interventions.

Figure 3.2 compares the performance per hospital in a box plot. The figure shows that there was considerable variation between and within the hospitals: the median scores of the participating hospitals ranged from 58 to 35%.

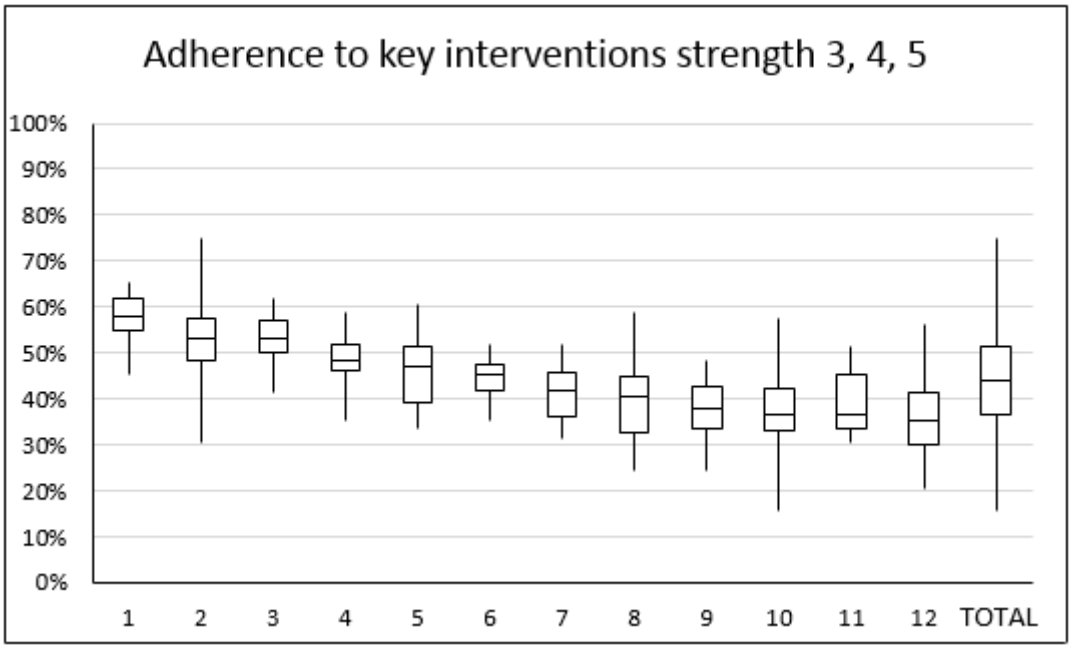

Figure 3.2 Variation between and within hospitals: percentage of documented key interventions the patient received

Numbers 1-12 represent the individual hospitals in descending order of median adherence rate, the final box represents the total / benchmark with all 230 patients.

DISCUSSION

Our data shows the baseline level of adherence to ERAS elements in 12 European hospitals in four countries with departments dedicated to colorectal surgery. A wide variability between the hospitals

was observed regarding the implementation of all single ERAS elements. Even within the hospitals there is considerable variation. The “whiskers” in figure 3.2, signifying the variation within a hospital (minimum – maximum score), were very long, notably so in hospital 2, 8, 10, and 12. Overall, the present study shows an average protocol adherence rate of 44%. This is comparable with data published in the “Quality of health care study” in 2003, which is regarded as a benchmark study on recommended care. This paper states that patients receive on average 55% of recommended care [13]. The study also included colorectal cancer (54% adherence rate). Since this study was published in 2003, ERAS has become the standard of care for perioperative management of colorectal cancer surgery. While the “Fast Track” ERAS program was originally designed for colorectal surgery, protocols have since then been established for gastrectomy, pancreatectomy, cystectomy and other procedures. ERAS represents a multimodal treatment bundle including items with different grades of evidence from prospective randomized studies [1]. The idea behind this bundle is that all interventions in the bundle should be performed, to improve patients’ outcome, A long term cohort study showed that the adherence to an ERAS protocol may be associated with improved 5-year cancer specific survival after colorectal cancer surgery. This study included 911 consecutive patients undergoing major colorectal cancer surgery. In total, 30% of patients had an adherence rate ≥70% to ERAS interventions. For this group, the risk of cancer specific death was reduced by 42%, compared to the group (of patients) with an adherence rate <70% [4]. The authors clearly state that there is a strong association between protocol adherence and survival, but that this may not be a cause-and-effect relationship. Nor did their study provide evidence on the mechanism behind the reported effect. A possible explanation given by the authors is that protocol adherence reduces the metabolic stress response, which in turn reduces tumor recurrence [4].

The necessity of some interventions, not supported by good evidence, is arguable. However, the results show a very low adherence to three strongly recommended key interventions of the ERAS protocol in all participating colorectal units. Early oral nutrition (fluid start day of surgery), mid-thoracic epidural anesthesia/analgesia, and early mobilization (sitting evening of surgery and walking postop day 1) were documented in a small fraction of patients. This is much lower than expected by the results of previous studies [3-7,9]. However, there may be traditional and/or practical barriers for

these interventions. Fasting is a surgical “tradition” promoting “safer” healing of any gastrointestinal anastomosis. Epidural analgesia means the introduction of modern techniques of regional analgesia. Early mobilization could be a challenge for the workload of restricted nursing staff capacities.

Implementation strategies for guidelines and treatment protocols are an important issue worldwide for the improvement of clinical care. Implementation is a central element in the Medical Research Council (MRC) framework for process evaluations of “complex interventions”. This framework links the *outcomes* of implementation efforts to *mechanisms* in daily practice, within the *context* (organization, society) [14]. Implementation of a guideline or protocol such as ERAS, is a complex intervention, and can be influenced by elements in the *context*. For example the availability or (lack of) qualified community nurses and home care staff may influence the protocol adherence. *Organizational features*, such as resources, and *mechanisms* in daily practice such as hierarchy, training etcetera, could also influence the implementation of and adherence to ERAS protocol. These concepts (context, mechanism, outcome) reflect the previously mentioned practical barriers of tradition (mechanisms), introduction of modern techniques (context), and workload for nurses (context). The ERAS Society is providing support for implementation of the ERAS protocol. Another relevant implementation resource is the International Consortium for Health Outcome Measures (ICHOM) Standard Set for colorectal cancer. This document provides recommendations or indicators to measure the outcomes that matter most to persons with colorectal cancer [15,16]. Finally, the development and implementation of care pathways can be a strategy to bring evidence to practice. A recent systematic review, defines care pathways as one of the proven interventions to reduce adverse events in surgery [17]. A recent meta-analysis by Song et al. on the effects of clinical pathways for patients with gastrointestinal cancer, shows a reduction in expenditure and average length of stay and higher patient satisfaction [18].

This study comes with strengths and some limitations. First of all, there might be selection bias, taking into account the limited number of patients included in every single hospital. This may not represent each hospital reliably. However, this study is focused on identifying process improvement opportunities, taken the resource and time constraints in the participating hospitals into account. A

number of 20 patients has been suggested as sufficient in previous care pathway research and methods papers [19-21].

The purposive sampling of the hospitals could have led to a positively biased selection of hospitals, with a focus already on structured (surgical) care for colorectal cancer patients. The inclusion of the patients was performed by local research coordinators, and not under control of the authors. This could have led to an over estimation of the protocol adherence.

A final limitation of the study is the retrospective design with some shortages in clinical documentation. Our data shows a median under-documentation of 20%. It is interesting to note that the level of documentation is higher in interventions with the higher strength. This could mean that these interventions are considered more important and are documented with greater attention. Because of the under-documentation, the results of our study may *under*estimate the ERAS protocol adherence. However, our study shows a comparable or even lower adherence rate than published in the “Quality of health care study”[13]. This makes us quite confident of the representativeness of our data.

If we assume the positive scenario that key interventions are performed, but not documented, the level of adherence would be approximately 20% higher. This percentage is certainly debatable. Moreover, a mean adherence of 44% as found in our study +20% documentation bias, is still below the 70% cut-off point from the Gustafsson et al. 2016 study [4]. Apart from the problem in determining the true adherence, the documentation shortages represent a potential or actual quality problem in daily practice, in terms of continuity and coordination of care.

We believe that our results provide a great opportunity for hospitals to learn from each other. Improvement priorities can be identified using the importance-performance method. Care pathways can be used as a method to implement the evidence-based key interventions in daily practice. Because adherence to the evidence seems so challenging in daily practice, we suggest to evaluate not only the effect of implementation on adherence and patient outcome, but also the process of implementation. This could help in designing a practical and effective implementation strategy.

CONCLUSION

The goals of this study were to examine the adherence to the individual protocol elements (“key interventions”) and the relationship between the importance (strength) of key interventions and the adherence rate, and to describe protocol adherence and variation for perioperative care in colorectal cancer surgery. Our data shows that the average protocol adherence in clinical practice is 44%. The variation within and between hospitals is considerable. Only in one patient the adherence rate was >70%. In total, only 30% of patients received 50% or more of the key interventions. This could mean a serious threat to quality of care, because patients are under-treated. A solid implementation strategy to bring evidence into practice seems to be needed to improve the uptake of the ERAS pathway. The importance-performance matrix can help in prioritizing the areas for improvement.

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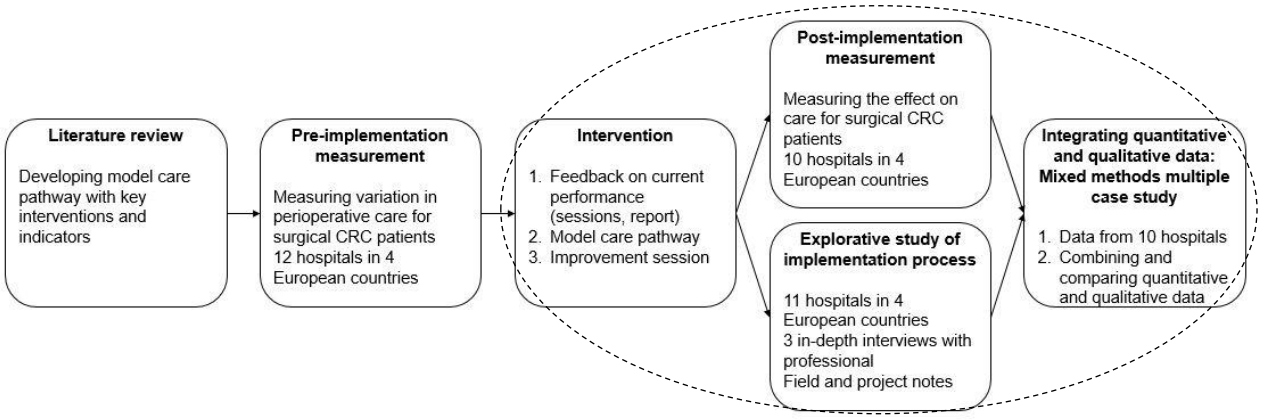
Chapter 4

PROTOCOL FOR PROCESS EVALUATION OF EVIDENCE-BASED CARE PATHWAYS: THE CASE OF COLORECTAL CANCER SURGERY



Published as:

Van Zelm R, Coeckelberghs E, Sermeus W, Aeyels D, Panella M, Vanhaecht K (2018) Protocol for process evaluation of evidence-based care pathways: the case of colorectal cancer surgery. International journal of evidence-based healthcare. doi:10.1097/xeb.0000000000000149

ABSTRACT

Background and aim

Care pathways are complex interventions, consisting of multiple “active ingredients”, to structure care processes around patient needs. Numerous studies have reported improved outcomes after implementation of care pathways. The structure – process – outcome framework and the context – mechanism – outcome framework both suggest that outcomes can only be achieved through a certain process within a context or structure. To understand how and why care pathways are effective, understanding of both this process and context is necessary. The aim of this paper is to propose a study protocol to evaluate the implementation process of evidence-based care pathways, including the influence of the context. This protocol is explained by applying it to the implementation of a colorectal cancer surgery pathway in an international setting.

Methods

The Medical Research Council (MRC) guidance on process evaluations for complex interventions is used as the basis for the protocol. The key components of process evaluation are intervention, context, implementation, mechanisms of impact, and outcomes. In process evaluations, these components are studied using quantitative and qualitative methods. Among them are patient record analysis, questionnaires, on-site visits and interviews.

Discussion

To guide our methodological choices, the MRC guidance for process evaluations of complex interventions, and published protocols for process evaluations of complex interventions were used. Our protocol is now tailored for the process evaluation of evidence-based care pathways and provides researchers and clinicians methods and tools, as well as a worked example, that can be used to study the process of care pathway implementation. As a result, healthcare professionals will be informed on context factors and implementation processes that can facilitate the implementation of care pathways, improving quality and effectiveness of care processes.

BACKGROUND

Care pathways, also known as critical pathways or clinical pathways, are used worldwide as a tool to structure or design care processes around patients' needs and, by doing so, to improve quality of care.[1,2] Care pathways are defined as a "complex intervention for the mutual decision making and organization of predictable care for a well-defined group of patients during a well-defined period".[3,4] Complex interventions are interventions consisting of multiple components, working interactively.[5,6] These components, or active ingredients, are defined for care pathways as a formative evaluation of quality and organization of the care setting (including feedback of the results), a set of evidence-based key interventions, and support of the development and implementation of the care pathway.[7] In essence, a care pathway is not merely a tool or product, but rather a process including formative evaluation and feedback, and a strategy to implement the care pathway.

Care pathways are widely used in surgical patient groups, where they are regarded as one of the proven interventions to reduce adverse events.[8] A meta-analysis by Song et al. on effects of pathways for patients with gastro-intestinal cancer, shows a reduction in expenditure and average length of stay (LOS), and higher patient satisfaction.[9]

Care pathways are used in quality improvement work with positive outcomes. However, to be able to understand the outcomes of care, it is necessary to understand *how* these outcomes were achieved. Two well-known frameworks suggest there are antecedents to outcomes. First, the "structure – process – outcome" framework on quality of care by Donabedian, implies that outcomes can only be achieved through processes within a structure.[10] The realist evaluation framework (context – mechanisms – outcomes) by Pawson and Tilley, suggest that interventions (e.g. care pathways) are not stand-alone mechanisms, but work in different contexts, that effect outcomes.[11] Gaining a comprehensive insight in the effects of a care pathway, as well as the underlying processes, ask for a process evaluation.

Process Evaluation

The Medical Research Council (MRC) has published guidance on process evaluation of complex interventions.[6,12] This guidance describes and links the key functions and components of process evaluation of complex interventions. These components are *context*, *implementation*, and *mechanisms of impact*. A description of the *intervention* which is evaluated, acts as input for the framework. The output is the actual *outcome* achieved with the intervention.

The case of a colorectal cancer surgery pathway

The process evaluation of the implementation of a care pathway for colorectal cancer surgery reported in this article, is part of a quality improvement project in 12 hospitals in four European countries: Belgium, France, Germany and the Netherlands. The project runs between January 2015 and April 2018. The project is performed by the KU Leuven Institute for Healthcare Policy (www.kuleuven.be/ligb) and is guided by the European Pathway Association (E-P-A, www.e-p-a.org), an international not-for-profit organization aiming to increase and disseminate knowledge on care pathways. In the project, the 12 participating hospitals perform a baseline measurement of their care process (outcome and process indicators), improve the care process where needed by implementing or revising a care pathway based on Enhanced Recovery After Surgery guidelines,[13] and perform an effect measurement. The hospitals are supported by the research team in a number of sessions, and are visited for a process evaluation in the summer of 2017. Ethical approval for this study was obtained by the ethical committee of the University Hospital Leuven (S57152 [ML11311]).

Aims and objectives

A care pathway consists of multiple “active ingredients” which leave room for local adoption and adaptation. To understand if the care pathway was effective, it is necessary to understand how the formative evaluation was performed, which evidence-based key interventions were adopted and adapted, and how the local implementation took place. This is where process evaluation is situated.

The aim of this article is twofold: first it proposes a study protocol to evaluate the implementation process of evidence-based care pathways. Second, it provides a worked example of the application of the study protocol to generate results that will help understand and inform future implementation

of (colorectal cancer surgery) care pathways. The evaluation of outcome is not described in this paper.

The specific research questions for the process evaluation of evidence-based care pathways are listed in figure 4.1, together with a summary of the proposed research methods. The methods are described in detail below.

METHODS/DESIGN

Where outcome evaluation focusses on the effect of an intervention, process evaluation investigates the process of implementing the intervention.[12] Richards and Rahm Hallberg (2015) as well as the MRC guidance suggest mixed method research to capture different elements of the evaluation of complex interventions. Both quantitative methods, such as measurement, patient file analysis to measure key process variables, as well as qualitative methods such as interviews or focus groups to capture experiences, can and should be used in process evaluations.[6,14] The design of process evaluation of the implementation of evidence-based care pathways is based on mixing quantitative with qualitative methods.

The rationale for the protocol is discussed in detail below, following the key components of process evaluation as indicated in the MRC guidance. The methods and instruments for data collection are described per component, followed by recommendations on data analysis. The proposed steps are illustrated by the process evaluation of the implementation of a care pathway for colorectal cancer surgery.

Data collection

Component: Intervention

To evaluate what exactly has been implemented, a process evaluation needs a thorough description of the implementation under evaluation.[6,12] When evaluating the implementation of a care pathway, a description is needed of all three active ingredients: first, formative evaluation of the care setting;

second, evidence-based key interventions; and third, support in development and implementation of the care pathway.[7]

To provide a comprehensive and transparent description of the intervention, the Template for Intervention Description and Replication (TIDieR) checklist is suggested. The TIDieR checklist is a 12-item format, developed by Hoffmann et al. in 2014.[15] It is a comprehensive format that gives authors and reviewers of research papers guidance in describing the intervention that is studied.

The TIDieR checklist was used to describe the complex intervention with its three active ingredients in the colorectal cancer surgery care pathway project. The formative evaluation of the current care process is the first active ingredient. It consisted of a baseline measurement of outcome and process indicators, including protocol adherence. The rationale behind this complex intervention is that providing feedback to a clinical team on their current performance, will show the areas for improvement and will spark a shared ambition to improve performance. The results were presented in a feedback report and two feedback sessions were organized. First, a feedback session per country was organized (n=4). The goal of these meetings was to share general findings, and to encourage the exchange of knowledge. Second, all but two of the participating hospitals (n=12) were visited to give on-site feedback to the interdisciplinary team. The two hospitals that were not visited already had extensive experience in working with care pathways, and decided an on-site visit was not necessary. These teams only received the full feedback report. The results of the formative evaluation have been published by Van Zelm et al. (2017). The main conclusions were that protocol adherence was low (44% on average) and that there is considerable variation within and between teams.[16] In eight out of 10 of the visited hospitals, the results were accepted by the teams as “benchmark”, showing room for improvement. One of the teams questioned the results, and in one case the results were even rejected during the feedback session. In this particular case, the head of abdominal surgery presented his own data to challenge the information given during the feedback session.

The second active ingredient of the complex intervention, the list of evidence-based key interventions, was shared with the participating hospitals after the feedback sessions. The hospitals

received the main clinical recommendations from the research literature.[17] Based on this summary, a proposal for a time-task matrix was developed. This matrix summarizes the key interventions on a day-to-day time frame in a so called model pathway.[17] The model pathway contains 27 interventions which the local teams can use as guidance to develop or adapt their own care pathway. There are nine interventions in the preoperative phase (e.g. patient education, no prolonged fasting, carbohydrate loading), ten in the perioperative phase (e.g. avoidance of salt and water overload, no use of nasogastric tubes), and eight in the postoperative phase (e.g. early mobilization and early oral nutrition, no use of opioids).

The third active ingredient, development and implementation of local care pathways, started with a second 3 hour on-site training session in which the goals for improvement of each individual hospital, based on the formative evaluation, were discussed in a multidisciplinary team meeting. Following that, the rationale behind the model pathway was explained and discussed. The session ended with practical considerations for the use of the model pathway in daily practice.

All sessions used a standardized format, and were led by the same person (R.v.Z.). In all sessions in the French speaking hospitals, R.v.Z. was supported by D.A. Although the project language is English, support of a bilingual person proved crucial to assure good communication. After the second on-site session, each hospital followed its own course in adapting and implementing the pathway, based on local context, barriers and facilitators. The number of interventions in the model pathway and the fact that teams can place their own focus on which areas to improve and how to do that, underline the “complex” nature of this intervention. The intervention as summarized above is described in more detail in the TIDieR checklist.[15] The completed TIDieR checklist is added as supplemental material.

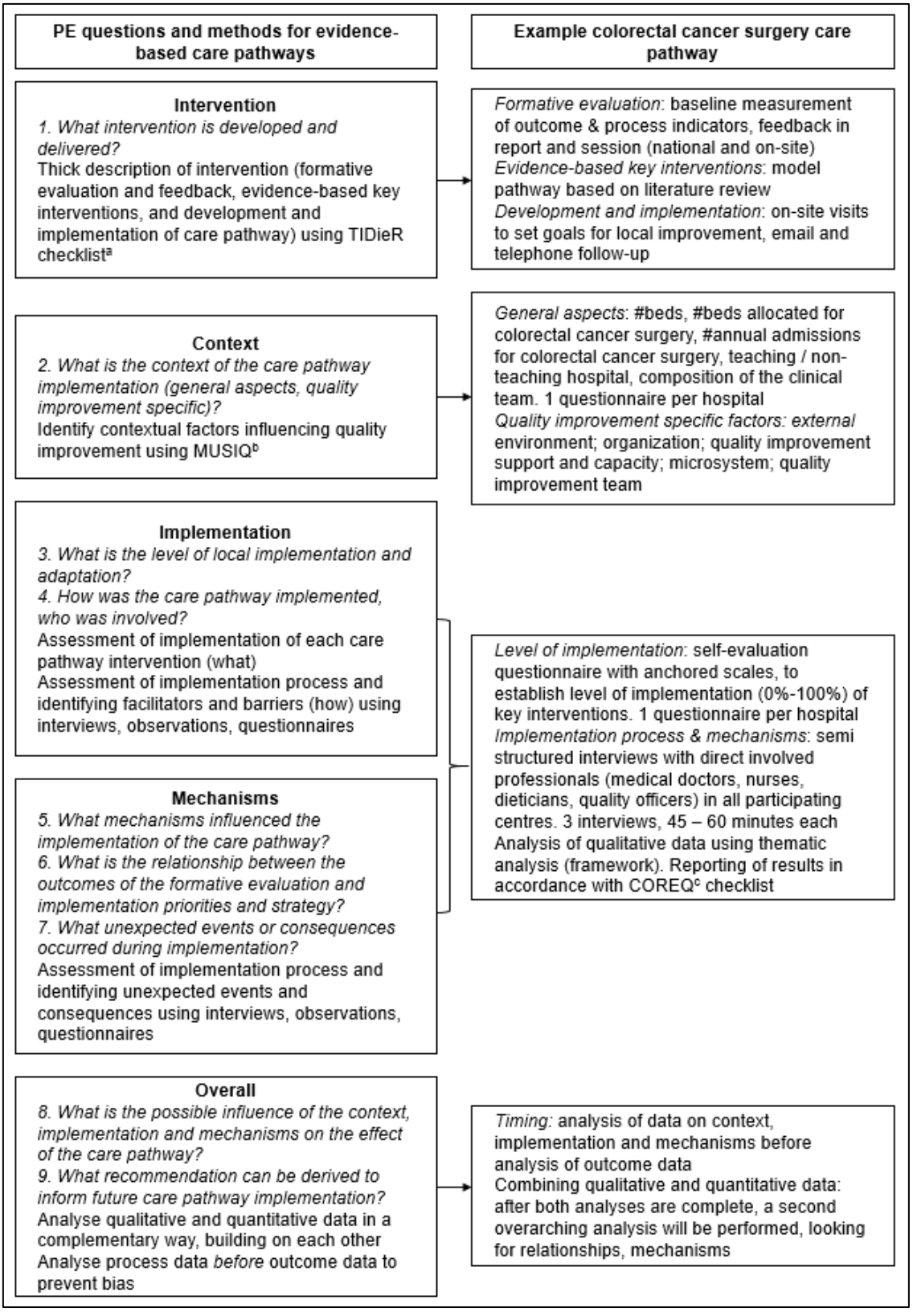


Figure 4.1 Protocol for process evaluation of care pathways – overview

Left: process evaluation questions and methods per concept from MRC guidance on process evaluation of complex interventions.
Right: application of the methods in colorectal cancer surgery care pathway process evaluation.
[a]TIDieR: Template for Intervention Description and Replication[15]
[b]MUSIQ: Model for Understanding Success In Quality[18,19]
[c]COREQ: Consolidated criteria for reporting qualitative research[34]

Component: Context

Process evaluation studies the context to understand how it affects the implementation of a complex intervention.[6,12] Implementation of care pathways is a form of quality improvement. An emerging framework to study the role of context in quality improvement, is the Model for Understanding Success In Quality (MUSIQ).[18,19] MUSIQ is developed as conceptual model to understand and optimize contextual factors affecting the success of a quality improvement project. The model defines 25 factors, which are divided in the following categories: external environment; organization; quality improvement support and capacity; microsystem; quality improvement team; miscellaneous.[18,19]

To understand the context in which the colorectal cancer surgery care pathway is implemented, general characteristics of each participating hospital were collected (total number of beds, number of beds allocated for colorectal cancer surgery, number of annual colorectal cancer surgery patients, teaching / non-teaching hospital, and the composition of the clinical team). Next to these general aspects, the concepts from MUSIQ[18,19] were used to develop an interview topic guide (see next section).

Components: Implementation and Mechanisms of Impact

To study the implementation, process evaluation focusses on “what” (fidelity, dose, adaptations, reach) is implemented, and “how” it is implemented (process).[6,12] When the intervention under evaluation is a care pathway, this means first establishing to what degree the interventions from the model pathway have been implemented, and if each intervention is implemented in part (e.g. not in full dose, not consistently over time) or in full (prescribed dose, timing, et cetera). Second, how the interventions were implemented, and who was involved.

For this purpose, a mix of quantitative and qualitative methods is used, such as questionnaires to study the level of implementation, interviews with involved professionals, direct observation and audit, and measurement of protocol adherence. The overview of facilitators and barriers to pathway implementation (Evans-Lacko, 2010), or the evaluation of pathway implementation (Deneckere, 2012) can serve as input to develop the evaluation questions.[20,21]

Process evaluation also tries to understand the mechanisms of how the intervention works, and to identify any unexpected events or consequences.[6,12] For this purpose, the same qualitative data as collected to evaluate the implementation process is used.

To measure the level of implementation of the care pathway for colorectal cancer surgery, a questionnaire was sent to the local study coordinator of the participating hospitals. The questionnaire is a self-evaluation tool, using a five-point anchored scale, to assess the level of implementation (0% – 100%) of each key intervention as described in the model pathway. The anchors, short and concise explanations of the ratings, provide a common frame-of-reference for users of the scale, improving interrater reliability and reducing rating errors.[22,23] The anchors from the EFQM (translated as Kwadrant in Flanders) self-evaluation compass[24] were used as basis for the questionnaire. The EFQM self-evaluation compass is focused on quality and organization of care, making the anchors highly applicable for the process evaluation of a care pathway, although translation was necessary. After translation, the anchors were ranked from “no implementation” to “full implementation”, and a draft of the questionnaire was developed, which was tested in a hospital not participating in the study. After this test, the questionnaire was approved for use during a consensus meeting with the research team. Per level of implementation, the anchors are defined as follows: (0%) “Little or no evidence of implementation, not really, usually not”; (25%) “Some evidence of implementation, not systematically, sometimes, more often not”; (50%) “Demonstrable, reasonably planned or systematic”; (75%) “Obvious, systematic, almost complete, all relevant staff”; (100%) “Example for others, imbedded in daily practice, regular evaluation of practice”. The full questionnaire is added as supplemental material.

The implementation process of the colorectal cancer surgery pathway was studied using semi-structured interviews during on-site visits to the hospital. Purposive sampling was used to select the interviewees. This is a non-probability sampling technique, in which known characteristics of the population are used to construct the sample. The goal is to select information-rich cases.[25,26] Interviews were conducted in all participating hospitals with a medical doctor (surgeon or gastroenterologist), a nurse from the clinical ward or a clinical nurse specialist, and a quality officer

or care pathway facilitator who supported the project. This sampling is comparable to a previously published process evaluation in colorectal surgery.[27] In our evaluation, we are looking for overall saturation across the participating hospitals, not saturation per case, to draw overarching conclusions. With this purposeful sample, we include not only the local “champions”, but also clinical team members, reducing the risk of bias.

If during analysis it becomes apparent that specific topics are underrepresented in the data, additional interviews with involved professionals in the participating centres are conducted. All interviews were audio recorded and transcribed verbatim.

To develop our interview topic guide, an overview of implementation influencing factors was created. First, more generic studies on implementation of care pathways and quality improvement were used to identify implementation influencing factors (both barriers as well as facilitators).[20,21,28] Second, a number of studies on implementation of an enhanced recovery protocol for colorectal cancer surgery was used to identify specific factors for this care pathway.[27,29,30] Next to these studies, the MUSIQ concept[18,19] was added to identify relevant contextual factors (refer to Component: context section).

The input (facilitators, barriers), from these studies were categorized in the five elements of the MRC guidance by R.v.Z. and D.A. This created a rich matrix (see online file 1), which was used as basis for the draft topic list.

Similar items from the matrix were grouped in topics. For each topic one or two example questions were formulated. The draft was circulated for commenting in the research team and then tested by R.v.Z. and D.A. in a pilot interview in a hospital with extensive experience in working with care pathways, but not participating in the project. Based on this test, the topic list was finalized in a research team meeting. The final topic list is added as supplemental material.

Finally, a retrospective patient record analysis was performed to measure the protocol adherence. This is the percentage of key interventions described in our model pathway a patients receives.[17] The local study coordinator was instructed to collect from the patient record which interventions the patient received. This was done for 20 randomly selected patients admitted between 1 December

2016 and 31 May 2017. This timing allowed the participating hospitals six months for the actual implementation of the care pathway.

Data analysis

For the analysis of process evaluation data, the MRC guidance gives a number of recommendations.[6,12] These recommendations are not specific for any type of complex intervention under evaluation, so can also apply to the evaluation of care pathways. For the analysis of quantitative data, descriptive statistic on measures such as fidelity, dose, and reach can be used. More detailed modelling can be used to explore if and how the implementation process varies in different contexts. The analysis of qualitative data should give insight in mechanisms through which the intervention brings about change and in the contextual factors. Preferably, qualitative data collection and analysis is an iterative process, occurring at the same time. The main recommendation is to use a mixed method approach: qualitative and quantitative analysis should complement each other. The MRC guidance recommends to "where possible, initially analyse and report process data before trial outcomes are known to avoid biased interpretation".[6,12]

The qualitative data in the process evaluation of the colorectal cancer pathway was analysed using a specific type of thematic analysis, referred to as the framework method, or framework approach.[31-33] This method consists of a data management stage [familiarization with the data, construction of initial thematic framework, indexing and sorting of data ("coding"), review of data samples, data summary and display], followed by an abstraction and interpretation stage (description of emerging categories, relationships between categories, and explanation of patterns found).[33] To improve the clarity and transparency of the qualitative findings, the results of the interviews will be reported in accordance with the Consolidated criteria for reporting qualitative research (COREQ) checklist.[34]

The protocol adherence will be reported as proportions, with median and interquartile range (IQR). Differences between the baseline and effect measurement will be analysed using Chi-square test. Correlation and regression analysis will be performed to analyse the relation between context, implementation, and mechanism factors versus adherence.

The process evaluation data (on context, implementation, and mechanisms) are analysed before the analysis of data from a separate outcome evaluation. When both analyses are complete, an integrated analysis of process and outcome data will be performed to answer the overarching research questions 8 and 9 (figure 4.1). The final report of the process analysis will be based on the MRC guidance for process evaluations of complex interventions[6] and the RAMESES II reporting standards for realist evaluations.[6,35]

DISCUSSION

The purpose of process evaluation is not to show an effect of the complex intervention under investigation, but rather to gain a comprehensive insight in the context, implementation process and mechanisms and how this works interactively to produce the outcomes. This can inform practitioners and policy makers on future quality improvements. Using both quantitative and qualitative methods to collect a variety of data as outlined in our protocol, enables us to answer the questions how the care pathway worked, and why or under what circumstances it worked. We believe that a process evaluation of a care pathway following our protocol and answering the research questions as listed in figure 4.1, generates a thorough understanding of the implementation process, mechanisms, and context factors. To guide our methodological choices, we have stayed close to the MRC guidance for process evaluations of complex interventions and earlier protocols for process evaluations of complex interventions.[12,14,36-38] In our experience, the MRC guidance is very applicable to evaluate this quality improvement initiative. Especially the distinction in implementation (what and how) proves useful to get a good understanding of the actual implementation activities, actors and results. The description of “Context” in the MRC guidance, is somewhat limited.

Like any study design, this protocol comes with strengths and limitations. For the quantitative data collection and analysis, these have been discussed in a previous paper.[16] For the qualitative data collection and analysis in our protocol, a strength is the use of proven methods and conceptual frameworks, tested in previous care pathway research, such as semi-structured interviews with direct

involved staff.[21,27,28,29,30] Adding the MUSIQ concept[18,19] to help understand the role of context in the implementation, is a new and promising approach. The MRC guidance recommends to evaluate “contextual factors”, without specifying these factors. We used the MUSIQ concept to distinguish four levels of context: the external context, organizational context, the clinical microsystem, and the quality improvement team. This helps in a more detailed understanding of contextual factors on different levels, with a focus on quality improvement. We recognize that broader contextual factors such as political forces, socioeconomic status et cetera, can influence the intervention. To effectively study this influence, larger samples are necessary. Based on the proposed sample size, we cannot extrapolate with regard to these factors. This is a limitation of our design.

Another strength is that our research methods are flexible, in order to collect the right data at the right time, as suggested in previous published protocol papers.[37] This flexibility, especially in the hospital visits, gives us the opportunity to shift our focus if new, unexpected themes emerge. In contrast with previous published studies with average interview length ranging between 20 and 33 minutes,[27,29] our interviews are planned to take 45-60 minutes, allowing flexibility to discuss multiple topics and to achieve depth in data collection. All hospital visits will be conducted by two researchers (R.v.Z. together with E.C. or D.A.), to allow for immediate reflection and briefing. We acknowledge that this is a resource intensive approach. However, we believe that using two researchers and have sufficient time to achieve depth are necessary to have a trustworthy and comprehensive data collection.

Our approach uses mixed methods and the analysis of both quantitative and qualitative data, which can be challenging. Several authors suggest to deploy a multidisciplinary research team, with specialists from different backgrounds.[14,31,32] Therefore, we added a public health specialist, a statistician, and colorectal surgeons to our research team for the integrated analysis.

Although the study protocol is tailored for the process evaluation of evidence-based care pathways, we believe it has a broader application. It can be used in any quality improvement initiative in which a (new) standard is introduced, accompanied by formative evaluation and implementation. For example the introduction of a safe surgery checklist, or a new diagnostic procedure, We believe that

the same research questions and methods as listed in figure 4.1 can be applied. In fact, we suggest to use the study protocol for future research, which can be used to refine the protocol. First, the protocol can be used for a process evaluation of a care pathway in a single centre setting. This can give insight in the applicability on a smaller, local scale. Second, the protocol can be used for process evaluations of other quality improvement initiatives than development and implementation of care pathways. This will give valuable insight in the range of applicability.

CONCLUSION

This paper presents a protocol for process evaluation of the implementation of an evidence-based care pathway, and illustrates this protocol with the case of a colorectal cancer surgery pathway. The protocol is developed in accordance with recommendations for the design, execution, and reporting of process evaluations as outlined in methodologic literature and previously published protocols. The paper gives researchers and clinicians methods and tools to use for studying the process of care pathway implementation.

The process evaluation of the colorectal cancer surgery pathway will provide insight in how a care pathway as a complex intervention works. It will help in understanding the context factors, processes and mechanisms that played a role in the development and implementation of the care pathway. Combined with information on the outcomes of implementation, these results can inform healthcare professionals, managers and policy makers on strategies for effective implementation of care pathways, improving quality and effectiveness of care processes.

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SUPPLEMENTAL MATERIAL – COMPLETED TiDIER CHECKLIST

No.	Item	Description
Brief name		
1	Provide the name or a phrase that describes the intervention	Implementation of a care pathway for surgical patients with colorectal cancer
Why		
2	Describe any rationale, theory, or goal of the elements essential to the intervention	A care pathway is defined as a complex intervention, with three active ingredients: 1. Formative evaluation of quality and organization of care (including feedback) – providing feedback on the actual care process is an essential step in creating awareness for improvement of the care process 2. Evidence-based key interventions – this is the core content of the care pathway, the interventions based on literature, which are provided as a bundle to the local multidisciplinary team 3. Support of the development and implementation of a care pathway – the improvement strategy and process, setting improvement goals and planning activities to achieve the goals
What		
3	Materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed (such as online appendix, URL)	• Formative evaluation of and feedback on the actual care process was delivered in the form of a confidential, anonymous feedback report and during feedback session. The report compares the performance of the 12 participating hospitals • The evidence-based key interventions were delivered in the form of a summary (“model pathway”) based on input from experts and a systematic literature review. During the local kick off meetings, participating teams proposed additional interventions, which were adopted • The support of the development of the care pathway was organized in an improvement session in each participating hospital. On-site implementation was carried out by hospital staff, with a MD as lead • Input for the formative evaluation was provided by a retrospective patient record analysis, of 20 consecutive patients. This was performed by the local study coordinator
4	Procedures: Describe each of the procedures, activities, and/or processes used in the intervention, including any enabling or support activities	
Who provided		
5	For each category of intervention provider (such as psychologist, nursing assistant), describe their expertise, background, and any specific training given	The same researcher (R.v.Z.), with 15 years of international experience in developing and implementing care pathways, provided the training and the feedback, and discussed these with the hospital teams, using a standardized agenda and PowerPoint presentation. In the French speaking hospitals, a bilingual research fellow (D.A.) with experience in care pathway research was present for support. The same researcher(s) assisted the teams in the improvement sessions
How		
6	Describe the modes of delivery (such as face to face or by some other mechanism, such as internet or telephone) of the intervention and whether it was provided individually or in a group	• Kick-off meeting: at the start of this quality improvement project, a kick off meeting to create buy-in and to explain the course of the project was organized in each country. For the participating hospitals in France and Germany, this session was extend with a 3 hour teaching session on care pathway (concept and methods). The target audience for this session was the local study coordinator (MD), 1 or 2 representatives of the multidisciplinary team (MD, nutritionist, nurse), and the pathway facilitator

		• National feedback session: at country level, a 4 hour feedback session was organized to share the results of the formative evaluation, and to promote information sharing and learning. We invited the same target audience as for the kick-off session • On-site feedback and improvement session: an on-site 4 hour feedback session was organized in each participating hospital. The goal of this session was to reach a bigger audience of involved disciplines in the hospital. The following day, a 3 hour improvement session was organized. The goal of this session was to discuss the areas or goals for improvement based on the formative evaluation and to explain the use of the evidence-based key interventions and "model pathway". Representatives of directly involved clinical disciplines (surgeons, nurses, dieticians, anesthetists) as well as care pathway facilitators or quality department staff were present • Telephone (1x) and quarterly email follow-up
Where		
7	Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features	• National sessions: in a central meeting facility (Germany, Netherlands) or in one of the participating hospitals (Belgium, France) • Local, on-site sessions: in the participating hospitals
When and how much		
8	Describe the number of times the intervention was delivered and over what period of time including the number of sessions, their schedule, and their duration, intensity, or dose	• Kick-off meetings: 4 times between January 2015 – June 2015 • Formative evaluation (retrospective patient record analysis): May 2015 – September 2015 • National feedback sessions: 4 times between October 2015 – November 2015 • On-site feedback and improvement sessions: 12 times between February 2016 – May 2016 • Quality improvement per hospital: from improvement session – December 2016

SUPPLEMENTAL MATERIAL – IMPLEMENTATION QUESTIONNAIRE

Implementation questionnaire CP4NutriGICan

Hospital name: _____

Study coordinator: _____

Date**:** _____

To which degree have the following key interventions been implemented?

Please circle or mark the appropriate number in the middle column and answer the questions in the final column.

0 = Little or no evidence of implementation, not really, usually not **25** = Some evidence of implementation, not systematically, sometimes, more often not **50** = Demonstrable, reasonably planned or systematical		**75** = Obvious, systematical, almost complete, all relevant staff **100** = Example for others, imbedded in daily practice, regular evaluation of practice		
Preadmission counseling Written and oral information	0 25 50 75 100	Implemented during CP4NutriGICan project? Y / N	If yes, how?	If no, why not?
Fluid and carbohydrate loading - 1-3 packages of carbohydrate drinks day before surgery - 1-2 packages of carbohydrate drinks until 2hr before surgery	0 25 50 75 100	Implemented during CP4NutriGICan project? Y / N	If yes, how?	If no, why not?
No prolonged fasting - Solid food until 6 hrs before surgery - Clear liquids until 2 hrs before surgery	0 25 50 75 100	Implemented during CP4NutriGICan project? Y / N	If yes, how?	If no, why not?
Bowel preparation No or selective (small enema) bowel preparation	0 25 50	Implemented during CP4NutriGICan project? Y / N	If yes, how?	If no, why not?

0 = Little or no evidence of implementation, not really, usually not **25** = Some evidence of implementation, not systematically, sometimes, more often not **50** = Demonstrable, reasonably planned or systematical		**75** = Obvious, systematical, almost complete, all relevant staff **100** = Example for others, imbedded in daily practice, regular evaluation of practice
	75 100	
Antibiotic prophylaxis - 30 min before incision - Repeated dose after 3.5 hrs if prolonged surgery	0 25 50 75 100	Implemented during CP4NutriGICan project? Y / N If yes, how? If no, why not?
Thromboprophylaxis - Low-molecular-weight-heparin until 28 days postoperatively - Well-fitting stockings	0 25 50 75 100	Implemented during CP4NutriGICan project? Y / N If yes, how? If no, why not?
Pre-medication No sedative pre-medication	0 25 50 75 100	Implemented during CP4NutriGICan project? Y / N If yes, how? If no, why not?
Nutritional status - Screening of nutritional status - If at risk: - formal nutritional assessment - nutritional care plan	0 25 50 75 100	Implemented during CP4NutriGICan project? Y / N If yes, how? If no, why not?
Measuring of CRP, Albumin level - At admission - At discharge - Calculate ratio	0 25 50 75 100	Implemented during CP4NutriGICan project? Y / N If yes, how? If no, why not?
Anesthesia Short acting anesthetic agents (consider propofol, remifentanil)	0 25 50 75 100	Implemented during CP4NutriGICan project? Y / N If yes, how? If no, why not?
Mid-thoracic epidural anesthesia/ analgesia Placement catheter between T6 - T12 (consider bupivacaine, ropivacaine), discontinue VAS < 4	0 25 50 75 100	Implemented during CP4NutriGICan project? Y / N If yes, how? If no, why not?
Skin cleansing Chlorhexidine	0 25 50	Implemented during CP4NutriGICan project? Y / N If yes, how? If no, why not?

0 = Little or no evidence of implementation, not really, usually not **25** = Some evidence of implementation, not systematically, sometimes, more often not **50** = Demonstrable, reasonably planned or systematical		**75** = Obvious, systematical, almost complete, all relevant staff **100** = Example for others, imbedded in daily practice, regular evaluation of practice
	75 100	
Drainage No drains	0 25 50 75 100	Implemented during CP4NutriGICan project? Y / N If yes, how? If no, why not?
Avoidance of salt and water overload - Free oral fluids (consider carbohydrate drinks) - Restricted IV: stop and remove IV day ≤ POD 3	0 25 50 75 100	Implemented during CP4NutriGICan project? Y / N If yes, how? If no, why not?
Maintenance of normothermia Body warmer/warm IV fluids	0 25 50 75 100	Implemented during CP4NutriGICan project? Y / N If yes, how? If no, why not?
Laparoscopic technique	0 25 50 75 100	Implemented during CP4NutriGICan project? Y / N If yes, how? If no, why not?
Wound infiltration	0 25 50 75 100	Implemented during CP4NutriGICan project? Y / N If yes, how? If no, why not?
Standard ASA monitors	0 25 50 75 100	Implemented during CP4NutriGICan project? Y / N If yes, how? If no, why not?
No NG tubes Remove NG tube before reversal of anaesthesia	0 25 50 75 100	Implemented during CP4NutriGICan project? Y / N If yes, how? If no, why not?
PONV	0 25	Implemented during CP4NutriGICan project? Y / N If yes, how? If no, why not?

0 = Little or no evidence of implementation, not really, usually not **25** = Some evidence of implementation, not systematically, sometimes, more often not **50** = Demonstrable, reasonably planned or systematical		**75** = Obvious, systematical, almost complete, all relevant staff **100** = Example for others, imbedded in daily practice, regular evaluation of practice
- Screen for risk factors of PONV - If ≥2 risk factors: multimodal prophylaxis - (Consider prophylactic medication / antiemetic medication)	50 75 100	
Early removal of catheter Remove POD 1 or POD 2	0 25 50 75 100	Implemented during CP4NutriGICan project? Y / N If yes, how? If no, why not?
Early oral nutrition - Fluid diet in the evening of surgery - Encourage normal diet POD 1 - Normal diet (POD 2)	0 25 50 75 100	Implemented during CP4NutriGICan project? Y / N If yes, how? If no, why not?
Non-opioid oral analgesia/NSAIDs - Consider paracetamol and/or NSAIDs - Opioid as rescue medication	0 25 50 75 100	Implemented during CP4NutriGICan project? Y / N If yes, how? If no, why not?
Early mobilization - Evening of surgery (bedside/ out of bed) - >6h out of bed, walks minimum 5m POD 1 - >8h out of bed; walks >100m by end of POD 2 - Fully mobilized	0 25 50 75 100	Implemented during CP4NutriGICan project? Y / N If yes, how? If no, why not?
Stimulation of gut motility (Consider prokinetics, magnesium oxide, chewing gum)	0 25 50 75 100	Implemented during CP4NutriGICan project? Y / N If yes, how? If no, why not?
Audit of compliance and outcomes Evaluate discharge criteria; discharge if fulfilled	0 25 50 75 100	Implemented during CP4NutriGICan project? Y / N If yes, how? If no, why not?
Measure bodyweight - At admission - At discharge	0 25 50 75 100	Implemented during CP4NutriGICan project? Y / N If yes, how? If no, why not?

SUPPLEMENTAL MATERIAL – INTERVIEW TOPIC LIST, APRIL 2017

Introduction

Hello mr / mrs <<name respondent>>. My name is Ruben van Zelm. This is my colleague Ellen Coeckelberghs / Daan Aeyels. Thank you for taking the time for this interview.
We are research fellows from the Catholic University Leuven Institute for Healthcare Policy. We study the implementation of the colorectal cancer pathway in your hospital. For this purpose we use interviews.

Based on the findings from the interviews in the 12 participating hospitals in the study, we hope to get a deep understanding of implementation of care pathways, so we can inform hospitals and professionals on effective ways to implement care pathways. Your contribution to this study is very valuable.

All data from this interview will be analysed anonymously. We would like to audio tape the interview in order to facilitate the analysis. Is this okay for you?

The interview will take approximately 45 minutes. You can indicate at any moment if you want to stop or pause the interview.

Have you received and read the information and consent form? Could you please hand us a signed copy of the last page?

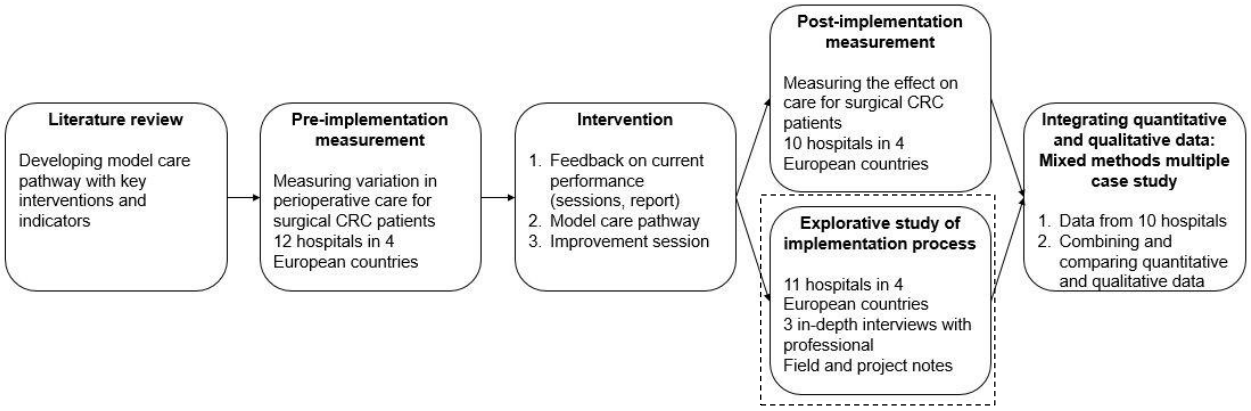
Do you have any questions before we start?

Topic	Possible question
Intro	Could you please tell us since when you have been working in this hospital and what your job is?
Respondents role in project	Your hospital participated in an international project on developing and implementing a colorectal cancer pathway. What was **your role** in this project?
Feedback session	During the project, the hospital received input in the form of feedback on the surgical care for patients with colorectal cancer (meetings and a report). Were you present at the **feedback session**? If yes: - who was present during the session? - what did you learn from this session? - what was your contribution?
Feedback report	Have you received or seen a copy of the **feedback report**? If yes: - what did you think of the feedback? - how was the feedback (report and session) received, by you and your colleagues? - how did it influence your contribution to the pathway project?
Improvement session	The hospital received input in the form of an improvement meeting and a model pathway. Were you present at the **improvement session**? If yes: - who was present during the session? - what did you learn from this session? - what was your contribution?
Model pathway	Have you received or seen a copy of the **model pathway**? If yes: - what did you think of the model pathway? Is it valid and/or useful, practical? - do you and your colleagues see the care pathway as “the right thing” to be doing?
Implementation activities and efforts	What **activities/efforts** are there to implement the care pathway: - can you tell us more about those and how they came about? - who was involved? - how were all involved professionals informed during the project? - was there a project plan?
Hospital support	How did the **hospital support** the project? What was the role of - staff personnel (quality dept.)? - were there resources (time, financial, personnel, training)?

Senior management	Was the **senior management** (director, board) of the hospital involved in any way?
Decision to join project	Could you tell us about **the decision to join** this project. - how did that happen? - why do you think you joined? - was there a specific event that made the hospital join? - how does the project fit with the hospitals policy?
Value quality improvement	How is **quality improvement valued** in your hospital? And in your team?
Desire and willingness to change	Does the multidisciplinary team involved in this care pathway have the **desire and willingness** to change their practice? Does the team leader facilitate and stimulate this?
Involved in CP project team	Who **was involved** in the care pathway project team? - who acted as team leader? - did these colleagues already know each other? - did they have experience in quality improvement projects? - how would you characterize the cooperation?
Skills	Did the project team had the **right skills** to perform the pathway project?
Compensation	Are project team members **compensated** for the time and effort? Are there financial incentives?
Data System	Is there a **system** available that can be used to provide the **data** needed for this project? Can this also be used for monitoring or follow-up of the care pathway?
Impact	What kind of **impact** has participation in the colorectal cancer pathway project had on clinical care and treatment, if any?
Unexpected effects	Were there any **unexpected effects**? Any unexpected factors working for or against the CP? Did the workload change because of the CP?
Outro	Is there anything else we should have asked you to understand the implementation process better?

CHAPTER 5

QUALITATIVE EVALUATION OF THE IMPLEMENTATION PROCESS OF A CARE PATHWAY FOR COLORECTAL CANCER SURGERY



Submitted as:

Van Zelm R, Coeckelberghs E, Aeyels D, Sermeus W, Wolthuis A, Panella M, Vanhaecht K (under review) Qualitative evaluation of the implementation process of a care pathway for colorectal cancer surgery

ABSTRACT

Background

Colorectal cancer surgery has become increasingly standardized with enhanced recovery protocols. Adherence to these protocols is challenging in daily practice. One strategy to improve adherence is development and implementation of care pathways (CPs). CPs are complex interventions that combine evidence-based key interventions with feedback and improvement methods. The purpose of this study is to explore the implementation process of an evidence-based CP in an international setting.

Methods

This qualitative study is based on the MRC guidance on process evaluations for complex interventions. In-depth interviews were conducted with 32 healthcare professionals from 11 hospitals in four European countries. Participants had various professional backgrounds and were directly involved in the implementation process. Data was analyzed using the Framework approach and visualized using a fishbone diagram.

Results

Based on the perceived outcomes, two groups of respondents were distinguished: those who perceived positive outcomes, and those who perceived no effect of care pathway implementation. A fishbone diagram was used to map the main themes reported by each group of respondents. Respondents who perceived positive outcomes reported clinical leadership, use of feedback, positive effect of standardization, and teamwork as factors that may contribute to positive perceived outcomes. Respondents who perceived no effect of the implementation reported lack of organizational support and challenging collaboration and standardization as mechanisms that may explain the low outcome perception.

Conclusions

The MRC guidance on process evaluations of complex interventions served as framework to explore the implementation process of an evidence-based CP. Important aspects that have to be taken into account during implementation are the evidence base of the CP, prolonged involvement of multiple

disciplines, and availability of a clinical data system. Multiple implementation activities are used, focusing on competence, behavior, or workplace. Different mechanisms are at work that impact implementation. When teamwork and collaboration are perceived as good, respondents perceive positive effects. Unexpected events during implementation of the CP that are perceived as positive, increase motivation. Our findings suggest that feedback is an important implementation activity used for goal-setting and motivation.

BACKGROUND

Enhanced recovery protocols (ERPs) (also called “fast track” or Enhanced Recovery After Surgery (ERAS) guidelines) are used extensively in surgery, especially in colorectal surgery, where they were first used.(1) These protocols aim to decrease risk of postoperative morbidity, by improving perioperative care. ERPs have been described as a “paradigm shift” in the delivery of surgical care.(2) Several studies, including a systematic review by Lau et al. (2017) and two studies based on (inter)national registries, have shown that ERPs can be used safely to reduce complications and postoperative length of stay.(3-5) Recently, a new version of the ERAS protocol has been published.(6)

Despite still growing evidence of effective and safe application of ERPs, adherence to these protocols seems difficult in daily practice. Protocol adherence ranging between 45 to 90% is reported, showing wide variation in clinical practice, and illustrating implementation of ERPs is challenging.(7-10) Other studies showed that improved protocol adherence leads to improved outcomes.(5, 11, 12) This suggests that sustainable implementation of an ERP with high adherence rates is needed. A recent review by Pedziwiatr et al. (2018) concluded that ERAS programs are safe, feasible and associated with improved outcomes. However, there remain challenges in maintaining a high level of compliance, and new implementation strategies may be needed.(13)

Gillissen et al. (2013) and Larson et al. (2018) both reported on collaboratives for the implementation of ERPs for colorectal surgery in respectively the Netherlands and the USA. Both studies concluded that participating teams were able to reduce length of stay and improve the standard of care. Learning with and from other participating teams was seen as important factor of success.(14, 15) Although both studies provided descriptions of the collaborative and associated activities, the focus is on outcome evaluation. Questions on the process of implementation remain unresolved.

Coxon et al. (2017) performed a literature review on implementation of ERPs (for several types of surgery). Using realist synthesis, the authors constructed so called “context-mechanism-outcome configurations” around two central program theories, on staff consultation and on change

agency.(16) The authors concluded that current literature is primarily focused on clinical and cost effectiveness, but less on implementation. They encourage others to use and test the proposed program theories.

Gotlib Conn et al. (2015) performed a process evaluation on normalization of ERP in everyday practice. The Normalization Process Theory was used as framework to describe and explain the implementation. The authors concluded that ERP implementation is achieved by complex cognitive and social processes in which a “champion”, external and internal relationship building, and strategic management of the project are key.(17) Stone et al. (2018) performed a systematic review to identify facilitators of and barriers to ERP implementation. They included 53 studies in multiple surgical specialties. The paper provides a useful overview of facilitators and barriers to implementation of ERAS, presented in frequency of discussion in the included papers. Facilitators include ongoing education for clinicians, a strong multidisciplinary team with good communication, continuous audit and feedback, leadership, alignment of the ERP with current practices, and standardization of protocol elements. Barriers were resistance to change. lack of resources, rotating staff and residents, the belief that implementation is too difficult, and a perceived low evidence-base. The authors also suggest that only few studies report ERP implementation in detail and that more high-quality studies on the implementation process are necessary.(18)

Rationale: care pathways as complex intervention

One strategy to improve the adherence to evidence-based protocols is developing and implementing care pathways (CPs).(19) CPs, by definition, are complex interventions, combining evidence-based key interventions, feedback on the actual care process with a strategy for quality improvement.(20, 21) The rationale for effectiveness of CPs is that a core set of evidence-based key interventions is delivered to an improvement team, together with feedback on their current performance (both patient outcomes and compliance to the key interventions). This feedback will identify the room for improvement. The teams then develop their strategy for improvement, including goal-setting and implementation activities, based on the feedback.(22)

The Medical Research Council (MRC), has published guidance on how to perform a process evaluation of complex interventions. A process evaluation determines the level to which a complex intervention is implemented as planned. The goal is to provide detailed understanding to inform both practice and policy.(23) This guidance links five elements for process evaluation (see table 5.1): intervention, context, implementation, mechanisms, and outcomes. The operationalization of these elements for this study are described in the protocol paper, including a description of the intervention.(22)

This study uses the MRC guidance to perform a comprehensive evaluation of the implementation process of a CP. The overall aim is to explore experiences of professionals with the implementation process of a CP for patients undergoing surgery for colorectal cancer, building on the previous mentioned studies, in an international collaborative setting. Research questions are:(22)

1. What is the context of the CP implementation?
2. How was the CP implemented, who was involved?
3. What mechanisms influenced the implementation of the CP?
4. What is the relationship between the outcomes of the formative evaluation and implementation priorities and strategy?
5. What unexpected events or consequences occurred during implementation?

Table 5.1 Key elements of process evaluation – MRC Guidance

Element	Description
Intervention	Description of intervention and its causal assumptions
Context	Contextual factors that shape theories how the intervention works Contextual factors that affect (or may be affected by) implementation, intervention mechanisms and outcomes Causal mechanisms present within the context which act to sustain the status quo, or potentiate effects
Implementation	Implementation process (how delivery is achieved; training, resources, etc) What is delivered: fidelity, dose, adaptations, reach
Mechanisms of impact	Participant responses to and interactions with the intervention Mediators Unexpected pathways and consequences
Outcome*	Perceived outcomes as expected by the respondents*

*Term not defined in MRC Guidance, but used in this study

METHODS

The methods section is described in accordance to the COREQ checklist for reporting qualitative research(24) (completed checklist can be obtained from author).

Sample – This qualitative study was part of a quality improvement project in 12 hospitals in Belgium, France, Germany and the Netherlands (see box 5.1 for additional information on the project).(7, 22) A purposeful sample of individual professionals from 11 participating hospitals was obtained, as one hospital dropped out due to local logistic reasons. The sample was designed to include the medical leader of the local projects, a quality officer or CP facilitator supporting the project, and a nursing leader involved in the project and/or direct patient care. The participants were contacted by the local study coordinator, and received written information and consent forms. All invited respondents gave informed consent to participate. In total 29 interviews with 32 interviewees were conducted, as three interviews were "duo interviews" due to planning preferences of the interviewees. Table 5.2 presents the characteristics of the interviewees, 26 of the interviewees were frontline staff working with the CP in daily practice.

Box 5.1 Outline of the project

Twelve European hospitals participated in the Care Pathways for cancer patients undergoing colorectal cancer surgery: a quality improvement project. The project started in January 2015 and ended April 2018. The project was performed by the KU Leuven Institute for Healthcare Policy (www.kuleuven.be/ligb) and was guided by the European Pathway Association (E-P-A, www.e-p-a.org), an international not-for-profit organization aiming to increase and disseminate knowledge on CPs. In the project, the 12 participating hospitals performed a baseline measurement of their care process (outcome and process indicators), improved the care process where needed by implementing or revising a CP based on ERAS guidelines, and performed an effect measurement. The hospitals were supported by the research team in a number of sessions. Below are the main activities:

- Pre-project: selection of hospitals, development of **model care pathway** (key interventions and indicators).
- National kick-off meeting per country: explaining project and CP methodology
- Pre-implementation patient record analysis: measuring protocol adherence and outcomes
- National **feedback session** per country: sharing and comparing performance (incl. extensive **feedback report**)
- Local sessions: **feedback** (for larger audience) and **improvement session**
- Post-implementation patient record analysis: measuring protocol adherence and outcomes
- International closing session for all participating teams: sharing lessons learned

Items in Bold are the "active ingredients" of the complex intervention.

Data collection – In-depth interviews with a duration of approximately 50 minutes were conducted with all participants. The interviews took place at the workplace of respondents, in a quiet room, with no other people present. Two interviews took place by telephone. The interviews were based on a semi-structured interview guide, focusing on key elements of process evaluation (see supplemental material chapter 4).(22)

All interviews were held in English or the primary language of the participant, recorded, and transcribed verbatim. If the interview was not performed in English or Dutch, it was transcribed and translated by a professional translation service. Since the interviews were transcribed literally, transcripts were not send to the participants for approval. Additionally, a second researcher took field notes during the interviews, capturing non-verbal reactions.

Table 5.2 Respondents characteristics (n=32)

Indicator	Number of respondents
Profession	
Clinical Nurse Specialist	2
Colorectal surgeon	9 (of which 6 project leaders)
Dietician	3 (of which 1 project leader)
Head nurse	5
Internist	3 (of which 1 project leader)
Nurse	4
Quality officer	6 (of which 1 project leader)
Country	
Belgium	10
France[a]	5
Germany	11
Netherlands[b]	6
Years of experience	Min 1 year – max 37 year (median 15)
Role in project	
Medical leader	7
Facilitator	9
Team member	16

[a]Three hospitals, but working closely together, 1 improvement team, with 1 project leader
[b]Two hospitals

Research team – All interviews were conducted by the same researcher (R.v.Z.). E.C. or D.A. were present as second researcher experienced in CP research, but independent of this project (not in the telephone interviews). Their role was to take field notes, and provide reflection during debriefing

after each interview. Prior to the interviews R.v.Z. and D.A. received training in qualitative interview techniques (see completed COREQ checklist for details on credentials of the interview team).

Data analysis – Data was analyzed using NVivo 11 software (QSR International). The thematic analysis method, referred to as Framework approach, was used for analysis.(25) This approach consists of two stages, each with several steps. Stage 1 is the *data management* phase, consisting of familiarization, constructing an initial thematic framework, indexing and sorting, reviewing data extracts, and data summary and display. Stage 2 is the *abstraction and interpretation* phase. This stage consists of developing descriptive categories, mapping linkages between the data, and explanation, accounting for patterns.(25)

Familiarization with the data started when the first interview was transcribed. Transcripts and field notes were read and re-read, to form a first impression of the data. The initial thematic framework was constructed both deductive, based on the interview guide, and inductive with emergent themes during the analysis. Indexing and sorting of data was performed by R.v.Z. All relevant text fragments were categorized and allocated to specific themes. After five interviews were coded, an independent, experienced qualitative researcher, also coded these interviews. Differences in codes were discussed, and codes refined, after which the remaining interviews were coded, indexed and sorted.

The next step was to critically review the data extracts and categories by the research team as a second quality control to improve robustness of the analysis. Per main category, a selection of themes was discussed, to retrace the steps to individual interviews. Finally, the data was displayed in matrices, containing data categories in columns and respondents per row, with the cells containing interview extracts for each specific theme.

The next stage, abstraction and interpretation, started with condensing the data by describing themes in the different categories (“vertical analysis” of the matrices). This phase resulted in a “thick description” of the major themes per element of the MRC Guidance on process evaluations. After this step, links between categories and themes were mapped, guided by the research questions, by exploring what different respondents reported about themes (“horizontal analysis” of the matrices).

The links and patterns found between the responses of the interviewees were analyzed using a fishbone diagram. A fishbone diagram (also referred to as cause-and-effect diagram, or Ishikawa diagram) is a visual representation used to collect, organize and summarize knowledge on potential causes to a certain effect.(26) A fishbone diagram was used here to summarize how different themes may affect the perceived outcomes of the CP implementation. The elements of process evaluations according to the MRC guidance were used as categories. Finally, patterns found were compared to existing literature in order to provide explanations.

RESULTS

After analysis of 16 interviews, no new themes emerged. However, all 29 interviews were included to provide extra depth to our data. The findings are presented in table 5.3, showing the main themes categorized in the MRC Guidance elements. Respondents perceived several effects of the CP implementation, including better patient information, reduction of length of stay, improved nutritional status and improved protocol adherence. Some respondents perceived no change in patient outcomes, either due to limited implementation or methodological issues (small sample size, lack of data).

> *"I think that it will definitely have a positive effect. Patients who are better informed, know what to expect, that they follow a certain route, that they do not remain with questions 'what happens next?'. I think that a well-informed patient will only benefit in his treatment process." (dietician)*
>
> *"Those 20 patients now, they will be the same as the 20 then. I think so, yes. Don't you think?" (colorectal surgeon)*

Unexpected events or consequences were reported as either positive or negative. Positive consequences mentioned were: more professional freedom, time it took for co-workers to cooperate ("much faster than expected"), and the detection of a hospital-wide problem with postoperative nausea and vomiting care by implementing this specific CP. These positive unexpected events

increased motivation, whereas negative consequences (less support than expected and (cynical) remarks by colleagues after set-backs) decreased motivation.

Table 5.3 Main findings per process evaluation element

Process Evaluation Element	Sub category	Main findings
Intervention	Care pathway	Practical; evidence-based key interventions valued, but complex; already known
	Feedback	Sessions' participants: medical leader, nursing leader, sometimes quality officer; local sessions also other professions (e.g. anesthesiology, nutrition, physiotherapy); feedback and comparison with other hospitals positively received and used for prioritization, motivation and quality control
	Improvement Session	Same participants; moderator as "critical friend"
Context	External	Stimulus (opportunity, pressure)
	Organization	Higher management involvement; CP development aligned with hospital strategy; resources; clinical data management system; role of quality department
	Clinical team	Leadership; team willingness to change
	Improvement team	Collaboration; training; previous quality improvement experience
Implementation	Competence focused activities	Changing or updating local protocols; (mandatory) training; variety of communication activities
	Behavior focused activities	Monitoring of and feedback on the pathway; use of reminders
	Workplace focused activities	Multidisciplinary meetings; changing team structure to work with dedicated staff
Mechanisms	People	Teamwork & collaboration; pathway depending on 1 person, possibility to deviate from the pathway
	Processes	Effect of feedback; standardization
	Consequences	Perceived effect on workload; unexpected consequences
Perceived outcomes	Effect on patient care	Improved patient information; reduced LOS; improved nutritional status; improved protocol adherence
	Effect on team work	Improved communication and coordination; broader involvement of disciplines; increased understanding of each other's contribution
	Sustainability of the care pathway	Create ownership within team rather than with champion; continuous development of the pathway

Based on the perceived outcomes, two groups of respondents were distinguished: those who perceived positive outcomes (group A), and those who perceived no effect of care pathway implementation (group B). Group A consisted of 15 respondents: four colorectal surgeons, four head nurses, three nurses, two quality officers and a clinical nurse specialist and a dietician. Group B consisted of 10 respondents: four colorectal surgeons, two internists, two dieticians, a head nurse and a clinical nurse specialist. Both groups had representatives from seven hospitals from all four countries. From our total of 32 respondents, seven could not be allocated to a group because outcomes were not discussed during their interview, e.g. a quality officer who was not aware of the

outcomes, or staff only involved since the implementation. For each group the responses on the main elements intervention, context, implementation, mechanisms and outcomes were analyzed to describe the different dimensions within each theme. A fishbone diagram was used to map relationships between the different themes. The fishbone diagram is presented together with illustrative quotes.

Intervention

The dimensions in which the intervention was discussed varied. The respondents in both groups generally reported the model pathway as a practical basis to be adapted to fit the local systems. The evidence-based key interventions were valued. Especially surgeons noted that the evidence base is important, Some respondents were somewhat skeptical of the model pathway and indicated a CP was already implemented. The individual interventions were not seen as complicated, but combining all, made implementation complex.

> *"I do not know from the top of my head if it contained much …. No, it did not contain much news." (nurse – group A)*
>
> *"So I think that the pathway is for sure better than for example the actual guidelines of the [national guideline body]. It is the oncology system, they made a new guideline in 2015, and you can read it, it's perfect for reading, but you cannot live it." (internist – group B)*
>
> *"I think that is the most important, because if you for example have to convince colleagues, you prefer doing that with evidence." (colorectal surgeon – group B)*
>
> *"Early mobilization of a patient, in itself it is not very complex, it is not big science. But to organize this on the floor, on the ward, that is really difficult … And if you consider this as one of the many items, then you should do this with all items. So in fact, it is an immense complex thing to implement." (colorectal surgeon – group A)*

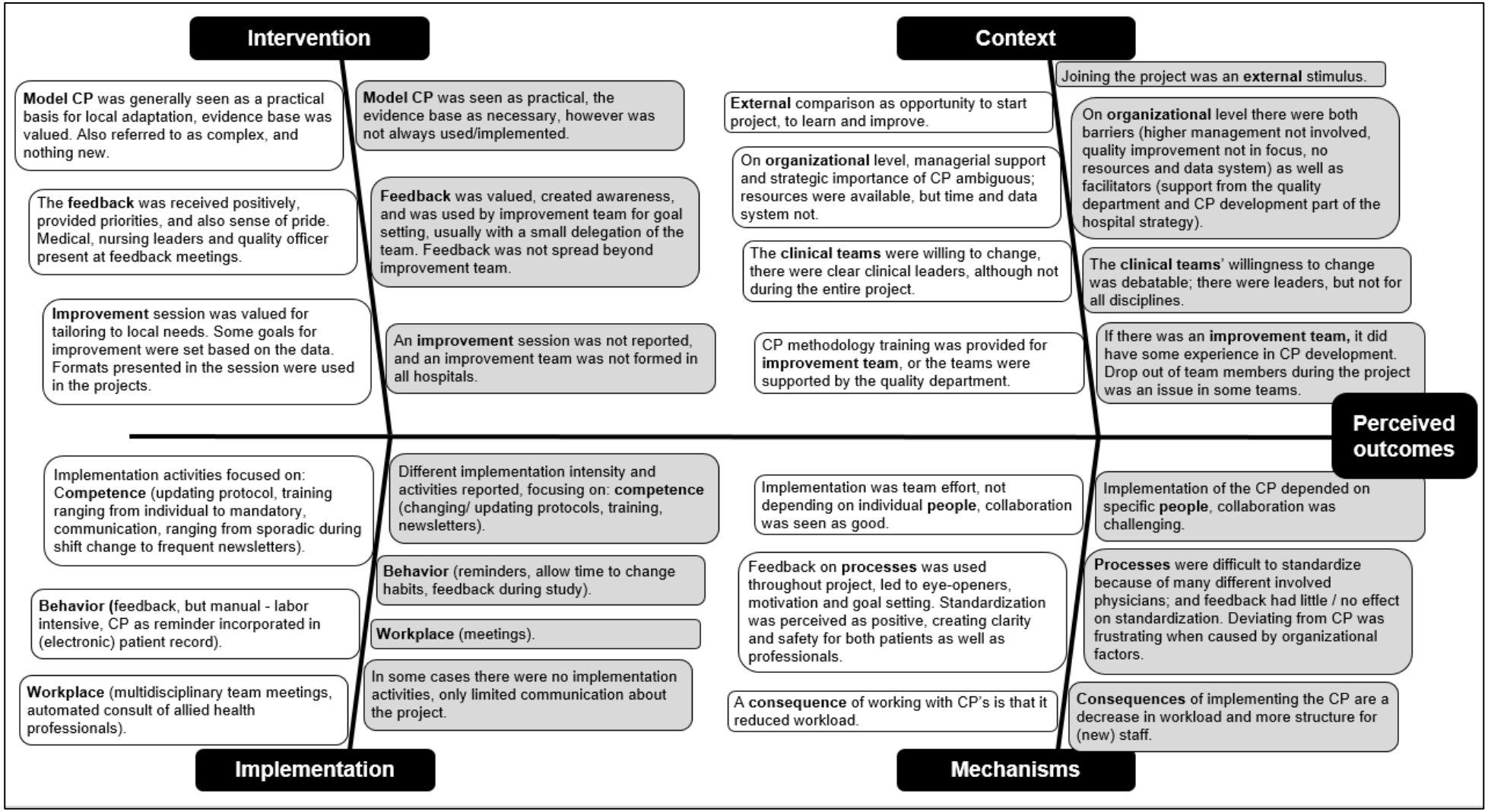


Figure 5.1 Experiences with care pathway implementation: intervention, context, implementation, mechanisms, and perceived outcomes

White boxes: group A – positive perceived outcomes. Gray boxes: group B – no perceived effect. Words in bold are sub categories from table 5.3.

Feedback on the current process was received positive, giving a sense of pride. Usually the medical leader, a nursing leader and quality officer were present at the feedback sessions. In exceptional cases, feedback was not spread beyond the improvement team.

> *"That we already do a lot like the other hospitals, just like providing a feeling of security, to work with standards and that we are very close to the top due to the fast track method." (head nurse – group A)*
>
> *"I only heard from my colleague about the results. And the professor told me this year it takes place again. So no real evaluation, because I was not present." (head nurse – group A)*

Some respondents in group B explained that feedback on their current care process was received, but that it was not spread further in the organization, and there was no improvement effort or CP implementation.

> *"I was very much attentive about what you were talking about with those slides. But afterwards it was just a rush all the time, and I must say I did not get further than that." (dietician – group B)*

Respondents in group A valued the local sessions, because they were tailored to local needs. Interviewees indicated that formats that were presented in the improvement session were used during the project.

> "*And simultaneously we started with it, huh, with that ladder [visualization of CP], let me put it like that. The intention was to deliver this ladder to the patients when they arrive at the ward." (nurse – group A)*

Context

Respondents in group A described the context for the CP implementation as supportive. The opportunity to join the project and compare with other hospitals worked as stimulus. Higher management support and CP development as part of the hospital strategy, were main themes discussed by the respondents. Both were deemed important, although not always present.

Availability of resources, including a clinical data system, and allocated time for the improvement work, varied.

> *"This is a strategic project, to work on care pathways and care programs, hospital wide." (quality officer – group A)*
>
> *"We have time within our hours, four hours a week for the two care pathway facilitators. All involved could invest their time." (nurse – group A)*
>
> *"Something in which we certainly fall short, but maybe we discus that later, is to receive enough feedback on what we were doing, which in fact is very important, but it proved a bit difficult with respect to IT to get enough feedback on what we are doing." (colorectal surgeon – group A)*

In contrast, respondents in group B characterized the context as unsupportive of CP implementation. There was negative external pressure, higher management was not involved, there were not enough resources, especially a data system was lacking.

> *"And you have to fight for patients against the other hospital in [city] as well, to get the numbers. R.v.Z.: Competition? Yes, competition. And therefore quality is an important point, to say 'We have high quality standards.' Get certifications and everything." (colorectal surgeon – group B)*
>
> *"Management is interested, but not more. I do not find my motivation in the management." (dietician – group B)*
>
> *"No. We have no statistics about that, that's for sure. And probably too bad because we could possibly communicate it." (colorectal surgeon – group B)*

Some facilitators in the context were also mentioned by interviewees in group B (e.g. CP as part of the hospital strategy and project support by the quality department). Several respondents mentioned experienced clinical leaders, but they were not reported by all. Drop-out of improvement team members over the course of the project was discussed by the interviewees.

> *"But for me, that was a disadvantage, when you have just started and have to develop the care pathway. You have some logistic problems, problems with people you do not know, and*

the disadvantage that your patient volume is not high enough to develop the pathway directly." (colorectal surgeon – group B)

The interviewees in group A indicated that the clinical team was open to change, and that there were clear and formal clinical leaders, although not for all disciplines, and not during the entire project (conflicting priorities, change of job).

"We are not very conservative, but also not changing all the time. The willingness to change, provided good arguments and clear objectives, is present." (colorectal surgeon – group A)

"*That is a bit my fault. We had several meetings, but since a few months I have not followed it." (colorectal surgeon – group A)*

Most respondents in group A indicated that members of the improvement team received training in CP methodology, or the teams were supported by the quality department. A challenge mentioned by the interviewees was the frequent changing of residents, threatening the continuity of CP implementation.

Implementation

The respondents in both groups indicated a wide range of implementation activities was used. These included, training, monitoring and feedback, use of reminders. Most respondents in group A reported that monitoring and feedback was performed manually and considered complicated and labor intensive. Changing or updating the local protocol was mentioned by all interviewees.

"Well, the doctors worked this into our treatment standards together with us. We then adopted some of the things there and then inserted them into our standards, so to speak." (head nurse – group A)

Different approaches to training and communication were discussed by the respondents in both groups, e.g. small group training versus mandatory training for the team, communication about the project during shift change, linking pin constructions.

"We made everyone responsible for communication within their own discipline. So every discipline present at meetings. That worked rather well, I think, yes." (nurse – group A)

"We are a small hospital, so most will have known each other before starting the project. But not each other's job. That was what people found interesting, to hear each other's contribution to the care pathway" (clinical nurse specialist – group A)

"But separate, just a ten minutes briefing. 'You want to do that for me? Let's do it together, let me know what happened, what was difficult.' In small groups, people feel interested, receive attention." (nurse – group A)

Some respondents in group B highlighted that there were no structural implementation activities performed in their hospital.

Mechanisms

Several mechanisms were reported that could affect the perceived outcomes. Interviewees in group A perceived the implementation process as team effort, with bottom-up ownership and good collaboration.

"I think when changes comes bottom-up, you should let that happen. Top-down often does not work. Takes more time and is less efficient." (colorectal surgeon – group A)

"I think it went pretty smooth. Everybody was joining in and everybody … Of course sometimes you had to wait a little, certainly when everything is communicated by email, because of busy schedules." (dietician – group A)

"I think that the guarantee to sustain the care pathway is that the disciplines themselves are aware of the importance of it, and that they become advocates. That is my hope that this will happen. But this is a risk." (colorectal surgeon – group A)

In contrast, respondents in group B reported challenging collaboration, and implementation depending on specific persons, which resulted in vulnerability.

"But, there are a lot of different things that have to work together. That is the important thing, the interference between different departments. From my point of view this study could be a good opportunity to do that." (internist – group B)

"So, when I am present or a few members of the team are in the specific positions, then it is rolling and if it is not then it is like not happening." (internist – group B)

Monitoring and feedback was used throughout the project, as indicated by both groups. However, only interviewees in group A discussed clear effects of feedback: it acted as trigger and eye-opener, increasing intrinsic motivation.

"When the topic is on the table, you act on it. It stimulates. You have a feeling, I can feel that, but that is not a real measurement. You better work with data. Than you can say 'Okay, let's focus on this topic and see how it evolves', huh." (head nurse – group A)

Standardization was perceived as positive by respondents in group A, creating clarity and safety for both patients and professionals.

"By standardizing, patients will recuperate sooner and have shorter length of stay, I think." (nurse – group A)

On the other hand, respondents in group B experienced challenging standardization, including the need to deviate from the CP due to organizational reasons,

"One of the problems is that we are with five surgeons. It would be better if only two would do colorectal surgery." (colorectal surgeon – group B)

Respondents in both groups perceived the effect on workload generally as positive: decreasing workload by organizing the care process and providing structure for the team.

"After all this had developed a little bit, it has become easier sometimes, because there were these fixed treatment standards, where one did not have to ask three times, how do we want to do it now, or how should we do it? Instead it just worked smoothly." (head nurse – group A)

No, it has not changed, because when things go not in a good direction then it takes much more time. Because you have to phone, call back or something is not working, there is trouble. So, when things are going smoothly then it is a gain of time. So, now it is only positive. (dietician – group B)

DISCUSSION

This paper explores the implementation process of a CP for colorectal cancer surgery in an international collaborative setting. The MRC guidance on process evaluation is used to describe intervention, context, implementation, mechanisms and perceived outcomes. Based on the perceived outcomes, we distinguished two groups of respondents for further analysis: respondents who perceived positive outcomes of the CP implementation (group A), and respondents who perceived no effect (group B). Respondents who perceived positive outcomes reported clinical leadership, use of feedback, positive effect of standardization, and teamwork as factors that may contribute to positive perceived outcomes. Respondents who perceived no effect of the implementation reported lack of organizational support and challenging collaboration and standardization as factors that may explain the low outcome perception. The main items per process evaluation element are discussed below.

For the *intervention*, importance of the evidence base of the CP, positive reception of feedback, and active participation from all involved disciplines are reported in several studies.(10, 15, 16, 18, 27, 28) This was reported in both groups of respondents. Our findings suggest that “drop-out” of disciplines during the implementation process could be an issue in group B. This is a nuance of the program theory of staff consultation by Coxon et al. (2017) (16), suggesting staff should not only be consulted, but involved for a prolonged time. Respondents in group A valued the local sessions because they were tailored to local needs.

Themes mentioned on *context* correspond with previous published barriers and enablers, and include the level of support from the hospital (higher management involvement and alignment with hospital strategy, quality improvement support), resources, clinical leadership.(10, 17, 18, 28-31) In a large European research project on quality improvement in hospitals, one of the findings is that quality on the agenda of higher management leads to better care.(32) This suggests that respondents who reported a lack of organizational support, might experience a disadvantage in quality improvement. The respondents in our study who perceived no effect from the CP implementation (group B) reported either an unsupportive context, or a context with clear barriers.

However, some respondents in group A also reported an unsupportive context with barriers, suggesting that quality improvement can still be perceived to be successful, despite an experienced lack of organizational support.

The importance of local champions is reported in previous research.(2, 10, 16-18, 27, 28, 31, 33) In line with the program theory on change agency by Coxon et al. (2017), our findings suggest that this champion should not only be clinically competent, but also knows his way around the hospital and has management and people skills. Respondents in group B reported a lack of, or unclear clinical leadership. As in our findings, the high turnover of residents is reported as barrier in previous studies, threatening communication and continuity.(10, 18, 34, 35)

Respondents who indicated that training for the improvement team was provided, or that the team was supported in CP methodology, perceived positive outcomes of the CP implementation.

Implementation activities reported include competence, behavioral, and workplace focused activities. Several studies looked at the implementation process, suggesting that implementing CPs requires complex cognitive, organizational and social processes. These processes include a variety of implementation activities, e.g. team meetings, educational activities, audit and feedback, project management, involvement of stakeholders and use of standardized CPs.(10, 17, 18)

Audit and feedback is an implementation activity used and promoted by different authors,(17, 18, 30, 32, 33, 36) and is a formal part of the ERAS approach, facilitated by the ERAS interactive audit system.(2) Our findings suggest that feedback on the current care process and especially the comparison with other, international centers, was valued. This is a main reason for setting up quality improvement collaboratives, as discussed in a systematic review on quality improvement initiatives by Wells et al. (2017), suggesting that teams learn faster and achieve better implementation when working together and comparing with others.(37)

Respondents in group B who did implement the CP, described the same sort of implementation activities used as respondents in group A.

Mechanisms affecting implementation of the CP reported in our study, included teamwork and collaboration, standardization, effect of feedback, and perceived effect on workload. These mechanisms are aligned with findings from previous research.(10, 18, 28, 31, 33, 34, 36) Our findings suggest that mutual respect is the basis for effective collaboration. Respondents in group A reported good collaboration, whereas the respondents in group B experienced challenging collaboration. Respondents in group A also experienced a motivating effect of receiving feedback, which worked as trigger for quality improvement and setting shared goals. Teamwork as basis for CP development was recently described in a study on CPs for heart surgery (38) and its importance for collective change has been theorized in organizational readiness for change theory.(39) At the same time, CPs can improve team outcomes (conflict management, burn-out), climate for innovation and organization level of care processes, by setting team-level goals.(40)

Overall, standardization was perceived as positive, providing clarity and safety, by respondents in group A, but less so by respondents in group B. The effect on workload was reported by both groups as positive. Most respondents indicated a decrease in workload (after an initial small increase).

We did not find differences in implementation approach based on how feedback was perceived, except for the step “prioritization”. We believe the logic assumption from our rationale that providing feedback automatically leads to quality improvement is far more complex in clinical reality. First of all, we observed that feedback does not always lead to perceived better outcomes. A number of respondents in group B clearly stated that there was no follow-up action after the feedback sessions. Indeed, feedback may have limited effect. A Cochrane review (2012) concludes that audit and feedback can lead to “small but potential important improvements”. Effect of feedback appears to depend on the baseline performance, and the way feedback is delivered (peer-to-peer, multiple times, written and verbal, and including goals and action plans).(41) It is recommended to provide feedback as close and timely to actual care as possible.(32) It is debatable if the way we provided feedback in our intervention was in line with these conditions. This could explain why in some cases, feedback did not lead to improvement activity.

Secondly, our findings show that availability of data can be a problem, leading to a labor intensive process to collect, present and interpret data. This was experienced by respondents in both groups. Previous research identified the use of data as enabler as well as barrier.(10) In this study, challenges with the volume of data and data collection (e.g. lack of electronic data, unreliable data) were reported. Still, audit and feedback was identified as key feature for success.(10) Frequent data feedback is regarded as essential but challenging, due to data collection problems.(17, 28) For this reason, implementation of pathway-oriented information systems is considered crucial.(32)

Methodological considerations

The choice for grouping the respondents based on perceived outcomes is debatable. Other groupings based on the MRC guidance elements (e.g. context) could have been used. There are three reasons that we believe justify our choice. First, as visualized by the direction of the arrows in the MRC guidance, outcomes are the quintessence element of the evaluation: what is the effect of the intervention context, implementation and mechanisms on outcomes? This is where implementation efforts are directed at.

Second, the topic outcomes was discussed in most interviews providing a large number of respondents in each group. As it turned out, seven respondents could not be allocated to a group, because outcomes were not discussed during their interviews. These respondents came from a variety of backgrounds (discipline, country and hospital), all of which were already represented in the two groups.

Third, we tried to develop other groupings based on the responses on the themes intervention (positive appreciation vs. neutral appreciation) and context (supportive vs. unsupportive), the responses on implementation and mechanisms being to divers to use. This led invariably to smaller potential groups than the two groups we used. Furthermore, the potential groups based on e.g. context, had nearly the same composition as the groups we used (except for the respondents who experienced an unsupportive context, but perceived positive outcomes – who we also identified in our fishbone diagram). This makes us quite confident that we used a meaningful and feasible grouping.

We advise caution in interpreting our fishbone diagram, because it is not a cause-and-effect diagram in the original meaning.(26) It is used here strictly as visualization. Relationships between elements may not be unidirectional and/or causal as suggested by the “flow” in the diagram.

A major strength of this study is the variety of contexts of both countries and hospitals. This gives a broad view of contextual factors influencing the implementation process. Additionally, there are three important methodological strengths. First, quantitative results of the outcome evaluation were not known to the researchers during the interviews, coding and description of data. This helps to reduce interpretation bias.

Second, there have been multiple quality controls during analysis (use of field notes, debriefings after each interview with the second independent researchers, discussing and refining codes), in both data management and interpretation stage, ensuring a transparent and auditable process.

Finally, all 29 interviews were analyzed, even after analysis of 16 interviews no new major themes emerged from the data. This gives us confidence that we collected ample and information rich data.

This study also has its limitations. There was no formal “member checking”; sending the data to respondents for an accuracy check. However, informal member checking was carried out during the interviews to check our understanding of the topics discussed. Techniques as paraphrasing and summarizing were used to this end.

By including directly involved professionals we may have introduced selection bias. However, to collect meaningful data, we wanted to include professionals that were involved in the CP project.

The study was performed in different countries, using different languages. In qualitative research, this can be an issue. Santos et al. (2015) suggest to translate early during analysis, to allow access to all data for researchers who do not speak the source language. The use of a professional translator is highly recommended.(42) Most interviews were performed in either Dutch or English, with interviewers proficient in German (R.v.Z.) or French (D.A.) present. Two interview transcripts in French and German were translated into English by a professional translator service. In the

abstraction and interpretation stage of data analysis, Dutch data were translated into English. This resulted in the lowest number of translations needed, reducing the risk of losing meaning in translation.

Recommendations for further research

The explorative nature of our study does not permit for easy generalizability of the findings. However, a number of recommendations for future research can be formulated. We suggest to further examine the particular relationships between process evaluation elements in the fishbone diagram and the effect on patient and implementation outcomes (adherence). Future research could study the relationship between how teams engage with the intervention (model pathway, feedback and improvement session) and quantitatively measured outcomes. The relationship between perceived outcomes and actual outcomes can be further explored. This will further develop and refine the fishbone diagram, and add to the generalizability of the implementation knowledge for CPs.

CONCLUSION

The aim of our study was to explore experiences with the implementation process of an evidence-based CP. The MRC guidance on process evaluations of complex interventions served as framework for this exploration. Important aspects that have to be taken into account during the implementation of a CP are the evidence base of the CP, prolonged involvement of multiple disciplines, clinical leadership, and support from the organization, including the availability of a clinical data system. However, even in an unsupportive context, respondents perceived positive effects.

A variety of implementation activities was used, focusing on competence, behavior, or workplace. Different mechanisms were at work that impact the implementation. When teamwork and collaboration were experienced as good, respondents perceived positive effects. Unexpected events during implementation of the CP that were perceived as positive, increased motivation. Delivering feedback on performance helped teams to prioritize their improvement goals, but had little effect on the implementation strategy. Our findings suggest that feedback is an important implementation and

follow-up activity. Respondents perceived the role of feedback (goal-setting, motivation) to be different than that of other implementation activities (supportive). The effect of these aspects in the implementation process on the outcome of the implementation needs to be checked in future research.

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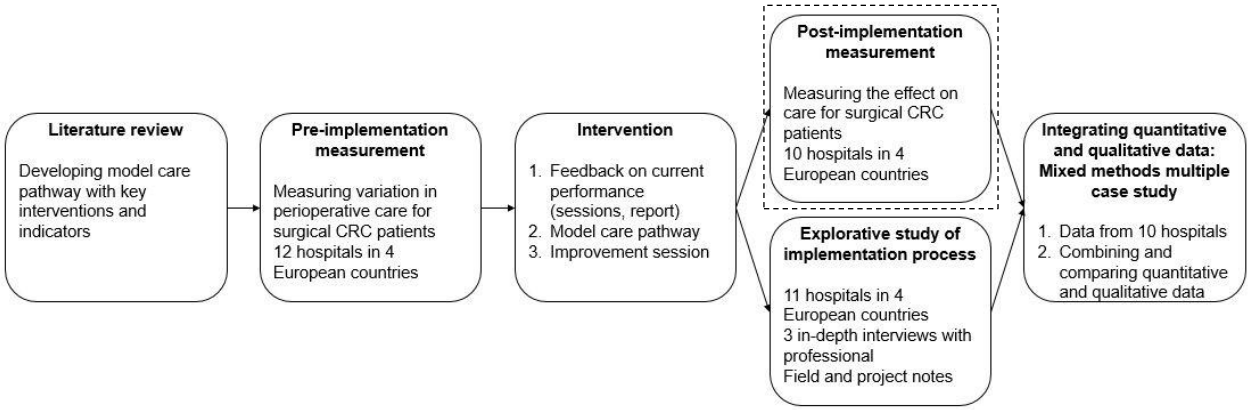
CHAPTER 6

EFFECTS OF IMPLEMENTING A CARE PATHWAY FOR COLORECTAL CANCER SURGERY IN 10 HOSPITALS: AN INTERNATIONAL MULTICENTER PRE-POST-TEST STUDY



Submitted as:

Van Zelm R, Coeckelberghs E, Sermeus W, Wolthuis A, Bruyneel L, Panella M, Vanhaecht K (under review) Effects of implementing a care pathway for colorectal cancer surgery in 10 hospitals: an international multicenter pre-post-test study

ABSTRACT

Background

Adherence to evidence-based recommendations is variable and generally low. Also in colorectal surgery, despite availability of the well-known ERAS® protocol. The aim of this study is to evaluate the effect of implementing a care pathway for perioperative care in adults undergoing colorectal cancer surgery on outcomes and protocol adherence.

Methods

International pre-test – post-test multicenter study, performed in 10 hospitals in four European countries. A model care pathway was developed, feedback on pre-implementation performance was provided, and quality improvement support to locally implement the care pathway was delivered. Measures used: length of stay, morbidity and mortality, and documentation and adherence on intervention and patient level, including improvement rate. Unadjusted pre-test – post-test differences were analyzed, followed by analysis adjusted for patient-mix variables. An importance-performance matrix was used to map the relationship between importance and performance of individual interventions.

Results

In total, 381 patients were included. Length of stay significantly decreased from 12.6 to 10.7 days ($p=0.0230$). Time to normal diet and to walking also decreased significantly. Overall protocol adherence improved from 56% to 62% ($p<0.00001$), but adherence to individual interventions remained highly variable. The importance-performance analysis showed that 30 interventions were scored as important, of which 19 had an adherence <70%, showing priorities for improvement. For some interventions, documentation improved, but adherence decreased. Across hospitals, change in overall protocol adherence ranged from a 13% decrease to a 22% increase.

Conclusion

Implementing a care pathway for colorectal cancer surgery reduced length of stay, time to normal diet and walking. Documentation and protocol adherence improved after implementing the care pathway. However, not in all participating hospitals protocol adherence improved. Only in 25% of

patients a protocol adherence of ≥70% was achieved, suggesting a large proportion of patients is at risk for underuse. The importance-performance matrix shows which interventions are important, but have low adherence, prioritizing improvement efforts.

BACKGROUND

Fifteen years ago, the “Quality of health care study”, regarded as a benchmark study on recommended care, was published in the New England Journal of Medicine. This paper stated that adherence to guidelines is low and highly variable. The authors concluded that patients receive on average 55% of guideline recommended care.(1) In September 2018, the National Academies of Sciences, Engineering and Medicine conclude in their Global Quality Chasm Report that variation in care and underuse of evidence-based care is still a worldwide problem.(2)

In colorectal cancer surgery, adherence to evidence-based interventions is in line with these general findings. Despite the availability of the well-established ERAS® protocol for almost 15 years,(3) there is considerable variation in protocol adherence, with reported adherence rates ranging between 45 and 92%.(4-9) A meta-analysis by Lau et al. (2017) showed that the implementation of the ERAS protocol in surgery programs, including colorectal cancer surgery, leads to significant reduced length of stay (LOS), complications and costs, and an earlier return of gastrointestinal function. There was no difference in overall mortality and readmission rates between ERAS groups and “usual care” groups.(10) Pedziwiatr et al. (2018) concluded in a recent review, that ERAS in colorectal cancer surgery is safe, feasible and associated with improved outcomes. The authors also state that there are challenges in maintaining a high level of compliance, for which alternative implementation strategies may be needed.(11)

One strategy to improve adherence to evidence-based guidelines is the introduction of care pathways.(12) Care pathways (CPs) are used to structure care around patients’ needs, and combine evidence-based key interventions, feedback on the current performance, and a strategy for improvement.(13)

The primary aim of this study is to evaluate the clinical effectiveness and safety of implementing a care pathway for perioperative care in adults undergoing colorectal cancer surgery. The secondary aim is to assess adherence to and documentation of the CP, and describe variation in adherence and improvement rates across and within hospitals.

MATERIALS AND METHODS

Study design and setting

This international pre-test – post-test multicenter study was performed in 12 hospitals in four European countries: Belgium, France, Germany and the Netherlands. The study was supervised by the European Pathway Association (E-P-A), an international not-for-profit organization aiming to increase and disseminate knowledge on care pathways (www.e-p-a.org). Three hospitals in each country were included using purposive sampling. Kick-off sessions were organized per country to inform the hospitals on the study.

For the pre-test, 20 consecutive patients per hospital who met the inclusion criteria were retrospectively included starting from January 1st 2014. For the post-test, 20 patients per hospital were included between December 2016 – May 2017. In low-volume hospitals, consecutive patients were included; in high-volume hospitals, patients were randomly included over the six month inclusion period. We included adult patients (≥18 years) undergoing elective colorectal cancer surgery (open or laparoscopic). Patients with severe dementia (DSM IV) / major neurocognitive disorder (DSM 5) or severe concomitant disease that may affect short-term outcome (life expectancy less than three months) were excluded.

Data were collected by the local study coordinator, who was instructed to collect the data from the patient record using a standardized data extraction form. Ethical approval for this study was coordinated with the ethics committee of the University Hospital Leuven (S57152 [ML11311]).

Intervention

The intervention consisted of the development and implementation of a care pathway, and included three steps:

1. Development of the model care pathway, based on the ERAS guidelines (see box 6.1) to adopt and implement by the local quality improvement teams. These teams consisted of representatives of medical, nursing, and allied health professionals involved in perioperative care for CRC surgery patients, and quality improvement staff.

2. Local quality improvement teams received feedback on their current care process based on the pre-test measurement in the form of: a). National feedback session organized within each country. This provided an opportunity to share experiences and knowledge and created a temporary learning collaborative. b). Local feedback sessions within each hospital. This allowed us to reach a larger audience per site and focus on local performance. c). Detailed feedback report to supplement the sessions.
3. Local quality improvement teams received the model care pathway, including the evidence-based key interventions, as base for the model pathway. It was delivered and explained on-site in all participating centers to the quality improvement teams, as support for their strategy for change. Per team, a three-hour training session was organized, to set local improvement priorities and to explain the practical use of the model pathway. Follow-up telephone and email support was provided.

All sessions used standardized formats and content and were delivered by the research team. After the training session, a transition period was foreseen, allowing teams six months to embed the care pathway. The intervention is described in detail in the study protocol paper.(14)

Measures

Primary outcome measures are in line with the meta-analysis by Lau et al. (2017): length of stay (LOS) (total hospital stay and stay on ICU), , and postoperative day of: first flatus and stool, tolerating normal diet, sitting and walking, meeting discharge criteria. Because of the importance of clinical nutrition, an additional nutritional indicator was measured: proportion of patients receiving total parenteral nutrition (TPN). To assess safety, 30-day mortality, morbidity (readmission and re-intervention rates) were measured.

Secondary outcome measures are the documentation of and adherence to the key interventions in the CP. First, the level of documentation and adherence for each of the interventions from the CP (box 6.1) was scored. Interventions were scored as “documented” if it was clear from the patient record that the intervention was or was not performed. If the data extraction form indicated there was no information in the patient record, the item was scored as “not documented”. Only for documented

interventions, “adhered to” or “not adhered to” was scored. Second, the proportions of relevant individual interventions in the protocol received by each patient were measured to establish protocol adherence.

In addition, the following patient-level variables were collected to account for patient-mix: age, gender, ASA classification, type of surgery (open, laparoscopic, started laparoscopic but converted to open) location of tumor (colon or rectum), stoma created during surgery (yes/no).

Statistical analysis

Unadjusted pre-test – post-test differences were analyzed using Student t-tests for continuous data and chi-squared tests for dichotomous data. Continuous data (e.g. LOS, time to normal diet) are reported as mean and standard deviation (SD). Dichotomous data (outcomes related to documentation and adherence as well as e.g. re-intervention rate) are presented as count and percentage. Protocol adherence rate is reported as median and inter quartile range (IQR).

Next, the analysis of the primary outcomes was adjusted for all previously described patient-mix variables. Multivariable linear regression analysis was performed for the continuous data. Multivariable logistic regression analysis was performed for dichotomous data. We recognized the hierarchical structure of our data, with patients clustered in hospitals, by including hospital as a fixed effect into our analysis.

Differences in pre- and post-test adherence rates were analyzed using Mann-Whitney U-tests. The analyses for this study were generated using SAS software, Version 9.4 of the SAS System for Windows.

Box 6.1 Monitoring of interventions from model care pathway

PREOPERATIVE
- Patient information (patient received leaflet, leaflet is discussed)
- Screening of nutritional status (incl. normal weight, weight at admission/day of surgery)
- No prolonged fasting (solid up to 6 hrs., and clear fluids up to 2 hrs. before anesthesia)
- Carbohydrate loading
- No or selective mechanical bowel preparation
- Antibiotic prophylaxis (incl. repeated dose if procedure prolonged)
- Thromboprophylaxis (well-fitting stockings and/or pneumatic compression, LMWH[a])
- No sedative premedication
- Measuring albumin and CRP[b] levels at admission

INTRAOPERATIVE
- Skin cleansing with chlorhexidine
- Midthoracic epidural analgesia (with short acting anesthetic)
- Avoidance of salt and water overload
- No nasogastric tubes
- No drains
- Laparoscopic technique
- Non-opioid analgesia

POSTOPERATIVE
- Prevention of nausea and vomiting
- Early nutrition (fluid day of surgery, solid as tolerated)
- Early mobilization (sitting evening of surgery, walking first postoperative day)
- Early removal of catheter (postoperative day 2)
- Postoperative patient information (patient received leaflet, leaflet is discussed)
- Measuring albumin and CRP[b] levels at discharge
- Discharge and follow-up weight

[a]Low Molecular Weight Heparin
[b]C-Reactive Protein

RESULTS

Two hospitals from two different countries were lost to follow up, due to internal organizational reasons. Only patients from hospitals that participated in both pre- and post-test were included, 381 in total (pre-test: 190, post-test 191). Table 6.1 shows the patient characteristics. Both groups were comparable except for the type of operation. The post-test group showed a lower percentage of open surgery (31.4% vs 21.2%, p=0.0448).

Table 6.1 Patient characteristics

Indicator	Pre (N=190)	Post (N=191)	P-Value
Age (in years) (mean ± SD)	69.3 ± 12.0	68.0 ± 13.4	0.3114
Female / Male	41.6 / 58.4%	51.1 / 49.0%	0.0641
Comorbidities (%)			
Hypertension	56.6%	46.7%	0.0653
Cardiovascular Disease	21.9%	20.2%	0.7162
Coronary Disease	21.3%	15.8%	0.2006
Diabetes	19.9%	16.9%	0.4638
Pulmonary Disease	11.3%	9.4%	0.5830
Liver Disease	2.0%	5.5%	0.1097
Renal Failure	1.9%	4.7%	0.1612
Location of tumor (%)			0.7693
Colon	67.4%	66.0%	
Rectum	32.6%	34.0%	
ASA classification[a] (%)			0.5400
I	14.0%	11.2%	
II	61.8%	58.3%	
III	23.1%	29.4%	
IV	1.1%	1.1%	
Type of surgery (%)			0.0448
Open	31.4%	21.2%	
Laparoscopic	57.1%	61.4%	
Laparoscopic converted to open	11.4%	17.5%	
Stoma created during surgery (%)	24.1%	31.5%	0.1254

[a]American Society of Anesthesiologists

Primary outcomes

The primary outcomes before and after implementing the CP are presented in table 6.2. The adjusted model is correcting for patient variables and clustering of patients. Length of stay decreased significantly, from 12.6 to 10.7 days (p=0.0466 unadjusted and p=0.0230 adjusted). Length of stay on the ICU also decreased, however not statistically significant. Postoperative day of tolerance of normal diet and early mobilization (walking) both improved significantly, from 7.2 to 4.9 days and from 3.7 to 2.8 days respectively. The proportion of patients receiving total parenteral nutrition (TPN) dropped significantly from 21.4% to 5.3% (p<0.0001). Our adjusted model shows that patients with ASA classification IV have significant longer LOS compared to ASA classification I-III. Also, patients with a stoma, had significant longer LOS. In contrast, patients who had laparoscopic surgery had significant shorter LOS, compared to patients with open surgery.

Table 6.2 Primary outcomes

	Unadjusted model[a]			*Adjusted model*[b]		
Indicator	**Pre (N=190)**	**Post (N=191)**	**P-Value**	**Estimate**	**SE**	**P-Value**
Length of stay (in days) (mean ± sd)	12.6 ± 9.8	10.7 ± 7.9	0.0466	-2.1	0.9	0.0230
Number of days on ICU (mean ± sd)	1.4 ± 3.3	0.9 ± 2.3	0.0967	-0.6	0.3	0.0865
30-day mortality	1.2%	0.6%	0.5379	-1.0	1.5	0.5315
Re-intervention rate	7.5%	7.4%	0.9651	-0.3	0.5	0,5403
Readmission rate	13.0%	17.1%	0.2822	-0.3	0.4	0.3987
Post Op Day of first flatus (mean ± sd)	2.7 ± 3.0	2.3 ± 2.6	0.2965	0.1	0.3	0.7978
Post Op Day of first stool (mean ± sd)	3.3 ± 2.2	3.1 ± 2.5	0.4792	0.2	0.3	0.4124
Post Op Day tolerance normal diet	7.2 ± 7.0	4.9 ± 3.9	0.0007	-2.5	0.8	0.0024
Post Op Day of first sitting	1.5 ± 1.5	1.4 ± 2.0	0.6692	0.0	0.2	0.9890
Post Op Day of first walking	3.7 ± 3.0	2.8 ± 2.6	0.0109	-1.4	0.4	0.0005
Post Op Day Meets discharge criteria	10.3 ± 8.0	9.5 ± 7.4	0.4693	-0.6	1.1	0.5472
Received Total Parenteral Nutrition	21.4%	5.3%	<0.0001	-2.1	0.5	<0.0001

[a]Unadjusted pre-post-test differences tested by t-test (continuous data) or chi-squared (proportions)
[b]Multilevel, multivariable linear (continuous data) and logistic regression (dichotomous data) analysis with hospitals as fixed effect, adjusted for age at admission, gender, ASA classification, type of surgery, location of tumor, and stoma created y/n.

Table 6.3 Documentation of and adherence to key interventions

Intervention	**S**	**Documented**			**Adhered to**		
		Pre	**Post**		**Pre**	**Post**	
		%	%	p-value	%	%	p-value
1. Antibiotic prophylaxis	5	98.4 (187/190)	99.5 (190/191)	0.3122	97.3 (182/187)	95.3 (181/190)	0.2895
2. Pharmacological anti thromboprophylaxis	5	93.2 (177/190)	99.5 (190/191)	0.0010	92.1 (163/177)	99.0 (188/190)	0.0013
3. No/selective mechanical bowel preparation – colon	5	87.9 (109/124)	81.3 (100/123)	0.1504	83.5 (91/109)	61.0 (61/100)	0.0003
4. Skin cleansing chlorhexidine	5	89.5 (170/190)	90.4 (170/188)	0.7583	78.8 (134/170)	57.7 (98/170)	<0.0001
5. Anti thromboprophylaxis stockings	5	88.4 (167/189)	91.1 (173/190)	0.3883	62.9 (105/167)	68.2 (118/173)	0.3007
6. No nasogastric tubes	5	97.9 (186/190)	94.8 (181/191)	0.1044	57.0 (106/186)	77.4 (140/181)	<0.0001
7. No drains – colon	5	98.4 (122/124)	88.6 (109/123)	0.0018	49.2 (60/122)	53.2 (58/109)	0.5407
8. Repeated dose antibiotics if procedure prolonged	5	96.3 (183/190)	81.4 (153/188)	<0.0001	35.3 (12/34)	31.2 (19/61)	0.6794
9. Avoidance of salt and water overload[a]	5	97.7 (171/175)	100.0 (176/176)	0.0437	28.1 (48/171)	36.4 (64/176)	0.0985
10. No drains – rectum	5	98.3 (59/60)	100.0 (64/64)	0.2997	27.1 (16/59)	26.6 (17/64)	0.9446
11. Mid thoracic analgesia	5	19.6 (37/189)	24.7 (47/190)	0.2265	19.6 (37/189)	24.7 (47/190)	0.2265

12. Pneumatic compression	5	73.7 (140/190)	81.8 (153/187)	0.0578	18.6 (26/140)	15.0 (23/153)	0.4175
13. No sedative medication	5	92.6 (176/190)	97.4 (185/190)	0.0341	9.1 (16/176)	27.0 (50/185)	<0.0001
14. No prolonged fasting – solid[b]	4	77.3 (146/189)	99.5 (189/190)	<0.0001	91.8 (134/146)	95.2 (180/189)	0.1955
15. No prolonged fasting – fluid[c]	4	77.9 (148/190)	99.5 (187/188)	<0.0001	62.2 (92/148)	38.0 (71/187)	<0.0001
16. Admission weight recorded	3	90.0 (171/190)	96.9 (185/191)	0.0069	90.0 (171/190)	96.9 (185/191)	0.0069
17. Pre-operative Info received	3	60.0 (114/190)	97.4 (186/191)	<0.0001	87.7 (100/114)	100.0 (186/186)	<0.0001
18. Pre-operative info discussed	3	49.5 (94/190)	96.3 (184/191)	<0.0001	76.6 (72/94)	100.0 (184/184)	<0.0001
19. Screening nutritional status	3	74.7 (142/190)	95.3 (181/190)	<0.0001	76.1 (108/142)	75.1 (136/181)	0.8489
20. Normal weight recorded	3	75.3 (143/190)	82.7 (158/191)	0.0739	75.3 (143/190)	82.7 (158/191)	0.0739
21. No opiates	3	71.4 (135/189)	42.6 (81/190)	<0.0001	71.4 (135/189)	42.6 (81/190)	<0.0001
22. Postoperative info received	3	53.2 (101/190)	89.5 (171/191)	<0.0001	69.3 (70/101)	90.6 (155/171)	<0.0001
23. PONV screening	3	65.3 (124/190)	86.2 (163/189)	<0.0001	58.1 (72/124)	65.6 (107/163)	0.1892
24. Postoperative info discussed	3	41.6 (79/190)	88.0 (168/191)	<0.0001	46.8 (37/79)	91.1 (153/168)	<0.0001
25. Early removal of catheter[d]	3	94.4 (167/177)	91.3 (158/173)	0.2726	38.3 (64/167)	44.3 (70/158)	0.2737
26. Carbohydrate loading	3	76.2 (144/189)	81.7 (156/191)	0.1898	30.6 (44/144)	55.8 (87/156)	<0.0001
27. Early nutrition – solid[e]	3	91.5 (172/188)	99.4 (179/180)	0.0003	29.1 (50/172)	43.6 (78/179)	0.0048
28. Early nutrition – fluid[f]	3	87.3 (165/189)	99.4 (159/160)	<0.0001	24.2 (40/165)	33.3 (53/159)	0.0706
29. Early mobilization – walking[g]	3	62.6 (119/190)	95.0 (151/159)	<0.0001	13.5 (16/119)	32.5 (49/151)	0.0003
30. Early mobilization – sitting[h]	3	70.0 (133/190)	96.9 (157/162)	<0.0001	7.5 (10/133)	20.4 (32/157)	0.0019
31. CRP level at discharge	2	71.1 (135/190)	65.5 (125/191)	0.2398	71.1 (135/190)	65.5 (125/191)	0.2398
32. CRP level at admission	2	55.3 (105/190)	44.0 (84/191)	0.0276	55.3 (105/190)	44.0 (84/191)	0.0276
33. No/selective mechanical bowel preparation – rectum	2	85.0 (51/60)	90.6 (58/64)	0.3371	31.4 (16/51)	39.0 (23/59)	0.4054
34. Discharge weight recorded	2	30.5 (58/190)	39.3 (75/191)	0.0735	30.5 (58/190)	39.3 (75/191)	0.0735
35. Albumin level at admission	2	25.3 (48/190)	28.8 (55/191)	0.4376	25.3 (48/190)	28.8 (55/191)	0.4376
36. Follow up weight recorded	2	21.6 (41/190)	17.8 (34/191)	0.3538	21.6 (41/190)	17.8 (34/191)	0.3538
37. Operation day weight recorded	1	70.5 (134/190)	84.3 (161/191)	0.0013	70.5 (134/190)	84.3 (161/191)	0.0013
38. Albumin level at discharge	1	15.8 (30/190)	20.4 (39/191)	0.2407	15.8 (30/190)	20.4 (39/191)	0.2407

S = Strength of key intervention, based on level of evidence and recommendation grade

[a]Removal of IV postop day 0-3
[b]Stop eating day before surgery
[c]Stop drinking day of surgery
[d]Removal of catheter post op day 0-2
[e]Start eating postop day 0 or 1
[f]Start drinking day of surgery
[g]Walking postop day 1
[h]Sitting evening of surgery

Documentation and Protocol adherence

Documentation of and adherence to the key interventions before and after implementing the CP are presented in table 6.3. Due to the nature of the study, some data were missing. A distinction between the level of documentation of and adherence to the key interventions was therefor made, as indicated in the methods section. For the interventions no use of drain and no or selective bowel preparation, a distinction was made between colon and rectal cancer.

Table 6.3 shows the individual key interventions sorted by strength. The strength of each key intervention was calculated based on levels of evidence, as reported in the ERAS 2013 protocol.(15) No (0 points), low (1 point), moderate (2 points), and high (3 points) and the grades of recommendations: weak (1 point) and strong (2 points), varying between 1 and 5.(4) The interventions are ranked based on the adherence in the pre-test.

Documentation improved for 17 out of 38 key interventions. For four interventions the level of documentation decreased significantly. Only half of the interventions had a documentation rate of > 90% in the post-test.

For 13 of the 38 interventions, adherence improved significantly. These include pharmacological antithrombotic prophylaxis, no use of nasogastric tubes, patient information, early mobilization and early nutrition. For five interventions adherence decreased, including no prolonged fasting (fluids), no or selective bowel preparation (colon), and the avoidance of opiate use.

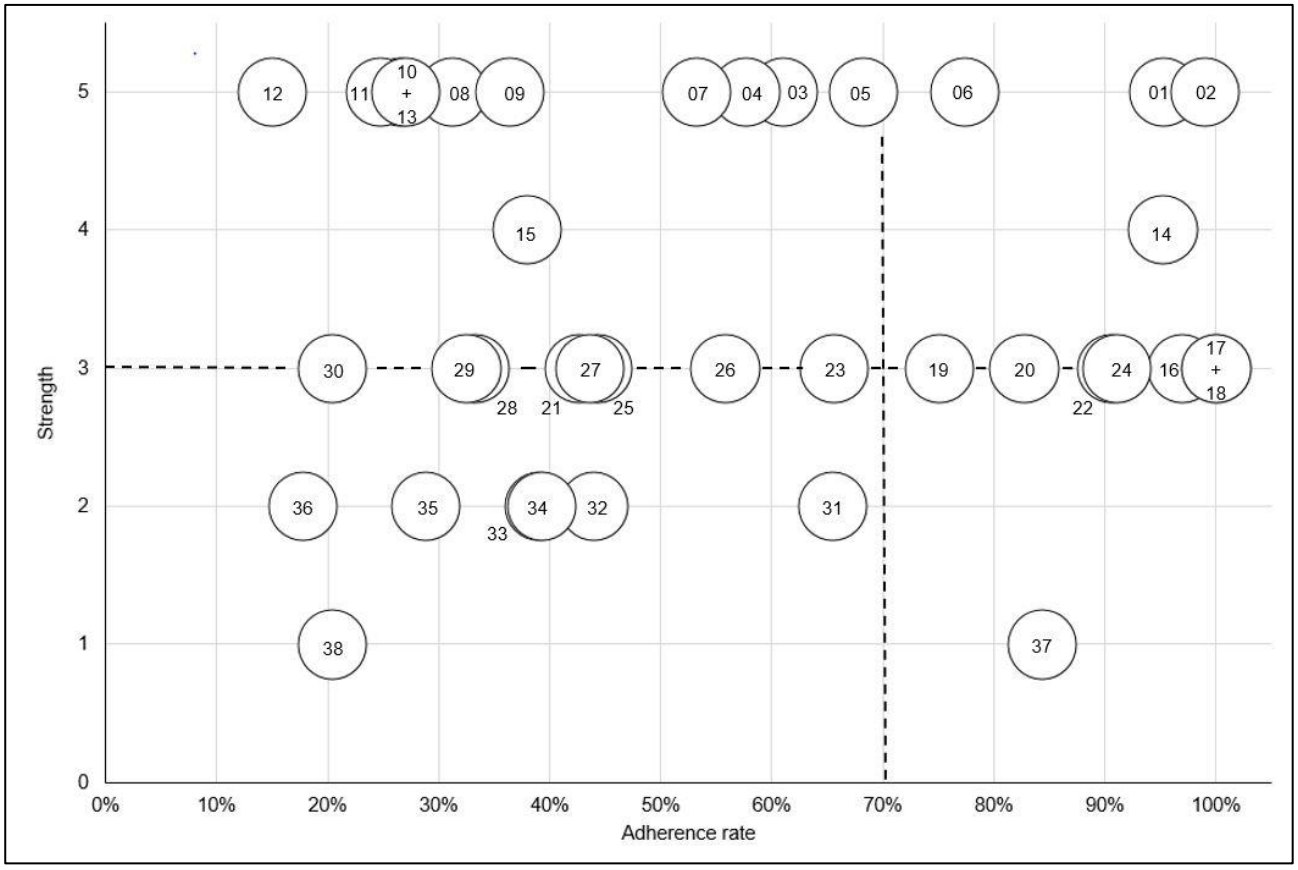


Figure 6.1 Importance-performance matrix post-test adherence

The numbers in figure 6.1 correspond to the numbers in table 6.3, identifying the interventions. Upper right quadrant: correct use; upper left quadrant: under use; lower right quadrant: over use.

Figure 6.1 provides an importance-performance-matrix of the adherence rate in the post-test. For the importance dimension, the strength of the interventions is used. A cut-off point was defined as ≥3 points. This includes interventions with a strong recommendation, even if the evidence base is low. Performance is the adherence rate. A cut-off of ≥70% was used, based on previous research.(16, 17) The cut-offs create four quadrants, with the upper two quadrants showing important interventions, with a high adherence rate (upper right) and a low adherence rate (upper left). The lower two quadrants show the less-important interventions, with high adherence rate (lower right) and low adherence rate (lower left). The matrix shows 11 interventions in the upper right quadrant, and 19 in the upper left quadrant, suggesting priorities for improvement.

Although overall adherence improved, the adherence to some interventions stayed relatively low. The adherence to “no sedative medication” for example, improved significantly, but is still only 27%.

At the same time, documentation of this intervention was already high and even improved (from 92% to 97%). The same pattern can be seen in the interventions no drains (rectum), pneumatic compression, no prolonged fasting (fluid), early nutrition and mobilization, and no or selective bowel preparation (rectum).

Protocol adherence, the percentage of key interventions delivered to each individual patient, for both pre- and post-test is shown in figure 6.2. In this analysis, only interventions with a strength of 3-5 were included, since these are considered the most important interventions.(4) The figure shows that in the pre-test only 18 patients (9%) had an adherence rate of 70% or higher, a cut-off established in previous studies.(16, 17) In 130 patients (68%) the adherence rate was ≥50%.

In the post-test, there was an adherence rate of ≥70% in 47 patients (25%), while in 162 patients (85%) the adherence rate was ≥50%. The total median adherence rate improved from 56 to 62% (p<.00001), with a minimum of 32%, and a maximum of 91%, showing considerable variation.

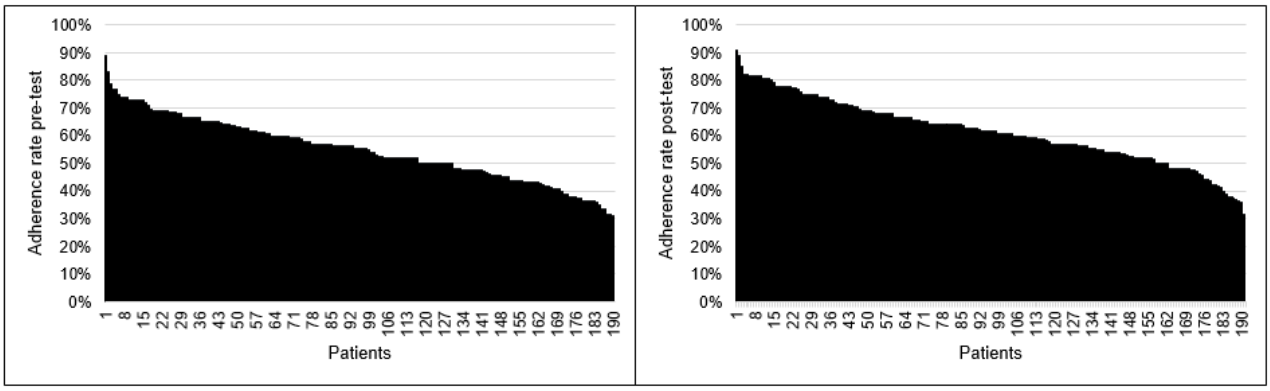


Figure 6.2 Adherence rates (strength 3-5 interventions) on patient level in pre- and post-test

There also was considerable variation in protocol adherence rate between the hospitals. Table 6.4 shows the median protocol adherence and inter quartile range per hospital, and the improvement of the adherence rate per hospital. The hospitals are ranked based on the pre-test adherence. The table shows that in three of the top-5 hospitals from the pre-test the adherence rates did not improve, while in the lower bound of the ranking four hospitals out of five were able to improve. Overall improvement was 6%.

Table 6.4 Median adherence and variance strength 3-5 interventions per hospital

Hospital	Pre-test median (IQR[a])	Post-test median (IQR[a])	Delta	p-value
1	69% (12%)	64% (7%)	-5%	p=0.25848
2	65% (6%)	75% (9%)	10%	p<0.00016
3	60% (10%)	47% (13%)	-13%	p=0.00012
4	57% (17%)	54% (12%)	-3%	p= 0.1141
5	56% (12%)	68% (14%)	12%	p=0.01078
6	54% (16%)	64% (7%)	10%	p=0.00062
7	52% (9%)	51% (9%)	-1%	p=0.7414
8	51% (13%)	67% (18%)	16%	p<0.00001
9	46% (10%)	55% (10%)	9%	p=0.00008
10	43% (12%)	65% (12%)	22%	p<0.00001
Total	56% (17%)	62% (13%)	6%	p<0.00001

[a]inter quartile range

DISCUSSION

As in many other studies in colorectal cancer surgery, we used LOS as primary outcome measure. LOS can be interpreted as a proxy for cost. However, LOS can also be seen as a measure for in-hospital recovery, having an equal construct-validity as “readiness for discharge”.(18)

The results of this study suggest that implementing a care pathway, including feedback on current performance (outcomes and adherence), and quality improvement initiatives, has a positive effect on outcomes and protocol adherence. These results are in line with previous reported results of studies on the implementation of the ERAS® protocol, on which our CP is based. The decrease in LOS, earlier recovery of bowel function (time to normal diet, stool) has been reported in the meta-analysis by Lau (2017), and more recent observational studies.(7, 8, 10, 19) However, both pre- and post-implementation LOS in our study is higher than reported in some studies. E.g. Pisarska et al. showed a median LOS of 5 days pre- and of 4 days post-test in a prospective study. These were patients undergoing laparoscopic surgery.(7) A study by Martin et al., using both open and laparoscopic technique, showed a median LOS of 6 versus 5 days.(19) Another study including both open and laparoscopic surgery, showed a median LOS of 13 vs 11 days.(8) The meta-analysis by Lau et al. showed a difference of -2.26 days between pre- and post-test.(10) This is comparable to

our findings. We also observed a difference of over 1 day between LOS and “time to meet discharge criteria”. Individual discharge criteria (e.g. first stool, 3.1 days) are met even sooner. However, we do not have insight in hospital specific discharge criteria, so we can not elaborate on this difference.

Our study did not find differences in mortality, readmission and re-intervention rates, suggesting implementation of a CP is safe. This is also in line with the already mentioned meta-analysis. In two recent observational studies in colorectal surgery, no difference in readmission and complication rates were found after introduction of an enhanced recovery pathway.(19, 20) However, other studies were able to show a difference in readmission and complication rates.(16, 21) The evidence on effect on readmission and complication rates seems inconclusive.

There are some notable outcomes in the documentation of and adherence to the interventions in the care pathway. Firstly, we see that overall documentation of the interventions has improved. Even for some interventions where the adherence is still low (e.g. no sedative medication, no drains and no or selective bowel preparation (rectum), early mobilization and nutrition), documentation has improved. This suggests that teams/professionals are consciously not performing these interventions. A possible explanation for this non-conformity could be the ongoing debate on the evidence base of these interventions. For example, in the new ERAS® protocol, the evidence levels for no sedative medication and early resumption of oral intake are “moderate”.(3) This could mean that in clinical practice, these interventions receive less attention. On the other hand, the evidence level for not using drainage is “strong”.(3) Our results show a post-implementation adherence rate of 53.2% (colon) and 26.6% (rectal), suggesting a preference for using drainage in rectal surgery.

Overall adherence rate improved after implementing the care pathway. Median adherence increased from 56% to 62% ($p<0.00001$), and the number of patients receiving 70% or more of the care recommended in the pathway increased from 9% to 25% (47 out of 191). This is especially important, because a “dose-effect” relationship is suggested between protocol adherence of ≥70% and outcomes.(16, 17, 19, 22, 23) A target adherence rate of 80% has also been described, suggesting an even bigger gap between actual and preferred adherence.(24) This shows that quality

improvement initiatives like in this study, focused on implementing evidence-based interventions in clinical practice, are important.

Secondly, we observed a decrease in adherence to a number of interventions. No mechanical bowel preparation, no prolonged fasting (fluids), no opioids all have significant lower adherence rates in the post-test. The ERAS® protocol makes a distinction between bowel preparation for colon ("not routinely") and rectal ("may be used") surgery.(3) However, the adherence data in our study shows the opposite: an increase in bowel preparation for colon surgery (significant), and a decrease for rectal surgery (although not significant). Avoiding opioids and no prolonged fasting both have a moderate evidence level.(3) This could account for the relative low adherence, but the reason why these interventions have lower adherence in the post-test compared to the pre-test is unclear. A possible explanation is that preoperative fluid/nutrition and analgesia are traditionally the domain of the anesthetist. From an ongoing qualitative study in the participating hospitals we know that anesthetists were not always "on board" in designing and implementing the CP. Other reasons for low adherence are workload (e.g. not enough staff for early mobilization), patient status (e.g. no tolerance of diet), and surgeons preference (e.g. use of drains) (Van Zelm et al., in preparation; chapter 5).

Thirdly, we observed that of 30 interventions deemed "important" (a strength of 3 and higher), 11 had an adherence rate of ≥70%. The other 19 interventions (e.g. carbohydrate loading, repeated dose antibiotics if procedure prolonged, early mobilization) represent the priorities for improvement.

Finally, we observed differences in improvement rates between the participating centers. Six teams managed to improve the adherence rate, while in three hospitals the adherence rate remained the same, and even significantly decreased in one other hospital. Subgroup analysis including only the hospitals that significantly improved adherence showed an increase of 15% in median adherence rate ($p<0.00001$). Previous research provides some explanation for these differences. A number of studies have identified facilitators and barriers for the implementation of ERAS®. Leadership, resources, collaboration and communication (or lack thereof) are a number of well-established facilitators or barriers.(25, 26) Other studies provide insight in the implementation process. Gotlib

Conn et al. (2015) performed a process evaluation on normalization of ERAS in everyday practice. The Normalization Process Theory is used as framework to describe and explain the implementation. The authors conclude that ERAS implementation is achieved by complex cognitive and social processes in which a “champion”, external and internal relationship building, and strategic management of the project are key.(27) Without a doubt, the context in the participating centers in our study differ on the mentioned facilitators and barriers and the implementation process, which could contribute to the observed differences.

Our study has a number of limitations. First, the possible selection bias due to the purposeful sampling of the hospitals and the limited number of patients per hospital. Based on the adherence rates and variation in care from our study in comparison to published data, we believe that the purposeful sampling of the hospitals did not lead to a biased sample. The limited number of 20 patients per hospital has been suggested as sufficient in previous CP research and methods.(28, 29) Because we included the patients consecutively (or randomly in the high volume hospitals), we believe our sample is sufficient to draw conclusions on the total sample for the primary outcomes, and for the secondary outcomes on hospital level, taking resource and time constraints in the participating hospitals into account.

Second, the observational, retrospective nature of our study has led to missing data because of documentation shortcomings. However, the documentation bias reported in a previous study, has been turned into a strength in this study, by distinguishing between documented and adhered to interventions. This gives a more realistic view of the actual adherence and documentation bias, compared to the previous study, where “not documented data” was interpreted as “not adhered to”, which could have led to a possible underestimation of adherence.(4)

The international multicenter design of this study facilitated the comparison of and learning from actual clinical practice in colorectal surgery between the participating hospitals. In contrast, differences in local circumstances (e.g. context, resources, implementation, teamwork) could have led to important between-hospital differences. In fact, our multilevel model shows there are statistical significant differences in LOS between hospitals. Further exploration and explanation of the

outcomes from this study in relation to the implementation process and context is therefore suggested.

CONCLUSION

In conclusion, implementation of a CP for patients undergoing colorectal cancer surgery, using a model pathway, feedback on current performance and quality improvement support, lead to shorter LOS, earlier tolerance of normal diet and walking, without negatively impacting mortality, re-intervention rate and readmission rate. This suggest CP implementation for colorectal cancer surgery is safe and effective for reducing LOS. Both documentation and protocol adherence improved after implementing the CP. However, only in 25% of patients a protocol adherence of ≥70% was achieved. There is considerable variation in adherence and improvement rates between the participating hospitals. This implies that patients are still at risk for underuse. The importance-performance matrix shows which interventions are important, but have low adherence, prioritizing improvement efforts. Knowledge on how the differences in the hospitals' context and implementation processes affect adherence could help to improve our understanding of quality improvement using care pathway methodology.

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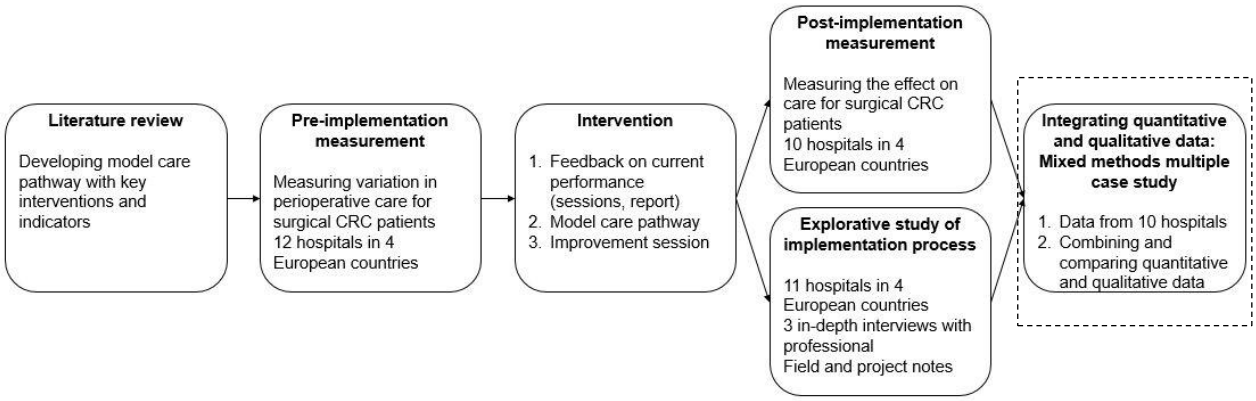
CHAPTER 7

MIXED METHODS MULTIPLE CASE STUDY TO EVALUATE THE IMPLEMENTATION OF A CARE PATHWAY FOR COLORECTAL CANCER SURGERY USING EXTENDED NORMALIZATION PROCESS THEORY



To be submitted as:

Van Zelm R, Coeckelberghs E, Sermeus W, Wolthuis A, Bruyneel L, Panella M, Vanhaecht K. Mixed methods multiple case study to evaluate the implementation of a care pathway for colorectal cancer surgery using extended Normalization Process Theory – Prepared for publication

ABSTRACT

Introduction

Colorectal cancer surgery has been standardized using enhanced recovery protocols. The introduction of these protocols is safe, effective and feasible. The implementation process, facilitators and barriers to implementation have been described in previous qualitative studies. The aim of this study is to evaluate the implementation of a care pathway for colorectal cancer surgery in 10 European hospitals, from a quantitative and qualitative perspective simultaneously.

Methods

A comparative mixed methods multiple case study design was used, based on an earlier purposefully selected sample of 10 hospitals in four European countries. These hospitals implemented a care pathway and performed pre- and post-implementation measurements of protocol adherence and length of stay. Post-implementation in-depth interviews were conducted with directly involved professionals. Based on the quantitative data, cases with diversity in effect were selected, after which the qualitative data per case was analyzed using the extended Normalization Process Theory as theoretical framework. The data was then combined and analyzed using joint data displays.

Findings

Data on 381 patients and 30 professionals were included. Two hospitals were identified as high performance cases, and three as low performance cases. Factors that could explain the differences in pre- and post-implementation performance were: the level of integration of the care pathway in daily practice (capability), the level of experience and support of the improvement team in care pathway methodology (capacity), the intrinsic motivation of the team, shared goals and level of management support and alignment of care pathway development and hospital strategy (potential), and finally the cognitive participation of relevant disciplines, most noticeably the physician (contribution).

Conclusions

Overall improvement (both adherence as well as length of stay) was achieved, but was highly variable between the cases. Factors in the implementation process that could explain the difference in performance between the cases were conceptualized using in eNPT. Our data suggest that teams that are able to integrate the care pathway, have experience or are supported with care pathway methodology, are intrinsically motivated, work towards shared goals, receive active management support, and care pathway development is in alignment with hospital strategy, contribute to successful implementation.

INTRODUCTION

For almost 15 years, colorectal cancer surgery has been standardized using Enhanced Recovery Protocols (ERPs), also known as enhanced recovery after surgery (ERAS) protocols. The fourth update of the international recognized ERAS protocol was published in 2018.[1] The effectiveness and safety of the application of ERPs has been studied extensively, leading to the conclusion that the application is safe, feasible, and improves postoperative outcomes.[2] However, adherence to the recommended interventions in ERPs seems challenging. Reported adherence rates vary greatly, and a dose-effect relationship between adherence rate and outcomes is suggested.[3-6]

Several studies have been published that explore the implementation of ERPs to identify relevant processes, facilitators and barriers. Gotlib Conn et al. (2015) and Gramlich et al. (2017) evaluated the implementation process of an ERP, suggesting that implementation involves complex cognitive and social processes. A local champion and relationship building capacity are perceived as important factors.[7,8] Other studies, including a systematic review of 53 studies of implementation of ERPs in multiple surgical specialties, identified facilitators including adapting the ERP to local circumstances, alignment with evidence-based practice, leadership, teamwork, staff education, monitoring and feedback. Barriers identified included resistance to change, lack of stakeholder buy-in, lack of resources, and rotating residents.[9-11]

The studies using qualitative research approaches provided detailed insight in the implementation process, and facilitators and barriers that are present in clinical practice. It is however unclear how quantitative data from effect studies and qualitative data on experiences can corroborate each other. Combining quantitative and qualitative data could potentially generate comprehensive insight in the implementation process of ERPs. This is the intent of this study, which is the final part of a series of connected studies in a process evaluation of the implementation of a care pathway for patients undergoing colorectal cancer surgery. One of the strategies to improve adherence to recommended care, is the introduction of care pathways.[12,13] Care pathways (CPs) are complex interventions, that structure care around patient's needs. They combine evidence-based key interventions with feedback on the current care process, and a strategy for improvement.[14]

The participating hospitals in this study received feedback on their care process, using feedback meetings and a feedback report. Next, a model CP (based on the ERAS protocol) was delivered to all teams and explained in an on-site quality improvement workshop. Subsequently, the participating teams implemented a CP or adapted their existing local CP. The intervention is described in detail in the study protocol.[15] A preceding qualitative study to explore the implementation process (chapter 5), and a quantitative effect study (chapter 6), generated a number of implications for further research, which are addressed in this study.

The aim of this study is to evaluate the implementation of a CP for colorectal cancer surgery in 10 European hospitals. A comparative mixed methods multiple case study design was used to identify information rich cases, and to interpret and explain relationships between quantitative data (on improvement of protocol adherence and length of stay [LOS]) and qualitative findings (perspectives of involved healthcare professionals). The rationale for using both quantitative and qualitative data is to enhance the understanding of the implementation process: How do the perspectives of healthcare professionals on the implementation process of a CP in different contexts, corroborate the effects of the implementation? The research questions are:

1. Which factors explain the difference between pre- and post-implementation performance (LOS and protocol adherence) and improvement rate?
2. What is the relationship between intended and measured adherence rate?

METHODS

Study design and setting

This international mixed methods study was performed in an earlier purposefully selected sample of 10 hospitals in four European countries. Our study used the comparative multiple case study design. The intent of this design is to understand and compare the complexity within and between cases.[16] Figure 7.1 provides a diagram of the study design. Ethical approval for this study was obtained with the appropriate ethics committees in the participating countries. All interviewees provided written informed consent for the interviews.

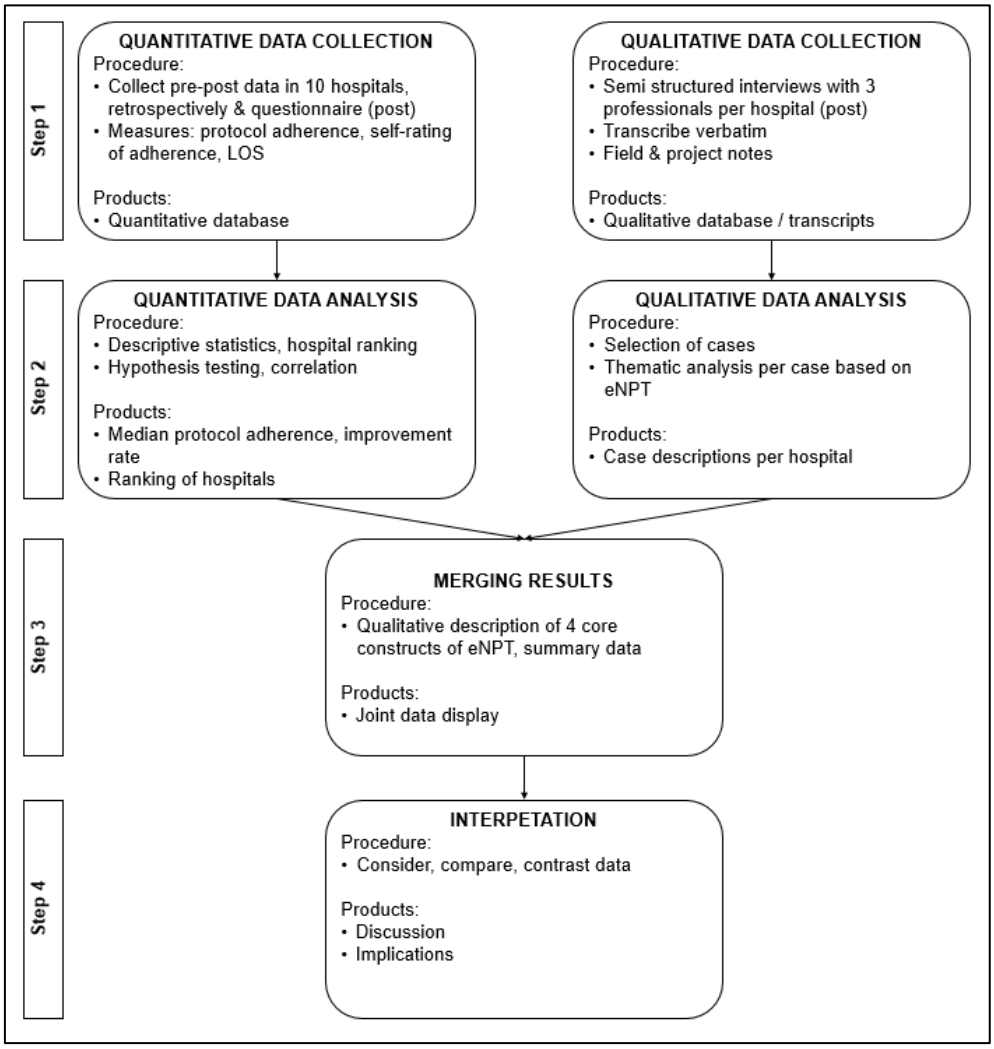


Figure 7.1 Diagram for comparative mixed methods case study *(based on Creswell et al., 2018)*

Data collection and measures

Quantitative – In step 1, data was collected pre- and post-implementation of the CP, through patient record analysis. Twenty patients were retrospectively included per hospital pre-pathway implementation (2014) and another 20 patients post-pathway implementation (December 2016) to study the effect of the CP on patient and implementation outcomes (chapter 6). Adult (≥18 years) patients undergoing elective colorectal cancer surgery (open or laparoscopic) were included. Patients with severe dementia (DSM IV) / major neurocognitive disorder (DSM 5) or severe concomitant disease that may affect short-term outcome (life expectancy less than three months)

were excluded. The local study coordinator was instructed to collect the data retrospectively from the patient record, using a standardized data extraction form (see chapter 6).

For step 2, we hypothesized that hospitals who scored lower adherence rates in the pre-test, achieved higher improvement rates. The primary outcome measures were median protocol adherence (the hospital median of the proportions of relevant interventions in the protocol received by each patient), and improvement rate (the difference between pre- and post-test adherence rates). Differences in improvement rates were analyzed using Mann-Whitney U-tests.

Secondary outcome measures are mean length of stay (LOS) and self-rated protocol adherence. To determine this last measure, additional quantitative data was captured post-implementation with a questionnaire using a five-point anchored scale. Each hospital received one questionnaire to assess the level of intended implementation (0% - 100%) of each key intervention described in the model pathway. Based on these findings, the self-rated protocol adherence rate was determined. We hypothesized that positive correlations exist between the self-rated adherence and the post-test adherence rate: teams who actively worked with the CP and intended to improve adherence, would indeed have a higher post-test adherence. The relationship between variables was quantified using Pearson's R.

Based on the absolute value and difference in median protocol adherence and mean LOS, an overall ranking of the hospitals was made. The hospital with the highest adherence ranked 1st (1 point), the hospital with the lowest adherence ranked 10th (10 points). The hospital with the biggest improvement in protocol adherence ranked 1st (1 point), the hospital with the lowest improvement ranked 10th (10 points). For LOS, the same method was used. This resulted in four rankings per hospital, which were then totaled to form the overall ranking, ranging between 4 and 40 points.

Qualitative – Step 1 was the data collection post-implementation, using in-depth interviews with three professionals per hospital involved in the care pathway project. The interviews were based on a semi-structured interview guide, focusing on the key elements of process evaluation. Additionally, a second researcher took field notes during the interviews, capturing non-verbal reactions. Finally,

project notes from feedback and improvement sessions during the project, were used to complete the qualitative data, resulting in a “thick description” of the intervention, context, implementation, mechanisms and perceived outcomes. The methods for the interviews and questionnaires are described in detail in the study protocol.[15]

In step 2, we set selection criteria for the cases based on the quantitative data. Since our research focus is on improvement, we opted to include cases at the top (≤10 points) and bottom (≥ 30 points) of the ranking developed in the quantitative strand. This way, we cover the whole spectrum of improvement, including the extreme cases.

Next, the result of the step 1 for the selected cases was carefully reviewed using the extended Normalization Process Theory (eNPT) as framework. eNPT was chosen because it defines, explains and links key elements that facilitate or impede normalization (i.e. turning a new practice into routine) of complex interventions in a social system.[17,18] A systematic review on the use of (e)NPT by May et al. (2018) shows that the theory has been applied in a wide range of practices and complex interventions, providing a combination of conceptual tools needed to understand implementation as a process.[18] In the third update of the eNPT, four core constructs are defined, two focusing on context, and two on agency (“the ability to make things happen” (May, 2013, p. 1). Each core construct is further operationalized in underlying components. The theory provides four propositions that explain the normalization of a complex intervention.[17] See table 7.1 for the main constructs, definitions and propositions of eNPT. Because the original interview guide was based on several theoretical frameworks, including eNPT, all components of eNPT were covered in the interviews.

The qualitative analysis was performed on case level, meaning that the data of different respondents in the same hospital (as well as the field and project notes) were combined. The cases were summarized in case descriptions (see additional file case descriptions). The case descriptions were discussed and reviewed in the research team to ensure that the descriptions were in concordance with the original data.

Data merging and analysis (step 3 and 4)

The cases were analyzed using so called joint displays. These are tables, bringing together both quantitative and qualitative data visually, to reach new insights. The specific type of joint display used is the "side-by-side" display.[16,19] The cases are presented in four displays, one per core construct of eNPT. Each row represents a case; the columns represent quantitative outcome data and professionals' experience. This enabled us to explore if and why cases differed in outcomes and experience per eNPT construct, and to look for patterns and explanations.

Table 7.1 Main constructs of eNPT and its 4 propositions *(May, 2013)*

Core construct	Components	Propositions
Capability Possibilities presented by the complex intervention	Workability Integration	The capability of agents to operationalize a complex intervention depends on its workability and integration within a social system.
Capacity Social-structural resources available to agents	Material resources Social roles Social norms Cognitive resources	The incorporation of a complex intervention within a social system depends on agents' capacity to cooperate and coordinate their actions.
Potential Social-cognitive resources available to agents	Individual intentions Collective commitment	The translation of capacity into collective action depends on agents' potential to enact the complex intervention.
Contribution What agents do to implement a complex intervention	Coherence Cognitive participation Collective action Reflexive monitoring	The implementation of a complex intervention depends on agents' continuous contributions that carry forward in time and space.

FINDINGS

In total, data on 381 patients and 30 professionals from 10 hospitals were included. Table 7.2 shows the hospital characteristics, number of included patients, and the number and professional background of interviewees.

Overall, the LOS decreased with 2.1 days (p=0.0230). However, there was considerable variation, ranging from a decrease of 5.06 days to an increase of 2.15 days. Overall improvement in adherence rate was 6%, an average increase from 56 to 62% (P<0.00001), varying between -13 up to +22%. In three hospitals there was no significant change in adherence rate, one hospital had a lower adherence rate in the post-test, six hospitals had significant higher adherence rates (see chapter 6).

Table 7.2 Hospital characteristics and number of patients and interviewees included

Hospital	A	B	C	D	E	F	G	H	I	J	Total
Beds total (dedicated)	200 (0)	1054 (15)	991 (39)	161 (10)	573 (22)	384 (12)	157 (-)	1995 (46)	270 (27)	322 (0)	n/a
CRC surgeries/y	110	250	120	-	200	-	86	340	80	-	n/a
FTE colorectal surgeons	3	4	3	5	3	1	2	3	2	-	
Teaching status	N	Y	Y	N	Y	Y	Y	Y	N	N	n/a
Patients pre post	20 20	20 20	20 17	20 20	10 20	20 20	20 20	20 20	20 20	20 14	190 191
Interviewees	CNS[a] CS N	CS N D QO	CS (2) HN (2)	CS D[b] QO[b]	CNS HN QO	CS G / I HN N[a] Q[a]	CS N QO	CS HN QO	G / I	CS	30

[a]Telephone interview
[b]Also provided information on hospital I and J
CNS = Clinical nurse specialist
CS = colorectal surgeon
D = Dietician
G / I – Gastroenterologist / internist
HN = Head nurse
N = Nurse
QO = Quality officer

Table 7.3 shows the main and secondary outcomes of the participating hospitals. Based on the pre-test median adherence we compared the top-5 with the bottom-5 hospitals to test the hypothesis that the lower performers in the pre-test had higher improvement rates. There was a difference in mean improvement rate for the top-5 hospitals versus the bottom-5 hospitals of 0.2% (range -13% to 12%) versus 11.2% (range -1% to 22%), although not statistically significant (p=0.17384).

Table 7.3 Protocol adherence, improvement rate, LOS and ΔLOS

H	Pre-test median adherence	Post-test median adherence (ranking)	Improvement rate (ranking)	Post-test mean LOS in days (ranking)	Δ mean LOS in days (ranking)	Overall ranking	Self-rated adherence
1	65%[a]	75% (1)	10% (4)	6.0 (1)	-3.1 (4)	10 (1)	88%
2	43%[b]	65% (4)	22% (1)	8.2 (2)	-4.2 (3)	10 (1)	60%
3	51%[b]	67% (3)	16% (2)	8.5 (3)	-2.0 (6)	14 (3)	71%
4	56%[a]	68% (2)	12% (3)	9.9 (5)	-2.4 (5)	15 (4)	88%
5	52%[b]	51% (9)	-1% (7)	10.2 (6)	-5.0 (1)	23 (5)	59%
6	46%[b]	55% (7)	9% (6)	9.5 (4)	-1.7 (7)	24 (6)	-
7	54%[b]	64% (5)	10% (4)	17.0 (9)	1.7 (8)	26 (7)	79%
8	60%[a]	47% (10)	-13% (10)	10.3 (8)	-4.4 (2)	30 (8)	71%
9	57%[a]	54% (8)	-3% (8)	10.2 (6)	2.1 (10)	32 (9)	72%
10	69%[a]	64% (5)	-5% (9)	18.8 (10)	1.8 (9)	33 (10)	64%

[a]Top-5 hospitals pre-test median adherence
[b]Bottom-5 hospitals pre-test median adherence

The correlation between intended adherence (self-rated), and measured adherence (median adherence post-test) is visualized in figure 7.2. The figure shows that there is a small positive correlation between self-rated adherence and median adherence (Pearson's R=0.5358, R^2=0.2871, p=0.13706).

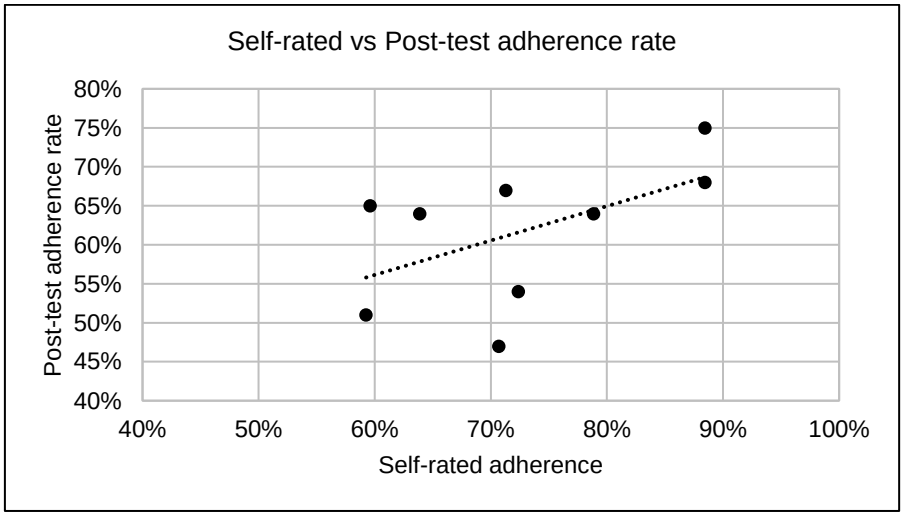


Figure 7.2 Self-rated improvement versus post-test median adherence rate

Case studies

The hospitals are ranked in table 7.3 as indicated in the methods section. This shows that hospital 1 and 2 (both 10 points) are included as high performance cases 1 and 2. Hospitals 8, 9, and 10 are included as low performing cases, case 3, 4, and 5 respectively. For each case, a short description is provided as additional file, covering the main quantitative findings, and the experience of the involved professionals described in the four core constructs of eNPT.

Per main construct of eNPT a joint display is presented showing the top (1 and 2) and bottom (3, 4, and 5) cases, followed by a short explanatory text including illustrative quotes, comparing the cases.

Table 7.4 Joint display capability

Capability: Possibilities presented by the complex intervention (Workability & Integration)					
	AR (IR)	**SrA**	**↑↓**	**LOS (ΔLOS)**	**Qualitative data**
Case 1	75% (10%)	88%	↑17 ↓5	(6.0d) (-3.1d)	• CP implemented before project, project used to update and adapt • CP integrated in electronic patient record • No effect on workload • Standardization, monitoring mentioned as standard ways of working

Case 2	65% (22%)	60%	↑18 ↓3	8.2d (-4.2)	• CP implemented during project • CP not integrated in patient record, but integrated in work processes • Initial increase in workload • Delicate process to reach consensus
Case 3	47% (-13%)	71%	↑6 ↓9	10.3d (-4.4)	• No CP implemented • Local protocol not integrated in the patient record • Using protocol decreases workload • Perioperative care is unstructured, depending on individual preferences
Case 4	54% (-3%)	72%	↑13 ↓6	10.2d (2.1d)	• CP partly implemented during project, not integrated in patient record • No effect on workload • Ambivalent perception of standardization: clarity versus "cook book medicine" and loss of autonomy
Case 5	64% (-5%)	64%	↑7 ↓8	18.8d (1.8)	• CP implemented during project • CP integrated in (paper based) patient record • Decrease in workload • Standardization perceived as positive providing clarity and safety

AR: Adherence rate post-test; IR: Improvement rate; SrA: Self-rated adherence; ↑↓: number of interventions on which adherence went up or down; LOS: length of stay post-test; ΔLOS: change in mean LOS (days)

Capability is defined as the possibilities offered by the complex intervention, in terms of workability and integration in a social system. In four of the cases, the workability of the CP was perceived as positive, with minimal effect on workload, and at the same time increasing structure, safety.

> *"At the start, yes, in the beginning. Now maybe we profit. But at the start we had to explain and tell everyone …. Now, it is … when it works, it works. When the patient arrives and everything is clear, it is a positive effect." (case 5)*

Only in case 4 there were doubts about the feasibility and standardization.

> *"So that's what we decided. Okay, because they were the same, it was dubious to get them up the first day. But, what they do recommend is that they have an evaluation by physio, or … well with them it is a … well an evaluation at least." (case 4)*

Case 1 and case 5 integrated the CP in the existing patient record. In case 2 the CP was not integrated in the patient record, but it was integrated in the work processes, in the social system, despite the perceived delicate process of reaching consensus. In contrast, in case 3 the perioperative care was characterized as unstructured, and the CP was not implemented. In case 4, part of the CP was implemented, but it was not integrated.

In summary, the implementation of the CP and related improvement in performance was facilitated by its workability and practical nature, providing clarity and safety, and by its integration in work processes.

Table 7.5 Joint display capacity

Capacity: Social-structural resources available to agents (Social roles, Social norms, Material & Cognitive resources)					
	AR (IR)	**SrA**	**↑↓**	**LOS (ΔLOS)**	**Qualitative data**
Case 1	75% (10%)	88%	↑17 ↓5	(6.0d) (-3.1d)	• Resources available, including time and data system • No support from quality department, but trained CP facilitator supported project • Clear clinical leader • Improvement team had no experience in CP methodology, project as opportunity to learn each other's contribution
Case 2	65% (22%)	60%	↑18 ↓3	8.2d (-4.2d)	• Resources and time constraints. Comprehensive data system available, but manual retrieval of data • Improvement team had experience with developing and implementing CPs, a detailed project plan was used, quality department supported the project • Medical champion present, but new in hospital, perceived as disadvantage in collaboration with surgeons
Case 3	47% (-13%)	71%	↑6 ↓9	10.3d (-4.4d)	• No resources and no time, no data system available • No clear local champion • Day-to-day teamwork perceived as good
Case 4	54% (-3%)	72%	↑13 ↓6	10.2d (2.1d)	• No resources nor time for improvement activities, no data system available. • No improvement team formed, and no clear clinical leader • Limited support from quality department • Day-to-day teamwork perceived as challenging
Case 5	64% (-5%)	64%	↑7 ↓8	18.8d (1.8d)	• Lack of resources and time, staff shortage, limited data available in data system • Both medical and nursing champions, but medical champion only working on 1 of 2 wards • Improvement team had no experience in CP methodology, champion had experience

AR: Adherence rate post-test; IR: Improvement rate; SrA: Self-rated adherence; ↑↓: number of interventions on which adherence went up or down; LOS: length of stay post-test; ΔLOS: change in mean LOS (days)

Capacity is defined as the social-structural resources available to agents. Only in case 1 it was reported that resources were available, including a data system. The other cases reported resource and time constraints. Especially the lack of automated data collection for performance monitoring acted as a barrier to implementation. It is interesting to note, that the case with the highest improvement rate, also reported limitations in resources.

In all cases except case 4, teamwork and collaboration was perceived as good.

> *"And in fact we have no departments-life. We are not meeting together, except in the corridor and so on, but we have no regular meeting for routine problems or so." (case 4)*

The improvement team in case 1 had no previous experience, but was supported by trained CP facilitators. The team in case 2 had experience in CP methodology, and was supported by the quality department. In case 5, only the medical champion had experience in CP development. In case 3 and 4, no improvement team was formed. This observed difference in CP methodology experience and support correlates with the performance.

The role of the local champion was different in all cases. In case 1 and 5 there were clear medical and nursing champions (but in case 5 only on one of two wards), whereas in case 2 there was a medical champion (but new in the hospital), and there was no clear champion in cases 3 and 4.

Thus, the implementation of the CP, was hindered by lack of automated data collection for feedback purposes, and was facilitated by improvement teams having experience or being supported in CP methodology. Lack of resources was no barrier in case 1 as opposed to the other cases, and the role of the champion as well as teamwork in relation to improvement was ambiguous.

Potential is described as the individual intentions and collective commitment of agents. In case 1, 2, and 5 willingness to change was perceived as intrinsic. The feedback of the pre-test performance acted as trigger. In case 3, it was reported that there were individual ways of working. The most striking differences between the high improvement and low improvement cases was found in the decision to join the project, and CP strategy. In case 3, 4 and 5, it was middle management or the team itself who took the decision to join the project, whereas in case 1 and 2, it was a higher management decision. In case 1 and 2, CP development is part of the hospital strategy, where in the other hospitals it is not.

Table 7.6 Joint display potential

Potential: Social-cognitive resources available to agents (Individual intentions & Collective commitment)					
	AR (IR)	**SrA**	**↑↓**	**LOS (ΔLOS)**	**Qualitative data**
Case 1	75% (10%)	88%	↑17 ↓5	(6.0d) (-3.1d)	• Willingness to change was present, team wanted to improve further • Quality improvement is considered important within hospital • CP development is team effort, with collective goals • CP development aligned with hospital strategy, higher management decided to join the project
Case 2	65% (22%)	60%	↑18 ↓3	8.2d (-4.2d)	• Improvement team was motivated • Motivation hampered by conflicting priorities • Identifiable collective reason to start project • CP development aligned with hospital strategy, higher management decided to join the project
Case 3	47% (-13%)	71%	↑6 ↓9	10.3d (-4.4d)	• Little motivation and collective commitment • Certification, external pressure as leverage for CP development • Conflict of views on quality: administrative vs clinical approach • CP development not aligned with hospital strategy, middle management decided to join the project
Case 4	54% (-3%)	72%	↑13 ↓6	10.2d (2.1d)	• Lacking shared goals and commitment • External pressure provides leverage for CP development • Management not involved, quality improvement as “part of the job” • CP development not aligned with hospital strategy, team decided to join the project
Case 5	64% (-5%)	64%	↑7 ↓8	18.8d (1.8d)	• Feedback of the pre-test data acted as trigger, team intrinsically motivated • Quality improvement perceived as important part of the job, project as opportunity to update local protocols, benchmark and learn • CP development is a team effort, with shared ambitions, but more so on the ward where medical champion worked • Little to no support by management, and different views on quality between management and clinicians • CP development is not aligned with hospital strategy, middle management decided to join the project

AR: Adherence rate post-test; IR: Improvement rate; SrA: Self-rated adherence; ↑↓: number of interventions on which adherence went up or down; LOS: length of stay post-test; ΔLOS: change in mean LOS (days)

There was a remarkable contrast in view on how “normal” quality improvement is between case 1 and 2 on the one hand, and case 3, 4 and 5 on the other hand. In case 3 and 5 it was indicated that there was a chasm in approach between management and clinicians.

> “*… always on the conflict between an administrative approach and a medical approach, huh. So it's that gap and it's been going on for years” (case 3)*

Case 3 and 4 reported that external pressure can work as facilitator to standardize care. This was not mentioned in the other cases. Finally, it was observed that case 1 and 2 both have clear objectives and priorities.

> *"And that fine-tuning… we first looked to see where there is room for improvement. So we set a number of general goals, of which the most remarkable was, say, reducing the admission, the length of stay, but also reducing nausea. In our analysis, these sprang out." (case 1)*

In short, implementation of the CP was facilitated by the intrinsic motivation of the team to work on specific goals and priorities, and by the fact that CP development is part of the hospital strategy. Individualism, external pressure, the difference between "managerial and clinical approach" and middle management decision to join the project were barriers to implementation.

Table 7.7 Joint display contribution

Contribution: What agents do to implement a complex intervention (Coherence, Cognitive participation, Collective action & Reflexive monitoring)					
	AR (IR)	**SrA**	**↑↓**	**LOS (ΔLOS)**	**Qualitative data**
Case 1	75% (10%)	88%	↑17 ↓5	(6.0d) (-3.1d)	• Model CP as refresher, evidence base valued, feedback shared in improvement team • Positive expectation of patient and team outcomes • Benchmarking with other hospitals valued • 9 disciplines involved • Activities: updating protocol, training, communication, meetings • Feedback and monitoring perceived as crucial, and routinely used • Plans ready for future development of CP
Case 2	65% (22%)	60%	↑18 ↓3	8.2d (-4.2d)	• Evidence base of model CP valued, feedback from pre-test discussed with individuals • Ambivalent outcome expectations • Benchmarking with other hospitals valued • 5 disciplines involved • Activities: updating protocol, meetings, mandatory training, laminated poster, development of CP took longer than expected • Follow-up of data, monitoring and feedback perceived as frustrating due to manual data retrieving • Plan for further development
Case 3	47% (-13%)	71%	↑6 ↓9	10.3d (-4.4d)	• Model pathway perceived as logical, clear (but not implemented) • CP could help to organize some of the care, positive • Unclear if and how feedback from pre-test was communicated • No improvement team, no activities

Case 4	54% (-3%)	72%	↑13 ↓6	10.2d (2.1d)	• CP desired, but unknown, questioning applicability of some interventions, unclear if feedback was spread • No change in patient outcomes was expected • Benchmarking with other hospitals valued • 4 disciplines involved • Activities: updating protocol, limited training, crucial role for head nurses • Feedback and monitoring perceived as crucial, but not used routinely • Desire to develop more CPs and work with improvement team
Case 5	64% (-5%)	64%	↑7 ↓8	18.8d (1.8d)	• Model CP valued, questioning applicability of some interventions, feedback shared beyond improvement team • Positive expectation of patient and team outcomes • Benchmarking with other hospitals valued • 4 disciplines involved • Activities: updating protocols, meetings, 1-on-1 instructions, communication, CP printed in patient record (reminder) • Feedback and monitoring is used, a number of indicators from the model CP was added for routine monitoring • Plan for new patient record analysis

AR: Adherence rate post-test; IR: Improvement rate; SrA: Self-rated adherence; ↑↓: number of interventions on which adherence went up or down; LOS: length of stay post-test; ΔLOS: change in mean LOS (days)

Contribution refers to what agents do to implement a complex intervention, in terms of sense making, cognitive participation, actions and reflexive monitoring. In all cases, the intervention was seen as "making sense". The model CP was practical, clear, and the evidence-base was valued. The feedback as part of the intervention was seen as important. Positive outcomes were expected in case 1 and 5, while in case 2 there where ambivalent expectations. In case 1, 2, and 5 the teams were critical to the content of the CP. Interventions were scrutinized, and in some cases adapted before implementation.

> *"Yes, I have seen that. Except … we already had everything [laughs]. So yes, it did not contain much news for us." (case 1)*

The number of involved disciplines was observably larger in case 1 and 2, and in case 3 and 4 the lack of physicians was noticeable. All cases, except case 3, described a variety of implementation activities, including training and updating the local protocol.

> *"And so the care pathway is explained step-by-step, with the intention to receive comments." (case 2)*
>
> *"The care pathway is in the patient record, it is printed for the colleagues, and also available in intranet. And I try to make sure everybody knows that." (case 5)*

An observable difference was that team training was not organized in case 5. Reflexive monitoring, the use of feedback to improve performance, was regarded as important in all cases. It was remarkable that one of the high performance cases reported the biggest struggle in collecting feedback data. The international benchmarking with other hospitals was valued, in all cases, however, it is not clear how feedback was shared and how the benchmarking was perceived in cases 3 and 4.

> *"And to be able to compare ourselves to other hospitals, which we have never ever done before, you know we rarely have some benchmarking." (case. 4)*

All teams that implemented the CP indicated they have ideas and plans for future developments, suggesting they "carry [the implementation] forward in time and space".[17]

In summary, implementation of the CP and high performance was facilitated by the fact the intervention made sense to the users. Positive expectation of outcomes, however, was not enough to achieve positive outcomes. Further facilitators of CP implementation are use of (international) feedback data, and involvement of relevant disciplines, where the absence of physicians was observed as a barrier to achieve better performance.

DISCUSSION

Main results

The aim of this study was to evaluate the implementation process of a CP using a mixed methods design, identifying factors that could explain the difference in pre- and post-implementation performance. Although there was a difference in mean improvement rate for the top-5 hospitals versus the bottom-5 hospitals (based on pre-test adherence) of 0.2% versus 11.2%, this difference was not statistically significant. This could be attributable to either the small sample size, and/or the variation in improvement rates. We were unable to establish a relation in self-rated adherence and post-test adherence rate. We did observe however, that seven of nine hospitals overestimate their performance. A systematic review by Adams (1999) of self-report bias in guideline adherence, shows

an absolute overestimation of 27%.[20] The difference between self-reported and measured adherence in our study is smaller than this 27%, but overestimation is a known problem.

A possible explanation can be found in the so called “intention-behavior” gap. This phenomenon explains that individuals or groups can have the intention to change, but fail to show the desired behavior.[21] The intention-behavior gap has also been described within health care, proposing the use of implementation intentions to close the gap. Implementation intentions are “if-then” plans, which detail an expected situation, and a planned reaction or response.[22] CPs have the potential to structure and operationalize these planned responses.

We observed a difference in improvement in adherence and improvement in LOS. LOS is used as primary outcome measure in most studies on ERAS or fast-track protocols. Recently, Balvardi et al. (2018) suggested that LOS can be used as a measure for in-hospital recovery, having an equal construct-validity as “readiness for discharge”.[23] However, due to the small number of patients per hospital (≤20), LOS (and change in LOS) has to be interpreted with caution. This is why we used two variables to make our ranking and case selection: LOS as well as protocol adherence.

Implementation process

The implementation process differed between the cases. There were minor differences in *capability*, where the workability of the CP was perceived positive by all, but integration in work processes was stronger in the cases with higher improvement rates. In case 1, a CP was already implemented before the project started. The project was used to update the local CP. Still, this hospital improved the adherence with 10%, suggesting that having a CP is not the same as actually using it. In the other high performance case, a CP was developed from the start, although some of the care was already delivered to patients (43% pre-implementation adherence). As eNPT proposes, the capability to work with a complex intervention, depends on its workability and integration.[17] Adapting the ERP to fit local circumstances is identified as a key facilitator to implementation.[11] Furthermore, the importance of integrating the new ways of working in systems was previously described using an earlier iteration of eNPT in colorectal surgery.[7] This provides some explanation for the observed differences between the high and low performance cases.

For *capacity* there were more noticeable differences between the high and low performance cases, which could explain the difference in improvement rates. The level of experience and support of the improvement team seems to have a relation with the achieved improvement rate. This is in line with previous published studies, in both colorectal surgery[7,10,24,25] and in other settings.[26,27] The role of a trained facilitator and a local champion are both described. In the high improvement rate cases, a trained facilitator or the quality officer supported the team. A lack of resources is a well-documented barrier to implementation.[9-11,28-31] However, our data suggests that both high and low performing cases experienced a lack of resources. A local champion was present in three of five cases. In case 1 there was a clear and institutionally sanctioned champion. In case 2 the champion was relative new to the hospital, which was perceived as a disadvantage. In case 5 the champion worked on one of two wards. Interviewees indicated that implementation of the CP was less successful on the other ward. Coxon et al. (2017) developed a program theory on "change agency" in which the change agent is a clinical champion. The authors suggest that champions not only should have clinical skill and know-how, but are familiar with the local situation, and have good management and people skills as well.[24] The proposition in eNPT is that the incorporation of a complex intervention in a social system depends an users' capacity to cooperate and coordinate their actions.[17] The teams in the high performing hospitals had better access to cognitive resources (experience, training, facilitation) enabling them to cooperate and coordinate their actions. The role of the champion and material resources in our cases is ambiguous.

The first observable difference between the high and low improvement cases in *potential* was that intrinsic motivation and shared goals and commitment were reported in case 1 and 2, but were lacking in case 3 and 4. In case 5, the team was also motivated, however the team on the ward where the medical lead worked showed more commitment than the team on the other ward. This could be an explanation for the low improvement in this case. Previous research supports the importance of staff morale and commitment. For example, Jabbour et al. (2018) identify strong commitment as facilitator for the implementation of CPs in a complex environment.[32] Other studies focusing on ERAS implementation also identified commitment as facilitator.[9-11,24] The lack of commitment in cases 3 and 4 could explain the low performance. Second, the fact that CP

development is part of the hospital strategy (case 1 and 2) and the perceived difference in view on quality improvement between clinicians and managers, which was reported in the low improvement rate cases but not in the high improvement rate cases, could explain the difference in performance. In eNPT, individual intentions and shared commitment are concepts used to operationalize potential. The theory proposes that the translation of capacity into collective action depends on the users' potential (and thus intentions and commitment) to enact the complex intervention.[17] Numerous papers have described the importance of management support in quality improvement, including a review of systematic review by Kringos et al. (2015), and studies specific on CP or ERAS protocol implementation.[7,10,11,28,33-35] These studies suggest that management support is a key success factor. The lack of management support in case 3, 4 and 5, including the level at which the decision to join the project was made, and the lack of alignment of CP development with hospital policy could explain the low performance.

The final core construct, *contribution*, showed a number of interesting results. In all cases, the intervention was valued and made sense to the users, although in case 1 the model CP and feedback were perceived as nothing new. Coherence or sense making in eNPT terms, involves assigning meaning to an intervention, on which the level of involvement depends.[17] This can be seen as first important step towards normalization, also described in previous research. Banks et al. (2017) describe that a "clear understanding and acceptance of the aims of the project, including the legitimacy of the research data and the process of pathway development" (p.109) can lead to agreement and implementation.[36] Both high and low performance cases exhibited sense making and positive outcome expectation, suggesting this is not enough to achieve positive outcomes.

We were unable to observe a meaningful distinction between the cases regarding the implementation activities used, except for case 3 where there was no implementation. In our previous research we identified implementation activities focused on competence, behavior or workplace (chapter 5). We noticed that in all cases implementation activities were used from all three categories. We did observe a difference in the involvement of relevant disciplines, where the absence of physicians in the project in the low performance cases 3 and 4 was noticeable. This

relates to the concept of cognitive participation from eNPT, the level to which users enroll themselves in a complex intervention and become members of a community of practice.[17] The importance of building a community of practice was also shown by Gotlib Conn et al. (2015), who identified it as a key component in the implementation. In this study, there was a community of practice on two levels: at the individual sites and at an overarching level.[7] In our study the focus was on creating a local community of practice: the improvement team.

All cases except for case 3, used feedback as important implementation activity. A systematic review of studies involving audit and feedback, shows audit and feedback is effective to change practice.[37] It was also identified as a key facilitator of implementation of an ERP.[11] Audit and feedback, or reflexive monitoring in eNPT terminology, is important to reconfigure the actions and social relations necessary to normalize the intervention.[17] We could not observe a difference in the perceived importance and use of feedback, that could explain the difference in performance between the cases.

As proposed in eNPT, the core constructs capability, capacity and potential have an impact on contribution, i.e. the actions people take to implement the intervention. In the end, the implementation and normalization of a complex intervention depends on users' continuous contributions.[17] Figure 7.3 shows the identified factors that could explain the difference between pre- and post-implementation performance. The figure is based on the "resources and possibilities for agents' contributions to implementation processes" (May, 2013, figure 3, p.4) and links the four main constructs. It shows the factors that were present in the high performance cases, but that were absent in the low performance cases. Other factors, e.g. the workability of the CP, the availability of resources, sense making, collective and diverse implementation activities, and use of feedback and monitoring (reflexive monitoring), were reported as important factors in the implementation process, and were present in both high and low performance cases.

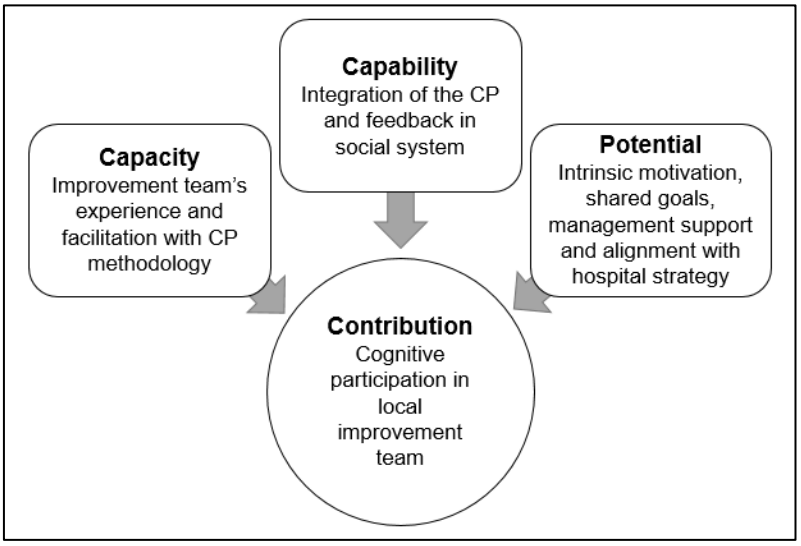


Figure 7.3 Factors explaining pre- and post-implementation difference *(based on May, 2013)*

Strengths and limitations

Our study showed that eNPT can be used to explain how different factors can influence the implementation of a CP. The study was performed in a time span of over two years, allowing the participating teams time to study their processes, develop or improve their CPs, and implement and normalize the CP. A major methodological strength of the study is that the interviews and initial coding of interviews were performed before the quantitative data was analyzed. This helps in reducing interpretation bias.[38] The selection of cases, from the high and low end of the spectrum, ensures that we have included information rich cases.

Our study also has its limitations. Because it was not feasible to include all hospitals in the study, we selected the top two and bottom three hospitals based on the ranking presented in table 7.3. This is an arbitrary selection of cases, other selections would have been possible. The ranking shows that hospitals ranked 1 to 4 have a total ranking score between 10 and 15 points. Hospitals ranked 5 to 7 have a score between 23 and 26 points, and finally hospitals ranked 8 to 10 have a score between 30 to 33 points (these three hospitals are included as case 3, 4 and 5). This suggests that there are three groups of hospitals: high, intermediate and low performers. To validate our selection of top and

bottom cases, we compared them with the not-selected hospitals. Hospitals ranked 3 and 4 showed similar characteristics as described in detail for case 1 and 2. Both hospitals have integrated the CP, feedback and monitoring (although manual) is used, standardization is perceived as positive. Care pathway development was aligned with hospital strategy, although it was a team decision to join the project. Teams were intrinsically motivated and received training and/or support in CP methodology, and used a variety of implementation activities. This gives us confidence to believe that hospital 3 and 4 provided no additional insights and we captured ample data on high performance by including only hospital 1 and 2.

The other not-included hospitals, the “intermediate group”, showed a more diverse picture. Some characteristics were similar to the high performance group (e.g. motivation, local champion, variety of implementation activities) and some characteristics were similar to the low performance group (e.g. lack of management support, resources, collective commitment, and support/training in CP methodology). This is what we expected to see, and we believe it supports our decision for including, analyzing and contrasting the top and bottom of our ranking.

In case 3 and case 4 there was a partly overarching team (quality officer, project support). Therefor it was not always clear to which case a response was applicable. Furthermore, for all cases the interviews were conducted with only three or four directly involved professionals, which could give a limited account of the implementation process. To mitigate this, we used data triangulation by checking the interview data with the field notes and project notes, which is an established method to enhance the trustworthiness of the data.[39]

There is some overlap in the eNPT constructs, e.g. feedback as part of our intervention (workability, integration) or feedback for reflexive monitoring. This overlap was previously described by Drew et al.[26] In this study, the data was first coded inductively by thematic analysis. After this, eNPT was applied. By using the thematic analysis from our previous study as input, we followed the same procedure as described by Drew et al.

Further research could explore a single case, aiming to reach data saturation on case level (rather than data saturation for the overall sample). To establish whether the CP was indeed normalized, a longitudinal quantitative study could be performed.

Conclusions

Combining quantitative and qualitative data, our study shows that a change in protocol adherence does not automatically lead to a change in length of stay. However, overall improvement (both adherence as well as length of stay) was achieved, but was highly variable between the cases.

There are multiple factors in the implementation process that could explain the difference in improvement of performance between the cases. Conceptualizing these factors in eNPT suggests that teams that are able to integrate the care pathway in their social system, have experience or are supported with working with CP methodology, are intrinsically motivated, work towards shared goals, and receive active management support and where care pathway development is aligned with the hospital strategy, contribute to the successful implementation of a care pathway for colorectal cancer surgery.

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ADDTIONAL FILE – CASE DESCRIPTIONS

Case 1

Quantitative – Case 1 had a post-test median adherence rate of 75%, with an improvement rate of 10%. The number of interventions on which adherence improved, was 17, of which seven scored an adherence <70% in the pre-test (priority interventions). Adherence decreased in five interventions. Mean LOS in the post-test was 6.0 days, a decrease of 3.1 days.

Capability – This hospital already had a CP in place and used the project to adapt this. Respondents did not experience an effect on workload after adaptation. The CP is integrated in the electronic patient record. Also, respondents noted that when required (e.g. due to complications), deviating from the CP was possible. Standardization, measuring and discussing results were mentioned as standard ways of working.

Capacity – Both material (time) and cognitive (training) resources were available, including a data system. There was no support from the quality department, but a trained CP facilitator supported the project, together with a formally appointed clinical leader, with good collaboration in the improvement team. The improvement team members knew each other before the start of the project, but had no experience in CP development and implementation. The project offered the possibility to learn each other's roles in the care process, and look at problems from different perspectives.

Potential – Interviewees indicated that willingness to change was present, and that quality improvement is considered important within the hospital. Despite the already good results, the team wanted to improve further. There was a high level of involvement of all disciplines during the project. A number of collective goals (e.g. reduce LOS, improve postoperative nausea) were set. CP development and implementation is perceived and organized as team effort. Development of CPs is anchored in hospital strategy, and the higher management decided to join the project.

Contribution – The model CP delivered to the hospital was perceived as "not much news", was used as a "refresher", although the evidence base of the CP was valued. The project was expected to deliver positive results, and interviewees indicated that teamwork had already improved because of the project. The benchmarking with other hospitals, as part of the intervention, was seen as inspiring, the feedback report was shared in the improvement team. Involved disciplines were: colorectal surgeon, gastroenterologist, nursing, clinical nurse specialist, anesthetist, dietician, patients, physiotherapist, CP facilitator. A wide range of implementation activities was used, including updating protocols, meetings, mandatory training, 1-on-1 instruction, and several communication modes (e.g. weekly email newsletter, linking pin in each involved discipline). This team indicated that they already monitor their performance every three months. And although the results from the pre-test were perceived as good, this did not make the team lean back. A number of goals and indicators were added to the monitoring. Several actions were mentioned to sustain improvement, e.g. repeated training, training for new employees.

Case 2

Quantitative – Case 2 had a post-test median adherence rate of 65%, with an improvement rate of 22%. The number of interventions on which adherence improved, was 18, of which 13 scored an adherence <70% in the pre-test. Adherence decreased in three interventions. Mean LOS in the post-test was 8.2 days, a decrease of 4.2 days.

Capability – The CP was seen as practical, although with an initial increase in workload. The CP was not integrated in the patient record, but was considered “nothing special” and integrated in the work processes. Developing the CP proved to be a delicate process to reach consensus, because of variation between the surgeons in the hospital.

Capacity – Interviewees indicated there were both resource and time constraints. The project was initially supported by a quality officer, but she was not replaced during leave. On the other hand, the improvement team had experience with developing and implementing CPs. The team used a detailed project plan to guide the project. A comprehensive data system was available in the hospital, but data had to be retrieved manually. The medical champion was relatively new in the hospital, impeding collaboration and teamwork with other surgeons, who do not all follow the CP.

Potential – CP development is part of the hospital policy, the chief medical officer supports the project. It was a higher management decision to join the project. The inter-doctor variation reported by the respondents, acted as a collective reason to join the project. The improvement team was motivated to develop and implement the CP, despite a struggle for priorities.

Contribution – The evidence base of the CP was valued, interviewees indicated it was needed to convince colleagues. The interviewees were ambivalent in the expected outcomes. Deviations from the pathway were deemed necessary, and were experienced as frustrating when caused by organizational problems. The opportunity to compare with and learn from other hospitals was sees as positive. The feedback was presented and used to introduce the new CP. The following disciplines were involved in the project: colorectal surgeon, nursing, dietician, anesthetist, quality officer. The improvement team used the following activities: updating the local protocol, meetings, mandatory training and used a laminated poster as reminder for the team. Follow-up of data was perceived as time consuming and difficult because of the manual data retrieving. This was perceived as frustrating and demotivating, making monitoring almost impossible. Development and implementation of the CP was perceived as time consuming, taking “longer than expected”. The interviewees expected that a newly developed patient brochure will further help, not only to better inform patients, but also to sustain the CP.

Case 3

Quantitative – Case 3 had a post-test median adherence rate of 47%, with an improvement rate of -13%. Despite the overall decrease in adherence, the number of interventions on which adherence improved, was six, of which five scored an adherence <70% in the pre-test. Adherence decreased in nine interventions. In the post-test, the mean LOS was 10.3 days, a decrease of 4.4 days.

Capability – In this hospital, interviewees indicated that the interventions presented in de model CP are used in practice, but in a different format, which is not integrated in the patient record. The use of a protocol, of the standardized interventions, was perceived to decrease workload and save time. However, preoperative care was characterized as an unsystematic process, depending on the individual surgeon.

Capacity – Physicians are encouraged to improve quality, but there are no resources and no time. There was no data system available. A clear local champion to promote the CP was not available; a study nurse was perceived as being the project leader. Daily teamwork is perceived as good; there is a well-structured surgical service.

Potential – The respondents indicated that individual doctors do as they want. CP development is not part of a central hospital strategy. There is a struggle between administrative quality (“ticking boxes”) versus clinical quality (focus on patient): “we are here because the patient is important”. Middle management decided to join the project. Certification of services is seen as central strategy, which according to interviewees, “unites people”. There is pressure from national health authorities which have imposed national indicators to which the hospital has to comply. This provides leverage to create a more standardized service and improve adherence.

Contribution – The model CP describes the same items as those used for certification, it has a logical and clear format. Implementing the CP could help to organize some of the care, which “would be good”. Interviewees indicated that feedback and monitoring are crucial for quality control. It was unclear if and how the feedback on the pre-test performance was communicated. The feedback report was send to all surgeons and the medical director. However, other interviewees did not recall to have seen the report, and were not aware of a meeting were the feedback was presented.

There was no improvement team in this hospital, and no improvement project or activities were performed. Interviewees agreed that internal communication regarding the project should have been better.

Case 4

Quantitative – Case 4 scored a post-test median adherence rate of 54%, with an improvement rate of -3%.The number of interventions on which adherence improved was 13, of which 9 were priority interventions. Adherence decreased in six interventions. In the post-test the mean LOS was 10.2 days, an increase of 2.1 days.

Capability – There were doubts about the feasibility of the CP in this hospital. Not all interventions were directly applicable. The CP was not integrated in the patient record, but protocols were updated. The respondents indicated workload had not changed. There were mixed feelings about standardization; this could enhance structure and safety, but there was also a fear of “cook book medicine”. Physicians have great autonomy to deviate from standards.

Capacity – Lack of resources, time and a data system was discussed by the respondents. Quality improvement work is regarded “part of the job”. There was limited support from the quality department, no facilitation. A clear clinical lead was not identified, involvement of physicians was low. Respondents agreed that collaboration and working relations within and across disciplines were not good.

Potential – Respondents indicated that the project had not been communicated to the hospital CEO. Management was interested, but did not support the project actively. It was perceived that the team decided to join the project, however, a sense of shared goals and commitment was lacking. CP development is not a part of the hospital strategy, but the new CEO favors it. The national authorities imposed a national indicator for colorectal cancer. The hospital has to show improvement in accreditations. This can provide leverage for CP implementation. On the other hand, accreditations take up time and resources of the quality department and teams.

Contribution – The CP was perceived as logic, but the format was different from local forms. Traditional care was perceived as barrier to implement the CP. After the feedback and improvement sessions, there was no follow-up by an improvement team and little improvement in outcomes was expected. There were some implementation activities, mainly updating the preoperative protocol and some training on specific interventions, not on the complete CP. Involved professionals in these activities were surgeons, dieticians, quality officer, and nurses. Respondents indicated that interventions were implemented because there are “good head nurses”. This team reported that feedback and feedback sessions are crucial for quality improvement. Providing information and benchmarking was seen as a mechanism to change practice. The feedback on performance, including the international comparison, was received positive. Results were perceived to be good, motivating the team. However, it was unclear if the feedback was spread within the hospital after the feedback sessions. Interviewees reported no structural use of feedback and monitoring. A desire to continue working with an improvement team was expressed during the interviews.

Case 5

Quantitative – Case 5 had a post-test median adherence rate of 64%, with an improvement rate of -5%. Still, the number of interventions on which adherence improved, was seven, of which only one scored an adherence <70% in the pre-test. Adherence decreased in eight interventions. Mean LOS in the post-test was 18.8 days, an increase of 1.8 days.

Capability – In this hospital, the perioperative care for colorectal surgery is provided in two separate wards. On both wards, the model CP was perceived as very practical, and expected to reduce workload. The CP was integrated in the patient record. The interviewees indicated that standardization provides clarity and safety, and a basis to evaluate the care process.

Capacity – The respondents reported resource and time constraints, and shortage of staff for multiple disciplines, including surgeons and nurses. A discrepancy in vision on priorities between management and staff on the wards was described. There was limited data available in a data system. There were experienced clinical champions (both medical and nursing), but the medial champion is working only in one of the two wards. The interviewees indicated that on the other ward, the implementation was less successful. The collaboration in the improvement team was perceived as good. The medical champion had experience in developing CPs, the improvement team not. The team received no assistance from the quality department.

Potential – The department head favors CPs, and decided to join the project, which was perceived as opportunity to update local protocols, and to learn from other hospitals. Quality improvement is seen as “vital”, were the hospital management considers this part of the job. The feedback after the pretest showed that the performance was close to the top. On other indicators there was room for improvement, which stimulated the intrinsic motivation. CP development is a team effort, with shared ambitions. CP development is not in the hospital policy, but the need for certification and quality of care is.

Contribution – Interviewees reported that the model CP was valued. However, the team was critical to some of the interventions in the model CP, questioning the local applicability. Positive outcomes for both patient care and teamwork were expected. The international comparison with other hospitals was valued. Involved disciplines in the project were: colorectal surgeons, nurses, dietician, and physiotherapist. The following activities were used by the improvement team: updating the local protocol, CP as printed reminder in all patient records, meetings, 1-on-1 instructions, and communication during shift handovers. The results of the pre-test were discussed on the wards, and presented to partner-hospitals in the region. Feedback and monitoring is used, and a number of indicators used in the study were added to the routine monitoring. This, and the plan to do another patient record analysis in a year’s time gives the interviewees the confidence that the CP implementation will be sustained.

CHAPTER 8

GENERAL DISCUSSION, CONCLUSION AND RECOMMENDATIONS

This study entailed a mixed methods process evaluation of the implementation of a care pathway for colorectal cancer surgery. In this final chapter we will first summarize the main findings per research objective. The detailed findings have been discussed in the previous chapters. Here, we present a synthesis of our main findings on understanding the implementation process. We will then highlight some future perspectives, and address a number of methodological strengths and limitations of the study. Finally, we will formulate an overall conclusion and recommendations for practice, policy and future research.

MAIN FINDINGS

This study had two main objectives:

1. To perform an international quality of care improvement initiative for patients undergoing surgery for colorectal cancer, by:

a. developing a model care pathway including key interventions and indicators;

A systematic review was performed to develop a model care pathway. We found considerable variation in the type and number of interventions used in the included studies. This ranged from nine to 20. In total 33 different key interventions were identified. Additionally, 25 outcome indicators were identified. Length of stay was the most common used indicator. This clinical content was summarized in a model care pathway (chapter 2).

b. studying the pre- and post-implementation adherence to and variation in perioperative care;

An observational cross-sectional multicenter study was performed in 12 hospitals in four European countries to study pre-implementation variation. A total of 230 patients were included. Mean length of stay was 13.76 (± 12.29) days. The protocol adherence ranged between 16 and 75%, with a median of 44%. An importance- performance analysis was used to show the relationship between the importance of each key intervention (the level of evidence) and its performance (the adherence). Only six interventions scored “important and high performant” (chapter 3).[1]

Post-implementation adherence and variation in care, and the effect of CP implementation was measured in 10 hospitals (two hospitals only included patients in the pre-implementation

measurement). In total, 381 patients were included. After implementation of the CP, mean length of stay decreased from 12.6 (± 9.8) to 10.7 (± 7.9) (p=0.0230) days. Protocol adherence increased from 56 to 62% (p<0.00001), still showing great variability between the hospitals. Eleven interventions scored “important and high performant” in the importance-performance analysis, but still 19 important interventions score an adherence of <70%, showing underuse (chapter 6).

In summary, the overall outcomes of our quality improvement initiative were positive. Mean length of stay, a measure used extensively in studies on enhanced recovery protocols, decreased with almost two days, without negatively impacting mortality, readmission and re-intervention rates. This is comparable to the decrease in LOS published in the meta-analysis by Lau et al.[2] Our results match the results published by Li et al. (2017). Patients in their study were divided in four groups based on protocol adherence rate. The patient group with 0 to 60% adherence had a median LOS of 12.5 days, while the group with an adherence rate of 60-70% had a median LOS of 10 days.[3]

Time to tolerating normal diet decreased from 7.2 to 4.9 postoperative days (p=0.0024) and time to first walking from 3.7 to 2.8 days (p=0.0005). These parameters are frequently used as discharge criteria. However, the time to “patient meets discharge criteria” in our study was 9.5 days in the post-test, suggesting there might be a difference between the patient being physically ready for discharge and the moment when the team decides the patient is ready for discharge. Further research is required to explore this difference

We observed hospitals in which the adherence rate increased and LOS decreased, and hospitals in which adherence rate decreased and LOS increased. This is what we expected based on previous studies: a “dose-effect” relationship between protocol adherence and outcomes has been suggested.[3-7] We also observed one hospital in which both adherence rate and LOS increased (10% and 1.7 days respectively) and one hospital in which both measures decreased (-13% and -4.4 days respectively). From the interviews we know that in the first hospital there were implementation and improvement efforts. In the second hospital there was no improvement team, the CP was not implemented. Moreover, perioperative care was characterized as “unstructured”, depending on individual preferences. This could provide some explanation for the decrease in

adherence. The LOS data from both hospitals seem contradictory to the “dose-effect” relationship suggested by the previous reported studies. However, we advise caution in the interpretation of the LOS of individual hospitals in our study as this is based on only 20 patients. This low number of patients may not represent each hospital reliably.

In a recent prospective study in open colorectal surgery, Lohsiriwat (2019) suggests that an ERAS team (with a single surgeon) needs to treat 76 patients before reaching >70% compliance and higher rates of postoperative recovery.[8] The teams in our study had a timeframe of only six months for the implementation of the CP. If we look at the number of surgeries reported in table 7.2, four out of the seven hospitals who reported the number of surgeries, treat on average 50 patients in six months, suggesting a longer timeframe is needed to fully implement all key interventions.

c. implementing a care pathway.

The implementation of the CP consisted of several steps. First, local improvement teams received feedback on their current care process in a national meeting, with the three hospitals form the same country. This was followed by two local in-house sessions: a feedback session, and an improvement session in which the model pathway was explained. Two hospitals with extensive experience in care pathway development declined to participate in local sessions. In three other hospitals, the feedback and improvement sessions were combined in one session. After the improvement session, the teams implemented the improvements using their own methods and tools, tailored to their situation and goals.

The teams who declined to participate in the local feedback session or combined the feedback and improvement session, are in the top of the ranking presented in chapter 7. This suggests these teams made a correct judgment about their ability to develop and implement the care pathway.

2. To evaluate the implementation process of a care pathway for colorectal cancer surgery by performing a process evaluation:

a. developing a method to perform process evaluation of evidence-based care pathways;

Primarily based on the Medical Research Council's guidance for process evaluations of complex interventions,[9] a protocol for studying the different components of process evaluation and its relationships was developed. This protocol formed the bases of this PhD study. It guided the research questions, and timing of both quantitative and qualitative methods (chapter 4).[10]

b. evaluating the context, implementation process, mechanisms of impact of the implementation of the care pathway;

A qualitative study was used to explore the individual experiences of involved professionals with the implementation of the CP. In-depth interviews with 32 professionals provided the data that were analyzed and summarized in a fishbone diagram (figure 5.1). Their experiences were grouped according to their overall perceived outcomes: "no effect" or "positive effect". A number of aspects that have to be taken into account during implementation of a CP were identified: the evidence base of the care pathway, prolonged involvement of multiple disciplines, and availability of a clinical data system. Furthermore, multiple implementation activities were used, focusing on competence, behavior, or workplace. Different mechanisms influenced the implementation: when teamwork and collaboration were experienced as good, respondents perceived positive effects. Feedback was used as important implementation activity used for goal setting and motivation (chapter 5).

The feedback, presented as part of the intervention, was generally received positive. Especially the comparison with other (international) centers was valued. It increased motivation for the project and helped in goal-setting (chapter 5 and 7). Monitoring and feedback is part of the official ERAS interactive system [11] and has been topic of multiple studies, e.g. a systematic review by Ivers et al. (2012) [12] and a publication of 15 recommendations based on research evidence by a group of international experts.[13] These recommendations are summarized in box 8.1.

Despite the importance of monitoring and feedback, both individuals (in chapter 5) as well as teams (in chapter 7) reported that in some hospitals feedback had been received, but that it was not always followed by implementation or improvement activities. We believe the way feedback was provided, was in concordance with the recommendations in Box 8.1, with the exception of numbers 5, 6, 7, and 10. Real-time feedback requires a full operational EPD, which was not available in all

1. Recommend actions consistent with established goals and priorities
2. Recommend actions that can improve and are under recipients control
3. Recommend specific actions
4. Provide multiple instances of feedback
5. Provide feedback as soon as possible, based on a frequency informed by number of new cases
6. Provide individual rather than general data
7. Choose comparators that reinforce desired behavior change
8. Closely link visual display and summary message
9. Provide feedback in more than one way
10. Minimize extraneous cognitive load for feedback recipients
11. Address barriers to feedback use
12. Provide short, actionable messages followed by optional detail
13. Address credibility of the information
14. Prevent defensive reactions to feedback
15. Construct feedback through social interaction

Box 8.1 Practice recommendations for feedback *(Brehault et al., 2016)*

participating hospitals in the project. The relevance of timely feedback is illustrated by Geisinger Healthcare. They are capable of delivering real-time feedback, which helps to achieve compliance rates of >95% in their “ProvenCare” concept.[14] Moreover, within Geisinger Healthcare, monitoring and feedback is embedded in a structure, including incentives for physicians.[15]

The level to which individual rather than general feedback was provided, and comparators that reinforce desired behavior change were used, is debatable. We provided feedback to teams, not to individual professionals, showing both the own performance as well as the performance of others. When performance on a specific indicator is low, but still higher than others, this could give the message that improvement is not necessary.

3. *exploring the relationships between context, implementation and mechanisms, in relation to the intervention and outcomes.*

A mixed methods case study was used to combine the outcomes (quantitative) with the experiences (qualitative) in high performance and low performance cases. The extended Normalization Process Theory [16] was used as theoretical framework, to identify and understand factors that explain differences in pre- and post-implementation performance. These factors are summarized in figure 7.3, and include the level of integration of the care pathway, the experience and support of the

improvement team in CP methodology, the motivation of the team, level of management support and alignment of CP development and hospital strategy, and participation of relevant disciplines, most noticeably the physician.

Although lack of resources is a well-documented barrier to CP implementation [17-19], we observed that a lack of resources was reported by professionals and cases irrespective of the (perceived) outcomes or performance after CP implementation. This suggests that despite a lack of resources, improvements can be achieved.

A possible explanation for this phenomenon can be found in the job demand-control model, originally published by Karasek in 1979, and since then applied in many settings including healthcare.[20,21] This model, developed to understand job stress, explains two dimensions: job demands (physical, emotional), and job control (decision latitude). High demand jobs that have low control, create the biggest risk of stress. In an update of the model, a third dimension has been added: that of support.[20] High demand jobs, with low support (e.g. lack of resources, time) create stress for professionals, which can be reduced by increasing the job control for the professional. Interviewees in our study indicated that implementing a CP leads to standardization, and provides clarity and safety, in fact increasing decision latitude, especially for nurses and junior doctors working under supervision of a specialist. This could mean that implementing a CP could mitigate the negative effect of a lack of resources.

IMPLICATIONS FOR CARE PATHWAY IMPLEMENTATION

The final research questions in the study protocol (chapter 4) are: “What is the possible influence of the context, implementation and mechanisms on the effect of the care pathway?” And: “What recommendation can be derived to inform future care pathway implementation?” These questions are included in the study protocol as “overall” questions, and have not yet been addressed in full. We will answer the first question below, focusing on the implications for CP implementation, and the final question at the end of this chapter.

As mentioned in the General introduction, in this PhD study, the E-P-A definition of CPs has been used. A critique from a recent publication by the European Observatory on Health Systems and Policies (WHO) (Rotter et al., 2019) on the E-P-A definition, is that it lacks specificity.[22] What Rotter et at. seem to overlook in their critique, is that the E-P-A definition also includes five defining characteristics, as mentioned in the General introduction.[23] These characteristics have been the focus of previous research, empirically validating the role of key interventions [24,25], teamwork [26], and operations management [27] in CPs. Moreover, our study expands the defining characteristic on documenting the variability of care to the tracking of adherence to guidelines.

Our study reports a process evaluation of implementing an evidence-based CP using the MRC guidance in combination with eNPT. This provides the opportunity to synthesize our findings on the implementation process from these two perspectives, expanding the body of knowledge on CP implementation and the application of the MRC guidance and eNPT. As described in the general introduction, extended Normalization Process Theory [16] is used to explain relationships between the different factors in the implementation process. eNPT includes “contribution” (what people do to implement a complex intervention), but has a broader view and includes characteristics of the intervention (“capability”) and of the context (“potential” and “capacity”). This enables us to combine the theoretical constructs from eNPT with the elements of process evaluations from the MRC guidance.[9] Care pathways affect and are affected by three levels in health care organizations: the organizational, team and individual level. We mapped the different factors per construct on these three levels, and have visualized the relationships we established based on our data and our experience in (inter) national CP implementation projects and master classes in a model, figure 8.1.

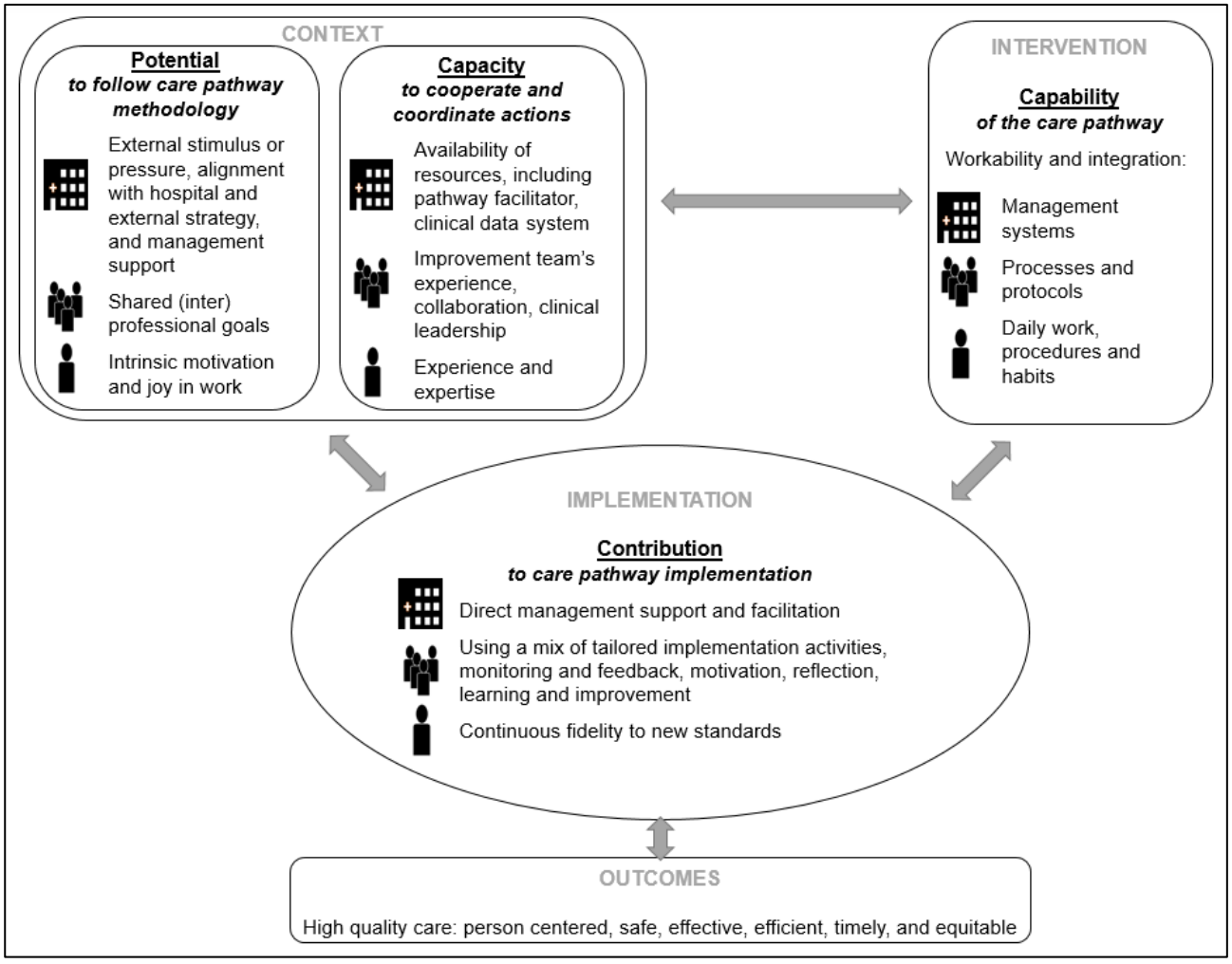

Figure 8.1 Model for implementation and normalization of a care pathway

Grey text: process evaluation elements according to MRC guidance

= Organizational level; = Team level; = Individual level

Intervention: capability

In eNPT the construct of capability refers to the opportunities presented by the complex intervention. This relates to the workability and (level of) integration of the complex intervention.[16]. This component contains the workability and integration of the care pathway in management systems (organizational level), in processes and protocols (team level), and daily work, procedures and habits (individual level), increasing decision latitude.

Context: potential and capacity

The context provides the potential to follow CP methodology, and the capacity to cooperate and coordinate actions.[16] For potential, at the organizational level this includes external stimulus or pressure, management support and alignment of CP development with hospital strategy. Care processes and care pathways are not restricted to a single organization. The surgical treatment of colorectal cancer for example is usually just an episode in the entire patient journey.[28,29] Therefore, CP development should also be aligned with external strategy, enabling transition of care and networking. We observed that teams in hospitals where CP methodology is aligned with the hospital strategy achieve better performance. Care pathway methodology in line with hospital policy, increases the likelihood that there is a support system including funding for CP development and implementation. We believe this is necessary, because CPs are organizational tools, not individual tools. At the clinical team level, shared (inter) professional goals are necessary for CP implementation. Intrinsic motivation is an already well-established enabler of CP implementation.[17,18,30] Since a few years there is considerable attention for joy in work. With burnout and staff turnover rates increasing, attention to joy in work tries to materialize the most essential aspects of positive daily work life.[31]

For capacity, at the organizational level the availability of resources, including a pathway facilitator to support the team, and a clinical data system, are factors we identified. However, CP development and implementation should not be a “one-(wo)man show”, which is owned by the CP facilitator. As mentioned in several cases, CPs ask for teamwork in a broad sense. At the team level the team’s collaboration and teamwork, and clinical leadership are important factors. At the individual level the experience with CP development and implementation and clinical expertise determine the capacity to cooperate and coordinate actions.

Implementation: contribution

In figure 8.1 we placed contribution at the center. Contribution is what people do to implement a CP. This entails direct support and facilitation by higher management. The team uses a mix of tailored implementation activities. Monitoring and feedback are used according to the previously mentioned

practice recommendations, for motivation, reflection, learning and improvement. These are mainly team level activities, although feedback can also be individual. At the individual level, “sense making” is necessary. It concerns giving meaning to the CP (both content and methodology) as prerequisite for continuous fidelity to the new standards. Implementation fidelity is the degree to which an intervention is delivered as intended.[32] Fidelity can be defined in several areas: content (intervention implemented as planned), frequency and duration (intervention implemented as often and long as planned), and coverage (proportion of target group reached by intervention).[32,33] Fidelity to a CP means following the new standard day-in and day-out.

The arrow between contribution and context goes both ways. Obviously, capacity to cooperate and coordinate actions, and potential to follow pathway methodology are conditions for contribution. Conversely, contribution of professionals can influence capacity (e.g. in clinical leadership) and potential (e.g. improving motivation of colleagues through sense making).
The connection between capability and contribution is also a two-way arrow: higher capability to implement, will make it easier to contribute. Conversely, we believe sense making and the willingness to participate in an improvement team make it easier to accept and integrate the CP in daily work.

Elements in the context shape how the intervention will be integrated. Conversely, successful integration of a specific CP in systems, processes, procedures et cetera, will influence the context (with regard to other CPs). Hence the two-way arrow.

Outcomes

The basis of the figure is formed by the goal of CP implementation: providing high quality care. We used the Institute of Medicine’s six domains of high quality care to operationalize outcomes.[34] There is a two-way arrow between outcomes and contribution: contribution leads to outcomes, and outcomes are monitored to provide feedback.

The mechanisms we identified in our study that affect CP implementation are not visualized separately, but are embedded in the other components. For example, “collaboration and team work”

was identified as a mechanism with an effect on performance. In our model, it is placed under capacity.

To clarify and explain our model, we use the two extreme cases from the mixed methods study reported in chapter 7, case 1 and case 5. We added a third case of a hospital that dropped out of the study. Team members from this hospital were included in the interviews reported in chapter 5, so we have an understanding of the interrupted implementation process in this specific case. This drop-out case can also be described and explained using our model The cases are described in short and compared to our model in table 8.1.

Table 8.1 shows the differences in how the various factors from our model were or were not present in the cases. In case 1, most factors worked together, so professionals could contribute to CP implementation. The organization actively supported the project. A CP was already implemented, and was updated during the project and fidelity to the new standards improved. In case 5 some factors from our model were missing. There was no support from the organization (facilitation, resources). Still, the improvement team was motivated and committed to improve. The level of implementation of the CP was perceived as higher on the ward where the medical leader works, compared to the other ward. In the drop-out case, there was no contribution to CP implementation, despite the fact that implementation of a CP made sense, and a comprehensive clinical data system was available. The negative impact of the feedback, negative leadership, lack of resources, lack of facilitation of a potential improvement team, and poor collaboration, made CP development and implementation impossible.

Table 8.1 Illustration of implementation model in three cases

		Case 1	Case 5	*Drop-out Case*
Description		Hospital which achieved improvements in adherence and outcomes. A CP was already implemented before the start of the project and was updated. CP development and implementation is part of hospital strategy. A multidisciplinary improvement team was supported by trained CP facilitators.	Hospital did not improve adherence nor LOS. Perioperative care for patients with colorectal cancer is delivered in two separate wards. The improvement team was led by a medical leader experienced in CP development. The medical leader only worked on one of the two wards. CP development was no part of the strategy, the team was not supported in CP methodology.	*Hospital which did not implement a CP. At the local feedback session, there was a dispute with the head of surgery regarding the data from the pre-implementation measurement. After this session, cooperation between the head of surgery and the local study coordinators ended. There was no improvement team.*
Potential		CP development and implementation is anchored in the hospitals' strategy. Higher management decided to join the project, which was seen as opportunity to learn and improve.	The need for certification is a priority for this hospital, CPs are not part of the strategy. Higher management considers quality improvement "part of the job" and did not support the project.	*External developments (merger, budget constraints) were seen as threats, preoccupying higher management, which was not involved. CP development and implementation is not part of the hospitals' strategy.*
		The improvement team set a number of collective interdisciplinary goals.	The department head decided to join the project. CP development was seen as team effort, with shared ambitions.	*There were no shared goals or ambitions.*
		Willingness to change was present, quality improvement was considered important.	Intrinsic motivation and joy in work (proudness) was increased by the feedback on the performance.	*Only two persons from the multidisciplinary team were motivated for the project. Over time, joy in work decreased.*
Capacity		Resources were available, including a clinical data system and a trained CP facilitator to support the team.	There was no support from the quality department. Lack of resources and staff were reported. There was limited data available in the data system, leading to manual data collection.	*There was no support from the quality department, no facilitation of the team. A lack of resources, especially staff time, was reported. There was a clinical data system, capable of delivering the necessary information.*
		There was a formally appointed clinical leader of the improvement team. The team had no experience in CP implementation. Team members knew each other before start of project, collaboration was good.	The improvement team had no experience in CP development and implementation. The medical leader had experience, but only worked on one ward. On the second ward, the CP was not completely implemented.	*There was negative clinical leadership, blocking the progression of the project. Collaboration across the departments was considered poor.*
		The individual team members had the clinical expertise to work with the CP.	The individual team members had the clinical expertise to work with the CP, experience in CP development was missing.	*The local study coordinator showed personal leadership trying to reanimate the project, unfortunately without result.*

Capability		Working with CPs is integrated in systems, the hospital supported integration of CP in electronic patient record.	The CP was not integrated in management systems.	*There was no implementation, so no integration.*
		CP was integrated in electronic patient record, standardizing processes. Local protocols were updated.	The CP was integrated in the patient record (paper based), care processes were standardized, providing clarity. However, at a different level at both wards.	
		The CP was experienced as practical. Standardization, monitoring and discussing results are habitual.	The CP was seen as practical and was implemented in daily work and procedures. It was used structurally to evaluate the care process.	
Contribution		Management supported the project.	There was no direct management support and facilitation.	*Although the idea of CPs was welcomed, there was no further contribution.*
		A well-supported multidisciplinary improvement team used mandatory training, 1-on-1 instructions, meetings, newsletters. Monitoring and feedback was already used routinely.	The team used 1-on-1 instruction, reminders, communication during shift handovers. Indicators from the CP were added to routine monitoring. Comparison with other hospitals was valued.	
		The CP was seen as “not much news”. Adherence to the protocol was 75%, showing an increasing fidelity to the new standards.	The applicability of some interventions in the CP was questioned. Fidelity to the new standards was not yet at 70%.	
Outcomes		Improvement in adherence rate: 10% ΔLOS: -3.1 days	Improvement in adherence rate: -5% ΔLOS: 1.8 days	*N/A*

 = Organizational level;  = Team level; = Individual level

ΔLOS = difference in post- and pre-implementation length of stay in days

FUTURE PERSPECTIVES

Enhanced recovery pathway: key interventions or "all or nothing"?

The literature review yielded 33 key interventions, listed in table 2.1 We used this list to form a model pathway, formatted as time-task matrix (see chapter 4). During the kick-off sessions in each country we received input on the model pathway, based on which we decided to exclude some of the identified interventions listed in table 2.1: three general recommendations regarding scheduling of surgery and dedicated ward and team, respiratory care and standard monitoring at medium care unit were seen as local organizational choices. Midthoracic analgesia and prevention of fluid overload were listed in both intra- and postoperative phases. Due to the format of the model CP, both were counted only as one intervention in the model CP. Measuring CRP and albumin were added to the model, resulting in 27 interventions in the model pathway (as mentioned in chapter 4).

Furthermore, for two interventions a distinction was made between colon cancer and rectal cancer: use of drains, and no mechanical bowel preparation. This means that these two interventions are operationalized in four different clinical activities. Other interventions were operationalized in multiple activities, because they are performed at multiple time points (e.g. measuring body weight), or because they focus on two areas (e.g. fluid and solid nutrition). This resulted in a higher number of activities in the model CP than the reported 27 interventions.

We realize that this can be confusing. However, it somewhat reflects the variation in enhanced recovery protocols used in studies, as shown in our literature review (nine to 20 interventions included) – see chapter 2. This variation still exists today. Two recent studies used different interventions, although both claim to use an ERP. Martin et al. (2019) use a protocol containing 22 interventions.[5] Pisarska et al. (2019) use a protocol which includes 16 interventions.[35] Kehlet, one of the earliest protagonists of enhanced recovery, stated in an editorial (2018) the five key elements of ERAS in colonic surgery (preoperative patient information, thoracic epidural anesthesia in open (but not laparoscopic) colonic surgery, avoidance of fluid overload and hypovolemia, no nasogastric tube, combined with early oral feeding and mobilization). Instead of performing more studies on effects of full adherence, Kehlet argues to increase knowledge on why the postoperative

interventions of ERAS fail to be implemented.[36] Nevertheless, the most recent ERAS guideline published in 2018 contains 25 interventions.[37] There is a recurrent discussion about which interventions are the most important to achieve positive outcome. Arguably, some interventions may have a bigger impact than others. The ERAS guideline states that this question does not have an evidence-based simple answer, but that it has been shown that increased adherence to items in the whole ERAS guideline, improves outcomes. That is why all interventions that potentially influence outcome, have been included in the guideline.[37]

This could cause challenges for both research and practice. A protocol containing 10 or 12 items might have a better workability, compared to a protocol containing 24 items, increasing the change of complete implementation and high fidelity. In implementation theory, a distinction between the core of an intervention and a “flexible periphery” is sometimes made.[38] The core is supposed to be implemented “as is”, the periphery can be adapted. We believe a distinction between core and periphery based on importance of the intervention alone is not enough to focus implementation effort. That is why we used the importance-performance analysis in both chapter 3 and 6. This combines the importance with the current adherence to any given intervention, and gives hospitals the opportunity to determine their starting point and priorities for improvement, as suggested in the ERAS guideline.[37] Because our final importance-performance matrix (figure 6.1) still contains 30 “high importance” interventions, further refinement may be desirable.

Several studies are published that aimed to identify the most effective ERAS interventions. A retrospective analysis including 328 patients by Jurt et al. (2017) was designed with this purpose: assess the impact of every individual protocol element and the entire ERAS protocol. The authors concluded that laparoscopic surgery is the strongest individual predictor for positive outcomes, and that the use of nasogastric tubes, drains and epidural analgesia were associated with complications. High adherence to the complete protocol however, decreased complication rate and reduced LOS, and should be the goal (70% adherence).[39] Aarts et al. (2018) suggested that postoperative ERAS interventions have the biggest impact on outcomes.[40] Very recently, Meillat et al. (2019) stated that full ERAS compliance is necessary to improve outcomes.[41] Future research may help in

selecting which interventions from the protocol should be part of the core, and which of the flexible periphery. The data in our study were too limited to perform a mediation analysis to help answer this question.

The CP in our study was limited to perioperative care. As mentioned previously, for many patients with colorectal cancer this surgical episode is just a part of the total patient journey.[28] In a systematic review by Mitchell et al. (2015) on effectiveness of integrated care models, CPs are recognized as one of six elements across different models for integrated care.[42] This suggests that CPs are not only used for integrated care, but are perceived as important element to improve integration. A recent publication by Bergin et al. (2019) on concordance between optimal care pathways and colorectal cancer care, suggests that compliance to recommended care is challenging across the continuum of care from presentation to treatment (all modalities).[43] A potential direction for further research could be to study and improve the adherence to a CP that spans the continuum of colorectal cancer care, using similar steps as in our study: (1) Develop a set of evidence-based key interventions, (2) measure performance and provide feedback, (3) local or regional improvement teams. These local teams should include stakeholders such as general practitioners, medical oncologists and radiotherapists.

Extending our understanding of implementation and normalization of care pathways

Our process evaluation used a mixed methods convergent design, which has a number of strengths. First, the design is flexible to allow for different methods to be incorporated to answer the research questions. Second, the design provides an overall framework for conducting multiple iterative studies over multiple years. And third, it provides different types of results of the evaluation.[44] Although this PhD study had multiple phases, lasting several years, data collection was confined to two distinct periods: before and after the implementation of the CP. A future study with a more longitudinal or an interrupted time series design could give more insight in the sustained implementation or normalization of the CP.

The main construct ***contribution*** from the eNPT has received much attention in our model as shown in figure 8.1. It is also the focus of the recently developed NoMAD instrument.[45] This tool measures

the underlying mechanisms of contribution: coherence, cognitive participation, collective action, and reflexive monitoring. This 23-item questionnaire has been validated recently. The instrument has good face and construct validity, and the four mechanisms and the overall instrument had internal consistency scores (Cronbach's alpha) ranging between 0.65 and 0.89.[46] The instrument is available in a number of different languages, including English, Dutch, French and German. To our knowledge, the instrument has not yet been used in care pathway research. This provides an opportunity to quantitatively measure these four mechanisms and compare with our qualitative data.

Finally, the other constructs in our model (capability, capacity, potential) could also be measured quantitatively. A tool that focuses on the CP document, and includes some items covering ***capability***, has been developed within the Belgian-Dutch Clinical Pathway Network (www.nkp.be – internal publication). A tool that focusses on the care process rather than the CP document, is the Care Process Self Evaluation Tool (CPSET), developed by Vanhaecht et al. (2007).[47] This 29-item self-evaluation tool provides teams who want to implement (or update) a CP with feedback on five dimensions of the organization of the care process: patient focused organization, coordination of care, communication with patient and family, collaboration with primary care, and follow-up of care. This tool could be used in the audit of a care process, creating awareness about the current level of organization.[47] This could contribute to sense making.

The constructs ***capacity*** and ***potential*** focus on context.[16] Important aspects of the context could also be measured to contrast or complement our qualitative data. We have used the Model for Understanding Success In Quality (MUSIQ) [48,49] to develop our interview guide. A measurement instrument based on MUSIQ is available, but it was not yet validated at the time of the study. However, it has been used in previous CP research and shows promising results.[50] The MUSIQ instrument measures context in several domains: environment (external context), organization, quality improvement support and capacity, microsystem (the clinical team), quality improvement team and miscellaneous. With the underlying 25 factors (e.g. resource availability in quality improvement support and capacity, or motivation in microsystem) it covers the constructs of capacity and potential. Instruments to quantitatively measure context are not restricted to MUSIQ. A

systematic review by Brennan et al. (2012) found 41 potentially relevant instruments to assess (elements) of context. The authors conclude that most require further use and testing to establish the measurement properties.[51] One more recent example is the development of measures for seven constructs from the “inner setting” of the consolidated framework for Implementation Research (CFIR).[52] The CFIR is a framework of implementation influencing factors, derived from 19 previously published implementation theories and models. The CFIR consists of five major domains: characteristics of the intervention, outer setting, inner setting, characteristics of involved individuals, and implementation process.[38] The study by Fernandez et al. (2018) provides measures for five constructs from the inner setting (organizational context): culture, implementation climate, learning climate, leadership engagement, and available resources. These measures were tested for reliability and validity. The authors conclude that the measures have structural and discriminant validity, and reliability.[52]

The instruments mentioned above can be used to collect quantitative data. These could then be combined with our model, to increase our understanding of implementation and normalization of a CP, expending or corroborating our model. As may be evident from our model, hospitals form a complex organizational context with numerous and interrelated components, including policy, systems, procedures, resources, culture and behavior. Although like every model, our model is a simplified representation of reality, some caution is required in the interpretation. The elements in the model are not quantified, and the qualitative data were collected in 11 very different hospital contexts in four national contexts. Despite this prudence and the focus on implementation of a CP, we think the model visualized in figure 8.1 is not limited to CPs. It can be used for multiple quality improvement initiatives in which a team implements knowledge into action.

METHODOLOGICAL CONSIDERATIONS

Strengths and limitations of the individual studies have been discussed in the respective chapters. Here we will address a number of overall considerations. The language restriction in the literature search to English, Dutch and German could mean we may have missed some local publications. A

mixed methods study brings its own methodological considerations. First, a major strength in this convergent design is that during the in-depth interviews, both interviewers and interviewees did not know the quantitative outcomes of the implementation, minimizing the risk of bias. This is in line with the recommendation in the MRC guidance.[9] Another strength of our study is the variety in contexts, both in hospitals and countries. This provided information rich individual and hospital cases.

When dealing with a mixed methods study, the limitations of both quantitative and qualitative methods have to be taken into account.[44] For the quantitative strand, the main limitation is the uncontrolled, pre-post-test design. Uncontrolled pre-post-test studies are superior to observational studies, but secular trends or sudden changes (in context) can make it difficult to relate the observed changes to the intervention. The results of this study type should be interpreted with caution, overestimation has been described.[53] We cannot rule out that there were secular trends in our study. However, the interviews and site visits were intended to also identify influencing factors, (e.g. staff shortage, accreditation) which are discussed in chapters 5 and 7. And we think that the fact we included hospitals from four different countries helped to spread and minimize the risk that such trends influenced the data.

Due to the international character of the study, data collection was performed by several people. This could lead to quality issues in data collection. To mitigate this, we provided written instructions, a standardized data extraction form and a logbook for the local researchers. Moreover, we believe using local researchers who know where to retrieve data in the local systems, is a strength and that data collection was of good quality.

For the qualitative strand, the main challenge lies in the generalizability. Although qualitative research cannot and should not be generalized on statistical basis, generalization is possible.[54] It lies at the level of the categories, concepts, and explanation rather than in counting the number of times views or experience are discussed. Three forms of generalization can be distinguished: (1) Representational generalization, (2) inferential generalization, and (3) theoretical generalization.[54]

Representational generalization is about the extent to which the findings in the research sample can be held equally true of the parent population of the sample. The accuracy of the field work and the inclusivity of the sample are key aspects.[54] The quality of the field work has been extensively described in the methods and discussions of the preceding chapters. We are confident that the quality level of field work is high enough to make representational generalizations. The samples for the interviews and the cases in the case study were purposefully selected to include information rich cases. We included professionals directly involved in the implementation work, while the majority was also working with the CP in daily practice. However, inclusion of patients and anesthesiologists needs some reflection. In a systematic review by Bombard et al. (2018) on the strategies and effects of patient engagement in quality improvement, the authors conclude that patient engagement can improve discrete products (e.g. patient education, tools) as well as improve service delivery (care process). A matrix is presented describing levels of engagement. Patient engagement is visualized as a continuum (consultation – involvement – partnership and shared leadership), which is combined with three levels of engagement (direct care – organizational design and governance – policy making).[55] The policy making level could be considered the “study level” in this PhD thesis. An important activity on this level was the development of the model CP. We did not involve patients, because we used the well-established ERAS protocol as basis, and the focus of the study was on how teams work with this protocol as part of our intervention. While developing the model CP, we observed that indicators covering the “service domain” of the clinical pathway compass were almost lacking in the studies included in chapter 2. Quality of life and patient satisfaction were both only used in one study.

The organizational design level deals with the engagement of patients in the local projects. In several of the hospitals patients were engaged, but this was not systematic (e.g. patient involvement in the improvement team, consultation). We opted to let the local teams decide on patient engagement in the project as part of their implementation plan. This means we cannot make a judgement on the effect of patient consultation or involvement with regards to implementation. Moreover, Bombard et al. suggest that the level of engagement affects the outcome: process improvements are achieved

by high-level engagement (co-design, partnership).[55] This level of engagement was observed in only one hospital.

Regarding engagement at the direct care level, we observed that patient information (both pre and postoperative) improved after implementing the CP (consultation). The role of patient involvement in perioperative care has been reported as a facilitator in ERAS protocol adherence previously. A well informed patient knows what to expect and can play an active role in his or her care process.[56] This was also echoed in a number of the interviews in our study (involvement).

Although the focus of our study was the organization of perioperative care including follow-up, and not just directly focused at the surgery, not including anesthesiologists in our sample could be a limitation, because of their heavy involvement in ERAS. However, we know from interviews with other professionals and from the project notes that anesthesiologists were involved in the local projects. Themes such as collaboration and motivation were discussed in interviews. Still, the inclusivity of our sample is something to take into account with respect to representational generalizability.

Inferential generalization deals with the question if the findings from our study can be generalized to other settings or contexts. The main issue here is the degree to which the research context is congruent with the context where the findings are generalized to (transferability). To facilitate this, the qualitative researcher provides ample information on the research context and sample, usually by providing a “thick description”.[54] This is what we have done in our study. We provided a thick description per theme derived from the interviews, case descriptions of the included cases, and context information on both the individual interviewees as well as the hospitals. We believe that with this information, readers of our study can make a judgement on the inferential generalizability: “Are the findings transferable to my context?”

Theoretical generalization, finally, focusses on more broad application of study findings in the form of ideas, theoretical propositions and principles. Qualitative studies can contribute to theory by providing explanations for beliefs, experiences, or behavior, or by providing evidence of social

process and structures underlying theories.[54] This is what we have tried to accomplish by using eNPT as theoretical framework, and combining the insights of the different studies in our model. This resulted in a refinement of eNPT focused on CP implementation. The relevance of this refinement should be established by further empirical research, whether qualitative or quantitative (using instruments as discussed above).

OVERALL CONCLUSIONS

We conclude that this international quality improvement initiative for patients undergoing surgery for colorectal cancer was successful in reducing the mean length of stay with almost two days. Mortality, re-intervention rate and readmission rate did not change. Adherence to evidence-based recommended care improved overall to a median of 62%. There is great variability in improvements achieved by the hospitals in the study, both in outcomes as well as adherence rate. The achieved improvements are statistically significant, but can be considered modest. The length of stay in our hospitals is relatively long. A possible delay between the time patients meet discharge criteria and actual discharge could contribute to this. The overall protocol adherence is below the target adherence of 70% as described in literature.

The implementation and normalization of a care pathway asks for the *contribution* of multiple involved professionals, including physicians, to achieve the desired outcomes. They must understand and appreciate the content, goals and related standardization of the care pathway, and play an active role in the improvement team. The team selects the appropriate implementation activities, focused on competence, behavior, or workplace, including the use of monitoring and feedback. The goal is to reach continuous fidelity. A practical care pathway with a clear evidence base which is workable and can be integrated in systems, processes, protocols, procedures and habits, improves the *capability*. The context in which the implementation takes place provides the *potential* to follow care pathway methodology. Support from higher management, alignment of care pathway development with hospital and external strategy, and intrinsic motivation, joy in work, and shared (inter)professional goals facilitate the contribution. The *capacity* to cooperate and to

coordinate actions to implement the pathway depend on the availability of resources, including a CP facilitator and a clinical data system, the improvement team's experience, collaboration and clinical leadership, and individual experience and expertise. The constructs contribution, capability, potential and capacity are connected reciprocally, but it is contribution that is connected to outcomes: success of care pathway depends on the activities people do to implement it.

RECOMMENDATIONS FOR PRACTICE AND RESEARCH

Recommendations for colorectal cancer pathway practice

1. Review discharge criteria in relation to ERAS criteria – we observed a delay in the time patients meet certain physical parameters (mobility, bowel movement, normal diet) and the time patients meet discharge criteria. We recommend that multidisciplinary teams in hospitals performing CRC surgery review their discharge criteria to make sure there are no unnecessary delays built in the care pathway.
2. View ERAS as "all or nothing approach" – although there is discussion about the relative value of certain protocol elements, we advise to strive for high adherence rates to the complete ERAS pathway. Plotting the own data in an importance-performance matrix can help to identify priority areas. Until the international consensus on key elements provides different insights in which interventions are core, and which are "flexible", the importance-performance matrix can act as guiding principle.

Recommendations for care pathway implementation

3. Invest in contribution – the prolonged contribution of multiple professionals is paramount for care pathway implementation. Create awareness and facilitate sense making by telling the right story: care pathways are a tool and process, including monitoring and feedback, to improve organization of care processes. Organize teams to form "communities of practice" around the care pathway population. Monitor and give feedback on fidelity to the new standard as defined in the CP.

4. Decision latitude more important than resources – obviously, providing resources, time, and training and facilitation in CP methodology will help in the implementation of care pathways. However, resources are scarce and time is limited in health care. Care pathways should be designed so that they facilitate decision making, and thereby create decision latitude (and in many cases also: time), which mitigates the stress of high demand jobs.
5. Invest in clinical data management systems – to facilitate reflexive monitoring, key component of contribution, correct and timely data is necessary. We recommend to invest not only in a data management system, but in the accompanying processes as well, to support clinicians and management in reflexive monitoring because of its effect on motivation and goal setting.

Recommendations for future research

6. Continue searching for key elements of ERAS – we recommend that clinical researchers will continue to study the possibility of determining a core set of interventions, supplemented with flexible interventions. We believe it is easier to achieve and sustain high adherence to a relative small set of interventions than to a large number of interventions. A smaller set of key elements could also help in sense making. However, until there is a more clear understanding of this issue, overall protocol adherence should be the goal (see recommendation 2). We propose a prospective study with a larger sample but from a smaller number of centers than in our study, using mediation analysis, to establish the effect and interactions of the different protocol elements.
7. Interrupted time series or longitudinal study – we recommend to set up a study with a more longitudinal or an interrupted time series design to provide more insight in the sustained implementation and normalization of care pathways.
8. Relevance of our implementation model – we suggest further empirical research, either qualitative or quantitative, to establish the relevance of our implementation model as presented in figure 8.1. For the quantitative research, various tools as discussed could be used: NoMAD, CPSET, MUSIQ.

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SUMMARY – SAMENVATTING

SUMMARY

There is a challenge in translating research knowledge into everyday practice in healthcare. Adherence to evidence-based recommended care is relatively low and highly variable. This also applies to patients with colorectal cancer. Colorectal cancer has the third highest incidence of all cancer types. Surgical resection of the tumor is the number one treatment option. The perioperative care for patients undergoing colorectal cancer surgery has been standardized by using so called Enhanced Recovery Protocols. Adherence to these protocols proves to be difficult. Adherence rates as low as 45% have been reported. Using care pathway methodology can be an effective way to increase adherence to evidence-based recommendation. A care pathway combines evidence-based key interventions, feedback on the actual care process, with a strategy for quality improvement. The aim of this PhD study is twofold: (1) To perform an international quality of care improvement initiative for patients undergoing surgery for colorectal cancer, and (2) to evaluate the implementation process of a care pathway for colorectal cancer surgery by performing a process evaluation.

In the first phase of the study, a literature review was performed to develop a model care pathway for the perioperative care of patients with colorectal cancer. A systematic literature search was conducted in three databases, and 15 studies were included. This review identified 33 key interventions to incorporate in the model pathway. We observed considerable variation in both the number (nine to 20) and content of the interventions used in the included studies. A total of 25 indicators was found that are used to measure the effect of enhanced recovery protocols. The clinical content was summarized in the model pathway which served as basis for teams to develop or adapt their own pathway.

Next, the variation in perioperative care was studied in 12 European hospitals (Belgium, France, Germany, the Netherlands). Based on the model pathway a retrospective patient record analysis was performed, including 20 consecutive patients per hospital, to assess outcomes (length of stay, morbidity), protocol adherence (the percentage of individual key interventions from the model pathway received by a patient), and to establish a relationship between importance of the intervention (level of evidence) and the performance (adherence). In total, 230 patients were

included in the study. An overall median adherence of 44% was measured, but with high variability between and within the hospitals. Only six interventions scored “important and high performant” in the importance-performance analysis.

The third phase of the study consisted of the intervention. Local quality improvement teams received feedback on their current care process based on the measurement in phase 2 in the form of: (1) a national feedback session organized within each country, (2) a local feedback session within each hospital, and (3) a detailed feedback report to supplement the sessions. The teams then received the model care pathway. It was delivered and explained on-site in all participating centers to the quality improvement teams, as support for their strategy for change.

In phase four, the implementation of the care pathway was evaluated. A qualitative exploration of the implementation process took place. The MRC guidance on process evaluations was used as framework. In-depth interviews with 32 direct involved healthcare professionals were conducted before quantitative results were known. We used the Framework approach to analyze the data. Based on the perceived outcomes, respondents were divided in two subgroups: those perceiving positive outcomes and those perceiving no effect. For each group the factors explaining the implementation process were mapped in the categories from the MRC guidance: intervention (the evidence base of the care pathway), context (prolonged involvement of multiple disciplines, availability of a clinical data system), implementation (several implementation activities, focusing on competence, behavior, or workplace), and mechanisms (teamwork and collaboration). The use of feedback is perceived as an important implementation activity used for goal-setting and motivation.

Parallel to the qualitative evaluation, a quantitative effect evaluation was performed. In this post-implementation measurement, 10 hospitals participated. We only included patients from hospitals that participated in both pre- and post-implementation measurement. Again, a retrospective patient record analysis was performed, using the same methods as in phase two. In total, 381 patients were included. Length of stay significantly decreased from 12.6 to 10.7 days ($p=0.0230$), while mortality, readmission and re-intervention rates did not change. Overall protocol adherence improved from 56 to 62% ($p<0.00001$). Across hospitals, change in overall protocol adherence ranged from a 13%

decrease to a 22% increase. Only in 25% of patients a protocol adherence of ≥70% was achieved, suggesting a large proportion of patients is at risk for underuse.

In the fifth and final phase, the quantitative and qualitative data were combined. We used a comparative mixed methods multiple case study design. The aim of this study was to evaluate the implementation of a care pathway from a quantitative and qualitative perspective simultaneously. From the 10 hospitals remaining in phase four, we developed a ranking based on improvements in protocol adherence and length of stay. From this ranking we selected the highest and lowest performing cases, and described them from a quantitative and qualitative perspective. The extended Normalization Process Theory was used as theoretical framework. Two hospitals were identified as high performance cases, and three as low performance cases. Factors that could explain the differences in pre- and post-implementation performance were: the level of integration of the care pathway, the experience and support of the improvement team in care pathway methodology, the motivation of the team, shared goals, level of management support and alignment of care pathway development and hospital strategy, and finally the cognitive participation of relevant disciplines, most noticeably the physician.

Overall, we concluded that this international quality improvement initiative was successful in reducing mean length of stay with almost two days. Protocol adherence improved overall to a median of 62%, with great variability between the hospitals. These outcomes are statistically significant, but can be considered modest.

We propose a model for the implementation of care pathways. The implementation and normalization of care pathways asks for the *contribution* of multiple involved professionals at organizational, team and individual level. Both the *capability* of the care pathway as well as the context, described in terms of *potential* (to follow care pathway methodology) and *capacity* (to cooperate and coordinate actions) influence the implementation and vice versa. But it is contribution that leads to *outcomes*: success of care pathway implementation depends on the activities people do to implement it.

SAMENVATTING

Er bestaat een uitdaging in het toepassen van wetenschappelijke inzichten in de dagelijkse praktijk van de gezondheidszorg. De naleving van wetenschappelijk onderbouwde aanbevolen zorg is relatief laag en kent veel variatie. Dit geldt ook voor colorectale kanker zorg. Colorectale kanker heeft de derde incidentie van alle typen kanker. Chirurgische verwijdering van de tumor is de primaire behandeloptie. De perioperatieve zorg voor patiënten met een colorectale tumor is gestandaardiseerd in zogenaamde Enhanced Recovery Protocols – versneld herstel protocollen. Naleving van deze protocollen blijkt ingewikkeld. Een protocolnaleving van 45% en hoger is beschreven. Het gebruik van de zorgpad methodiek kan een effectieve manier zijn om naleving van aanbevolen zorg te verhogen. Een zorgpad combineert evidence-based zorg, feedback op het huidige zorgproces met een strategie voor kwaliteitsverbetering. Het doel van dit onderzoek is tweeledig: (1) Het uitvoeren van een internationaal kwaliteitsverbeteringsinitiatief voor patiënten met colorectale kanker die een operatie ondergaan, en (2) het evalueren van het implementatieproces van een zorgpad voor colorectale tumor chirurgie door het uitvoeren van een proces evaluatie.

De eerste fase van het onderzoek was een literatuurstudie om een model zorgpad voor de perioperatieve zorg voor patiënten met colorectale kanker op te stellen. Een systematische literatuur review in drie elektronische databases werd uitgevoerd, waaruit 15 studies werden geïncludeerd. Er werden 33 sleutelinterventies gevonden die in het model zorgpad konden worden opgenomen. Er was veel variatie in zowel het aantal (negen tot 20) als de inhoud van de interventies die in de geïncludeerde studies werden gebruikt. In totaal werden 25 indicatoren gevonden om het effect van enhanced recovery protocollen te meten. Deze klinische inhoud werd samengevat in een model zorgpad dat als basis diende voor de teams om hun eigen zorgpad te ontwikkelen of aan te passen.

Vervolgens werd de variatie in perioperatieve zorg in 12 ziekenhuizen in België, Duitsland, Frankrijk, Nederland bestudeerd. Op basis van het model zorgpad werd een retrospectieve dossieranalyse van 20 opeenvolgende patiënten uitgevoerd, om uitkomsten (verblijfsduur, morbiditeit), protocolnaleving (het percentage sleutelinterventies uit het model zorgpad dat werd toegepast bij elke patiënt) en om de relatie tussen belang van de interventie (mate van bewijs) en prestatie

(naleving) vast te stellen. In totaal werden 230 patiënten geïncludeerd. Een totale protocolnaleving van 44% werd gemeten, met grote variatie tussen en binnen de ziekenhuizen. Slechts zes interventies scoorden “belangrijk en hoge naleving”.

De derde fase van het onderzoek bestond uit de interventie. Lokale verbeterteams ontvingen feedback op hun huidige prestaties, gebaseerd op de metingen uit fase 2, in de vorm van: (1) een landelijke feedback sessie, (2) een lokale feedback sessie per ziekenhuis en (3) een gedetailleerd feedback rapport als aanvulling op de sessies. Vervolgens ontvingen de teams het model zorgpad. Dit werd aangeleverd en toegelicht tijdens een verbetersessie in elk ziekenhuis, als ondersteuning van de verbeterstrategie.

In fase 4 werd de implementatie van het zorgpad geëvalueerd met een kwalitatief onderzoek. De richtlijn Procesevaluaties van de MRC werd als leidraad gebruikt. Dataverzameling vond plaats via diepte-interviews met 32 direct betrokken professionals. De interviews vonden plaats voordat de kwantitatieve uitkomsten bekend waren. Gebaseerd op ervaren uitkomsten van de implementatie werden de geïnterviewden in twee groepen gedeeld: zij die positieve uitkomsten ervaarden en zij die geen effect ervaarden. Voor beide groepen werden de factoren die het implementatieproces kunnen verklaren, geplaatst in de categorieën van de MRC richtlijn: interventie (wetenschappelijke basis van het zorgpad), context (langdurige betrokkenheid van meerdere disciplines, beschikbaarheid van een klinisch datasysteem), implementatie (diverse implementatieactiviteiten, gericht op competentie, gedrag, en werkomgeving) en mechanismen (teamwork en samenwerking). Gebruik van feedback werd gezien als belangrijke implementatieactiviteit, voor het stellen van doelen en ter motivatie.

Parallel aan de kwalitatieve evaluatie werd een kwantitatieve uitkomstevaluatie uitgevoerd. Alleen patiënten uit de 10 ziekenhuizen die zowel in de pre- als post-implementatie meting participeerden, werden geïncludeerd. Opnieuw werd een retrospectieve dossieranalyse uitgevoerd met dezelfde methode als in fase twee. In totaal werden 381 patiënten geïncludeerd. Verblijfsduur daalde van 12.6 naar 10.7 dagen ($p=0.0230$), terwijl sterfte, en het percentage heropnames en heroperaties gelijk bleven. De totale protocolnaleving steeg van 56 naar 62% ($p<0.00001$). De verandering in

protocolnaleving varieerde tussen de ziekenhuizen van 13% afname tot 22% toename. Slechts bij 25% van de patiënten werd een protocolnaleving van of ≥70% bereikt. Dit suggereert dat een grote groep patiënten het risico loopt op ondergebruik van zorg.

In de vijfde en laatste fase werd een vergelijkende mixed methods case studie uitgevoerd om de implementatie van het zorgpad gelijktijdig vanuit een kwantitatief en kwalitatief perspectief te evalueren. Van de 10 ziekenhuizen uit fase 4 werd een rangorde gemaakt op basis van verandering in protocolnaleving en verblijfsduur. De hoogst en laagst presterende werden cases geselecteerd en beschreven vanuit kwantitatief en kwalitatief perspectief. De extended Normalization Process Theory vormde het theoretisch kader. Twee ziekenhuizen werden geïdentificeerd als hoog presterende cases en drie als laag presterende cases. Factoren die het verschil in pre- en post-implementatie prestaties kunnen verklaren zijn: het niveau van integratie van het zorgpad, de ervaring en ondersteuning van het verbeterteam met de zorgpad methodiek, de motivatie van het team, gedeelde doelstellingen, mate van steun vanuit management en overeenstemming van zorgpad methodiek met de strategie van het ziekenhuis, en tenslotte de cognitieve betrokkenheid van de relevante disciplines, met name de arts.

Afsluitend concluderen we dat dit internationale kwaliteitsverbeteringsinitiatief de verblijfsduur met bijna twee dagen heeft gereduceerd. Protocolnaleving steeg van 56 naar 62%, met grote variatie tussen de ziekenhuizen. Deze uitkomsten zijn statistisch significant, maar bescheiden.

We stellen een implementatiemodel voor zorgpaden voor. De implementatie en normalisatie van zorgpaden vraagt om de *bijdrage* van meerdere betrokken disciplines op organisatie, team en individueel niveau. Zowel de *geschiktheid* van het zorgpad als de context, beschreven in termen van *potentie* (om de zorgpad methodiek te volgen) en *capaciteit* (om samen te werken en acties te coördineren) beïnvloeden de implementatie en vice versa. Maar, het is bijdrage die tot *uitkomsten* leidt: het succes van zorgpad implementatie hangt af van de activiteiten die mensen uitvoeren om het te implementeren.

CURRICULUM VITAE – LIST OF PUBLICATIONS

ACKNOWLEDGEMENTS, PERSONAL CONTRIBUTIONS, AND CONFLICT OF INTEREST STATEMENTS

CURRICULUM VITAE

Ruben van Zelm (21-4-1970, Alkmaar, the Netherlands) obtained a bachelor's degree in nursing from the Hogeschool Alkmaar in 1992, and a master's degree in health sciences from Maastricht University in 1994. Following graduation, Ruben worked in several hospitals as nurse, researcher and educator, with a focus on quality of care. In 2000, Ruben was the care pathway facilitator in the OLVG Hospital, Amsterdam. A fruitful cooperation with professor Walter Sermeus and professor Kris Vanhaecht started when the OLVG Hospital joined the Belgian-Dutch Clinical Pathway Network, a networking and training initiative on care pathway methodology from the former KU Leuven Center for Health Services and Nursing Research.

In 2001, Ruben joined the former Dutch Institute for Healthcare Improvement CBO, and became a facilitator of national evidence-based guideline development groups. Guidelines in which Ruben was involved include prevention of accidental falls, postoperative pain management, and perioperative nutrition management. Initiated by Ruben, the Institute became the Dutch partner to support the Belgian-Dutch Clinical Pathway Network in 2003. Ruben had the role of project coordinator and trainer, and is until the present day one of the trainers in the Network's training activities.

From 2007 Ruben joined Q-Consult zorg, a Dutch consultancy company in healthcare. His focus is on quality and process improvement, including care pathway methodology, Lean management, and patient flow. Since 2015 he started working part-time at the University of Applied Science (UAS) Utrecht, as senior lecturer in the master's program integrated care design. He teaches implementation management and quality and safety in healthcare, and coordinates the scientific tract, one of the three programs curricular tracts. Over the past years, Ruben's position at the UAS Utrecht has increased to nearly full-time. He still holds a part-time position at Q-Consult zorg.

Ruben is secretary of the European Pathway Association (E-P-A), a not-for-profit international association to promote care pathway methodology. To date, the E-P-A has more than 1.500 members in 75 countries, and coordinated several research projects, hosted three scientific conferences and seven masterclasses on care pathways and organization of care processes.

Ruben started his PhD in January 2016 under supervision of professor Walter Sermeus and professor Kris Vanhaecht. His research evaluates the implementation process of an evidence-based care pathway for colorectal cancer care in Belgium, France, Germany and the Netherlands.

Ruben is married to Carolien Rijpkema. They live in Woerden, the Netherlands, with their two sons, Job and Oscar.

A full and updated description is available at: www.linkedin.com/in/rubenvanzelm/

PUBLISHED PAPERS

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- van Zelm R, Janssen I, Vanhaecht K, de Buck van Overstraeten A, Panella M, Sermeus W, Coeckelberghs E (2018) Development of a model care pathway for adults undergoing colorectal cancer surgery: Evidence-based key interventions and indicators. Journal of evaluation in clinical practice 24 (1):232-239. doi:10.1111/jep.12700
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ACKNOWLEDGEMENTS

Chapter 3 – We thank the local coordinators and improvement teams in the participating hospitals:

Belgium: AZ Groeninge, Kortrijk (Dr. D. Devriendt / Mrs. K. Vandendriessche & Mrs. D. Verhelst), Institute Bordet, Brussels (Dr. G. Liberale), University Hospital Leuven (Dr. A. de Buck van Overstraete / Mr. D. Michiels & Mr. K. Op de Beeck).

France: American Hospital of Paris / Institute Hospitalier Franco-Britannique, Paris / Clinique Hartmann – Ambroise Parre, Paris (Dr. A. Toledano / Mr. P. Ihout).

Germany: Kreisklinikum Ebersberg (Dr. D. Plecity), Städtischen Klinikum Frankfurt Höechst (Dr. M. Ferschke & dr. J. Reusch), Klinikum St. Georg, Leipzig (Prof. Dr. A. Weimann / dr. M. Braunert / dr. M. Wobith).

The Netherlands: Groene Hart Hospital, Gouda (Dr. L. Tseng / Mrs. J. Verkerk), Onze Lieve Vrouwe Hospital, Amsterdam (Mrs. H. Hiemstra), Wilhelmina Hospital Assen (Dr. W. Bleeker / Mrs. G. Boekeloo & Mrs. H Bouwman).

Chapter 5 – We thank the participating hospitals and professionals who allowed us to collect data for this study. We thank Anneke de Jong, PhD, senior lecturer University of Applied Science Utrecht, for her valuable assistance in the quality control of the sorting and indexing of data.

Chapter 6 & 7 – We thank the local coordinators and improvement teams in the participating hospitals:

Belgium: AZ Groeninge, Kortrijk (Dr. B. Van Geluwe / K. Vandendriessche / D. Verhelst), Institute Bordet, Brussels (Dr. G. Liberale / S. Timmermans), University Hospital Leuven (Prof. Dr. A. D'Hoore / Prof. Dr. A. Wolthuis / D. Michiels / K. Op de Beeck / I. Vandessel).

France: American Hospital of Paris (Dr. J. Pitre / P. Broumalt / P. Ihout / J. Tuall), Institute Hospitalier Franco-Britannique, Paris (Dr. S. Houhou / P. Ihout), Clinique Hartmann – Ambroise Parre, Paris (Dr. P. Wintringer / P. Ihout).

Germany: Kreisklinikum Ebersberg (Dr. D. Plecity / I. Schwarz), Klinikum St. Georg, Leipzig (Prof. Dr. A. Weimann / Dr. M. Braunert / Dr. M. Wobith).

The Netherlands: Onze Lieve Vrouwe Hospital, Amsterdam (H. Hiemstra / E. Gooskens), Wilhelmina Hospital Assen (Dr. W. Bleeker / G. Boekeloo / H. Bouwman).

PERSONAL CONTRIBUTIONS

Chapter 2 – R. van Zelm was a major contributor to the conception an design of the study, selected, analyzed and summarized the studies, and drafted the manuscript. I. Janssen performed the literature search and selected the studies. K. Vanhaecht made substantial contributions to the conception and design of the study, supervised the review and commented on the draft. A. de Buck van Overstraeten supervised the review and commented on the draft. M. Panella and W. Sermeus made substantial contributions to the conception and design of the study and commented on the final draft. E. Coeckelberghs analyzed and summarized the studies, and prepared the draft.

Chapter 3* – R. van Zelm made substantial contributions to conception and design of the study, acquisition, analysis and interpretation of data and drafted the manuscript. E. Coeckelberghs contributed substantially to acquisition, analysis and interpretation of data, and was involved in drafting the manuscript. W. Sermeus was a major contributor to interpretation of data, and to conception and design of the study. A. de Buck van Overstraeten and A. Weimann made substantial contributions to interpretation of data and commented on the draft. D. Seys was a major contributor in analysis and interpretation of data and commented on the draft. M. Panella made substantial contributions to conception and design of the study and commented on the draft. K. Vanhaecht made substantial contributions to conception and design of the study, analysis and interpretation of the data, and was involved in drafting the manuscript.

**Van Zelm & Coeckelberghs contributed equally*

Chapter 4 – R. van Zelm made substantial contributions to conception and design of the study protocol, acquisition, analysis and interpretation of data and drafted the manuscript. E. Coeckelberghs was a major contributor to acquisition, analysis and interpretation of data, and was involved in drafting the manuscript. W. Sermeus was a major contributor to interpretation of data,

and to conception and design of the study. D. Aeyels was a major contributor in acquisition of data and commented on the draft. M. Panella made substantial contributions to conception and design of the study and commented on the draft. K. Vanhaecht made substantial contributions to conception and design of the study, analysis and interpretation of the data, and was involved in drafting the manuscript.

Chapter 5 – R. van Zelm was a major contributor to conception and design of the study, acquisition, analysis and interpretation of data and drafted the manuscript. E. Coeckelberghs was a major contributor to acquisition, analysis and interpretation of data, and was involved in drafting the manuscript. D. Aeyels made substantial contributions to acquisition, analysis and interpretation of data. W. Sermeus was a major contributor to interpretation of data, and to conception and design of the study. A. Wolthuis made substantial contributions to interpretation of data. M. Panella made substantial contributions to conception and design of the study. K. Vanhaecht made substantial contributions to conception and design of the study, analysis and interpretation of the data, and was involved in drafting the manuscript.

Chapter 6 – R. van Zelm made substantial contributions to conception and design of the study, acquisition, analysis and interpretation of data and drafted the manuscript. E. Coeckelberghs was a major contributor to acquisition, analysis and interpretation of data, and was involved in drafting the manuscript. W. Sermeus was a major contributor to conception and design of the study, and to interpretation of data. A. Wolthuis made substantial contributions to interpretation of data. L. Bruyneel made substantial contributions to analysis and interpretation of data. M. Panella made substantial contributions to conception and design of the study. K. Vanhaecht made substantial contributions to conception and design of the study, analysis and interpretation of the data, and was involved in drafting the manuscript. All authors read, critically revised for important intellectual content, and approved the manuscript.

Chapter 7 – R. van Zelm was a major contributor to conception and design of the study, acquisition, analysis and interpretation of data and drafted the manuscript. E. Coeckelberghs made substantial contributions to acquisition, analysis and interpretation of data, and was involved in drafting the

manuscript. W. Sermeus was a major contributor to conception and design of the study, and to interpretation of data. A. Wolthuis made substantial contributions to interpretation of data. L. Bruyneel made substantial contributions to analysis and interpretation of data. M. Panella made substantial contributions to conception and design of the study. K. Vanhaecht made substantial contributions to conception and design of the study, analysis and interpretation of the data, and was involved in drafting the manuscript.

CONFLICT OF INTEREST STATEMENTS

Funding – Research made possible by an unconditional, unrestricted educational grant by Baxter SA, Baxter Belgium, Baxter France, Baxter Germany and Baxter the Netherlands to the European Pathway Association. Baxter had no role in the study design, data collection, data analysis, interpretation of results, or manuscript creation.

van Zelm, Ruben – declared no conflict of interests

Aeyels, Daan – declared no conflict of interests

Bruyneel, Luk – declared no conflict of interests

Coeckelberghs, Ellen – declared no conflict of interests

de Buck van Overstraeten, Anthony – declared no conflict of interests

Janssen, Ingrid – declared no conflict of interests

Panella, Massimiliano – declared no conflict of interests

Sermeus, Walter – declared no conflict of interests

Seys, Deborah – declared no conflict of interests

Vanhaecht, Kris – declared no conflict of interests

Weimann, Arved – has received lecturer's honoraria from Baxter, B.Braun, Berlin-Chemie, Fresenius Gabi, Lilly, Medtronic, Nestlé, Nutricia, and has received research grants from Baxter and Danone

Wolthuis, Albert – declared no conflict of interest

Maier's law

E = Q x A

Effectiveness = Quality x Acceptance

Norman Maier, 1963


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