The added value of oncological care pathways

Data supported with health care professionals'
and patients' perspective

Jolanda van Hoeve

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and patients' perspective**

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ADDED VALUE OF ONCOLOGICAL CARE PATHWAYS

**DATA SUPPORTED WITH HEALTH CARE PROFESSIONALS'
AND PATIENTS' PERSPECTIVE**

PROEFSCHRIFT

Ter verkrijging van
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CHAPTER 1

Introduction

INTRODUCTION

Cancer incidence and mortality are rapidly growing worldwide¹. Cancer is the second leading cause of death globally, accounting for an estimated 9.6 million deaths, or one in six deaths, in 2018. The main reasons of the increased incidence of cancer are both aging and growth of the population, as well as changes in the prevalence and distribution of the main risk factors for cancer, several of which are associated with socioeconomic development¹. Because cancer care is complex it requires collaboration among care professionals with complementary skills, who work together to share the latest evidence, pool their expertise and exchange information through a regular flow of communication².

Professionals working in oncological care face numerous challenges nowadays. Patient volumes are increasing, demographics are shifting to older and more medically and socially complex patients, and financial limitations and administrative burden are increasing. Moreover, as treatment options for tumor sites expand, treatment plans are becoming increasingly multidisciplinary and complex whereby the involvement of multiple hospitals is necessary³.

The complexity of cancer care continually increases with new and expensive drugs and technologies, demanding for clinical expertise, budget and close monitoring of the clinical benefits^{4,5,6}. On the one hand advances in science and technology have improved the ability of the health care system to treat diseases, on the other hand the amount of new discoveries demand the system to be capable of effectively generate and manage knowledge and apply it to regular care⁵. To be able to deliver high-quality health care and meet all the domains: effectiveness, safety, timeliness, efficiency, equitably, and patient-centeredness care it might be needed to concentrate certain care in a limited number of organizations⁷.

Care pathways are used worldwide in almost all management models and settings as methods for the patient-care management of a well-defined group of patients during a well-defined period of time⁸. They are based on guidelines, best practices and patient expectations by facilitating communication, coordinating roles and sequencing the activities of the multidisciplinary care team, patients and their relatives; by documenting, monitoring and evaluating variances; and by providing the necessary resources and outcomes⁸. Furthermore, care pathways may serve as useful and evidence-based tools to reduce variations in clinical practice and improve quality and outcomes of health care interventions. Pathways can provide patients with clear expectations of their care, provide a means of measuring patient's progress, promote teamwork on a multidisciplinary team, facilitate the use of guidelines, and may act as a basis for a payment system⁹. In addition, multidisciplinary team (MDT) meetings are considered best practice in the management and decision-making for cancer patients. MDT meetings mainly consists of surgeons, medical oncologists, organ specialists, radiologists, radiation oncologist pathologists and in some cases specialized oncology nurses and psychologists. The aim of MDT meetings is to achieve evidence-based, collaborative and multidisciplinary decision-making for cancer treatment and patient management¹⁰.

However, pathways are not always well defined and many terms are used to define pathways, leading to confusion. The following terms were most used in literature: critical pathway, clinical pathway, care pathway, integrated care pathway, transmurial care pathway and care map^{8,11}. Care pathways were first developed in the 1980s in the United States and the United Kingdom. In the United States pathways were mainly used as a framework for balancing costs and quality, as a response to the escalating costs of health care. During the 1990s, pathways in the United Kingdom were considered as a way of achieving a continuum of care across care settings. Somewhat later, nursing care pathways were developed, incorporating all aspects of patients care, ranging from medical care, psychosocial support, to palliative care and including prospective plans for all disciplines involved in patient care^{8,12}. Based on all the developments of pathways in health care the main aim of pathways can be formulated as: to improve the multidisciplinary quality of care, reduce risks, increase patient satisfaction and increase the efficiency in the use of resources⁸.

In order to achieve these targeted effects of a pathway adequate implementation of pathways is obliged. This demands consideration of facilitators and barriers, planning, and incorporation of the pathway directly into clinical practice with full engagement among clinical and management staff⁹. However, evidence on the most optimal process of pathway implementation is limited and variation in how organizations deal with the implementation process is large. As with any quality improvement intervention, implementation and evaluation are a continuous process, covering evaluation, monitoring, and the incorporation of results of the pathway into ongoing quality improvement. Therefore, this process needs to involve all those taking part in the care process, including management⁹.

Although the use of care pathways seems rather new for health services, the thoughts and theories on this already exist for decades within the industry. In the 1950s, the critical path method (CPM) became popular¹³. In the 1980s, the company Motorola has further elaborated statistical approach from CPM and the Program and Evaluation Technique and Review into Six Sigma: a quality management approach to improve operational performances of an organization by identifying weaknesses and improving processes within the organization¹⁴. In the 1990s, the concept of business process redesign (BPR) came up. This defined a production process or business process as: the logic organization of people, materials, energy, equipment and procedures into work activities designed to produce a specified end result (work product)^{15,16}. The concept of care pathways can be linked to the above-mentioned management theories¹⁷. For example: the reduction of the cost of the production process through standardization, by avoiding employee waiting times and underutilization of equipment, and by avoiding duplication, which is a characteristic of the CPM, Lean Six Sigma, BPR and the Theory of Constraints (TOC) is linked to care pathways. Furthermore, shortening the duration of the production process by reducing waiting time between divisions of the same organization, and by simultaneously running sub-processes that take place analogously is linked to the management strategies BPR, and TOC and reducing the risk of errors is linked to Lean Six Sigma.

From 1970 onwards, a focus was developing in the health care research on the statistical and business-like approach to health care processes or Health Operations Management¹⁷. Health Operations Management aims to help health care management and working professionals find ways to improve the delivery of health care and make processes as efficient and effective as possible, with its complex web of patients, providers, reimbursement systems, physician relations, workforce challenges, and intensive government regulation¹⁸.

Health Operations Management is a modern framework for health care planning and control that integrates all managerial areas in health care delivery operations and all hierarchical levels of control, to ensure completeness and coherence of responsibilities for every managerial area. Furthermore, Health Operations Management is concerned with the optimization of care processes, which is achieved through redesigning or improving their planning and implementation. Because local optimization without adequate coordination leads to a sub-optimal situation throughout the chain, coordination within the chain is of great importance. Health Operations Management can be used to structure the various planning and control functions and their interaction. It is applicable to an individual department, an entire health care organization, and to a complete supply chain of cure and care providers¹⁹. Care pathways in Dutch health services were developed based on the above-mentioned new paradigms, with a constant focus on the core process of the organization. In the course of time, a variety of formats and concepts were developed, the creation of multidisciplinary guidelines provided a huge boost for the design of care pathways¹⁷.

Nowadays, oncology networks are used, integrating multiple hospitals and health care organizations. Care pathways can have a facilitating role in these oncology networks to formalize regional agreements overarching the walls of the individual organizations. In the United States the goal of forming oncology networks for academic centers was mainly to acquire community practices to expand their clinical care and research footprint²⁰. Little evidence is available about the application of care pathways within oncology networks. However, the process of integration in the United States seems to facilitate the ability to standardize cancer practice and provides a platform for quality improvement. In the Netherlands, in oncological care more and more networks have been formed between hospitals in order to jointly take responsibility for cancer care. For more than ten years oncology networks exist for high-complex low-volume tumor types, which can be enforced by the trend of concentration²¹. An oncology network can be of interest for health care professionals to keep close contact, to organize (regional) MDT meetings and to make patient' referrals efficient. In addition, networks also have been formed for low-complex high-volume tumor types, which shows an awareness of the need for working together within networks to facilitate highly qualified cancer care²¹. For these tumor types regional care pathways can be helpful to standardize care as the number of patients are sufficient to deliver care and treatment in each hospital. However, exchange of information with other centers will be necessary in case patients are participating in clinical trials.

Multiple motives can lead to the initiative to organize care within a network. Firstly, networks aim to jointly meet the (volume) norms, and retain care and treatment within a specific region based on agreements, for example about the division of care and treatment. Secondly, within networks the connection is being sought with primary, secondary and tertiary health care. This connection is focused on providing the best quality of care to patients making use of the capacity of participants to offer the best possible care on the right moment and close to the patient. Oncology networks can be very divers in the number of participating hospitals, the inclusion of an academic center, historical connections through educational programs, the tumor type(s) on which the network is focusing, and current volume standards²¹.

Care pathways can provide patients with clear expectations of their care, provide a means of measuring patients' progress, promote teamwork on a multidisciplinary team, facilitate the use of guidelines, and may act as a basis for a payment system. In order to achieve adequate implementation, full engagement among clinical and management staff is of great importance^{9,22}. Impediments of successful implementation of pathways and clinical engagement can occur at the staff (clinician or management) or health care organization (management, resources, and financial or institutional structures) level or can be influenced by external factors (broader health and social policies or patient characteristics)^{23,24}. Most literature, however, focuses on clinician-related barriers⁹. Clinicians may have mixed or negative attitudes regarding standardization of health care through the use of pathways. Even though clinicians may appreciate the guidance and information that pathways can provide, they may also feel that pathways are externally imposed and threaten clinical autonomy by being overly prescriptive and leading to additional work^{25,26}. Besides these clinician-related factors, other barriers for pathway engagement are time constraints, available resources/facilities, insufficient staff, staff turnover, variation in implementation across teams, poor reimbursement, lack of training in the use of pathways, and increased costs (practice and liability). In addition, not one implementation strategy can be expected to be successful in all contexts, and the literature suggests a multifaceted intervention which is setting-specific is most likely to be effective²⁶ and it is indicated that the context and implementation process may be as important as the intervention itself²⁷.

Besides the involvement of clinical and management staff, patient involvement is mostly missing in the current strategies to improve the organization of care pathways. On the one hand care pathways are intended to reduce unnecessary practice variation, improve coordination and continuity, and ultimately improve outcomes of clinical care²⁸. And at the same time care pathways are supposed to deal with personalization of care based on the needs and preferences of the individual patient, recognizing flexibility for patients' conditions, problems and priorities²⁹. According to Faber and colleagues, to narrow the gap between organizational demands and the quest for patient involvement, patients should be moved to the frontline of care pathway design, maintenance and dissemination, fostering the self-reported needs of patients³⁰.

OUTLINE OF THIS THESIS

Because care pathways are directly related to health care organizations and the patients care processes, this thesis has two aims. The first aim was to get insight in the deployment of care pathways in cancer care. The second aim was to study the added value of (regional) care pathways within oncology networks of collaborating (academic) hospitals and other health care organizations from the clinical and organizational point of view, including the professionals' and patients' perspective.

In the first part of this thesis the available literature about care pathways in cancer care was synthesized. **Chapter 2** describes a protocol which was written prior to the systematic review of effects on cancer care pathways. **Chapter 3** presents the results of this systematic review and discusses these in the light of clinical practice. Because cancer care is highly multidisciplinary and involves many health care professionals, **Chapter 4** focuses on the transitions in cancer care and themes were generated from the evidence, based on reviewed literature. Furthermore, to get more insight in the organization and personalization of follow-up for patients with breast cancer, **Chapter 5** presents the results of a study on variation in follow-up for breast cancer patients, including best practices and steps for the future.

The second part of this thesis investigates the added value of (regional) care pathways for patients with a low-complex high-volume tumor type as well as high-complex low-volume tumor types. **Chapter 6** presents an evaluation of a regional care pathway for breast cancer patients in three hospitals. In this study quantitative data was supplemented with qualitative data based on interviews with health care professionals. In **Chapter 7** the effects of a regional care pathway for patients with rectal cancer are discussed. This study applied a mixed methods research design and focusses on the long term results after implementation of the rectal cancer care pathway within four participating hospitals. In **Chapter 8** the evaluation of a regional collaboration for patients with esophagogastric cancer in seven hospitals and two radiotherapeutic institutions was presented. In this study quantitative data was combined with qualitative data from health care professionals and patients. To interpret the outcome measures more adequate, a national benchmark was included. In addition, **Chapter 9** shows insight in the variation of care within a network for esophageal cancer care of 17 hospitals in the Northern region of the Netherlands, including a national benchmark.

Part I

- 2 Effects of oncological care pathways in primary and secondary care on patient, professional, and health systems outcomes: protocol for a systematic review and meta-analysis
- 3 Effects of oncological care pathways in primary and secondary care on patient, professional and health systems outcomes: a systematic review and meta-analysis
- 4 Transitional Care in Clinical Pathways for Cancer Patients. Transitional care for the cancer patient: an evidence base
- 5 Follow-up after breast cancer: variations, best practices, and opportunities for the future according to health care professionals. Assessment of personalized aftercare for patients with breast cancer: best practices and steps for the future

Part II

- 6 Quality improvement by implementing an integrated oncological care pathway for breast cancer patients
- 7 Long-term effects of a regional care pathway for patients with rectal cancer
- 8 Evaluation of a regional network for esophagogastric cancer care: results based on data and from the perspective of health care professionals and patients
- 9 Variation in esophageal cancer care within a Managed Clinical Network. Trends in treatment strategies, lead time, and 2-year survival

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PART I

The evidence base for cancer care pathways

CHAPTER 2

Effects of oncological care pathways in primary and secondary care on patient, professional, and health systems outcomes: protocol for a systematic review and meta-analysis

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ABSTRACT

Background

The high impact of a cancer diagnosis on patients and their families and the increasing costs of cancer treatment call for optimal and efficient oncological care. To improve the quality of care and to minimize health care costs and its economic burden, many health care organizations introduce care pathways to improve efficiency across the continuum of cancer care. However, there is limited research on the effects of cancer care pathways in different settings.

Methods

The aim of this systematic review and meta-analysis described in this protocol is to synthesize existing literature on the effects of oncological care pathways. We will conduct a systematic search strategy to identify all relevant literature in several biomedical databases, including Cochrane library, MEDLINE, Embase, and CINAHL. We will follow the methodology of Cochrane Effective Practice and Organisation of Care (EPOC), and we will include randomized trials, non-randomized trials, controlled before-after studies, and interrupted time series studies. In addition, we will include full economic evaluations (cost-effectiveness analyses, cost-utility analyses, and cost-benefit analyses), cost analyses, and comparative resource utilization studies, if available. Two reviewers will independently screen all studies and evaluate those included for risk of bias. From these studies we will extract data regarding patients, as well as professional and health systems outcomes. Our systematic review will follow the PRISMA set of items for reporting in systematic reviews and meta-analyses.

Discussion

Following the protocol outlined in this article, we aim to identify, assess, and synthesize all available evidence in order to provide an evidence base on the effects of oncological care pathways as reported in the literature.

BACKGROUND

Description of the condition

Cancer (malignant neoplasm) is a generic term for a large group of diseases that can affect any part of the body. One of its defining features is the rapid growth of abnormal cells beyond their usual boundaries that can then invade adjoining parts of the body and/or spread to other organs; this process is referred to as metastasis formation, and is the major cause of death from cancer¹.

As one of the leading causes of morbidity and mortality worldwide, cancer is a major public issue. Data from 2012 showed 14 million new cases and 8.8 million cancer related deaths worldwide². The most commonly diagnosed cancers were lung (1.82 million), breast (1.67 million), and colorectal (1.36 million). Similarly, the most common causes of cancer death were lung cancer (1.6 million deaths), liver cancer (745,000 deaths), and stomach cancer (723,000 deaths). The incidence data were derived from population-based cancer registries: however, these cancer registries do not cover all national populations². Advances in medical technology have contributed to the growth of an aging population with a greater life expectancy, but will at the same time lead to an ever-increasing cancer burden over the next decades, particularly in low and middle income countries, where over 20 million new cancer cases are expected annually by 2025³.

Given the global incidence of cancer and its mortality, cancer imposes a substantial economic burden on society. Considerable health care costs are associated with its prevention and management, and indirect costs result from patients' inability to work⁴. Warren et al. state that the costs of initial cancer treatments are steadily increasing, as more patients are receiving surgery and adjuvant therapy, and the costs of these treatments are rising⁵.

To minimize the burden of cancer for patients, health care professionals, and health care organizations, effective and efficient organization of cancer care is vital. Cancer care is complex and depends upon careful coordination between various health care organizations and providers. Regular communication and exchange of technical information between all those involved in treatment (including patients, general practitioners, medical specialists, and other specialty disciplines) must be guaranteed⁶. One way to provide patient-centered care, reduce waiting times, and improve the quality of cancer care is to introduce care pathways^{7,8}.

Description of the intervention

Care pathways, also known as 'integrated care pathways', 'clinical pathways', 'critical pathways', or 'care plans', have been implemented since the 1980s as tools to facilitate evidence-based health care. Kinsman et al. developed five criteria to define a care pathway⁹. Rotter et al. tested these criteria and refined the definition into four criteria, including a structured multidisciplinary plan of care, which translates guidelines into local structures, detailing the steps in a course of treatment or care in a plan of actions, and aiming to standardize care¹⁰.

From the perspective of health care professionals and organizations, care pathways are emerging as welcome strategies for quality improvement. They help to improve multidisciplinary communication and care planning, optimize the safety and quality of care, and increase patient satisfaction¹¹. Focusing on the whole pathway of care, including the care delivered to patients from diagnosis, through treatment, to living with and beyond cancer, care pathways organize efficient transitions between health care organizations. They are able to link evidence to practice via integration of guidelines into local systems and, consequently, optimize patient outcomes and maximize clinical efficiency¹². The systematic review of Rotter et al. showed that care pathways reduced in-hospital complications and improved documentation among health care professionals. These authors also found that most studies reported a decreased length of stay and a reduction in hospital costs after care pathways were implemented¹². However, in spite of some evidence for the use and effects of oncological care pathways, this evidence is often limited to only a small number of pathways or only a limited part of a pathway; available studies report the effects of care pathways for breast cancer^{13,14,15,16}, colorectal cancer¹⁷, lung cancer¹⁸, and prostate cancer¹⁹.

Evidence is not only lacking about the use and effects of care pathways, but also about the implementation of these pathways. Studies of strategies for implementation of guidelines, rather than pathways, are more common^{20,21}. Furthermore, Jabbour et al. stated that the true impact of pathways has been limited because the implementation strategies are variable and the research designs are suboptimal²². Therefore, it is important to identify the existing knowledge about implementation and the circumstances under which care pathways lead to improved care.

Although care pathways are frequently applied in cancer care, to our knowledge systematic reviews of the whole pathway of oncology care and its effects are not available. We therefore present the systematic review as described in this protocol, for which we follow the preferred reporting items for systematic review and meta-analyses (PRISMA)(see PRISMA Checklist)²³, in order to improve the current knowledge base on the effects of oncological care pathways.

METHODS

Review questions and objectives

1. The primary question is: What are the effects of oncological care pathways on patient, professional, and health system outcomes within primary and secondary (hospital) care settings?
2. The secondary review questions are: 1) What are the differences in the implementation of oncological care pathways in primary and secondary (hospital) care? And 2) Can we explain how these differences might lead to different outcomes?

For the purpose of this review, we will define usual care as treatment determined at the discretion of the attending health care professional. Unless studies specify that the control group utilizes some form of standardized care, we will assume the control group utilizes this definition of usual care.

Criteria for considering studies for this review

We will include all studies that address the questions and objectives of our systematic review. We will include studies which tested the implementation of care pathways in primary and secondary (hospital) care and of intersectional care pathways in all health care settings.

Types of studies

We will include all primary, quantitative studies which utilize the following study designs: randomized trials, non-randomized trials, controlled before-after studies, and interrupted time series studies according to the EPOC study design criteria²⁴. Where available, we will include full economic evaluations (cost-effectiveness analyses, cost-utility analyses, and cost-benefit analyses), cost analyses, and comparative resource utilization studies. We will exclude retrospective cohort studies, prospective cohort studies, cross-sectional studies, and case-control studies.

Definition of care pathways

Because there are many definitions of 'care pathways'⁹, we will use the working description which was tested and refined in a previous review by Rotter et al.¹⁰:

1. The intervention was a structured, multidisciplinary plan of care.
2. The intervention was used to translate guidelines or evidence into local structures.
3. The intervention detailed steps in a course of treatment or care in a plan, pathway, algorithm, guideline, protocol or other "inventory of actions" (i.e. the intervention had time-frames or criteria-based progression).
4. The intervention aimed to standardize care for a population of cancer patients.

An intervention is considered to be a care pathway only if it meets all four criteria. Otherwise, the study will be excluded.

Types of institutions and participants

Participants will include patients, care providers, and health care organizations in primary and secondary care. All cancer types will be included. Regarding the care providers, we will consider all health professionals, including general practitioners, doctors, nurses, physiotherapists, pharmacists, occupational therapists, social workers, dietitians, psychologists, psychiatrists, and dentists involved in oncological care pathway utilization. Finally, we will group the included studies into primary and secondary care pathways. Also, we will synthesize and report on the studies according to the context in which they have been implemented (primary or secondary care).

Primary outcomes

Objectively measured patient outcomes include: (in-patient) mortality, mortality at the end of follow-up, re-admissions (hospital setting), (in-hospital) complications, hospital admissions, adverse events, discharge destinations, performance status, patient satisfaction, quality of life, and absence from work.

Objectively measured professional outcomes include: quality measures appropriate to the specific aim of the care pathway, staff satisfaction, team functioning, guideline adherence, and adherence to evidence-based practice.

Objectively defined systems level outcomes include: length of stay, waiting times, and costs.

Secondary outcomes

Any reported measure of the following implementation strategies and methods will be included. We will use the evidence-informed strategies identified and employed by the Cochrane authors in their systematic review, although Rotter et al.¹² found that reporting of implementation processes was generally poor. Further, we will extract the reported evidence-based processes for developing and implementing care pathways in primary and secondary care. We will group the reported implementation activities according to whether they used evidence-informed strategies. We will categorize reported strategies into: (1) pathway development^{12,25}, (2) implementation planning^{12,26}, (3) pathway education^{12,25,27}, and (4) feedback & reminder systems^{12,27,28}.

Potential activities involved in pathway implementation include: project groups, clinician involvement, local consensus processes, use of an implementation team, identification of potential barriers to change, identification of evidence-practice gaps, local opinion leaders, educational meetings and outreach, printed educational materials, audit and feedback, and electronic reminder systems.

Search methods

We will search the Cochrane Database of Systematic Reviews and the Database of Abstracts of Reviews of Effects (DARE) to identify related systematic reviews. The initial search strategy has been developed for OVID MEDLINE and will be translated for other databases (see search strategy). We will apply three methodological filters: randomized controlled trials; EPOC designs (controlled before-after studies, interrupted time series studies, and quasi-experimental designs); and economic studies to identify cost-effectiveness analyses, cost-utility analyses and cost-benefit analyses. Search strategies will use controlled vocabulary such as Medical Subject Headings (MeSH) and Emtree (Embase), and keyword phrases. All databases will be searched from date of inception forward with neither date nor language limits.

Databases

- Cochrane Central Register of Controlled Trials, Cochrane Library (Wiley)
- DARE, NHS Economic Evaluation Database (EED), Health Technology Assessment Database (HTA) (Wiley)
- MEDLINE, Epub Ahead of Print; In-Process & Other Non-Indexed; MEDLINE R; MEDLINE R Daily (OVID) 1946 to present
- Embase (OVID) 1947 to present
- CINAHL (EBSCO) 1981 to present
- Latin American and Caribbean Health Science Information database (LILACS); via Virtual Health Library, <http://lilacs.bvsalud.org/en/> 1982 to present
- Scientific Electronic Library Online (SciELO) <http://www.scielo.org/php/index.php> 1940 to present
- The American Economic Association's database for economic literature, EconLit (EBSCO) 1969 to present

Searching other resources

Trial Registries

- ClinicalTrials.gov - US National Library of Medicine <https://clinicaltrials.gov>
- International Clinical Trials Registry Platform (ICTRP)- World Health Organization <http://apps.who.int/trialsearch/>

Grey Literature

We will search a selection of grey literature sources to identify citations not indexed in the standard bibliographic databases above. Sites will include, but not be limited to, the following:

- Open Grey www.opengrey.eu/
- The Grey Literature Report, New York Academy of Medicine (1996 to present) <http://www.greylit.org>
- Open Clinical <http://www.openclinical.org/home.html>
- Organizational web sites and professional organizations related to clinical pathways and implementation.
 - European Pathway Association <http://e-p-a.org>

We will also:

- Screen the following individual journals (e.g. hand search):
 - International Journal of Care Pathways
 - International Journal of Integrated Care
- Review reference lists of all included studies, relevant systematic reviews/primary studies.
- Contact authors of relevant studies/reviews to clarify reported published information and/or to seek unpublished results/data.
- Contact researchers with expertise relevant to the review topic/ EPOC interventions.
- Conduct a cited reference search Studies included in our review in Web of Science.
- Contact the corresponding author to request full text in case of the full text is missing.

Data extraction

Two reviewers will independently screen all titles and abstracts, using Covidence²⁹. A third reviewer will be consulted in case of disagreement between the two reviewers. We will further examine potentially relevant studies, using full-text copies.

Two review authors will independently extract data, directly from included studies. Where necessary, we will request additional information from the authors of primary studies. When we include systematic reviews in the analysis, we will assess the methodological quality of these reviews using the Assessing the Methodological Quality of Systematic Reviews (AMSTAR) tool³⁰.

When data are missing, we will not impute any values.

Areas of data extraction will include:

- Study characteristics: publication year, country, length of follow-up period, urban vs. rural location, and inclusion criteria.
- Population characteristics (of patients): age, gender, number of patients, and type of cancer.
- Population characteristics (of professionals): types of health care professionals, number of health professionals involved in development, and health care setting.
- Intervention characteristics: evidence based development and implementation strategy(ies) reported.
- Outcomes: patient, professional, and systems (means, averages, and other uncertainty measures).

Risk of bias assessment

For randomized trials, non-randomized trials, controlled before-after studies, and interrupted time series studies we will use the validated criteria suggested by the Cochrane EPOC group to assess the risk of bias in studies with control groups²⁴.

The review team will identify criteria for assessing randomized trials, non-randomized trials, and controlled before-after studies: sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, similarity of baseline measures, similarity of baseline characteristics, management of incomplete outcome data, selective outcome reporting, and other risks of bias.

The review team will also identify criteria assessing interrupted time series studies: intervention independent of other changes, shape of effect pre-specified, intervention unlikely to affect data collection, blinding of outcome assessment, management of incomplete data, selective outcome reporting, and other risks of bias.

We will summarize the results of the risk of bias assessment across studies and present them in a tabular format.

Data analysis

We will undertake meta-analyses if we find more than two comparable studies which report similar outcomes, within similar contexts, and without statistical heterogeneity. To perform a meta-analysis, we will use RevMan³¹ for calculating a pooled effect (if the clinical and statistical homogeneity across groups of studies is sufficient), using both fixed and random effect models to assess the robustness of the results³².

Data synthesis

We will report details on the number of retrieved references, obtained full-text papers, and the included and excluded articles. We will present results of meta-analyses using forest plots. We will adjust cost data for inflation and present these data in US dollars for a common price year.

Assessment of heterogeneity

We will assess heterogeneity within the review and analyze the comparability of the results from individual studies ($I^2 = [(Q \text{ df})/Q] \times 100\%$). The cut off for substantial statistical heterogeneity will be an I^2 greater than 50%. In addition to considering the quantitative measure of I^2 , we will perform the Cochran's Q test statistical test for heterogeneity³³.

Assessment of reporting biases

In cases where we find more than 10 studies we will assess potential reporting biases by visual inspection of counter-enhanced funnel plots^{34,35}. To test for funnel plot asymmetry, we will use the test proposed by Egger³⁶ or the modified version of the Egger test proposed by Harbord in case of small study effects in meta-analyses of controlled trials with binary endpoints³⁷.

Subgroup analysis

We will perform a subgroup analysis of the reported primary and secondary outcomes.

We will group studies according the following categories:

- Country(ies) where the study was carried out.
- Setting(s) where the implementation of care pathways occurred.
- Year of publication, to assess differences in outcomes reported over time.
- Quality of studies: high versus low risk of bias.
- Age of population: studies including children versus adults.
- Cancer type for which the care pathway was developed and implemented.

In our subgroup analyses we will be using the quantity I^2 for estimating heterogeneity, based on Cochran's Q test, and both statistics will be provided in our forest plots to depict the pooled estimates.

Sensitivity analysis

We will use sensitivity analyses to explore the robustness of the results by investigating the effects of including and excluding studies with high and unclear risks of bias from the analysis.

Ongoing studies

We will describe identified ongoing studies, where available, detailing the primary author, research question(s), methods, and outcome measures. In addition, we will contact the authors of ongoing studies to request raw data for inclusion in our review.

DISCUSSION

The systematic review outlined in this protocol aims to identify, assess, and synthesize all quantitative studies on the effects of care pathways for oncological care meeting the EPOC study design criteria. As a result, the review will provide an evidence base for cancer care pathways regarding patient effects, cost effectiveness, and implications for implementation. Disseminating the results of the systematic review will be done by publishing the systematic review in a peer-reviewed journal and presenting the results at relevant symposia. The methodological quality of our systematic review will be reported by using the AMSTAR tool³⁰.

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CHAPTER 3

Effects of oncological care pathways in primary and secondary care on patient, professional and health systems outcomes: a systematic review and meta-analysis

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ABSTRACT

Background

Pathways are frequently used to improve care for cancer patients. However, there is little evidence about the effects of pathways used in oncological care. Therefore, we performed a systematic review and meta-analysis aiming to identify, and synthesize existing literature on the effects of pathways in oncological care.

Methods

All patients diagnosed with cancer in primary and secondary/tertiary care whose treatment can be characterized as the strategy “care pathways” are included in this review. A systematic search in seven databases was conducted to gather evidence. Studies were screened by two independent reviewers. Study outcomes regarding patients, professionals and system level were extracted from each study.

Results

Out of 13,847 search results, we selected 158 articles eligible for full text assessment. 150 studies were excluded and the remaining eight studies represented 4,786 patients. Most studies were conducted in secondary/tertiary care. Length of Stay (LOS) was the most common used indicator, and was reported in five studies. Meta-analysis based on subgroups showed an overall shorter LOS regarding gastric cancer (Weighted Mean Difference (WMD)): -2.75, CI: -4.67--0.83) and gynaecological cancer (WMD: -1.58, CI: -2.10--1.05). Costs were reported in six studies and most studies reported lower costs for pathway groups.

Conclusions

Despite the differences between the included studies, we were able to present an evidence base for cancer care pathways performed in secondary/tertiary care regarding the positive effects of LOS in favor of cancer care pathways.

BACKGROUND

Care pathways are also known as 'integrated care pathways', 'clinical pathways', 'critical pathways' or 'care maps'¹. Care pathways are tools to guide evidence-based health care and have been implemented since the 1980s². Care pathways provide a means to improve multidisciplinary communication and care planning, including primary and secondary/tertiary care. Further, pathways aim to improve communication between clinicians and patients as well as patient satisfaction³. In addition, care pathways are described to have a positive impact on quality of care, efficiency and teamwork^{4,5}. Rotter et al. conducted a systematic review on the effects of clinical pathways and concluded that clinical pathways are associated with reduced in-hospital complications and improved documentation without negatively impacting on length of stay and hospital costs⁶. Although care pathways are frequently applied in cancer care, the evidence of its effects is often limited. Furthermore, most study designs which were used to evaluate pathways were relatively weak. To our knowledge, a systematic review of the effects of pathways in cancer care is not available⁷.

Cancer care is complex and relies upon careful coordination between multiple health care organizations and providers. Technical information exchange and regular communication flow between all those involved in treatment (including patients, general practitioners, specialist physicians, and other specialty disciplines) is needed⁸. Therefore, care pathways are often used in cancer care and are seen as a method to provide patient-centered care, reduce waiting times and improve quality of cancer care^{9,10}.

The aim of this systematic review is to assess the effects of oncological pathways according an unambiguously definition of cancer care pathway in studies providing a high level of evidence. In this systematic review effects of cancer care pathways were assessed in comparison with usual care. In addition, an overview of the outcome measures regarding patients, professionals and system level will be presented. Because cancer care is characterized by coordination and multidisciplinary communication within and between health care organizations, we searched for literature in primary as well as secondary/tertiary health care. Furthermore, information about the implementation of oncological care pathways was assessed. By conducting this systematic review and meta-analysis we aimed to present the available high evidence in a substantiated and concise way, in order to improve the current evidence base regarding the effects of oncological care pathways.

METHODS

Types of studies

We limited our study selection to the following study designs: randomized controlled trials (RCT), non-randomized studies (NRS), controlled before-after studies (CBA), and interrupted time series studies (ITS), as well as economic evaluations (cost-effectiveness analyses, cost-

utility analyses and cost-benefit analyses, cost analysis and comparative resource utilization studies), where available. Based on the suggested study designs of the Cochrane Effective Practice and Organisation of Care (EPoC) Group for inclusion in reviews, retrospective cohort studies, prospective cohort studies, cross-sectional studies, and case-control studies were excluded¹¹. An additional file shows an overview of the inclusion criteria for this systematic review [see additional file 1].

Types of participants

Eligible participants for inclusion in this systematic review were patients in primary and secondary/tertiary care which includes the coordination and continuity of health care as patients transfer between different locations or different levels of care. As potential patients we considered all patients of every age and diagnosed with every type of cancer in primary and secondary care/tertiary care.

Types of interventions

In this review cancer care pathways were compared to usual care or care and treatment given to patients in a control setting. For the purpose of this review, we will define usual care as treatment determined at the discretion of the attending health care professional. This care may present the best current care, and may also be highly variable across different settings. Due to the different terminology used for cancer care pathway we applied the definition of clinical pathways based on four operational pathway criteria: 1) multidisciplinary (two or more clinical professions involved), 2) protocol or algorithm based (i.e. structured plan/treatment-protocol or algorithm), 3) evidence based or based on practice guidelines, and 4) aiming to standardise cancer care¹². Every pathway characteristic could be met as (1) “yes” criterion; (2) “not sure” because of poor reporting or when the authors did not reply to our emails and phone calls and therefore we were not able to retrieve more information about the study or (3) “criterion not met”. If one or more pathway criteria was not met, we excluded the study. In the results section additional information relating to the included studies and differences between the studies is presented.

Types of outcome measures

Every measured patient, professional, and system level outcome was considered for inclusion. Patient outcomes include (in-patient) mortality, mortality at the end of follow-up, re-admissions (hospital setting), (in-hospital) complications, hospital admissions, adverse events, discharge destinations, performance status, patient satisfaction, quality of life, and absence from work. Professional outcomes include quality measures appropriate to the specific aim of the care pathway, staff satisfaction, team functioning, guideline adherence, and adherence to evidence-based practice. System level outcomes include length of stay, waiting times, costs, and hospital charges. Furthermore, any reported measure regarding implementation strategies and methods were also assessed.

Information sources and search strategy

Systematic searches were performed in the Cochrane Library, Medline (1946-2019), Embase (1946-2019), Cinahl (1981-2019), Lilacs, ClinicalTrials.gov, and the World Health Organization International Clinical Trials Registry Platform, including conference abstracts. Because this systematic review aimed to present evidence regarding the effects of oncological care pathways, our literature search focussed on “research” rather than “quality improvement”. Furthermore, grey literature was searched in Open Grey, the Grey Literature Report (1996-2017), and Open Clinical. Also organizational websites and professional organizations related to care pathways and implementation were assessed. Moreover, we employed citation tracking and examined included studies and previous reviews. We also contacted investigators to identify any study missed by the electronic searches. The most recent searches were conducted on July 1, 2020. Two reviewers independently screened all titles and abstracts (JvH,RV), using Covidence¹³. A third reviewer (TR) was available for consultation in the case of disagreements between the two reviewers. The potentially relevant studies were further examined using full-text copies. All databases were searched from the date of inception forward with neither date nor language limits. For the complete search strategy, see additional file 2.

Summary of most important search terms

Pathway:	critical pathway, clinical pathway, patient care pathway, pharmacotherapeutic pathway, therapeutic pathway, treatment pathway, care plan, structured care, intensive management care, care algorithm, treatment algorithm, therapeutic algorithm, standardized (patient) care, standardized treatment, (care) map, process map
Cancer	oncology, neoplasm, carcinoma, malignant, tumor
Oncology:	medical oncology, radiation oncology, surgical oncology, oncologist, radiation oncologist
Guideline:	interdisciplinary guideline, cross-disciplinary guideline, multidisciplinary guideline, team guideline, standardized guideline, practice guideline
Health professional:	clinician, provider, professional, doctor, nurse, family doctor, family physician, family practitioner, GP, practitioner, physician, hospital, pharmacy, primary care, regulatory, team
Intervention:	intervention study, intervention care, intervention health, demonstration project, pre-test, post-test, improvement, impact, individualized, interdisciplinary, multicomponent, multidisciplinary, multifaceted, multimodal, personalized, standardized, usual care

Study design: randomized controlled trial, (controlled) clinical trial, placebo trial, quasi-experiment, experimental method, experimental study, experimental design, (interrupted) time series, multicentre study, controlled before-after study, interrupted time series analysis, evaluation study, prospective studies, retrospective study, meta-analysis, pilot project, systematic review, scoping review, concept analysis

Data collection process

From every included study we extracted data regarding study characteristics, population characteristics, interventions characteristics and outcomes.

Hospital costs and charges were assessed and calculated for the individual studies. Cost and charges data were calculated in US\$ for the common price year 2016 by using the “CCEMG-EPPI-Centre Cost Converter”¹⁴. This Cost Converter is a web-based tool that can be used to adjust and estimate of cost expressed in one currency and price year to a target currency or price per year¹⁴.

Statistical analysis

For calculating the pooled effects estimate, called Weighted Mean Difference (WMD), we used Review Manager from the Cochrane Collaboration¹⁵. To assess the comparability of the results from individual studies and included subgroups, we used the statistic for quantifying inconsistency: $I^2 = [(Q \text{ df})/Q] \times 100\%$ ¹⁶. We considered an overall test-value greater than 60% to serve as evidence of substantial heterogeneity of a magnitude where statistical pooling is not appropriate¹⁶. We used a random effects model since the model estimates the effect with consideration to the variance between studies, rather than ignoring heterogeneity by employing a fixed effects model. Subgroup analysis based on differences in the setting, on the risk of bias of the studies and on the age of the study population were not possible because these characteristics were not distinctive enough between the studies to form different subgroups.

Quality assessment

Two reviewers independently assessed the quality of the studies (JvH,RV). Therefore, we adhered to the validated criteria suggested by the Effective Organisation of Care Group (EPOC) and defined three risk of bias classes: Class I (low risk of bias), Class II (moderate risk of bias) and Class III (high risk of bias)¹⁷. A third reviewer was available for consultation in case of disagreements between the two reviewers (TR). To appraise the methodological quality of the included cost evaluations the Evers checklist was used, which is recommended for Cochrane Reviews¹⁸.

Dealing with missing data

If a study did not provide information about the standard deviation, this was calculated based on the reported p-value and mean difference. For calculating the standard deviation of the mean we used the Revman Calculator¹⁹. By using this calculator the assumption was made that the standard deviations of outcome measurements are the same in both study groups. For calculating the mean as well as the standard deviation from the reported median and range, we used the Mean Variance Calculator²⁰.

RESULTS

Search results

The specialized search strategy led to 13,870 results. After removing duplicates, all of the 13,847 titles and abstracts were screened for inclusion. The remaining 158 possibly relevant studies were retrieved as full text articles. Based on the full text assessment, 150 studies were excluded. The majority of the excluded studies did not meet our study design criteria (79 studies). In addition, a number of studies compared different medical treatments and medication, the intervention did not meet our definition of cancer care pathways, or information was lacking (25 studies). Finally, eight studies matched our methodological requirements. In an additional file the PRISMA flow diagram is presented [see Additional file 3]. The excluded full text studies and the reason for exclusion are listed in Additional file 4. For the references of all excluded full text studies, see Additional File 5.

Below we present the studies conducted in the secondary/tertiary health care setting separately from the study conducted in both primary and secondary health care, because the settings in which the studies were performed, intervention characteristics, and outcomes differed greatly.

Quality assessment

Based on the validated criteria suggested by the Effective Organisation of Care Group (EPOC)¹⁷, all studies were assessed as “high risk of bias”, except for two studies^{25,27}. In an additional file the results of the risk of bias assessment are shown [see Additional file 6]. The results of the cost evaluation according the Evers checklist¹⁸, is presented in Additional file 7.

Results of studies conducted in the secondary/tertiary health care (hospital care) setting

The majority of the included studies (seven studies) were conducted in the setting of secondary health care, within hospitals or in oncology centers²¹⁻²⁷. These studies represented 1,494 patients.

Study characteristics

In this paragraph a description is given of the following study characteristics: study designs, tumor location, sample size, country, and health care setting. In Table 1 the study characteristics of the included primary studies included are presented.

Study designs

The specification of the study designs of the included studies were based on the description of the Cochrane Effective Practice and Organisation of Care (EPOC) Group¹¹.

We included two studies which applied randomized study designs^{25,27}. In these studies patients were randomized to either a pathway group or a non-pathway group. Two studies used an interrupted time series study design (ITS), in these studies a pre-pathway group was compared to two or more pathway groups^{22,23}. In one study pathway groups at 12 and 36 months after implementation were compared to a pre-pathway group²², and in the other study a pre-pathway group and pathway groups at six, 12, and 18 months after implementation were used²³.

Furthermore, in three studies a non-randomized controlled trial study design was applied^{21,24,26}. In these studies patients in the non-pathway group received general care, and simultaneously patients in the pathway group were managed based on the pathway. In one study a historical control group was compared with two other groups; a pathway group and a non-pathway group²¹.

Tumor location

In the articles patients with different tumors were studied: three studies described the effects of pathways for head and neck cancer^{21,22,27}. Other studies presented the results of pathways for gastric cancer^{24,25}, gynaecological cancer²³, and breast cancer²⁶.

Sample size

The number of included participants varied, and ranged from almost 70 patients to more than 600 patients²¹⁻²⁷.

Country

Three studies were conducted in Korea, Japan and Turkey²⁴⁻²⁶. In addition, three studies were performed in the United States of America (USA)²¹⁻²³, and one in United Kingdom²⁷.

Setting

Three studies were conducted in general and non-academic hospitals or oncology centers²⁵⁻²⁷. Other studies were performed in an academic hospital^{21,22,23}. In one study the setting was not clearly reported²⁴.

Table 1 Study Characteristics of Included Primary Studies

	Study ID	Study design	Tumor location	Sample Size	Country	Setting
1	Chen et al. 2000 ²¹	Non-randomized controlled trial* (with a historical control group)	Unilateral neck dissection	190	USA	Academic cancer Center, secondary/tertiary care
2	Dahl et al. 2017 ²⁹	Non-randomized controlled trial* (with a historical control group)	Cancer patients (colorectal, lung, melanoma, breast, prostate & other)	3292	Denmark	Danish hospitals, primary and secondary care
3	Gendron et al. 2002 ²²	Interrupted time series study*	Head and neck cancer surgery	212	USA	Tertiary care academic medical center
4	Ghosh et al. 2001 ²³	Interrupted time series study*	Hysterectomy cervical or endometrial cancer	151	USA	Academic Medical Center, tertiary care
5	Jeong et al. 2011 ²⁴	Non-randomized controlled trial*	Treatment of gastric cancer (early vs advanced; non-CP vs CP)	631	Korea	Unclear, secondary care
6	Kiyama et al. 2003 ²⁵	Randomized Controlled Trial	Gastric cancer	85	Japan	Nippon Medical School Hospital, secondary care
7	Tastan et al. 2012 ²⁶	Non-randomized controlled trial*	Breast cancer	69	Turkey	Military Medical Academy, secondary care
8	Williams et al. 2015 ²⁷	Randomized Controlled Trial	Pain screening and treatment in head and neck cancer	156	UK	Hospital, secondary care

Abbreviations: USA: United States of America; CP: Care Pathway; UK: United Kingdom.

*study design is not mentioned in the article; specification is based on the Cochrane study designs

Population characteristics

The population characteristics of the study groups included in the studies was listed in table 2. All studies, except one²³, reported patient characteristics on gender and age. Two studies reported also characteristics about socioeconomic status^{22,26}.

Table 2 Population Characteristics of Included Primary Studies

Study ID	Study groups	Gender (male vs female)	Age	Socioeconomic status
1	Chen et al. 2000 ²¹ historical control group nonpathway group pathway group	76% vs 24% 64% vs 36% 73% vs 27%	58 years (median) 59 years (median) 60 years (median)	No information available
2	Dahlet al. 2017 ²⁹ Before implementation After implementation total After implementation pathway referred After implementation non-pathway referred	45% vs 55% 52% vs 48% 49% vs 51% 54% vs 46%	11.3/14.8/25.3/28.5/20.2* 7.0/12.2/24.9/33.1/22.8* 6.4/10.4/25.5/33.2/24.6* 7.3/13.3/24.6/33.1/21.6*	No information available
3	Gendron et al. 2002 ²² Control group (pre-pathway) 1 year after pathway implementation 3 years after pathway implementation	71% vs 29% 79% vs 21% 73% vs 27%	65 years (median) 61 years (median) 60 years (median)	Smoking (yes): 96%; alcohol use (yes): 75% Smoking (yes): 90%; alcohol use (yes): 73% Smoking (yes): 90%; alcohol use (yes): 54%
4	Ghosh et al. 2001 ²³ Separate groups for cervical and endometrial cancer Preintervention group Postintervention group Postintervention group Postintervention group	No patients characteristics were reported and stage of disease only.		Patients were matched for age, comorbid conditions, and stage of disease only.
5	Jeong et al. 2011 ²⁴ Non care pathway group early gastric cancer Pathway group early gastric cancer Non care pathway group advanced gastric cancer Pathway group advanced gastric cancer	71% vs 29% 64% vs 36% 69% vs 31% 65% vs 35%	59.7 (mean) 58.2 (mean) 59.1 (mean) 59.3 (mean)	No information available
6	Kiyama et al. 2003 ²⁵ Traditional care group Clinical pathway group	66% vs 34% 62% vs 38%	66.8 years (mean; $\pm$ 12.9) 63 years (mean; $\pm$ 12.1)	No information available

7	Tastan et al. 2012 ²⁶	Control group	No information available	53.2 (mean; ± 12.3)	Marital status (married vs single): 82.4% vs 17.6; ownership child (no vs yes): 11.8% vs 88.2; education (primary/secondary/high school/college or higher): 8.8%/50%/17.6%/23.6%; occupation (yes vs no): 32.4% vs 67.6%.
		Clinical pathway group		51.7 (mean; ± 11.3)	Marital status (married vs single): 82.9% vs 17.1; ownership child (no vs yes): 2.9% vs 97.1; education (primary/secondary/high school/college or higher): 11.4%/45.7%/28.6%/14.3%; occupation (yes vs no): 17.1% vs 82.9%.
8	Williams et al. 2015 ²⁷	Usual care group Intervention group	64% vs 36% 66% vs 34%	58 years (mean; range 19-80) 60 years (mean; range 39-82)	No information available

* this information was reported in the following categories: 18-44 years; 45-54 years; 55-64 years; 65-74 years; ≥75 years.

Intervention characteristics

In this paragraph the intervention characteristics reported in the studies were described: study groups, intervention and care pathway. See table 3 for more detailed information.

The specific interventions regarding the pathways described in the included studies, showed considerable variation. Most studies focused on pathways for the perioperative phase in order to guide surgical management²¹⁻²⁶, and one study investigated pain management²⁷. In the studies focussing on for surgical care, the following key components which were addressed in these pathways were described: nutrition and diet^{21,23-26}, diagnostic modalities and laboratory tests^{21-24,26}, medication^{21,24-26}, patient education^{23,25,26}, preoperative consultation and visits^{21,24,26}, drains^{22,24}, activity^{21,26}, clinical procedures and treatment^{21,26}, discharge planning or -instruction^{21,26}, assessment and preadmission testing and evaluation^{21,24}, and psychosocial support and education^{21,26}. Other components which were mentioned in one study only: performance status, outcome criteria, follow-up criteria, and follow-up care²¹, pain management and pain control, and deep vein thrombosis prophylaxis²³, preoperative bowel preparation and fasting, and removal of nasogastric tube²⁴, removal of a catheter and mobility²⁵.

The study included in this review investigating pain management, included an initial consultation with a control pain doctor and weekly follow-up sessions²⁷.

In addition, in three studies the pathway was presented in detail providing a description of the pathway as well as a figure of the pathway^{21,24,26}. Further, one study presented a pathway for the hospital staff as well as a pathway for patients²⁴. In the other studies no detailed information about the pathway was available.

Table 3 Intervention Characteristics of Included Primary Studies

Study ID	Study groups	Intervention	Care pathway*	Outcomes
1	<ul style="list-style-type: none"> Chen et al. 2000²¹ <ul style="list-style-type: none"> Historical control group (prepathway, Sep 1993-Dec 1994) Contemporaneous nonpathway group (Sep 1996-Aug 1998) Clinical pathway group (Sep 1996-Aug 1998) Patients in the underwent the same surgical procedure during the time of implementation, but were not managed based on the pathway. The treated physician decided solely to place patients on the pathway. 	<p>The neck dissection pathway was presented in a tabular format and consists of the following aspects: assessment/evaluation, consult, diagnostic test, treatment, medication, performance status/activity, nutrition, teaching/psychosocial, discharge planning, outcome criteria and follow-up criteria. The activities were described for the initial evaluation, preoperative visit and same day admit surgery.</p>	Meets criteria 1 - 4	<p>Length of hospital stay (median)</p> <p>Complications</p> <p>Readmission</p> <p>Costs of care</p>
2	<ul style="list-style-type: none"> Dahl et al. 2017²⁹ <ul style="list-style-type: none"> Before implementation (Sep 2004-Aug 2005) After implementation total (May-Aug 2010) After implementation pathway referred (May-Aug 2010) After implementation non-pathway referred (May-Aug 2010) 	<p>The framework of the Danish cancer pathways includes three different descriptions of the pathway: a flowchart, a narrative text and a table providing an organizational overview. A pathway in the Danish context is a standardized pathway that most patients suspected of cancer will be able to follow. It describes the patient's pathway from clinical suspicion of a certain cancer through diagnostic procedures and treatment. The pathway describes the medical procedures, the necessary organization encompassing both primary and secondary sectors of the health system, and timeframes in accordance with the political agreement. Main emphasis in the pathways are on information to be given to the patient, explicit identification of the responsible health professional or department in all phases, procedures for referral, description of multidisciplinary teams in each pathway as a forum for decisions on diagnosis and recommended treatment, and timeframes of all phases. An example of a pathway is shown³⁰.</p>	Meets criteria 1 - 4	<p>Patient dissatisfaction with long term waiting times</p>
3	<ul style="list-style-type: none"> Gendron et al. 2002²² <ul style="list-style-type: none"> Control group (pre-pathway) (1995) 1 year after pathway implementation (July 1996-July 1997) 3 years after pathway implementation (1999) 	<p>The pathway for patients undergoing major resection for upper aerodigestive tract cancer was implemented in July 1996. The format for the pathway is a 1-page table containing a list of goals and interventions for each postoperative day, followed by a page for each day on which accomplishments are recorded. When goals were not met, the variances are recorded in detail on the flow sheet.</p>	Meets criteria 1 - 4	<p>Length of stay (median, range)</p> <p>Readmission</p> <p>Complication rates</p> <p>Hospital charges</p>

4	Ghosh et al. 2001 ²³	<p>Separate groups for cervical and endometrial cancer:</p> <ul style="list-style-type: none"> • Preintervention group (Jan 1997-June 1998) • Postintervention group (July 1998-Dec 1998) • Postintervention group (Jan 1999-June 1999) • Postintervention group (July 1999- Dec 1999) 	<p>Care pathways for patients with gynecologic malignancies were developed based on the results of clinical trials and on the consensus of experts. The pain control team and a pharmacist were involved. The nursing team played an active role in the practicality of the execution of these care plans. Documentation including preprinted orders were created and approved by hospital committees. Postoperatively, patients were placed on preprinted orders, which addressed patient education, rapid diet advancement, a reduction in laboratory tests, deep vein thrombosis prophylaxis, and pain management.</p> <p>The pathway was first implemented in September 2004. The pathway for patients with gastric cancer following gastrectomy were developed in 2006 to provide care for these patients. The pathway was electric medical record based. In the pathway for hospital staff which is presented in figure 1, the aspects: Lab, Treat, Activity, Diet, Mx, Education and Evaluation were described for the day before surgery, the day of surgery until 2/3 days after surgery (preoperative laboratory tests and diagnostic modalities, assessment of concomitant diseases, consultation for operative safety, bowel preparation and antibiotics at preoperative day 1 and postoperative day 1, removal of nasogastric tube, start of semi-fluid diet, removal of closed suction drain before discharge. There is also a pathway for patients; this is presented in figure 2.</p> <p>The care pathway employed standardized postoperative management using printed order sets, which included instructions for such matters as medication, diet, removal of the catheter and the mobility of the patients.</p>	<p>Meets criteria 1 - 4</p>	<p>Length of hospital stay (mean, SD) Total costs Direct costs Patient satisfaction Readmission rates</p>
5	Jeong et al. 2011 ²⁴	<p>Separate groups for early gastric cancer and advanced gastric cancer:</p> <ul style="list-style-type: none"> • Non care pathway (general care) group • Pathway group <p>Both groups: Dec 2006-Nov 2007</p>	<p>The pathway was first implemented in September 2004. The pathway for patients with gastric cancer following gastrectomy were developed in 2006 to provide care for these patients. The pathway was electric medical record based. In the pathway for hospital staff which is presented in figure 1, the aspects: Lab, Treat, Activity, Diet, Mx, Education and Evaluation were described for the day before surgery, the day of surgery until 2/3 days after surgery (preoperative laboratory tests and diagnostic modalities, assessment of concomitant diseases, consultation for operative safety, bowel preparation and antibiotics at preoperative day 1 and postoperative day 1, removal of nasogastric tube, start of semi-fluid diet, removal of closed suction drain before discharge. There is also a pathway for patients; this is presented in figure 2.</p> <p>The care pathway employed standardized postoperative management using printed order sets, which included instructions for such matters as medication, diet, removal of the catheter and the mobility of the patients.</p>	<p>Meets criteria 1 - 4</p>	<p>Length of hospital stay (pre, post and total) (mean) Costs (pre, post and total)</p>
6	Kiyama et al. 2003 ²⁵	<ul style="list-style-type: none"> • Traditional care group (control) • Clinical pathway group <p>Both groups: January 2001 to December 2001.</p>	<p>The pathway was first implemented in September 2004. The pathway for patients with gastric cancer following gastrectomy were developed in 2006 to provide care for these patients. The pathway was electric medical record based. In the pathway for hospital staff which is presented in figure 1, the aspects: Lab, Treat, Activity, Diet, Mx, Education and Evaluation were described for the day before surgery, the day of surgery until 2/3 days after surgery (preoperative laboratory tests and diagnostic modalities, assessment of concomitant diseases, consultation for operative safety, bowel preparation and antibiotics at preoperative day 1 and postoperative day 1, removal of nasogastric tube, start of semi-fluid diet, removal of closed suction drain before discharge. There is also a pathway for patients; this is presented in figure 2.</p> <p>The care pathway employed standardized postoperative management using printed order sets, which included instructions for such matters as medication, diet, removal of the catheter and the mobility of the patients.</p>	<p>Meets criteria 1 - 4</p>	<p>Length of hospital stay: pre- and postoperative (mean, SD) Morbidity rate Postoperative complications</p>

7	Tastan et al. 2012 ²⁶ <ul style="list-style-type: none">Control group (clinical pathway was not used)Clinical pathway group Both groups: March 2004-April 2005	The clinical pathway was constructed after conducting a literature survey. The clinical pathways were organized to make them suitable for the clinic by considering work order and resources of the clinic along with the doctors and nurses. For this study, a standard clinical pathway that included possible problems of the patient, clinical goals, and the medical team's interventions for reaching the treatment goals was designed. Primary components of the breast surgery care protocol are: consultation/visit (physician, anesthetist, and nurse), diagnostic processes, patient evaluation/diagnosis processes, medication, treatment and clinical procedures, diet, activity/security, and psychological/educational/discharge planning (Appendix 1). This was described for the admission day, the operation day and the postoperative days 1 until 4.	Meets criteria 1 - 4	Patient anxiety Quality of life Patient satisfaction
8	Williams et al. 2015 ²⁷ <ul style="list-style-type: none">Usual care groupIntervention group Both groups: Feb 2011-Jan 2013 The usual care treatment is based on the Royal Marsden Hospital Pain and Palliative Care treatment guidelines. The intervention group received combined screening, treatment and educational approach. Patients in the usual care group were not proactively assessed at baseline, nor did they receive a timetable weekly pain assessment conducted by their pain physician. They also did not receive the pain education brochure.	Pain assessment and treatment was conducted by two pain clinic doctors and two nurses who were independent of the research team. Treatment took place immediately after allocation to the intervention group, and continued throughout the three month study period. Treatment was individualized according to analgesic needs and requirements according to the Royal Marsden Hospital Palliative Care & Pain Control guidelines, which are based on the WHO and British Pain Society guidelines. First the initial consultation took place. Further, follow-up sessions took place weekly either by telephone or in a pain clinic consultation. Each patient was also given an educational brochure about cancer pain and its treatment and this was discussed with a control pain doctor at the baseline time point. Subjects were asked proactively about their suitability for these additional pain control treatments. Different analgesic drugs and their expected benefit and side-effects were discussed.	Meets criteria 1 - 4	

* the described pathway was defined using the following definition of 'care pathways':

1. the intervention was a structured multidisciplinary plan of care.
 2. the intervention was used to translate guidelines or evidence into local structures.
 3. the intervention detailed steps in a course of treatment or care in a plan, pathway, algorithm, guideline, protocol or other "inventory of actions" (i.e. the intervention had time-frames or criteria-based progression).
 4. the intervention aimed to standardize care for a population of cancer patients.
- An intervention is considered to be a care pathway if it meets all four criteria.

Outcomes

The most frequently used patient outcomes reported in the included studies, were complications^{21,22,25} and readmission²¹⁻²³. Other reported patient outcomes were: patient satisfaction^{26,27}, patient anxiety^{26,27}, morbidity²⁵, and quality of life²⁶. However, these quality outcomes measures were not comparable between the studies.

Professional outcomes such as staff satisfaction and team functioning, were not reported in the included studies. Furthermore, Length of stay (LOS) was the most common used indicator for system level outcomes and was reported in five studies²¹⁻²⁵. For this outcome measure we were able to carry out a meta-analysis, see the paragraph about Effects on Length of Stay. Other system level indicators which were reported focussed on costs and hospital charges^{21-25,27}, but these studies showed considerable differences in definitions and results. Nevertheless, in most studies the actual costs instead of charges were reported^{21,23-25,27}, because costs are set constant over time. In one study the median total charges per patient was used as the primary outcome²². In addition, in all studies in which costs were reported, fixed as well as variable costs were included in the total costs. Besides, the studies showed differences in aspects which were included in the total costs. In four studies patient visits, consultation, assessment and diagnostic- and laboratory tests, as well as treatment were included^{21,23,25,27}. Medication was included in five studies^{21,22,23,25,27}. Facilities, like inpatient ward costs, operation room, medical and surgical supplies were reported in two studies^{22,23}. One study included professionals fees²¹. And in another study the costs for patient monitoring and patient education were included²³.

Additional, two studies reported extra information about the methods for conducting the cost analysis: in one study the hospital and professional costs were combined into a model that has been developed to set costs constant over time²¹ and in another study quality adjusted life days (QALD's) were generated and the results were presented in a Cost Effectiveness Acceptability Curve (CEAC) related to the willingness to pay²⁷. See table 3 for a summary of the outcomes reported in the studies.

Effects on patient outcomes

Patient outcome measures were reported in four studies^{21-23,25}. However, only two studies reported the measured effects in terms of complications^{22,25}, and one study reported outcomes measures in terms of readmissions²². Therefore, statistical pooling of quality outcomes could not be performed. Both studies reporting effects of complications described less observed complications among the pathway groups^{22,25}. The study reporting effects of readmissions described less readmissions for the pathway group within 30 days after surgery²². See for the results of the reported complications figure 1 and the reported readmissions figure 2.

Figure 1 Reported complications **Figure 2** Reported readmissions

Effects on Length of Stay (LOS)

The effects of cancer care pathways on LOS were reported in five studies²¹⁻²⁵. All included studies that measured LOS, reported results in favor of cancer pathways. In two studies both mean and standard deviation were reported^{23,25}, and three studies did not provide information on the standard deviation (SD)^{21,22,24}. One study reported the mean LOS, and the SD was calculated by using the Revman Calculator¹⁹. In another study the median and range was reported and the mean as well as the standard deviation were estimated²² (see 'dealing with missing data' in the methods section). In one study the median was reported only²¹, therefore we were not able to calculate the mean and standard deviation. Two studies consisted of two subgroups which were separately studied^{23,24}. See figure 3 for the results of all reported effects on LOS.

After conducting a meta-analysis with data of four studies²²⁻²⁵, which represented a study population of 1079 patients, substantial heterogeneity between the studies was observed ($I^2=72\%$). Therefore a forest plot with the total results without the pooled effects of all included studies reporting on LOS was presented in figure 3. The results of the meta-analysis of subgroups is presented in the section 'subgroup analysis'.

Figure 3 Reported effects on LOS

Effects on costs

Out of nine studies, six studies reported on costs effects^{21-25,27}. In four studies, including two studies with each two subgroups, lower costs were reported for pathway groups^{21-23,25}, and three of these studies reported a significant reduction of costs related to cancer care pathways^{21,24,25}. However, in one subgroup of a study the total hospitals costs and the preoperative costs were lower in the pathway group, but the postoperative costs were higher in the pathway group²⁴. Another study reported lower total and medication costs, but higher total daily costs in the pathway group²⁵.

Nevertheless, we observed a considerable methodological variation regarding the different methods used for cost calculation. In some studies a full cost approach was used, whereas other studies included only direct hospital costs. In Table 4 the costs differences are presented. In addition, we have provided the un-discounted cost data in a separate table shown in Additional file 7, to allow readers recalculate the results using any discount rate.

Table 4 Cost / charges data, standardized to the year 2016 (CCEMG EPPI tool used)

Study ID	Country	Currency	Costs included	Pathway	Control	Reduction of costs, per patient
Chen et al. 2000 ²¹	USA	US\$	Total costs including hospital and professional fees: surgery-related costs, treatment-related costs, medications, consultations, and assessment and diagnostic tests.	\$8448.62	\$11476.93 (historical control group, HCG) \$9341.37 (non-pathway group, NPG) \$137769.62	HCG vs pathway: -\$3028.31 NPG vs pathway: -\$892.75
Gendron et al. 2002 ²²	USA	US\$	The charge summary was divided into the following 6 categories: total, hospital room, pharmacy, operating room, laboratory, and other charges. Professional fees were not included.	\$103160.57 (>1 year, group 1) \$86155.35 (>3 years, group 2) \$5204.43	Control vs pathway group 1: -\$34609.05 Control vs pathway group 2: -\$51614.27 -\$215745 (-29%)	
Ghosh et al. 2001 ²² (cervical cancer)	USA	US\$				
Ghosh et al. 2001 ²² (endometrial cancer)	USA	US\$	Direct costs were obtained including hospitalization, pharmacy, laboratory, operation room, radiological, and other miscellaneous costs (the last includes: physical therapy, respiratory therapy, patient monitoring, and patient education).	\$5031.83	\$6327.63	-\$1295.80 (-32%)
Jeong et al. 2011 ²⁴ (advanced gastric cancer)	Korea	US\$	Total hospital costs There is no description available of which costs are included.	\$9297.65	\$9329.28	-\$31.63
Jeong et al. 2011 ²⁴ (early gastric cancer)	Korea	US\$	Preoperative costs	\$1330.75	\$1651.92	-\$321.17
			Postoperative costs	\$7966.90	\$7681.14	+\$285.76
			Total hospital costs There is no description available of which costs are included.	\$9997.61	\$11119.04	-\$1121.43
			Preoperative costs	\$1475.00	\$1975.97	-\$500.97
Kiyama et al. 2003 ²⁵	Japan	US\$	Postoperative costs	\$8522.61	\$9143.07	-\$620.46
			The total costs The total direct costs reported were the total medical costs (including medication and examinations). Medication costs only	\$13380.86	\$17206.63	-\$3825.77
			Daily total costs	\$1695.01	\$2410.03	-\$715.02
Williams et al. 2015 ²⁷	UK	US\$		\$519.91	\$495.58	+\$24.33
			Costs included: analgesic drug costs, pain clinic visits, use of physiotherapy, psychology and other resources.	\$629.64	\$336.79	+\$292.85

Abbreviations: USA: United States of America; US\$: United States Dollar; UK: United Kingdom.

Implementation of cancer care pathways

Information about the implementation of pathways was reported in five studies^{21-24,26}. To categorize the detailed information about the reported implementation process of the pathways, we used the refined taxonomy for guideline implementation of Mazza and colleagues²⁸. This taxonomy was based on the Cochrane Effective Practice and Organisation of Care (EPOC) data collection checklist and developed to classify the nature and content of implementation strategies. The taxonomy consisted of four domains: professional, financial (health care professionals, patients), organizational (health care professionals, patients, structural) and regulatory.

Professional domain

Present materials at meetings: in two studies health care professionals were given information regarding the pathway in order to implement the pathway adequately^{21,26}. Also several conferences and seminars were organized for outpatient and inpatient health care teams working with a disease site working group. Further, physicians were briefed on the pathway²¹. In another study nurses underwent a two-hour training session to refresh their information on cancer risk factors, symptoms, diagnostic methods, treatment, pre-operative and post-operative nursing care for patients, and discharge procedures. In addition, doctors and nurses were given information about the clinical pathway and their duties and responsibilities while implementing it²⁶.

Organizational domain

Creation of an implementation team: in three studies a multidisciplinary group was involved in the development of the pathway^{21,22,24}. In one study a core group determined which pathways were developed and a disease site working group was organized to draft the pathway²¹. In another study the pathway was developed and continued to be modified by a multidisciplinary team which included surgeons, nurses, and allied health care representatives²². In addition, in one other study the involvement of the multidisciplinary team was less clear²³. In this study the development of the pathways within a multidisciplinary team was not mentioned, but the pathways were based on the results of clinical trials and consensus of experts. Furthermore, these pathways were developed in cooperation with the department of anesthesia pain service and a pharmacist reviewed the recommendations. Moreover, the nursing team played an active role in developing these pathways²³.

Change in information & communication technology: in one study was described that almost one year after the pathway was implemented, an electronic medical record (EMR)-based care pathway was being used²⁴.

No implementation activities in the regulatory and financial domains were described in the primary studies.

Subgroup analyses

Subgroup analyses were conducted in order to formulate more thorough conclusions relevant for clinical practice. These analyses were performed according to the protocol described previously.

Type of tumor

The included studies were subdivided by type of tumor. We created subgroups of the study with subgroups including patients with gynaecological cancer²³ and studies including patients with gastric cancer^{24,25}. Based on the random effects model, pathways for patients with gastric cancer showed a statistical significant pooled reduction of more than two and a half days compared to usual care (WMD: -2.75; CI: -4.67--0.83). In the study with subgroups including patients with cervical and endometrial cancer, we observed a statistical significant pooled LOS reduction of more than one and a half day (WMD: -1.58; CI: -2.10--1.05). Furthermore, the total pooled LOS reduced almost 2 days (WMD: -1.87; CI: -2.42--1.31), which was a statistical significant result, associated with a moderate amount of heterogeneity ($I^2=50\%$). Nevertheless, it should be mentioned that the effects on LOS for pathways regarding patients with gynaecological cancer was based on one overall study, which contained two subgroups. See figure 4 with the subgroup analyses of the effects on LOS.

Figure 4 Subgroup analyses of the effects on LOS

Country

The primary studies were ordered by country to examine possible different market effects. Therefore studies carried out in North America versus the studies performed in Asia (Korea and Japan) were analyzed. However, no association between country and the impact of pathways on LOS was detected.

Year of publication

Subgroup analysis based on the year of publication was similar for the subgroups subdivided by country, which showed no association.

Sensitivity analysis

First, the robustness of the pooled LOS effects was determined by the available information about the standard deviation on LOS. In two studies both mean and standard deviation were reported^{23,25}, and for three studies the standard deviation was calculated due to missing information^{21,22,24}, see Effects on Length of Stay.

We tested the robustness of the pooled LOS effects using different statistical calculation models, i.e. fixed versus random effects model. The pooled effects changed slightly when using the fixed effects model which indicates reliable pooled results.

In addition, sensitivity analysis were performed to test whether the effects size of LOS varied by the countries where the studies were carried out. Subsequently, we tested the hypothesis that different market forces are possibly confounding the conclusions of our meta-analysis. After stepwise exclusion of the studies carried out in North America, the pooled LOS effect increased, while the statistical heterogeneity reduced (WMD: -2.75; $I^2=59\%$).

Sensitivity analysis were also performed to analyze the variation in the year of publication in order to test our hypothesis that pathways which were developed and implemented in more recent years could have had more success in reducing the LOS than less recent studies (or vice versa). After stepwise exclusion of all studies published before 2003, one study with two subgroups showed no statistical heterogeneity and a statistically significant pooled LOS effect of -2.03 days.

Results of studies conducted in the primary and secondary health care (hospital care) setting

Study characteristics

This paragraph provides a description of the following study characteristics: study designs, tumor location, sample size, country, and health care setting of the study covers both the primary setting as well as the secondary setting²⁹. This study used a non-randomized controlled trial study design. A control group was compared to two post-pathway groups, i.e. a pathway group and a non-pathway group. The study focused on cancer pathways for patients with colorectal cancer, lung cancer, breast cancer, prostate cancer, melanoma and other types of tumors. This study was performed in Denmark and represented 3,292 patients²⁹. See table 1.

Population characteristics

Information about the group of patients before the implementation of pathways and three groups after implementation of the pathways was available regarding gender and age. No information was available about the socioeconomic status. See table 2 for more information.

Intervention characteristics

This study was based on the implementation of standardized cancer patients pathways in 2008. Therefore, dissatisfaction of cancer patients with long waiting times was investigated. Although the cancer pathways did not include the diagnostic workup performed in general practice, the study focused on the time between referral by patients general practitioner (GP) to the first consultation at the hospital. Besides using registered data, patients were questioned about their satisfaction with the waiting times and GP's were questioned about their involvement in diagnosing the cancer. In the Danish health care system the GP serves as a gatekeeper to secondary care and GP's refer patients to other clinicians when there is a reasonable suspicion of cancer. The authors concluded that the waiting time during the diagnostic process was reduced and patients were more satisfied after implementation of cancer pathways²⁹.

More detailed information about the specific pathway which was studied, was found an article included in the list of references³⁰. In this publication it was stated that a pathway in the Danish context is a standardized pathway that most patients suspected of cancer will be able to follow. It describes the patient's pathway from clinical suspicion of a certain cancer through diagnostic procedures and treatment. The pathway describes the medical procedures, the necessary organization encompassing both primary and secondary sectors of the health system, and timeframes in accordance with the political agreement. Main emphasis in pathways is placed on information to be given to the patient, explicit identification of the responsible health care professional or department in all phases, procedures for referral, description of multidisciplinary teams in each pathway as a forum for making decisions on diagnosis and recommended treatment, and timeframes of all phases³⁰. In addition, the framework of the Danish cancer pathways includes three different descriptions of the pathway: a flowchart, a narrative text and a table providing an organizational overview. An example of a Danish cancer pathway was presented³⁰. See table 3 for more information about the intervention characteristics.

Outcomes

Patient satisfaction was the reported measured, which was measured using a patient questionnaire and a general practitioner questionnaire. This information was supplemented with register data²⁹. See table 3.

Quality assessment

To assess the quality of this study conducted in both primary and secondary, we adhered to the validated criteria suggested by the Effective Organisation of Care Group (EPOC), see 'results studies in the secondary/tertiary care setting, quality assessment' in the result section¹⁷. This study was assessed as being at high risk of bias (Additional file 6).

Implementation of cancer care pathways

The included study described the development of cancer care pathways rather specific, but little information was given about the implementation process. Based on the description regarding the development, we may assume there was multidisciplinary involvement of clinicians and other health care professionals. But it remains unclear which role the regional representatives and other relevant health care professionals had in the implementation process of the pathway. Using the taxonomy for guideline implementation²⁸, the organizational domain was addressed for at least the development of the presented pathways.

Organizational domain

Creation of an multidisciplinary team: in this study the development of cancer care pathways was based on a common framework. Subsequently, health care professionals formulated the medical content in accordance with the consensus-based framework and finally the pathways were approved by a two-step process involving all stakeholders. This framework ensured that all stakeholders were able to influence the process which could be characterized as a 'bottom-up and top-down' approach with involvement of both local and central actors, and in which administrators, health care professionals, and politicians cooperated to strike a balance. Further, agreeing on a framework and the integration of needs from the view of various professional disciplines, created a common understanding on how the best possible pathway was acquired. The framework was used for all cancer types to ensure consistency and ease the implementation of the various pathways.

In addition, for the development of these pathways working groups developed the content using a consensus-making process where all stakeholders participated actively and contributed to the final product. The clinical working groups were asked to describe standard timeframes for the various elements involved in each pathway. These timeframes were further estimated without consideration of existing capacity and resources and thus indicate the minimum time needed to treat an "ideal patient" in an "ideal health system".

Once a pathway had formally been approved, the five health regions had three months to ensure implementation at the local level. The regional representatives in the working groups knew the pathways in details which was an important factor in ensuring the implementation process³⁰.

DISCUSSION

We screened more than 13,000 published studies to assess the effects of cancer care pathways in primary and secondary/tertiary care. Finally, eight studies met our inclusion criteria with a total of 4,786 patients. The included studies were conducted in six different countries and the investigated care pathways covered for more than 10 different types of tumors in general hospitals or academic hospitals in the primary and secondary health care setting.

Most studies were conducted in secondary/tertiary care and concerned the perioperative surgical care process. One study was carried out in both primary and secondary care, measuring dissatisfaction with waiting times. However, we observed considerable variance between the included studies regarding the pathways which were measured, the settings in which the studies were performed as well as the reported outcomes, especially the reported costs. Despite these differences, all included studies that measured LOS reported results in favor of cancer care pathways. Further, as a consequence of the clinical variability between the included studies, we observed a considerable statistical heterogeneity and therefore meta-analysis was often inappropriate. However, we were able to calculate the pooled effects of LOS for subgroups based on type of tumor and observed positive impact of cancer care pathways for patients with gastric and gynaecology cancer which can be of interest for clinicians and managers.

In order to answer the secondary research question, we collected and analyzed information about the implementation of cancer care pathways in the included studies. In more than half of the included studies implementation activities regarding cancer care pathway were described. Almost all these activities could be categorized as 'professional' aspects (such as presenting materials in order to inform health care professionals, educating groups, and providing feedback) and 'organizational' aspects (such as creating a multidisciplinary team, and changing the information & communication system). We observed that all studies which reported a positive impact on LOS in favor of the pathway described the involvement of a multidisciplinary team in the development of the pathway. Based on these observations, it is likely that the involvement of a multidisciplinary team could be a success factor in achieving positive outcomes of cancer care pathways. In addition, literature confirmed that implementation strategies have been poorly reported and evidence on successful clinical pathway implementation is limited and varies significantly in how health care organizations implement pathways³¹. Due to the differences in activities which were used for implementing care pathways, we could not formulate thorough conclusions about implementation strategies related to the differences in outcomes based on this review.

Although we searched for studies in primary and secondary/tertiary health care, we mainly found studies performed within secondary cancer care and only one study was related to both primary care and secondary health care. A possible reason why we did not find many publications in the primary care setting could be because pathways are widely used in inpatient and secondary/tertiary care, but their potential benefit in primary care is largely unclear¹².

This systematic review has several limitations. Despite our electronic search strategy, the additional search in grey literature and the independent screening of the search results, it is possible that some studies are overlooked. In addition, in order to present an evidence base regarding the effects of oncological care pathways we focussed in our literature search on "research" rather than "quality improvement", which may have contributed to publication

bias. However, we included all studies meeting our definition of care pathways, also when the term pathway was not mentioned in the text. Furthermore, due to the clinical variability of the included studies as well as the low number of included studies reporting on the outcome measures the pooled effects on LOS should be interpreted carefully.

Furthermore, from the perspective of clinical relevance the correlation between the presence of complications and readmission is interesting, because patients can be readmitted to the hospital after a complication occurs. In addition, there is evidence that complications are a risk factor for in hospital readmissions³². However, we did not find any results of correlation analysis on this in the included studies.

CONCLUSION

This systematic review was conducted in order to identify, assess and synthesize all quantitative studies on the effects of oncological care pathways. Despite of the differences between the included studies, we were able to present an evidence base for cancer care pathways regarding the subgroup effects of LOS. However, the effects on complications, readmissions and costs as well as the implications of differences in implementation of cancer care pathways were not conclusive enough.

Finally, cancer care pathways have shown their value for clinical practice, however a comparison of care pathways is challenging and the impact of the implementation process on the outcomes remains rather unclear. Because of the paucity of high-quality evidence on the important questions covered by the review, there is a need for further well-designed research and audit.

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Additional file 1 Overview inclusion criteria**Inclusion criteria:**

- Participants: patients, care providers, and health care organizations in primary and secondary/tertiary care.
- Intervention: care pathway based on four operational pathway criteria.
- Comparators: cancer care pathway versus usual care, cancer care pathway versus control, cancer care pathway versus non-pathway.
- Outcomes: patient, professional and system level outcome (primary) and measures regarding implementation strategies and methods (secondary).
- Study designs: randomized controlled trials (RCT), non-randomized controlled trials (NRCT), controlled before-after studies (CBA), and interrupted time series studies (ITS), cost-effectiveness analyses, cost-utility analyses and cost-benefit analyses, cost analysis and comparative resource utilization studies

Additional file 2 Prisma flow diagram**Care pathways search strategy Ovid Medline: 1946 to June 1, 2020**

- 1 exp Neoplasms/
- 2 exp medical oncology/ or radiation oncology/ or surgical oncology/
- 3 oncologists/ or radiation oncologists/
- 4 (cancer or oncolog\$ or neoplasm?).ti,ab,kw,kf.
- 5 (cancer or carcinoma\$ or oncolog\$ or malignanc\$ or neoplasia? or neoplasm?).ti,ab,kw,kf.
- 6 (tumo?r? adj3 (malignan\$ or neoplas\$)).ti,ab,kw,kf.
- 7 or/1-6 [Cancer]
- 8 Critical Pathways/
- 9 care plan?.ti,ab,kw,kf.
- 10 structured care.ti,ab,kw,kf. clinical pathway/
- 11 intensive management.ti,ab,kw,kf.
- 12 (standardi?ed adj2 (care or patient care or treatment?)).ti,ab,kw,kf.
- 13 (care algorithm? or treatment algorithm? or therapeutic algorithm?).ti,ab,kw,kf.
- 14 (care path\$ or clinical path\$ or critical path\$ or patient care path\$ or pharmacotherap\$ path\$ or therapeutic\$ path\$ or treatment? path\$).ti,ab,kw,kf.
- 15 ((care or clinical or patient care or pharmacotherap\$ or therapeutic\$ or treatment?) adj2 pathway?).ti,ab,kw,kf.
- 16 ((care or treatment) adj2 (map or maps)).ti,ab,kw,kf.
- 17 process map\$.ti,ab,kw,kf.
- 18 or/8-17 [Critical Pathways]
- 19 7 and 18 [Cancer & Pathways]
- 20 ((guideline or guidelines) adj4 (local\$ or adapt\$ or customi\$ or tailor\$)).ti,ab,kw,kf.
- 21 ((guideline or guidelines) adj4 (pathway? or path way?)).ti,ab,kw,kf.
- 22 ((guideline or guidelines) adj4 (interdisciplin\$ or inter-disciplin\$ or crossdisciplin\$ or cross disciplin\$ or multidisciplin\$ or multi-disciplin\$ or team? or standardi?)).ti,ab,kw,kf.
- 23 or/20-22 [Guidelines--customized, locally adapted]
- 24 guideline/ or practice guideline/
- 25 (local or local?y or adapted or customi\$ or interdisciplin\$ or inter-disciplin\$ or crossdisciplin\$ or cross disciplin\$ or multidisciplin\$ or multi-disciplin\$ or standardi\$).ti,ab,kw,kf.
- 26 and/24-25 [MeSH GUideline & customization terms]
- 27 or/23,26 [Customized Guidelines]
- 28 7 and 18 [Cancer & Pathways]
- 29 (7 and 27) not 28 [Cancer & Customized Guidelines]
- 30 (randomized controlled trial or controlled clinical trial).pt. or randomized.ab. or placebo.ab. or clinical trials as topic.sh. or randomly.ab. or trial.ti.

- 31 exp animals/ not humans.sh.
- 32 30 not 31 [Cochrane RCT Filter 6.4.d Sens/Precision Maximizing]
- 33 intervention?.ti. or (intervention? adj6 (clinician? or collaborat\$ or community or complex or DESIGN\$ or doctor? or educational or family doctor? or family physician? or family practitioner? or financial or GP or general practice? or hospital? or impact? or improv\$ or individuali?e? or individuali?ing or interdisciplin\$ or multicomponent or multi-component or multidisciplin\$ or multi-disciplin\$ or multifacet\$ or multi-facet\$ or multimodal\$ or multi-modal\$ or personali?e? or personali?ing or pharmacies or pharmacist? or pharmacy or physician? or practitioner? or prescrib\$ or prescription? or primary care or professional\$ or provider? or regulatory or regulatory or tailor\$ or target\$ or team\$ or usual care)).ab.
- 34 (pre-intervention? or preintervention? or "pre intervention?" or post-intervention? or postintervention? or "post intervention?").ti,ab.)
- 35 (hospital\$ or patient?).hw. and (study or studies or care or health\$ or practitioner? or provider? or physician? or nurse? or nursing or doctor?).ti,hw.
- 36 demonstration project?.ti,ab.
- 37 (pre-post or "pre test\$" or pretest\$ or posttest\$ or "post test\$" or (pre adj5 post)).ti,ab.
- 38 (pre-workshop or post-workshop or (before adj3 workshop) or (after adj3 workshop)).ti,ab.
- 39 trial.ti. or ((study adj3 aim?) or "our study").ab.
- 40 (before adj10 (after or during)).ti,ab.
- 41 ("quasi-experiment\$" or quasiexperiment\$ or "quasi random\$" or quasirandom\$ or "quasi control\$" or quasicontrol\$ or ((quasi\$ or experimental) adj3 (method\$ or study or trial or design\$))).ti,ab,hw.
- 42 ("time series" adj2 interrupt\$).ti,ab,hw.
- 43 (time points adj3 (over or multiple or three or four or five or six or seven or eight or nine or ten or eleven or twelve or month\$ or hour? or day? or "more than")).ab.
- 44 pilot.ti.
- 45 Pilot projects/
- 46 (clinical trial or controlled clinical trial or multicenter study).pt.
- 47 (multicentre or multicenter or multi-centre or multi-center).ti.
- 48 random\$.ti,ab. or controlled.ti.
- 49 (control adj3 (area or cohort? or compare? or condition or design or group? or intervention? or participant? or study)).ab. not (controlled clinical trial or randomized controlled trial).pt.
- 50 "Controlled Before-After Studies"/ or "Interrupted Time Series Analysis"/
- 51 evaluation studies as topic/ or prospective studies/ or retrospective studies/
- 52 (utili?ation or programme or programmes).ti.
- 53 (during adj5 period).ti,ab.
- 54 ((strategy or strategies) adj2 (improv\$ or education\$)).ti,ab.
- 55 "comment on".cm. or review.pt. or (review not "peer review\$").ti. or randomized controlled trial.pt.

- 56 exp animals/ not humans.sh.
- 57 (animal? or beaver? or beef or bovine or breeding or bull or canine or castoris or cat or cattle or cats or chicken? or chimp\$ or cow or dog or dogs or equine or foal or foals or fish or insect? horse or horses or livestock or mice or monkey? or mouse or murine or plant or plants or pork or porcine or protozoa? or purebred or rat or rats or rodent? or sheep or thoroughbred).ti. or veterinar\$.ti,ab,kw,kf,hw.
- 58 (or/33-54) not (or/55-57) [EPOC Filter for Non-RCT designs]
- 59 ((systematic adj2 review) or metaanaly\$ or meta=analy\$ or scoping review or concept analysis).ti,kw,kf.
- 60 cochrane.jw.
- 61 meta-analysis/
- 62 or/59-61 [ad hoc SR/MA Filter--Cochrane Library will also be searched for related reviews]
- 63 (or/28-29) and (32 not 57) [RCT Results]
- 64 (or/28-29) and 58 [NRCT Results]
- 65 (or/28-29) and 62 [SR Results]
- 66 remove duplicates from 65 [SR results to export]
- 67 remove duplicates from 63 [RCT Results to export]
- 68 67 not 66 [RCT Results to export]
- 69 remove duplicates from 64
- 70 69 not (or/66,68) [NRCT Results to Export]

Additional file 4 Excluded studies: reason for exclusion

	Study ID	Reason for exclusion	Patients/ subjects	Study design	Country	Outcomes
1	Abou-Haidar H, et al. 2014	Study did not meet Cochrane EPOC study design criteria	prostate cancer	retrospective study	Canada	Duration of hospital stay, complications, post-discharge emergency department visits and readmissions
2	Adams J. 2000.	Unavailable full-text				
3	Afonso A, et al. 2017	Not cancer patients	patients undergoing microsurgical breast reconstruction (not cancer patients)	retrospective cohort study	USA	Hospital length of stay and total postoperative opioid consumption
4	Aggarwal R, et al. 2014	Study did not meet Cochrane EPOC study design criteria	esophageal cancer surgery	systematic review	NA	Pre-, intra-, and post-operative measures: epidural analgesia, early catheter and tube removal, and early post-operative mobilization
5	Andtbacka RH, et al. 2006	No control	breast cancer surgery	retrospective and retrospective cohort study?	USA	Postoperative venous thromboembolism (VTE) within 60 days
6	Baade PD, et al. 2010	Protocol only	prostate cancer	longitudinal epidemiological study without a control group	Australia	Demographics, medical history, patterns of care, disease and treatment characteristics, quality of life and psychological adjustment, detailed treatment information, road travel distances from patients' residences to treatment centers
7	Bae HW, et al. 2017	Study did not meet Cochrane EPOC study design criteria	colorectal cancer patient	retrospective study	Korea	Length of hospital stay, incidence of postoperative complication, the value of preoperative prognostic nutritional index (PNI), disease free survival (DFS), overall survival (OS)
8	Baffert S, et al. 2015	Protocol only	breast cancer	observational, prospective, multicenter study	France	Cost of pathway, patient satisfaction and work reintegration, quality, coordination and access to innovation

9	Bakens MJAM, et al. 2016	Abstract only	pancreatic cancer	retrospective study, with before and after pathway groups		Unclear
10	Bao H, et al. 2016	No information about CP	Breast, colon and rectal cancer	Interrupted time series study	China	Length of hospital stay (median, IQR), complications, quality indicators about the compliance with the care process
11	Barrett J, et al. 2008	Study did not meet Cochrane EPOC study design criteria	lung cancer	retrospective case-control study	UK	Referral and time to diagnosis
12	Barrett J, et al. 2006	Study did not meet Cochrane EPOC study design criteria	colorectal cancer	observation study	UK	7 clinical features: diarrhea, constipation, rectal bleeding, abdominal pain, the finding of an abdominal or rectal mass on examination, anaemia, positive faecal occult blood tests. And time intervals: first consultation to first referral, first referral to diagnosis
13	Barrett J, et al. 2010	Study did not meet Cochrane EPOC study design criteria	ovarian cancer	cohort study	UK	Patients taking specific routes to diagnosis, together with the time taken to diagnosis
14	Bosch C, et al. 2010	Abstract only	breast cancer	??	Germany	Hospitalization
15	Brannstrom M, et al. 2016	Not cancer patients only	patients in the last days of their lives	exploratory, controlled before-after study	Sweden	Patients' symptoms: distress and well-being during the last days of life
16	Chan RJ, et al. 2016	Study did not meet Cochrane EPOC study design criteria	patients in the last days of their lives	systematic review	NA	Primary outcomes: physical symptom severity, psychological symptom severity, harms. Secondary outcomes: advanced care planning, communication between health care teams and families, carers' well-being, grief and bereavement, patient/staff/carers' satisfaction, staff confidence, cost of intervention, cost of care, medication/treatment use, spiritual needs
17	Chang PL, et al. 2002	Other intervention	renal cell carcinoma	??	Taiwan/UK	Length of stay, admission charges, six quality indicators and the advantages of the web based pathway.

18	Chang PL, et al. 2000	Study did not meet Cochrane EPOC study design criteria	renal cell carcinoma	retrospective cohort study	Taiwan	Length of stay, average admission charges, and 8 quality indicators
19	Chang SS, et al. 2002	Not cancer patients	radical cystectomy (no oncology patients)	??	USA	Complication rate, post-operative ileus, blood loss, mortality rate
20	Chang SS, et al. 2002	Study did not meet Cochrane EPOC study design criteria	germ cell carcinoma	retrospective study	USA	Clinical/pathological stage, hospital stay, postoperative care and complications rate
21	Chang WC, et al. 2003	Not cancer patients only	patients who recieved laparoscopy assisted vaginal hysterectomy (mostly patients with myoma uteri)	retrospective study	Taiwan	Delay of operation, blood transfusion, duration of post-operative antibiotics, patient mortality, complications, readmissions, length of stay, duration of operation, duration of anesthesia
22	Chang WC, et al. 2003	Not cancer patients only	most patients with myoma uteri (a few patients with cancer)	retrospective study	Taiwan	Costs, operation time, length of stay
23	Chase DM, et al. 2008	Study did not meet Cochrane EPOC study design criteria	gynaecologic oncology patients	retrospective study (with-out control group)	USA	Readmissions, mortality, complication rates
24	Choi JW, et al. 2013	Other intervention	gastric cancer	retrospective study	Korea	Discharge, readmission, complications
25	Choi JY. 2011	Study did not meet Cochrane EPOC study design criteria	hepatocellular carcinoma	descriptive article about treatment algorithm	Korea	
26	Cohen J, et al. 1997	Other intervention	head and neck cancer	before-after trial	USA	Length of stay, costs of hospitalization, and variance tracking
27	Costantini M, et al. 2011	Protocol only		Randomized cluster trial	Italy	Overall quality of life
28	Costantini M, et al. 2014	Other outcomes	cancer patients	before after cluster phase II trials	Italy	Outcomes reported by family members
29	Costantini M, et al. 2014	Does not meet CP definition	cancer patients	pragmatic cluster randomised trial	Italy	Overall quality of life

30	Dautremont JF, et al. 2016	Study did not meet Cochrane EPOC study design criteria	Head and neck onco-logic surgery	before-after study	Canada	Emergency department visits, outpatient visits, inpatients admissions, physician claims, post discharge costs: inpatient costs, outpatients costs, emergency department costs, medical doctor claims costs
31	Dautremont JF, et al. 2013	Study did not meet Cochrane EPOC study design criteria	Head and neck surgery	before-after study	Canada	Length of stay, return to operation room, readmission to Intensive Care Unit, time to decannulation, pneumonia
32	de Luc K. 2000	Study did not meet Cochrane EPOC study design criteria	breast disease patients (including cancer patients as subgroup)	quasi experimental case study	UK	Waiting times, diagnostic procedures performed. For cancer patients: discussion in multidisciplinary meeting, seeing the specialist breast nurse, first seeing specialist breast nurse in the outpatients, number of times patients seeing specialist breast nurse.
33	Delgado A, et al. 2013	No control	oncology patients	unclear	USA	Unclear
34	Dyrop HB, et al. 2013	Study did not meet Cochrane EPOC study design criteria	bone and soft tissue sarcomas	retrospective study	Denmark	Milestones, time intervals, performed diagnostics, and tumor size
35	Fackler-Schwalbe I, et al. 2014	Abstract only		unclear	Germany	Unclear
36	Fields KK, et al. 2017	Other intervention		adherence to pathways		Unclear
37	Fiore JF, et al. 2016	Study did not meet Cochrane EPOC study design criteria	patients undergoing elective lung resection	systematic review	NA	LOS (ie, time from surgery until first discharge), post-operative complications, readmissions, mortality rates, and patient-reported outcomes (PROs)
38	Forrest LF, et al. 2017	Study did not meet Cochrane EPOC study design criteria	lung cancer	systematic review and meta-analysis	NA	Stage at diagnosis or the length of time spent within an interval on the care pathway, socio-economic position
39	Gasbarrini A, et al. 2010	Other intervention	spinal metastases.	semiprospective clinical study	Italy	Neurologic function, local recurrence/development rate comparison, postoperative survival time

40	Gerardi MA, et al. 2008	Does not meet CP definition	advanced ovarian and primary peritoneal cancers	case-control methodology	USA	The median time to flatus, median time to tolerance of diet, length of hospital stay, 30-day post-operative hospital cost, 30-day readmission rate, hospital cost
41	Gordon SA, et al. 2016	Study did not meet Cochrane EPOC study design criteria	head and neck cancer surgery	a systematic review	NA	Setting, length of stay, complications, readmission, costs, and case length
42	Grau C, et al. 2011.	Study did not meet Cochrane EPOC study design criteria	patients with squamous cell carcinoma of the oral cavity, pharynx, and larynx	retrospective study	Denmark	Total time from first health care contact to start of definitive treatment, median time used for diagnosis, median time from diagnosis to treatment start
43	Gustafsson UO et al. 2011	Study did not meet Cochrane EPOC study design criteria	colorectal cancer surgery	before-after study	Sweden	Postoperative symptoms, complications, length of stay, 30-day morbidity, mortality
44	Hingh IDE, et al. 2014	Study did not meet Cochrane EPOC study design criteria	pancreatic cancer	retrospective study	Netherlands	Proportion of patients without pre-operative biliary drainage, duration of referral to surgery, duration of 1st outpatient visit to final treatment and the number of preoperative outpatient visits prior to treatment
45	Hirasaki S, et al. 2004	Study did not meet Cochrane EPOC study design criteria	mucosal gastric carcinoma	retrospective study	Japan	Total length of hospitalization, preoperative stay, postoperative stay, hospital costs, total costs, the number of endoscopic examination, operation times
46	Hoverman JR, et al. 2011	Study did not meet Cochrane EPOC study design criteria	colon cancer	retrospective cohort design	USA	Disease-free survival in patients receiving adjuvant treatment and overall survival and costs
47	Hsu YC, et al. 2008	Study did not meet Cochrane EPOC study design criteria	localized prostate cancer	retrospective study?	Taiwan	Pathway variations and length of hospital stay
48	Hubner M, et al. 2015	Study did not meet Cochrane EPOC study design criteria	colorectal surgery	a retrospective cohort study	Switzerland	Return of bowel function (flatus/stool), postoperative complications, length of stay, total hospital stay, number of preoperative days, early readmissions within 30 days after surgery

49	Husbands JM, et al. 1999	Study did not meet Cochrane EPOC study design criteria	head and neck onco-logic surgery	before-after study	USA	Median charge per patient, length of stay, readmission rate, complication rate, mortality rate
50	Iijima K, et al. 2003	Study did not meet Cochrane EPOC study design criteria	patients with neoplastic diseases	retrospective study	Japan	Differences in procedures and therapy between the pathway group and control group, postoperative complications, readmissions, or overall deaths for one year
51	Ise Y, et al. 2003	Other intervention	stomach cancer	cost-effectiveness analysis.	Japan	Pre- and postoperative stay at the hospital, length of stay, costs
52	Ishiguro S, et al. 2008	Study did not meet Cochrane EPOC study design criteria	colorectal cancer	retrospective study	Japan	Hospital stay, mortality, morbidity, reoperation, readmission
53	Jackman DM, et al. 2017	Study did not meet Cochrane EPOC study design criteria	lung cancer	before-after study	USA	Costs of care & clinical outcomes (survival times)
54	Jakobsen JK, et al. 2016	Study did not meet Cochrane EPOC study design criteria	penile cancer	observational study	Denmark	Median time intervals (in calendar days) with inter-quartile range were the main outcome measure
55	Jensen KH, et al. 2015	Study did not meet Cochrane EPOC study design criteria	colorectal cancer	retrospective cohort study	Denmark	Median referral time from GP to endoscopy, time from referral to oncological treatment, long-term survival rate
56	Kagan SH, et al. 2002	No control	head and neck surgery	retrospective study?	USA	LOS and age
57	Kardos SV, et al. 2016	Abstract only	bladder cancer	unclear	USA	LOS, complications, readmissions
58	Katterhagen G. 1996	Unavailable full-text				
59	Keetch DW, et al. 1998	Other control	adenocarcinoma of the prostate	prospective study	USA	Hospital stay, hospital costs
60	Kennedy EP, et al. 2009	Other patient population	patients underwent distal pancreatectomy (44% malignant in prepathway group and 56% in postpathway group)	retrospective study	USA	Operative length, post-operative complications, Perioperative mortality, length of postoperative hospital stay, readmission rate, hospital costs

61	Khan SA, et al. 2013	Study did not meet Cochrane EPOC study design criteria	patients undergoing elective colorectal surgery (83% colorectal cancer in laparoscopic group, 76% in the open-ERAS group)	prospective observational study	UK	Length of stay and quality of life (HQoL)
62	Khoo CK, et al. 2007	Other intervention	patients undergoing elective resection for colorectal cancer	prospective randomized controlled trial (RCT)	UK	Postoperative stay, and achievement of independence milestones. Secondary endpoints were postoperative complications, readmission rates, and mortality.
63	Kim HS, et al. 2015	Other intervention	gastric cancer	retrospective study	South Korea	Unclear
64	Kiyama T, et al. 2003	Study did not meet Cochrane EPOC study design criteria	gastrectomy patients	economic analysis	Japan	Length of hospital stay, costs of hospital stay: cost per bed
65	Klinkhamer-Schalke M, et al. 2012	Other intervention	breast cancer	randomised controlled trial (RCT)	Germany & UK	'diseased' QoL (any QoL measure below 50 points) using a QoL profile
66	Klinkhamer-Schalke M, et al. 2015	Protocol only	colorectal cancer patients	RCT	Germany	Quality of life
67	Kobayashi ST, et al. 2017	Study did not meet Cochrane EPOC study design criteria	rectal cancer	a retrospective study	Brazil	The interval between the first medical consultation date and postoperative day 30. The resources considered: consultations (medical, multidisciplinary, dental), computed tomography (CT) scans, MRI scans, colonoscopies, emergency room care, the chemotherapy regimen, radiotherapy sessions, and the surgery, as well as hospital stays, ICU stays, day hospital stays, and costs.
68	Konety BR, et al. 1996	Study did not meet Cochrane EPOC study design criteria	radical retro-pubic prostatectomy	before-after study	USA	Hospital charges, length of stay, operating room time, units of packed red cells transfused, morbidity, mortality

69	Kreys ED, et al. 2013	Study did not meet Cochrane EPOC study design criteria	breast, lung, or colorectal cancer treatment	a retrospective single-group, pre-test–post-test design.	USA	Compliance rate for chemotherapy, supportive care site compliance, patient drug costs, hospitalization costs
70	Langham J, et al. 2013	Study did not meet Cochrane EPOC study design criteria	diagnoses such as cancer	??	UK	Unclear
71	Lee L, et al. 2013	Study did not meet Cochrane EPOC study design criteria	elective oesophag-ectomy	before-after study	Canada	Length of hospital stay, complication rates, readmission within 30 days of surgery, in-hospital mortality rate, costs (pathway dependent & total)
72	Leibman BD, et al. 1998	Does not meet CP definition	prostate cancer	retrospective study?	USA	Total hospital charges and length of stay, physician volume, patient satisfaction, Incidence of postoperative urinary tract infections, atelectasis, wound infection, and paralytic ileus
73	Lemmens L, et al. 2009	Study did not meet Cochrane EPOC study design criteria	patient undergoing oncology surgery of the gastrointestinal tract	systematic review	NA	Postoperative outcome measures
74	Letton C, et al. 2013	Abstract only	gynaecological oncology	unclear	UK	Duration of intraperitoneal drains, urethral catheters, intravenous fluids postoperatively, time to eat and drink, time to mobilization, length of hospital stay
75	Lindberg P, et al. 2016	Other intervention	colorectal cancer patients	RCT	Germany	Quality of life
76	Llobera J, et al. 2017	Protocol only	palliative care patients (oncology and non-oncology)	RCT	Spain	Early identification, evaluation of case complexity, level of case complexity, use and cost of hospital and primary care services, and quality of life during the last month of life
77	Lorenz W, et al. 2005	Abstract only	breast cancer	prospective trial	Germany	Unclear

78	Lyhne NM, et al. 2013	Study did not meet Cochrane EPOC study design criteria	head and neck cancer: patients with squamous cell carcinoma of the oral cavity, pharynx and larynx	retrospective study?	Denmark	Time intervals: Time from first health care contact with a cancer suspicion until final histopathological diagnosis was presented to the patient; Time from diagnosis to first day of either RT or definitive surgery; Time from suspicion of cancer to start of definitive treatment. Number of diagnostic imaging procedures performed (ultra sound (US), CT, magnetic resonance imaging (MRI) and (MRI) and positron emission tomography (PET)-CT).
79	Markar SR, et al. 2015	Study did not meet Cochrane EPOC study design criteria	oesophagus cancer	systematic review	NA	Incidence of postoperative mortality, anastomotic leak and pulmonary complications, and secondary outcomes were length of hospital stay and the incidence of 30-day readmission.
80	Markar SR, et al. 2014	No control	oesophagus cancer	prospective study?	USA & UK	Use of neo-adjuvant therapy, blood loss, intraoperative fluid administration, ICU stay, length of hospital stay, post-operative complications
81	Maruyama R, et al. 2006	Study did not meet Cochrane EPOC study design criteria	lung cancer, metastatic lung cancer, or a nodule that was suspected to be malignant	retrospective study	Japan	Length of hospitalization, hospital charges, and the outcome for video-assisted thoracoscopic pulmonary resection (VATPR)
82	Mashhad University of Medical S. 2014	Protocol only	colorectal cancer patients	prospective randomized trial	Iran	Length of stay, postoperative complications and patient satisfaction
83	McCray DK, et al. 2017	Study did not meet Cochrane EPOC study design criteria	breast cancer	retrospective review	USA	Pre-operative MRI utilization
84	Mori T, et al. 2017	Study did not meet Cochrane EPOC study design criteria	lung cancer	retrospective study	Japan	Mean duration of the pathway, mean distance between patients' home and our hospital

85	Muehling BM, et al. 2008	No information about CP	Fast track lung resections	Prospective randomized controlled pilot study	Germany	Complications (pulmonary, cardiovascular, technical), reoperation, morbidity, mortality, length of stay at the ICU (median), day of discharge (median)
86	Munitiz V, et al. 2010	Study did not meet Cochrane EPOC study design criteria	oesophageal neoplasia	retrospective study	Spain	Morbidity rates, pulmonary complications, length of hospital stay
87	Neo PS, et al. 2012	Does not meet CP definition	patients in oncology ward	retrospective study?	Singapore	Five types of end-of-life symptoms
88	Nunez Mora C, et al. 2001	Study did not meet Cochrane EPOC study design criteria	bladder tumors	retrospective study	Spain	Duration of hospital stay
89	Nussbaum DP, et al. 2014	Other patient population	patients undergoing distal pancreatectomy (DP) of which 26% in each groups Pancreatic cancer	retrospective review	USA	Complication rates, 30-d resurgery, readmissions
90	O'Connell DA, et al. 2015	Does not meet CP definition	patients undergoing major head and neck cancer resections for cancer treatment	retrospective case-control study	Canada	Length of hospital stay, complications (minor and major)
91	Ogawa T, et al. 2004	Study did not meet Cochrane EPOC study design criteria	patients with thyroid and parotid tumors	retrospective review	Japan	Clinical outcomes, length of hospitalization and costs
92	Oh JK, et al. 2014	Study did not meet Cochrane EPOC study design criteria	uterine cervix cancer	retrospective review	Korea	Overall and postoperative hospital stay, catheter time. In questionnaire for the ward nurses: their perception on patient's satisfaction, subjective benefits and relative incidence of complications.
93	Ortega-Lucea SM, et al. 2015	Does not meet CP definition	patients with localized muscle-invasive bladder cancer	ambispective cohort study	Spain	Intraoperative variables, postoperative complications (according to the Clavien classification), hospital stay and recovery stay.

94	Page BJ, et al. 2013	Other intervention	lung cancer	retrospective study	Australia	Interval times: (A) from receipt of referral to first specialist appointment (FSA), (B) FSA to first pathological (cytology or histology) diagnosis (FPD), (C) FPD to first multidisciplinary team discussion (MDT) and (D) MDT to first definitive treatment (FDT).
95	Pease NJ, et al. 2004	Study did not meet Cochrane EPOC study design criteria	patients with suspected malignant spinal cord compression	two retrospective audits	UK	Early mobilization, complication rate, patient survival, neurological function
96	Pellino G, et al. 2017	Study did not meet Cochrane EPOC study design criteria	colorectal cancer	systematic review	NA	Primary outcomes: symptoms of colorectal cancer in pregnancy (CRC-p), and the outcome of the mother and foetus according to CRC features and location, gestational age and treatment delivered. Secondary outcomes: incidence of CRC-p, exposure to chemotherapy in utero and the development of a treatment algorithm suitable for these patients.
97	Pengfei LUO, et al. 2015	Study did not meet Cochrane EPOC study design criteria	liver cancer	unclear	China	Time to functional recovery, postoperative length of stay, postoperative complications, hospital costs, time to mobility, time to first passage of stool, readmission and mortality.
98	Peters M, et al. 2016	Abstract only	cancer care pathways	systematic review	NA	Effective implementation, sustainability, and evaluation of cancer care pathways.
99	Pfau PR, et al. 2004	Not cancer patients only	patients with acute upper nonvariceal GI hemorrhage (probably not only cancer patients)	prospective study?	USA	Length of stay, time to endoscopy, utilization of potentially unnecessary radiological tests, acid suppression, and cost of care

100	Pirnejad H, et al. 2013	Other intervention	cancer patients	retrospective study	Netherlands	Turn-around-time 109 Paclitaxel–Carboplatin chemotherapy courses. The chemotherapy-postponing rate, administration record completion rate, and admission rate of day care unit before and after the implementation.
101	Porteous GH, et al. 2015	Study did not meet Cochrane EPOC study design criteria	esophageal cancer	retrospective study	USA	Intensive care unit and hospital length of stay, surgical complications, and morbidity and mortality rates.
102	Porter GA, et al. 2000	Not cancer patients only	patients undergoing elective pancreaticoduodenectomy (PD), mostly patients with carcinoma, but a few with pancreatitis or other diseases			Perioperative mortality, postoperative morbidity, length of stay, readmissions, and postoperative clinic visits.
103	Preston SR, et al. 2013	Does not meet CP definition	oesophageal cancer	unclear	USA	Intraoperative blood loss, fluid administration and duration of surgery. Postoperative outcomes: length of hospital and critical care stay, and postoperative complications.
104	Quraishi T, et al. 2012	Abstract only	uro-oncology surgical services	unclear	UK	LOS, mortality, morbidity, readmissions within 30 days
105	Raman V, et al. 2016	Study did not meet Cochrane EPOC study design criteria	esophagectomy for patients with cancer	retrospective review	USA	Mortality, major complications, hospitalization, and total charges
106	Rashid OM, et al. 2016	Study did not meet Cochrane EPOC study design criteria	patients with borderline resectable pancreatic adenocarcinoma	retrospective study	USA	Pancreatectomy rates, margin status, pathologic response, disease-free survival (DFS), disease-specific survival (DSS), and overall survival (OS)

107	Rich-Ruiz M, et al. 2006	Other patient population	patients undergoing surgery for benign prostatic hyperplasia or cancer of the bladder through transurethral resection	randomized study	Spain	Length of hospital stay, complication rate, patient satisfaction
108	Richter-Ehrenstein C, et al. 2012	No control	breast surgery patients with benign and malignant disease	unclear	Germany	Hospital stay, total costs per case, readmission rate, and patients' satisfaction.
109	Roberts HC, et al. 2004	Not cancer patients	patients aged 65 years and over with a femoral neck fracture (no cancer)	prospective controlled before and after study	UK	Primary outcome: length of stay on the orthopaedic unit. Secondary outcomes: ambulation at discharge, discharge destination, in-hospital complications, 30 day mortality, readmission within 30 days of discharge, postoperative days the patient sat out of bed and walked.
110	Sancho C, et al. 2010	No control	rectal cancer (RC) treatment	unclear	Spain	Imaging methods for staging, neoadjuvant therapy, surgical treatment and pathology, and use of resources.
111	Santillan A, et al. 2008	Other intervention	gynecologic cancers	retrospective and prospective cohort study?	USA	PAP test rate and costs
112	Santoso U, et al. 2002	Study did not meet Cochrane EPOC study design criteria	breast cancer	before-after study	Singapore	Length of stay, total hospital costs, postoperative complications, unscheduled readmissions within 15 days of surgery
113	Schwarzbach M, et al. 2010	Other patient population	patients undergoing lobectomy: (15,7% in CP group and 4,7% in prepathway group had benign tumors)	unclear	Germany	Duration of catheter placement, pain intensity, respiratory exercising, and mobilization. Outcome quality: morbidity, mortality, reoperations, readmissions, and cost of hospital stay

114	Schwarzbach MH, et al. 2010	Other patient population	patients undergoing video-assisted thoracoscopy (VATS) (more or less 40% malignant)	unclear	Germany	Duration of catheter placement, pain intensity, respiratory exercising, and mobilization. Outcome quality: morbidity, mortality, reoperations, readmissions, and cost of hospital stay
115	Scott JA, et al. 2013	Abstract only	patients with breast, colon and lung cancer	retrospective study?	??	Sum of allowed cancer costs 270 days after chemotherapy, and probability of inpatient admission
116	Seo HS, et al. 2012	No control	gastric cancer surgery	prospective study?	Korea	Length of stay, complication rate, total cost paid at the patient's discharge, and the daily hospital income
117	Shamji FM, et al. 2013	Study did not meet Cochrane EPOC study design criteria	lung cancer	observational?	Canada	Time intervals
118	Sherman D, et al. 2001	Abstract only	larynx and hypopharynx cancer	retrospective study	Canada	Length of postoperative inpatient stay, readmissions, complications
119	Shetiwy M, et al. 2017	Does not meet CP definition	colorectal cancer	controlled clinical trial	Egypt	Length of hospital stay. Secondary outcomes: times of removal of nasogastric tubes (NGTs), successful enteral feeding, and removal of drains, postoperative complications, intra-hospital mortality, and rate of readmission.
120	Sivakumaran Y, et al. 2013	Study did not meet Cochrane EPOC study design criteria	colorectal cancer	retrospective observational cohort study	Australia	(A) mode of presentation: emergency versus elective (B) key time intervals and (C) performance against recommended guidelines
121	So JB, et al. 2008	Does not meet CP definition	gastric cancer	retrospective study	Singapore	Postoperative length of hospital stay, hospital costs
122	Song XP, et al. 2014	Study did not meet Cochrane EPOC study design criteria	gastrointestinal Cancer	meta-analysis	NA	Length of stay, costs and patient satisfaction
123	Soria-Aledo V, et al. 2011	Does not meet CP definition	colorectal Cancer	ambispective presurgery and postsurgery study	Spain	Postoperative stay, compliance with antibiotic prophylaxis, compliance with the staging study, mortality, rate of infection, and reoperations.

124	Stephen AE, et al. 2003	Not cancer patients only	colorectal cancer (83% in pre group and 67% in post group) and diverticular disease	retrospective study	USA	Length of stay, postoperative complications, readmissions, and cost per patient
125	Stocker R, et al. 2013	Study did not meet Cochrane EPOC study design criteria	non cancer and cancer	systematic review	NA	Number of patients placed on the LCP, length of time patients spent on the LCP
126	Takagi J. 1996	Unavailable full-text				
127	Tateno Y, et al. 2012	Study did not meet Cochrane EPOC study design criteria	cancer patient (different cancers)	retrospective study	Japan	Pain management
128	Tomaszek SC, et al. 2010	Study did not meet Cochrane EPOC study design criteria	oesophageal cancer or Barrett's oesophagus with high-grade dysplasia	retrospective study	USA	anastomotic leak rates, length of hospitalization, re-admission and other complications.
129	Tomiki Y, et al. 2015	Study did not meet Cochrane EPOC study design criteria	colorectal neoplasms	retrospective study	Japan	Hospital stay
130	Turini IG, et al. 2016	Study did not meet Cochrane EPOC study design criteria	patients who underwent Robot Assisted Laparoscopic Radical Prostatectomy (RALRP)	retrospective chart review	??	Clinical patient care outcomes, quality of life and satisfaction
131	Una E, et al. 2010	Study did not meet Cochrane EPOC study design criteria	Rectal Cancer	retrospective cross-sectional study	Spain	Time intervals, patient satisfaction
132	Valentin-Lopez B, et al. 2012	Study did not meet Cochrane EPOC study design criteria	colorectal cancer	retrospective study and prospective data collection of pathway group	Spain	Referral criteria met, waiting times, number of cancers diagnosed, endoscopic polypectomies performed, surgery for CRC and the stage of disease at surgery.
133	Vallverdu-Cartie H, et al. 2011	Study did not meet Cochrane EPOC study design criteria	colorectal cancer	longitudinal and observational study	Spain	Origin of patient's referral, date of entry in FTDP, date of first hospital visit, date of colonoscopy, date of colorectal surgeon consultation and date of surgical intervention

134	Van Beek K, et al. 2016	Study did not meet Cochrane EPOC study design criteria	cancer patients	systematic literature review	NA	ICP criteria
135	van Dam PA, et al. 2013	No control	breast cancer	prospective systematic evaluation	Belgium	Clinical outcome measures, service indicators, team indicators, process indicators and financial indicators: treatment according the guidelines, patient satisfaction, progression free 4-year survival, overall 4-year survival
136	van Hoeve J, et al. 2014	Study did not meet Cochrane EPOC study design criteria	breast cancer	retrospective study	Netherlands	Clinical outcomes and time intervals
137	van Hoeve JC, et al. 2015	Study did not meet Cochrane EPOC study design criteria	rectal cancer	retrospective study	Netherlands	Clinical outcomes and time intervals
138	Van Houdt S, et al. 2013	Study did not meet Cochrane EPOC study design criteria	radical prostatectomy patients (cancer patients?)	exploratory trial	Belgium	Quality of care was translated into process and outcome indicators. Quality of care was translated into patient-perceived quality indicators. And the Distress thermometer.
139	van Zelm R, et al. 2017	Study did not meet Cochrane EPOC study design criteria	colorectal cancer surgery	systematic search	NA	Key interventions
140	Varela-Centelles P, et al. 2017	Study did not meet Cochrane EPOC study design criteria	oral and oropharyngeal cancer patients	quantitative systematic review	NA	Five measures (patient, primary care, diagnosis, total diagnosis and total treatment intervals).
141	Verhofstede R, et al. 2012	Study did not meet Cochrane EPOC study design criteria	patients dying in an acute geriatric ward	study protocol	Belgium	Symptom frequency and symptom burden of patients in the last 48 hours of life
142	Wang ML, et al. 2017	Not cancer patients	colorectal polyps	retrospective study	China	The hospitalization cost, medicine cost, hospitalization time, satisfaction
143	Wu CL, et al. 2015	No control	colorectal surgery patients	unclear		Length of stay and patient satisfaction
144	Xuping S, et al. 2014	Study did not meet Cochrane EPOC study design criteria	patients with the first diagnosis as uterine fibroids	meta-analysis	NA	Length of stay, days of waiting for surgery, inpatient expenditures

145	Yetzer JG, et al. 2017	Study did not meet Cochrane EPOC study design criteria	patients undergoing maxillofacial head and neck surgery		USA	Length-of-stay metrics, infection rates, transfers to the intensive care unit, and unplanned return to the operating room.
146	Yeung JK, et al. 2014	Study did not meet Cochrane EPOC study design criteria	head and neck cancer	before-after study	Canada	Pulmonary complications, hospital length of stay, rate of flap reoperation
147	Yueh B, et al. 2003	Other control	head and neck cancer	cohort study?	USA	LOS after laryngectomy
148	Zauner G, et al. 2014	Study did not meet Cochrane EPOC study design criteria	lung cancer	exploratorive study	Austria	
149	Zhang Y, et al. 2017	Other control	lung cancer	cost and survival analysis	USA	Clinical outcomes: survival, and costs
150	Zhu L, et al. 2014	Study did not meet Cochrane EPOC study design criteria	hepatocellular carcinoma	retrospective study and prospective data collection of pathway group	China	Hospital costs, LOHS and early clinical outcomes

Abbreviations: CP: Care Pathway; NA: Not Applicable.

Additional file 5 References excluded studies

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Additional file 6 Risk of Bias of included studies

Risk of bias										Overall score* High or Unclear or Low Risk
Study ID	Was the allocation sequence adequately generated?	Was the allocation adequately concealed?	Were baseline outcome measurements similar?	Were baseline characteristics similar?	Were incomplete outcome data adequately addressed?	Was knowledge of the allocated interventions prevented during the study?	Was the study protected against contamination?	Was the study free from selective outcome reporting?	Was the study free from other risk of bias?	
1 Chen et al. 2000 ²¹	+	+	?	?	-	+	?	-	-	High risk
2 Dahl et al. 2017 ²⁹	+	+	-	+	?	+	-	-	-	High risk
3 Gendron et al. 2002 ²²	+	+	?	+	-	-	-	-	-	High risk
4 Ghosh et al. 2001 ²³	+	+	-	+	?	?	-	-	-	High risk
5 Jeong et al. 2011 ²⁴	+	+	?	-	-	-	?	-	-	High risk
6 Kiyama et al, 2003 ²⁵	+	+	?	+	+	?	?	+	+	Low risk
7 Tastan et al. 2012 ²⁶	+	+	?	-	-	-	?	-	-	High risk
8 Williams et al. 2015 ²⁷	-	?	-	-	-	-	-	-	-	Low risk

"-" is low risk, "?" is unclear risk, "+" is high risk of bias.

* We will consider studies with low risk of bias for all key domains or where it seems unlikely for bias to seriously alter the results. We will consider studies where risk of bias in at least one domain is unclear or judged to have some bias that could raise doubts about the conclusions as having an unclear risk of bias. We will consider studies with a high risk of bias in at least one domain or judged to have serious bias that decreases the certainty of the conclusions as having a high risk of bias (Higgins, 2011).

Additional file 7 Quality assessment of cost evaluation studies, based on the Evers checklist available in the Cochrane Handbook

	Chen et al. 2000²¹	Gendron et al. 2002²²	Ghosh et al. 2001²³	Jeong et al. 2011²⁴	Kiyama et al. 2003²⁵	Williams et al. 2015²⁷
1. Is the study population clearly described?	y	y	n	y	y	y
2. Are competing alternatives clearly described?	n	n	n	y	y	y
3. Is a well-defined research question posed in answerable form?	n	n	n	n	y	n
4. Is the economic study design appropriate to the stated objective?	y	y	y	y	y	y
5. Is the chosen time horizon appropriate to include relevant costs and consequences?	y	y	y	y	y	y
6. Is the actual perspective chosen appropriate?	y	y	y	y	y	y
7. Are all important and relevant costs for each alternative identified?	y	y	y	y	y	y
8. Are all costs measured appropriately in physical units?	y	y	y	n	y	n
9. Are costs valued appropriately?	y	y	y	y	y	y
10. Are all important and relevant outcomes for each alternative identified?	y	y	y	y	y	y
11. Are all outcomes measured appropriately?	y	y	y	y	y	y
12. Are outcomes valued appropriately?	y	y	y	y	y	y
13. Is an incremental analysis of costs and outcomes of alternatives performed?	n	n	n	n	n	n
14. Are all future costs and outcomes discounted appropriately?	n	n	n	n	n	n
15. Are all important variables, whose values are uncertain, appropriately subjected to sensitivity analysis?	n	n	n	n	n	n
16. Do the conclusions follow from the data reported?	y	y	y	y	y	y
17. Does the study discuss the generalizability of the results to other settings and patient/ client groups?	n	n	n	y	n	n
18. Does the article indicate that there is no potential conflict of interest of study researcher(s) and funder(s)?	y	y	y	y	y	y
19. Are ethical and distributional issues discussed appropriately?	n	n	n	n	n	n

Additional file 8 Original reported costs / charges data

Study ID	Country	Currency	Costs included	Pathway	Control	Reduction of costs, per patient	P value
Chen et al. 2000 ²¹	USA	US\$	Total costs including hospital and professional fees: surgery-related costs, treatment-related costs, medications, consultations, and assessment and diagnostic tests.	\$6,227	\$8,459 (historical control group, HCG) \$6,885 (non-pathway group, NPG)	HCG vs pathway: -\$2,232 NPG vs pathway: -\$658	p<0.001*
Gendron et al. 2002 ²²	USA	US\$	The charge summary was divided into the following 6 categories: total, hospital room, pharmacy, operating room, laboratory, and other charges. Professional fees were not included.	\$78930 (>1 year, group 1) \$65919 (>3 years, group 2) \$3,920	\$105410	Control vs pathway group 1: -\$26480 Control vs pathway group 2: -\$39491 -\$1,625 (-29%)	-
Ghosh et al. 2001 ²³ (cervical cancer)	USA	US\$	Direct costs were obtained including hospitalization, pharmacy, laboratory, operation room, radiological, and other miscellaneous costs (the last includes: physical therapy, respiratory therapy, patient monitoring, and patient education).	\$3,790	\$5,545 \$4,766	-\$976 (-32%)	-
Ghosh et al. 2001 ²³ (endometrial cancer)	USA	US\$					
Jeong et al. 2011 ²⁴ (advanced gastric cancer)	Korea	KRW	Total hospital costs There is no description available of which costs are included.	7,359,437 Won	7,384,470 Won	-25,033 Won	p=0.96
Jeong et al. 2011 ²⁴ (early gastric cancer)	Korea	KRW	Preoperative costs Postoperative costs Total hospital costs There is no description available of which costs are included.	1,053,341 Won 6,306,096 Won 7,913,477 Won	1,307,558 Won 6,079,912 Won 8,801,131 Won	-254,217 Won +226,184 Won -887,654 Won	p=0.00* p=0.64 p=0.08*
			Preoperative costs Postoperative costs	1,167,514 Won 6,745,964 Won	1,564,053 Won 7,237,078 Won	-396,539 Won -491,114 Won	p=0.00* P=0.27

Kiyama et al. 2003 ²⁵	Japan	JPY	The total costs The total direct costs reported were the total medical costs (including medication and examinations).	1502587 Yen	1932197 Yen	-429610 yen	p<0.001
			Medication costs only	190339 Yen	270631 Yen	-80292 yen	p<.001
			Daily total costs	58383 Yen	55651 Yen	+2732 yen	N.S.
Williams et al. 2015 ²⁷	UK	GBP	Costs included: analgesic drug costs, pain clinic visits, use of physiotherapy, psychology and other resources.	£ 430 (640)	£ 230 (450)	+£200	-

Abbreviations: USA: United States of America; US\$: United States Dollar; KRW: Korean Won; JPY: Japanese yen; N.S.: not significant; UK: United Kingdom; GBP: Pound sterling.

CHAPTER 4

Transitional Care in Clinical Pathways for Cancer Patients

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In preparation

ABSTRACT

Purpose

The objectives of this mixed methods review were to ascertain the availability of evidence on and nature of clinical pathways involving the transition of patients with non-metastatic cancer between primary, secondary or tertiary hospital care.

Methods

MEDLINE (Ovid) was searched with a systematic search structure for publications in the English language from 1946 to May 2019 supplemented by a forward citation search. Titles, abstracts and articles were screened and appraised according to predetermined criteria on transitional care. Findings were clustered in descriptive themes that guided the framework synthesis.

Results

Out of 158 search results, a total of 16 papers on clinical pathways in cancer care featured aspects of transitional care were included covering 2000-2018. Twelve papers were restricted to the diagnostic phase. The remaining papers described transitional phases also for treatment or follow-up. The papers were clustered into three descriptive themes: transition outcomes, coordination between settings, and translation of guidelines.

The transition of the cancer patient between the GP and hospital settings involved various time intervals. Shorter intervals were associated with implemented guidelines in clinical pathways and enhanced coordination of care between settings/professionals. Particularly in Denmark, clinical guidelines served as pretext for the optimization of intervals and transitions of patients between settings.

Conclusion

Evidence is available for achieving more efficient transitions in the diagnostic phase of cancer care after implementing clinical pathways. Further improvements should focus on reducing fragmentation, improving coordination of care and using clinical pathways along the complete cancer care continuum in daily practice.

INTRODUCTION

Clinical pathways have been used for decades in the hospital setting across specialties and health systems. Originally developed to reduce unwarranted variability in the delivery of health services, clinical pathways are “road maps” to describe the sequence and timing of care and treatment, and the multi-professional teams that should be involved in the delivery of health care¹. Moreover, clinical pathways seek to reduce variation in services delivered and improve care by bringing more focus on evidence-based health care using available guidelines^{2,3}. In discouraging the use of less effective therapies or those that cause side effects necessitating hospitalization or other expensive interventions and by decreasing fragmentation in connecting phases within the care continuum clinical pathways, likewise, deal with the efficiency of provision of health care. Clinical pathways have most added value in complex care delivery, such as seen in cancer care.

As with pathways for other complex multidisciplinary conditions, clinical pathways in cancer care have seen rapid proliferation and widespread adoption as tools to enhance patient care and improve utilization of resources in the United States and beyond^{2,3}. Standardization of protocols have been achieved in many clinical pathways within one phase (such as treatment) and one setting (such as within one hospital) and evidence of achievement of their effectiveness is available. Less is known about clinical pathways between settings. These pathways between settings cover transitions of care within the care continuum between primary, secondary or tertiary care, and transition points⁴⁻⁶.

Following the World Health Organization (WHO), transitions of care refer to the various points where a patient moves to, or returns from, a particular physical location or makes contact with a novel health care professional for the purposes of receiving health care⁷. This includes transitions between home, hospital, residential care settings and consultations with different health care providers in out-patient facilities⁶. Transitions of care are an integral part of a cancer patient’s journey through the health care system and a continuum associated with the individual’s condition which can change over time⁵. Important transitions between settings are mainly seen in the diagnostic phase and in the survivorship phase both requiring transitions from primary care, the general practitioner (GP), to medical specialists working in hospitals (secondary care) or specialized/academic hospitals (tertiary care) or vice versa.

All transitional care within the cancer care continuum cover clinical pathways and require close coordination. In the diagnostic phase, where close collaboration between the GPs and medical specialists is needed, the symptomatic individual gets diagnosed as a patient with cancer and with it transitions between the primary care and hospitals settings to commence active treatment^{4,8}. These transitions of care are especially important in health systems where primary care physicians or GPs act as gatekeepers to specialists in secondary or tertiary facilities^{9,10}. Considering that health and non-health outcomes in cancer care are associated with timely diagnosis at the earliest possible stage, rapid access to a specialist opinion or diagnostic test for patients with specified alarm symptoms is a feature of clinical pathways¹¹.

Similarly, clinical pathways after the completion of treatment are important in the context of non-metastatic cancers since care may move back and forth from primary care to subspecialty services if an abnormality arises, when nononcologic problems need attention and to monitor recurrent or residual cancer¹⁰. Transitions also occur between secondary and tertiary care for cancers for which bundling of expertise in diagnosis and treatment is needed to achieve optimal outcome^{12,13}. Lack of expertise and volume norms^{14,15} as well as limited resources for expensive technologies (to offer FDG-PET scan or Da Vinci robotic surgery) force hospitals to decide whether or not to offer specific services and refer their patients to more specialized hospitals.

The objectives of this paper were to ascertain the availability of evidence on and nature of clinical pathways involving the transition of patients with non-metastatic cancer between primary, secondary or tertiary hospital care.

METHODS

We applied a mixed methods approach involving a systematic review based on a search conducted in a previous study¹⁶ and a framework synthesis to provide a more complete picture of the availability and implementation of clinical pathways in oncology on transitional in non-metastatic cancer care, focusing on the transitions of care between primary, secondary or tertiary care^{17,18}. Features of the clinical pathway and transitional care frameworks served as the bases for the selection of papers that were included in the review as well as reading the full texts to reveal key themes grounded in the included studies.

Data sources and searches

MEDLINE (Ovid) was searched with a systematic search structure for randomized controlled trials, non-randomized controlled studies, controlled before-after studies, and interrupted time series studies, cost-effectiveness analyses, cost-utility analyses and cost-benefit analyses, cost analysis and comparative resource utilization studies and was re-run in May 2019. The search was limited to publications in the English language from 1946 to June 2017.

Additional studies were identified by using a forward citation search to identify more recent studies that had cited included studies. EndNote X5 software was used to manage the references.

Article selection

Each (captured) article was read and critically appraised according to predetermined inclusion criteria covering aspects of transitional care: the study reported on the transfer of the patient (1) between providers and between settings (from the general practitioner to (sub)specialist; or, primary care to secondary or tertiary care; and (2) a change in the health state of the patient (from symptomatic to clinical; and/or outpatient to inpatient or inpatient to outpatient)^{4,7}.

Abstracts were hand screened by JvH and PC independently to establish appropriateness for inclusion in the review. The potentially relevant studies were further examined using full-text copies.

Analysis

Data analysis was a combination of induction (data-driven generalization) and deduction (theory-driven exploration of hypotheses)^{18,19}. Patterns in the data and comparing the findings of studies positioned differently within the frameworks, allows for grouping themes in an analytical manner rather than a statistical manner^{19,20}.

RESULTS

After screening the titles and abstract of 158 search results, a total of 16 papers on clinical pathways in cancer care were selected, which featured aspects of transitional care as stated by the inclusion criteria covering the years 2000-2018. Twelve papers concerned the referral and diagnosis phases. Treatment planning and treatment phases, and the entire cancer continuum each had two papers. The papers covered a variety of cancer types. Of the 13 papers that focused on a specific type of cancer, four covered colorectal cancer and three covered lung cancer. More than half of all papers (10) came from the United Kingdom and Denmark. (See Table 1.)

Three descriptive themes could be identified with which the papers could be clustered, namely: transition outcomes, coordination between settings and translation of guidelines. These themes guided the framework synthesis.

Table 1. Characteristics of Included Studies

Authors	Country	Cancer type	Transition phase	Design	Transition Outcomes	Between health care settings	Involved providers
Barrett and Hamilton ²¹	United Kingdom	Lung	Diagnosis	Cohort study	Time intervals between first symptoms, referral and diagnosis	General practices, respiratory clinics, outpatient departments	GPs, respiratory physicians
Barrett et al. ²²	United Kingdom	Colorectal	Diagnosis	Observational audit	Time intervals: 1st consultation-1st referral, 1st referral-diagnosis, 1st consultation through to diagnosis	Primary and secondary care	GPs, medical specialists (surgery/gastroenterology/other)
Barrett et al. ²³	United Kingdom	Ovarian	Diagnosis	Cohort study	Numbers of patients taking specific routes to diagnosis, time interval to diagnosis	General practices, gynecology department	GPs, gynecologists
Dahl et al. ²⁴	Denmark	All	Diagnosis	Comparative cohort study	Patient-reported dissatisfaction, time intervals: GP-consultation, GP referral for first hospital consult	Primary and secondary care	GPs, hospital-based physicians
de Luc et al. ²⁵	United Kingdom	Breast	All	Quasi-experimental case study	Patient satisfaction levels, views of staff involved in the pathways	Primary and secondary care	GPs, members of the multidisciplinary group
Dyrop et al. ²⁶	Denmark	All	Diagnosis	Unclear	Milestones, time intervals, performed diagnostics, and tumor size	Primary and secondary/tertiary care	GPs, diagnosing hospital-based physicians
Forrest et al. ²⁷	United Kingdom	Lung	Diagnosis	Review	Stage at diagnosis, time intervals: 1st symptom-1st presentation; 1st presentation-referral, GP referral-1st specialist appointment, secondary care investigation-diagnosis, diagnosis-treatment	Primary and secondary care	GPs, hospital-based physicians
Grau et al. ²⁸	Denmark	Head and neck	Diagnosis	Systematic review (ORAL/abstract)	Time intervals: 1st health care contact (GP, ENT or hospital)-start treatment; total time used for diagnosis; diagnosis-start treatment, diagnostic imaging	Primary and secondary care (ENT and other departments)	GPs, hospital-based physicians
Jakobsen and Jensen ²⁹	Denmark	Penile	Diagnosis, Treatment	Comparative before-and-after study	Time intervals: total, patient, pre-referral, system and tertiary center intervals. Proportion of patients within the time limits defined by the CPP	Primary and secondary care (including private-based specialists)	GPs, private practice dermatology/ urology, specialists from urology, other hospital departments

Lyhne et al. ³⁰	Denmark	Head and neck	Diagnosis	Cohort study	Diagnostic intervals, treatment intervals, total time in health care.	Primary and secondary care	GP, dentist, community otolaryngologist or ENT physician
Page et al. ³¹	Australia	Lung	Diagnosis	Retrospective study	Time intervals: referral-1st specialist appointment (FSA), FSA-1st pathological diagnosis (FPD), FPD-1st multidisciplinary team discussion (MDT), MDT-treatment	Primary (rural and remote) and secondary/tertiary care	Lung cancer (diagnostic and treatment) specialists
Sivakumaran et al. ³²	Australia	Colorectal	Diagnosis	Retrospective observational cohort study	Mode of presentation, time intervals: GP referral-primary treatment, GP referral-appointment with colorectal surgeon, colorectal appointment-primary treatment	Primary and secondary care	GP, colorectal surgeon, gastro-enterologists
Valentin-Lopez et al. ³³	Spain	Colorectal	Diagnosis	Three-year audit	Referral criteria met, waiting times, cancer diagnosed, stage of disease	Primary and secondary/tertiary care	GPs, medical specialists at the tertiary hospital
Vallverdú-Cartié et al. ³⁴	Spain	Colorectal	Diagnosis	Longitudinal and observational study	Time intervals: admission-1st diagnostic colonoscopy, admission-surgery visit, surgery visit-surgery, admission-surgical intervention	Primary and secondary care	GPs, doctors from the department of gastroenterology, colorectal surgeons
Van Hoeve et al. ¹⁶	The Netherlands	All	All	Systematic review (protocol)	Effects on patient, professional and health system outcomes within primary and secondary health care	Primary and secondary care or intersectional care	GPs, surgeons, medical oncologists, nurses, nurse specialists
Varela-Centelles et al. ³⁵	Spain	Oral	Diagnosis, Treatment	Systematic review	Time intervals: symptom onset-1st visit with a HCP, 1st visit HCP-1st referral to specialist, first visit HCP-diagnosis, 1st symptom-treatment	Primary and secondary care	Physicians, dentists

Abbreviations: GP: General Practitioner; ENT: ear-nose-throat; HCP: health care professional

Transition outcomes

The transition of the cancer patient in the diagnostic phase between the GP and secondary/tertiary care settings involved various settings which have been generally classified in the literature into two: 1) GP referral for medical specialist consult; and, 2) referral from secondary to tertiary care. Depending on the health care system²⁶ and the clinical pathway³¹, the medical specialist to whom the GP may initially refer the patient can be based either at a secondary or a tertiary care facility.

1) GP referral for medical specialist consult

The time between first contact with the GP or another health care professional and the first consultation with a medical specialist in secondary care was studied in seven papers^{21-23,29,32,34,35}. One paper reported a reduced time interval after implementation of the clinical pathway. Jakobsen and Jensen found a significant reduction of time between referral by any medical practitioner to the first visit in the tertiary center from 13 days in 2000-2002 to 7 days after the implementation of the pathway for patients with penile cancer in 2013-2014²⁹. Furthermore, Varela-Centelles and colleagues reported in their systematic review of clinical pathways in symptomatic oral cancer in several European countries an interval from the first presentation in primary care to first referral to secondary care of 15.8 days³⁵.

In Australia, Sivakumaran and colleagues found that the time from GP referral to a medical specialist appointment in the surgical management of colorectal cancer lasted a median of 76 days and for a GP emergency referral it was 7 days³². In addition, for elective referrals, the overall time from GP referral to colorectal treatment was longer for tertiary referrals compared to secondary referrals. Meanwhile, Vallverdú-Cartié and colleagues studied the time interval for patients diagnosed with colorectal cancer and found a median time interval from administrative registration, which is the date of request for referral to the fast track pathway by primary health centers, to the first hospital visit of 3 days³⁴. Barrett and Hamilton found that the interval from the first recorded symptom to diagnosis was significant longer for patients misdirected to other outpatient departments than those sent directly to respiratory clinics²¹.

2) Referral from secondary to tertiary care

Nine papers investigated the time interval between visits or consultations with medical specialists^{22,26,28-30,32-34,35}. Four of these papers studied the intervals between secondary and tertiary care over time and found statistically significant reductions in the time to diagnosis after implementation of a clinical pathway^{26,28-30}. Dyrop and colleagues observed that following the implementation of the cancer patient pathways for sarcomas in Denmark in 2009, the time interval from the local orthopedic hospital to a specialized Danish sarcoma center was (statistically significantly) reduced from 8 days in 2008 to 3 days in 2010 for soft tissue sarcomas, from 9 to 4 days for benign soft tissue and bone conditions, and from 6 to 3 days for other bone malignancies²⁶. Grau and colleagues found following the referral from a

GP, the referral from an ear-nose-throat specialist (ENT) to a head and neck oncology center resulted to a significant reduction of time to a head and neck cancer diagnosis of 13 days in 2010 compared to 17 days in 2002²⁸. In addition, Lyhne reported the same results concerning head and neck cancer including the median of 20 days for the diagnostic interval in 1992³⁰.

For more detailed information regarding the time intervals, see Table 2.

Table 2. Time Intervals in the diagnostic phase Reported in Included Studies

Authors	Time between presenting 1st symptom GP/ HCP and 1st consultation	Time between 1st visit / investigation and diagnosis (or decision to treat*)	Other time intervals
Barrett and Hamilton ²¹	Median 66 days (IQR: 37, 110) for patients referred to outpatient departments Median 29 days (IQR:17, 61) for patients sent to respiratory clinics: Median 16 days (IQR: 8, 40) for patients admitted as emergency (p < 0.001)	NA	NA
Barrett et al. ²²	Median 6 days (IQR: 0, 56.25)	Median 42 days (IQR: 21, 76): 1st referral to diagnosis Median 69 days (IQR: 35, 188): 1st consultation through to diagnosis NA	NA
Barrett et al. ²³	Median 2.5 days (IQR: 0, 27.5)	NA	The median interval from 1st symptom reported in primary care to diagnosis 74.5 days (IQR: 32, 159)
Dyrop et al. ²⁶	NA	Median 10-17.5 work days in 2007 to 5-12 workdays in 2010*	Time from referral to start treatment: reduction from median 28 to 18 work days (soft tissue sarcomas), median 31 to 14 work days (bone sarcomas)
Grau et al. ²⁸	NA	Median 13 days in 2010 compared to 17 days in 2002 (p < 0.001)	Total time from first health care contact to start of treatment: median 41 calendar days in 2010 to 69 days in 2002 (p < 0.001).
Jakobsen and Jensen ²⁹	Median 13 days (IQR: 7, 20) in 2000-2002 to 7 days (IQR: 4, 11) in 2013-2014 (p < 0.0001)	See "other time intervals"	Time from referral to initiation of treatment: median 32 days (IQR: 21, 58) in 2000-2002 to 20 days (IQR: 14, 29) in 2013-2014 (p < 0.0001)*
Lyhne et al. ³⁰	NA	Median 13 days (2010) versus 17 days (2002; p < 0.001) and median 20 days (1992; p < 0.001)	Total pre-treatment time: median 41 days in 2010 versus 69 days (2002) (p < 0.001) and median 50 days (1992; p < 0.001).
Sivakumaran et al. ³²	See "other time intervals"	Elective tertiary versus secondary referrals: median 28 vs. 7 days for specialist appointments (p < 0.001) and 21.5 vs. 9 days for endoscopic assessment (p = 0.004)	Time from GP referral to decision about treatment: median 7 days (emergency) versus 76 days (elective referrals) (p < 0.001). The overall time from GP referral to treatment was median 78 days (elective tertiary referrals) versus 56 days (elective secondary referrals) (p = 0.003).

Valentin-Lopez et al. ³³	NA	Average 13.8 days (SD 8.8) for patients in rapid referral pathway and 33.8 days (SD 38.7) in the standard pathway. (p < 0.001). Median 11.5 days (range 1-41).	Overall average waiting time for patients in the rapid referral pathway: 52.7 days (SD 32.9); for patients in the standard pathway: 71.5 days (SD 57.4) (p = 0.002).
Vallverdú-Cartié et al. ³⁴	The time interval from entry into the pathway to the first hospital visit was median 3 days (range 1-8)		
Varela-Centelles et al. ³⁵	Weighted average 15.8 days	The shortest diagnostic periods (1st visit with HCP to diagnosis), 21-22 days, were reported from European countries. The weighted average diagnostic interval was 47.9 days.	The total interval (time between 1st symptom and start of treatment): average 186.7 days.

Abbreviations: HCP: health care professional, NA: not available

Coordination between settings

Optimizing the coordination of care was associated with shorter waiting times and a more efficient care pathway for cancer patients^{29,34}. Jakobsen and Jensen found that reduced waiting times were mainly achieved through pre-booking of appointments and diagnostic time slots by a dedicated clinical coordinator²⁹. This clinical coordinator was included in the program and was considered as pivotal in the gain in time. The tasks of the clinical coordinator involved personal calls with the patient and coordination of appointments, ideally, all on one day. Furthermore, this coordinator was also observed to help alleviate the patient of anxiety and stress before the first appointment and supporting the patient's own coping strategy²⁹.

In Spain a program of referral and diagnostic coordination was implemented in 2005 with the aim of reducing the time of delay in the diagnosis and treatment of patients with suspicion of colorectal cancer. Because these programs were complex they required the involvement and coordination of a multidisciplinary team. According to Vallverdú-Cartié and colleagues, in hospital settings where a team is responsible for the management of the process of patients with cancer, such a multidisciplinary team may have been indispensable in the time optimization and the correct management of resources throughout the complete pathway³⁴. This team could also play a role in coordinating processes and act as a link between the patient and other centers of health assistance. The authors conclude that collaboration with Primary Health Centers and Emergency teams was essential to update and improve these pathways and also to coordinate efforts in the struggle for an early diagnosis of cancer³⁴.

Translation of guidelines to pathways

In Denmark, Australia and Spain diagnostic cancer pathways were based on evidence based guidelines for different cancer types including time intervals for transitions, which were based on the norms. In Denmark fast track referral pathways for cancer patients were developed based on the national cancer plans from the National Board of Health^{24,26,28-30}. GPs and other clinicians can refer patients to a cancer pathway within secondary care in cases with a reasonable suspicion of cancer²⁴.

Varela-Centelles and colleagues referred in their Spanish review of time intervals in pathways to the suggested time interval norms from Denmark being part of the Aarhus guidelines on treatment of oral cancer³⁵. Using such as a framework for the development of dynamic and bidirectional pathways to treatment which allows multiple paths to reach a (final) diagnosis, they found that the patient interval (patient delay), rather than primary care interval (referral interval) or diagnostic interval (professional delay) represented the major component of delay.

The introduction of clinical guidelines in Australia to improve the efficiency of cancer care delivery, Sivakumaran and colleagues evaluated the referral pathway of surgically managed colorectal patients at a tertiary center, specifically the performance of lower gastro-intestinal (GI) endoscopy within four weeks of GP referral, with explicit comparison to published

guidelines³². The authors concluded that measures to reduce waiting times for lower GI endoscopy are required to achieve better performance to conform to guidelines.

DISCUSSION

Considering that transitions of care are an integral part of a cancer patient's journey, we sought evidence on clinical pathways in cancer care for patients with non-metastatic cancer between primary, secondary or tertiary care. In our framework synthesis of transitional care in the diagnostic phase of cancer care we found, three related themes: transition outcomes, coordination between settings and translation of guidelines to clinical pathways.

Firstly, we have noted a diversity in the reference time frames considered in the included papers. In particular, the transition of patients in the diagnostic phase occurred within relative short time intervals which reduced over time. This finding is important for patients because delay before diagnosis, generates anxiety for patients³⁹ which can have deleterious consequences in patient well-being as well as health outcomes³⁴. Meanwhile, there is evidence that patient delay is the main component of the total delay in the diagnostic phase³⁵. However, for rare cancer types also early recognition by clinicians might be difficult, due to the fact they present unspecific complaints and are often detected at advance stage resulting in an overall poor prognosis. In these types of cancer much gain could be obtained by earlier detection.

Secondly, we found evidence for the coordination of activities such as planning of patient's appointments and correct management of resources leading to a more efficient care process. This coordination included special attention to the psychosocial and interpersonal needs of patients provided by a dedicated coordinator within a multidisciplinary team^{29,34}. Oncology nurses or case managers can fulfill such a role³⁶. Lack of communication and coordination at transition points between health care professionals within settings as well as between settings contributes to numerous quality and safety problems, including suboptimal disease management, adverse events, medication errors, unnecessary declines in patient health and functional status and preventable hospital readmissions³⁷. Moreover, research indicates that health systems that are supported by a strong primary care foundation result in better health outcomes at lower total health-service costs³⁸.

Thirdly, evidence is available that clinical pathways were derived from national standards or evidence based guidelines in Denmark, Australia and Spain. Lyhne and colleagues pointed out, nonetheless, that the national cancer standards or guidelines are not applicable to all patients and improvements in the transitions between health care settings are needed³⁰.

Challenges for improvement of transitions in the future cover reducing fragmentation, improving coordination and enhancing the consistency of implementation of clinical pathways based on guidelines between health care settings. Valentijn and colleagues conclude that to deliver integrated, person-focused, and population-based care, integration

across the care continuum through inter-sectorial partnerships within the health and social service system is needed³⁹. As noted by Easley and colleagues⁴⁰ in their qualitative study on physician perspectives and contextual factors related to the coordination of cancer care and the role of family physicians in Canada, the coordination of cancer care, management of comorbidities and provision of psychosocial care to patients and their families are three key roles in the delivery of cancer care patients.

Although our study focused on the diagnostic phase transitions within the clinical pathways after the completion of treatment are important in the context of non-metastatic cancers. Care may move back and forth from primary care to subspecialty services if (late) effects of treatment or psychosocial problems arise and to monitor recurrent or subsequent cancer and unmet needs of patients might occur⁴¹⁻⁴³. Compared to the diagnostic phase along the cancer care continuum, we came across little evidence on the transition of the cancer patient from the end of cancer treatment to follow-up in our selection of papers. Follow-up studies focusing on transitions between the treatment phase and cancer survivorship or palliative care phase can complete insights in the whole cancer care continuum.

CONCLUSION

The transition of the cancer patient between primary care, secondary or tertiary care involved various phases. Actionable themes were found in transition outcomes, coordination between settings and translating of guidelines in the diagnostic clinical pathway. Shorter time intervals were associated with the implementation of clinical pathways and enhanced coordination of care usually involving an intermediary between settings. Improvements for the future should focus on reducing fragmentation and improving coordination for patients from the presentation of the first symptom through diagnosis until the treatment phases. Further research could gain more insight in the transitions of care, as patients with cancer move across settings and receive care from various providers, especially after treatment to the phase of palliative care or survivorship back in their community.

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CHAPTER 5

Follow-up after breast cancer: variations, best practices, and opportunities for the future according to health care professionals

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ABSTRACT

Purpose

It remains unclear how follow-up for breast cancer patients can ideally be organized from the perspective of health care professionals (HCPs). Follow-up can be divided into surveillance (detection of recurrence or new cancers) and aftercare (identifying and managing side and late effects of cancer). The aim of this study was to gain insight into the similarities and differences in the organization of follow-up in seven Dutch teaching hospitals and to identify best practices and opportunities for the future of follow-up for patients after breast cancer as proposed by HCPs.

Methods

Semi-structured in-depth group interviews were performed with in total 16 HCPs of the participating hospitals. To describe the organization of follow-up, transcripts were analyzed using a deductive approach. Best practices and opportunities were derived from the transcripts using an inductive approach.

Results

Variation was found in the organization of aftercare, especially in timing and frequency and in disciplines of involved HCPs. Less variation was observed for surveillance, which was based on the national guideline. Best practices focused on case management, adequate collaboration between HCPs, and personalization of aftercare. Opportunities mentioned lied in improving the monitoring of patients' needs (such as PROMs), a comprehensive guideline for organization and content of aftercare, integration of surgical, radiotherapeutic and medical oncology follow-up trajectories, and personalization of surveillance.

Conclusions

Variation in follow-up existed between breast cancer centers. Improvement in monitoring patients' needs, collaboration between HCPs, and coordination of care might lead to optimal and more personalized follow-up for every individual patient.

INTRODUCTION

Worldwide, breast cancer is the most common cancer among women, impacting 2.1 million women each year and causing the greatest number of cancer-related deaths among women¹. In the Netherlands, almost 15.000 women are diagnosed with breast cancer every year. The average survival rate after 5 years has increased by 10% in the last 30 years to 88% for patients diagnosed in the period from 2011 to 2017². The increased incidence and survival rate results in increasing prevalence, stretching resources for follow-up³⁻⁵.

The Dutch guideline for breast cancer defines follow-up as the regularly scheduled contacts between the patient and health care professionals (HCPs) in relation to the cancer treated⁶. Follow-up can be subdivided in surveillance and aftercare. In the Dutch guideline for General Practitioners (GPs)⁷, the term surveillance is defined as: “the regularly scheduled medical examination for early detection of recurrent breast cancer or secondary primary tumors”. According to the Dutch guideline, surveillance is equal for each curatively treated breast cancer patient: an annual mammogram and physical examination for at least five years following treatment⁶. Aftercare focuses on “limiting the burden of disease, rehabilitation and signalling, guiding and treating (late) consequences of (the treatment of) cancer”⁷. In clinical practice, a clear distinction between surveillance and aftercare is often missing.

Follow-up has changed over time. The traditional idea of monitoring cancer recurrence has broadened to a concern for recovery and wellbeing that includes comprehensive management of psychosocial and physical effects, promotion of healthy lifestyles, and care coordination of the various HCPs involved⁸. Currently, routine follow-up often still focusses on the surveillance and fails to meet patients’ supportive care needs, resulting in feelings of abandonment during the transition from patient to survivor^{9,10}. Besides, there is a growing demand for personalized care planning within cancer follow-up^{4,11,12}. Following the current Dutch guideline, a personalized aftercare plan should be composed containing information about the received treatment, the risk of potential late effects, the risk of recurrence, and a personalized schedule for surveillance⁶. This plan should be available for GPs too. However, in practice these plans often fail due to barriers for implementation¹³.

There is a diversity in follow-up practices, the intensity of which can be defined by the frequency of clinical visits and/or physical examinations (e.g. intensive, standard, patient-initiated or low intensity)³. There is also evidence for diversity in the way follow-up is implemented in clinical practice. Grunfeld and colleagues¹⁴ reported substantial variation in adherence to guideline recommendations, with both overuse and underuse of surveillance visits and tests based on a population-based study in Ontario, Canada. Davies and colleagues¹⁵ conducted a systematic review about cancer follow-up. They observed a trend towards more personalized patient-led follow-up for low to moderate risk breast cancer survivors as long as some conditions were guaranteed, such as having a clear indication of their future risk profile, receiving annual

mammographic surveillance, and when they were provided with a safe, reliable, and quick route back to specialist care if needed.

A more personalized patient-led model for follow-up asks for patient involvement, for example through shared decision making (SDM) about follow-up. SDM is described by Elwyn et al. as: “a process in which decisions are made in a collaborative way, based on trustworthy information about a set of options”¹⁶.

To our knowledge, no studies are available about the ideal organization of follow-up, taking into account the wishes of HCPs and efficiency, and personalization of care. Therefore, the aim of this study is to gain insight into the similarities and differences in the organization of follow-up in seven teaching hospitals in the Netherlands and to identify best practices and opportunities for the future of follow-up for patients with breast cancer as proposed by HCPs.

METHODS

Study Design and Setting

We used an explorative research design, including semi-structured in-depth group interviews with multiple HCPs involved in breast cancer care. This study took place in seven teaching hospitals, which together form the Santeon hospital group. The Santeon hospitals are large teaching hospitals spread over the Netherlands with dedicated breast centres, treating about 11% of all Dutch breast cancer patients. Active value-based health care (VBHC) teams are mutually benchmarking and improving logistics, outcomes and quality of breast cancer care on a regular basis since 2016.

Respondents

In each of the hospitals, the leading medical specialists of the VBHC breast cancer teams (mainly breast surgeons) indicated which HCPs are involved in the follow-up of patients with breast cancer in their hospital. By e-mail, involved HCP's were approached for a group interview. Table 1 displays the interviewed HCPs and their discipline per hospital. In each of the hospitals, a nurse practitioner (NP) from the surgery department and/or a breast cancer nurse (BCN) was interviewed. In four out of seven hospitals a breast surgeon was present during the interview.

Table 1 Respondents

	Hospital 1	Hospital 2	Hospital 3	Hospital 4	Hospital 5	Hospital 6	Hospital 7	
Breast surgeon	X		X	X	X			4
NP surgery department	X	X	X	X			X	5
NP oncology department		X				X		2
Breast cancer nurse			X		X	X	X	4
General physician					X			1
Total HCPs interviewed	2	2	3	2	3	2	2	16

Procedures

Before the interviews took place, the HCPs were asked to send the following documents (if available): 1) the transmural care pathway; 2) the follow-up care pathway; 3) an example of an aftercare plan for patients; and 4) if available, outcomes on Patient Reported Experience Measures (PREMs) and Patient Reported Outcome Measures (PROMs). These documents served as input for the interviews. The interviews lasted about one hour each and were conducted at the hospital location by two researchers (JA and JvH), both trained in conducting interviews. All interviews were audio-recorded - with prior permission of respondents - and transcribed verbatim. After each interview, a summary based on notes was sent to the respondents for approval.

Interview Scheme

The interviews focused on the following topics: 1) tasks and responsibilities of HCPs within the process of follow-up, 2) frequency and pacing of structured care moments, 3) referral to other HCPs for aftercare, 4) instruments and/or tools used in follow-up, 5) personalization of follow-up and, 6) Shared Decision Making (SDM) regarding follow-up. Additionally, to assess best practices for follow-up, respondents were asked to define what made them proud regarding follow-up in their hospitals. Furthermore, respondents were asked to identify 'opportunities' for the future of follow-up. Respondents were explicitly invited to elaborate on their motivations and considerations by probes such as: Can you tell us more about that? Can you explain why? Can you give an example?

Data analysis

Two researchers (JA and JvH) independently coded all transcripts. The coders read and reread all transcripts to familiarize themselves with the content. Then, relevant fragments were selected and categorized in one of the main themes, either related to the organization of follow-up or best practices or opportunities for the future of follow-up. All data were analyzed on hospital level. This means that quotes of individual respondents in each hospital

were gathered and labelled with a hospital number. Fragments related to the organization of follow-up were analyzed in three steps using deductive analysis. First, fragments related to the organization of follow-up were deductively categorized into the five main themes: tasks and responsibilities, frequency, referrals, tools, personalization and SDM. These fragments were summarized for each hospital. Second, different variations in the organization of follow-up were identified and their prevalence was counted. Third, if appropriate, motives for these different variations were sought in the fragments categorized for the specific main theme. Fragments related to best practices and opportunities for the future of follow-up were analyzed using an inductive approach, which means that the fragments were categorized into subcategories that are derived from the data, instead of pre-defined categories.

The coders (JA and JvH) discussed their individual findings several times and any differences in coding were solved based on consensus. Remaining inconsistencies in coding were discussed with a third coder (CD) until consensus was reached.

RESULTS

Organization and variation in follow-up

The organization and variation in follow-up are reported regarding the following main themes: roles of HCPs in follow-up, frequency of structured care moments, referrals, tools and information, personalization and SDM. The results mainly represent the follow-up trajectories in the surgery department, with the exception of Hospital 2, in which the surgery trajectory is integrated with the follow-up trajectory in the oncology department.

Roles in follow-up

Aftercare and surveillance

Figure 1 displays the HCPs involved in follow-up and the structural care moments for aftercare and/or surveillance. Wide variation was found between the hospitals regarding the HCPs involved in aftercare. Regarding surveillance, less variation was found. In most hospitals, surveillance was conducted by the breast surgeon or the NP of the surgery department. Depending on the received treatment, patients visited the medical oncologist or the radiotherapist during the follow-up phase, often in a separate aftercare trajectory. The degree of coordination between these trajectories differed between hospitals. The HCP who acted as a case manager for the patient during the follow-up phase differed per hospital. In most cases, the case manager was a HCP with a nursing background such as a BCN or a NP of the surgery or oncology department.

Anti-hormonal therapy

Regarding the guidance of the specific group of patients that had anti-hormonal therapy, little variance was found. In most of the hospitals, this guidance was performed by NPs of the

oncology department or a medical oncologist. In two of the hospitals, breast surgeons or NPs from the surgery department were counselling patients during their anti-hormonal therapy.

Role of the general practitioner

In most hospitals (4), the GP did not have an active role in the follow-up for patients with breast cancer. However, they were actively informed about the patient’s aftercare and surveillance. Furthermore, the GP was consulted by HCPs in case patients suffered from non-breast cancer-related (multi-) problems.

Frequency structured care moments

The moments at which aftercare takes place during the first and second year after surgery vary (figure 1). Two of the seven hospitals follow the proposed aftercare schedule from the guideline for the first two years after treatment (a consultation every 3 months in the first year and every 6 months in the second year). In the other hospitals, aftercare was provided at a lower frequency. In two of the hospitals, every patient had a aftercare consultation in which the patient was informed about aftercare and next aftercare visits were arranged based on the patients’ needs.

The structured care moments for surveillance were similar in all hospitals and correspond to the Dutch national guideline (an annual mammogram and physical examination for five years following treatment).

Figure 1 Roles of health care providers and structured care moments for follow-up

Note. This figure only represents the follow-up trajectories in the surgery department of the hospitals. Hospital 2 is the only hospital in which this trajectory is integrated with the follow-up trajectory in the oncology department.

Referrals

Respondents mentioned that patients are referred to other (specialized) HCPs based on their needs and preferences in the follow-up phase. For example, patients with physical complaints were referred to (oncological) physiotherapists and lymphedema therapists. For (psycho-) social problems related to the disease or treatment, patients were mostly referred to social workers or medical psychologists within the hospital. In case of more general (psycho-)social complaints, referral was made to external psychologists or general practice-based nurse specialists.

Patient's referral to rehabilitation and re-integration mainly took place in case of multidimensional problems. In one hospital an internal rehabilitation program was offered as a standard for patients during chemotherapy. Patients were referred to more specialized centres in case of specific problems regarding rehabilitation and re-integration.

Tools

Follow-up care pathway and aftercare plan

In most hospitals (6), a follow-up care pathway was available for HCPs (either digitally or on paper). However, none of the respondents referred to actively using these described care pathways during follow-up care. In two hospitals, participants explicitly mentioned not using the care pathway. A BCN in one of these hospitals said, *"I think that the care pathway broadly represents clinical practice. However, I don't check it daily nor monthly."* In three hospitals, respondents mentioned that the care pathway for follow-up was in revision. In one of the six hospitals the care pathway was recently transformed into a flowchart and integrated into the Electronic Medical Record (EMR).

A personalized aftercare plan was provided to patients as recommended by the Dutch guideline in only one hospital. This plan was developed within a regional collaboration with other regional hospitals and aimed to provide insight into different treatments the patients had undergone and the possible late effects of these treatments and to inform patients about aftercare and surveillance. In three hospitals an aftercare plan was under development at the time of the interview.

Other tools

In most hospitals, multiple instruments were used for patients with breast cancer within the follow-up phase (table 2). In one hospital, no tools were used yet, but the HCPs were looking for tools to use. One of the mentioned tool was the distress thermometer (DT), which was used in five hospitals to detect psychosocial problems. The DT is a short self-report measure to assess distress in the emotional, practical, physical, spiritual and social functioning domains^{17,18}. Additionally, in all hospitals the use of PROMs to detect and monitor needs of patients in follow-up was being explored at the time of the interview. For self-management support during follow-up, patients were actively referred to the website of the Dutch Breast

Cancer Patients Association (BVN) and to the Untire app, a self-help app for fatigue complaints. Two hospitals used the INFLUENCE-nomogram, a prediction tool for the risk of locoregional recurrence¹⁹. They did not use the calculated risk estimation to personalize follow-up yet, but were using it to inform patients about their risk to put fear of recurrence in perspective. To evaluate and improve care, respondents in three hospitals indicated that they made use of PREMs outcomes and in one hospital, focus group meetings with patients were organized to collect input for improvements.

Table 2 Instruments used in the follow-up phase

Tools to screen for (psychosocial) problems:

- Distress thermometer (hospital 1, 3, 4, 5 & 6)
https://www.nccn.org/patients/resources/life_with_cancer/pdf/nccn_distress_thermometer.pdf

Tools for self-management

- Website of the Dutch Breast Cancer Patients Association (BVN) (with online information and apps) (hospital 2 & 4)
<https://borstkanker.nl/nl/keuzehulp/nazorg>
- Untire app (self-help app for fatigue complaints) (hospital 4 & 6)
<https://untire.me/>

Tools for prediction of risks of recurrence

- INFLUENCE nomogram (hospital 2 & 3)
<https://www.evidencio.com/models/show/721>

Tools to evaluate and improve care

- PREMs (hospital 1, 5 & 6)
 - Focus group meetings with patients (to collect input for improvements) (hospital 5)
-

Information Provision, Personalization and Shared Decision Making

Information provision about follow-up

In most hospitals, information provision about follow-up did not take place in a structural manner. Mostly, written information about follow-up was provided to the patients in the form of a patient information folder, including information leaflets, usually handed to the patients after diagnosis containing practical information about treatments and procedures. The content of these folders regarding follow-up was not very elaborate in comparison with information on treatments and varied from a flowchart about structured care moments for surveillance to an overview of resources and instruments for detection and self-management of late effects of cancer and treatment. Additionally, face-to-face information about follow-up was usually provided by a BCN or NP at several moments in the care process, with the post-surgery consultation in which the pathology report was discussed with the patient as an explicitly mentioned moment.

Personalization

According to the respondents, aftercare was already more personalized than surveillance because it was in particular organized according to the needs of patients. Personalization of aftercare took, however, mostly place in an informal and unstructured way. In one of the hospitals (hospital 1), aftercare was personalized based on PROMs and the results of the distress thermometer. In another hospital (hospital 2), respondents mentioned that they would like to give patients more responsibility in organising and personalizing their own aftercare.

Surveillance was mainly offered according to the Dutch general guideline (an annual mammogram and physical examination for at least five years following treatment) and not considered as care that is personalized. Yet, HCPs indicated that in some cases, surveillance deviated from the guideline based on patient or treatment-related factors, which can be seen as informal personalization. In two hospitals (hospital 4 & 7), respondents indicated that there was a desire for more personalization of surveillance based on tumor- and patient characteristics.

Shared Decision Making

In none of the hospitals, structured SDM was practiced when making decisions about the planning of aftercare or surveillance. However, in three hospitals, HCPs mentioned that decisions about the organization of the aftercare and surveillance took place preferably after discussion with the patient. In two of the hospitals (hospital 1 & 2), a wish for more SDM regarding follow-up was expressed by HCPs. For example, HCPs mentioned an ideal situation in which the HCP and patient jointly consider the patients' wishes and discuss the need for extra support, aftercare and surveillance, taking into account the evidence-based guideline and tumor- and patient characteristics.

Best practices and opportunities for the future of breast cancer follow-up

To identify best practices, respondents were asked to indicate what makes them proud regarding follow-up care for breast cancer patients in their hospital. Furthermore, respondents were asked to identify opportunities for the future of follow-up. An overview of mentioned best practices and opportunities is provided in table 3.

Table 3 Best practices and opportunities follow-up

Best practices

- Case management and good collaboration between HCPs in follow-up phase (hospital 1, 2, 3, 4, 5 & 7)
- Sufficient possibilities for referral and close contact with primary care providers (hospital 5 & 6)
- Personalized aftercare visits (hospital 1 & 3)
- Integrated follow-up surgery and oncology department (hospital 2)
- Integration of follow-up pathway and PROMs in EMR (hospital 4)

Opportunities for the future

- Further exploration use of PROMs for monitoring needs in follow-up phase (hospital 1, 2, 3, 4, 5 & 7)
- Guideline organization and content of aftercare (hospital 1, 2, 5 & 6)
- Better collaboration HCPs and integration follow-up trajectories (hospital 1, 4 & 5)
- Using SDM to personalize follow-up (hospital 1 & 2)
- Attention to and financing of rehabilitation and re-integration of patients (hospital 6)
- Improving insight of referral options for specific patient needs (hospital 6)
- Improving patient communication and information provision about follow-up (hospital 6)
- Use of patient portals for communication in follow-up (hospital 5)

Best practices

In five out of seven hospitals, respondents valued their case management and good collaboration of involved HCPs in the follow-up phase as a best practice. HCPs had the impression that patients positively experienced the flexibility, accessibility and continuity of such a case manager. In these hospitals, the good collaboration of HCPs (e.g. breast surgeons, medical oncologists, NPs and BCNs) in the follow-up phase was also named as a best practice since this collaboration provides the opportunity to deliver efficient and adequate care. In two hospitals, respondents indicated that they were proud of the ample possibilities for referral and close contact with primary care providers (PCPs). A specific example was mentioned in hospital 6, where all patients receive physical rehabilitation after chemotherapy as standard care. Respondents in two hospitals mentioned the personalization of aftercare visits based on patients' needs as a best practice. In these hospitals patients are actively asked about their preferences for the frequency of aftercare consultations. In one hospital, the follow-up trajectories of the surgery and oncology department were integrated to reduce the amount of structured care moments and involved HCPs. Respondents in this hospital were proud of this practice, because it enables efficient follow-up care. In another hospital, respondents indicated the integration of PROMs in their EMR as a best practice, because it provides the opportunity to discuss the outcomes of PROMs at structured moments in the care pathway. Furthermore, the patient-specific outcomes of the PROMs are easily accessible.

Opportunities for the future

The HCPs described some opportunities for the future. The further exploration of the use of PROMs for monitoring patient's needs in follow-up was mentioned in six out of seven hospitals. Obstacles for this implementation were, however, also mentioned and included: the burden of the current extensive PROMs, required resources for implementation, low uptake by patients, different IT systems in the participating hospitals, and lack of knowledge on how to use the outcomes in clinical practice. A second opportunity, mentioned by respondents from four hospitals, was to have a (nation-wide) guideline about the ideal organization and content of aftercare. Examples of what this guidelines should include according to the respondents are: 1) organizational aspects (e.g. a specific starting point for aftercare), 2) a description of the role of the case manager during follow-up, 3) possibilities for follow-up outside of hospital, 4) an oversight of referral options for specific patients' needs (e.g. sexuality, fatigue or neuropathy). Third, whereas six hospital indicated the collaboration between HCPs in follow-up as their best practice, a wish for better collaboration between HCPs and integration of follow-up trajectories of the surgery and oncology department was mentioned as an opportunity in three hospitals. Integration of these trajectories and reduction of the number of involved HCPs and structured care moments provides the possibility to organize efficient and adequate follow-up. Fourth, the use of SDM to personalize follow-up to the patients' needs and risks for recurrence or secondary tumors was mentioned as an opportunity for the future by two hospitals. Finally, respondents from one hospital, indicated that there should be more attention to rehabilitation and re-integration of patients and that trajectories or referrals with this purpose should be financially covered by the basic health insurance package. Other, less frequently mentioned opportunities for the future were: improving patient communication and information provision about follow-up and the use of EMR linked patient portals for communication.

DISCUSSION

The results of this study showed substantial variation in the organization of aftercare, but less variation in surveillance. Best practices focused on case management, personalization of aftercare, and adequate collaboration between HCPs, which was also suggested as opportunity for the future. Other opportunities were seen in improving the monitoring of patients' needs, a more comprehensive guideline for aftercare, and integration of follow-up trajectories of the surgery and oncology department.

Variation in aftercare, mainly presented itself in the frequency and pacing of aftercare consultations and the tasks and responsibility of different HCPs in aftercare. HCPs in this study indicated perspectives on the frequency of aftercare widely ranging from leaving the responsibility for organization of aftercare with the patients to organising as many structural care moments for aftercare as possible to make sure that patients receive sufficient aftercare. Additionally, the HCPs involved in aftercare varied considerably in disciplines and

coordination of care. These findings confirm earlier findings of Neuman et al.²⁰ and Tucholka and colleagues²¹, who concluded that the lack of a standard protocol on which HCPs should be involved in aftercare leads to significant variation and that some of this variation likely reflects inefficiency in clinical care. One way to streamline care and to possibly reduce inefficiency is to appoint a case manager that oversees the care process and acts as a contact person for patients. In our study, we saw that many hospitals started with case management and reported to be proud of it. Meanwhile, HCPs recognize that the concept of case management in their care pathways can be optimized in the future.

According to the interviewed HCPs, PCPs currently have a limited role in aftercare and surveillance. Opinions on involving PCPs, such as GPs and general practice-based nurse practitioners in aftercare and surveillance are strongly divided. On the one hand, involving PCPs may create opportunities for the future in terms of reducing the workload of HCPs, and improvement of meeting the wishes and needs of patients and reducing distress levels combined with a higher satisfaction of care (e.g. by providing aftercare closer to home in a familiar environment)²². On the other hand, barriers still exist regarding communication and coordination between PCPs and secondary HCPs and especially doubts regarding the level of expertise of PCPs on breast cancer specific aftercare¹⁹.

In some hospitals, HCPs expressed the wish for more personalization of surveillance. The INFLUENCE-nomogram - a prediction tool for the risk of locoregional recurrence - can be used to personalize surveillance for breast cancer survivors, but it was not yet used for this purpose but only to predict the risk of locoregional recurrence¹⁹. De Ligt and colleagues²³ defined decisions about surveillance for recurrent or secondary breast cancer as preference-sensitive, meaning that decisions need to be based on the best available (medical) evidence and that these should reflect patient needs and values. SDM is advised as an optimal decision making process for this type of decisions. A tool to guide SDM regarding personalized surveillance integrating relevant outcome information (e.g. personal risks of LRR and SP or relevant PROs) is therefore necessary. A tool in under construction in co-creation with relevant stakeholders (clinicians, patients and other experts) to ensure alignment with the needs and requirements.

Although aftercare was described as highly personalized care, it was mainly personalized in an unstructured way, without the support of a systematic strategy or tools. HCPs indicated the need for more structured tools to personalize aftercare. Already existing tools such as the aftercare patient decision aid (PtDA) developed by Klaassen and colleagues²⁴ could be used for personalisation of aftercare. PROMs can also be used for this purpose as a tool for monitoring and meeting the needs of patients. Respondents in our study indicated that the use of PROMs could be an opportunity for the future. At the same time, they mentioned barriers for the implementation and use of PROMs such as: the extensiveness of the current questionnaires, required resources for implementation, low uptake by patients, and a variety of IT systems for the collection of PROMs and a lack of options to show and communicate outcomes and give patients feedback when they visit the hospital. Van Egdom et al.²⁵ and

Riis and colleagues²⁶ reported similar barriers, which should be addressed to increase overall impact of PROMs. They stated that the use of PROMs to personalize aftercare can be useful in improving post-treatment symptom management during follow-up by a comprehensive view of patients' needs. Based on this study, we recommend to develop a standard set of patient and HCP-friendly PROMs to support implementation in clinical practice.

In this study, we observed that HCPs used relatively few tools. The tools that were used had different aims: screening for (psychosocial) problems, self-management, prediction of risks of recurrence and tools for evaluation and improvement of care. An individualized aftercare plan as proposed in the Dutch guideline and recommended in international literature was seldomly used²⁷. HCPs indicated that it was unclear how and when this aftercare plan should be applied in the care process. A recent study among survivors of gynaecological cancer has shown that the use of aftercare plans does not always have a positive effect and can even have a negative impact on quality of life (QoL) and anxiety due to more threatening illness perception²⁸. Moreover, in systematic reviews by Jacobsen and colleagues and Høeg et al., no compelling evidence was found that the integration of survivorship care plans in follow-up leads to better outcomes regarding health-related quality of life (HRQOL), anxiety or depression levels, or costs^{27,29}. De Rooij and colleagues found that the benefits of aftercare plans for patients are mediated by information coping styles of patients, which advocates for a tailored delivery of such aftercare plans³⁰. Further research is needed on how patient aftercare plans should be applied, in order to develop a relevant guideline.

Another remarkable result was that HCPs referred patients to a relatively limited range of self-management tools, while there are many tools and interventions available^{31–33}. In a previous study by Jansen et al, cancer survivors expressed a high need for supportive care and a positive attitude towards self-management and e-health³⁴. Initiatives such as the Dutch website 'www.verwijsgidskanker.nl' and Oncokompas provide insight in supportive care options for specific needs of patients³⁵. The Netherlands Comprehensive Cancer Organization (IKNL) is currently working on an inventory of eHealth applications for cancer patients. Although these comprehensive overviews of care options and applications are available, they were not used by the HCPs interviewed in this study. We recommend the use of existing comprehensive overviews in clinical practice.

Little reference was made to the opportunity for distant care and telemedicine in follow-up in the interviews (e.g. the use of telemedicine, EMRs or patient portals in follow-up). However, these interviews were performed just before the COVID-19 pandemic. COVID-19 gave rise to the use of these types of technologies in follow-up and may cause a long-lasting shift in care delivery in follow-up.

Strengths and limitations

To our knowledge, this study is the first study to assess the similarities and differences in the organization of follow-up and to identify best practices and opportunities for the future of follow-up for patients with breast cancer as proposed by HCPs. A strength of this study is the use of semi-structured group interviews, which seemed the appropriate choice due to the type of data collected: motives for and perspectives on the organization of follow-up. Due to the group interviews, HCPs could complement each other and therefore we can be more sure about the follow-up practices that were described during the interview.

A limitation of this study lies in the focus on the surgical follow-up trajectory. Information obtained in the interviews about the oncological trajectory to follow-up on the use of endocrine therapy was not sufficient to be reported separately. More information about the oncological trajectory would provide a more comprehensive picture of follow-up and the interaction between the surveillance for recurrences, psychosocial support and endocrine therapy monitoring. Even though this study was focussed on the perspective of HCP's view on follow-up, effort was made to take into account patients' views. The Dutch Breast Cancer Patients Association (BVN) provided input for the study design and patient representatives were present at two interviews. Yet, a great amount of information about the needs and preferences of patients in breast cancer follow-up is present in literature^{21,36-42}.

CONCLUSION

Variation was present in the organization of aftercare. In contrary, little variation was observed regarding surveillance, for which guidelines are leading. Case management is seen as a best practice and opportunities for aftercare lie in improving the monitoring of patients' needs, a more comprehensive guideline for aftercare, better collaboration and determination of roles between HCPs and integration of aftercare trajectories of the surgery and oncology department. Concurrently, there is a wish to personalize surveillance based on risk for (local) recurrences and secondary primary tumors taking into account the wishes and needs of patients.

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PART II

The added value of (regional) cancer care pathways

CHAPTER 6

Quality improvement by implementing an integrated oncological care pathway for breast cancer patients

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ABSTRACT

Background and aim

In cancer care, more and more systemized approaches such as care pathways are used to reduce variation, reduce waiting- and throughput times and to improve quality of care. The aim of this study was to determine whether the implementation of a multidisciplinary breast cancer pathway in three hospitals has improved the care for breast cancer patients.

Methods

Retrospectively almost 800 patients with breast cancer were selected from the Netherlands Cancer Registry (NCR). The patients were divided in two groups: before implementation of the pathway in 2006-07 (baseline measurement) and those after implementation in 2009 (post measurement). Fourteen quality indicators were compared before and after the implementation of the care pathway. To estimate the impact of the care pathway relative to evidence based guidelines and profession-based norms, involved project leaders were interviewed.

Results

Seven out of eight indicators with medical information and four out of five indicators with information about waiting- and throughput times improved. With the multidisciplinary meeting as key in the breast cancer care, more compliance to national guidelines was observed. For example: For more patients a HER2neu test was performed after implementation of the pathway (from 92% to 96%, $p = 0.016$) and more patients started with their first chemotherapy (from 33% to 45%) or their first radiotherapy (from 55% to 59%) within 4 weeks after surgery.

Conclusion

Implementing a multidisciplinary breast cancer pathway leads to better compliance with the national guidelines and can improve breast cancer care.

INTRODUCTION

Breast cancer is the most common cancer in women worldwide, with 464,000 cases in 2012¹. The Netherlands Cancer Registry (NCR) showed a 1-year incidence of breast cancer of 13.257 women in 2010². Due to this large number, the high impact of the diagnosis cancer and the multidisciplinary character of cancer care processes, health care organizations put much effort in improving breast cancer care. Besides, external parties such as the Health Care Inspectorate (IGZ) stimulate and demand transparency of care through publication of indicators to get insight in the patient-focused care and the delivered quality of care. Nowadays patients can choose between hospitals, based on the quality indicators. One of the methods to realize patient-focused care and re-organize care processes is the development and implementation of care pathways in order to improve the quality and efficiency of evidence-based care, teamwork and to achieve better accessibility of care^{3,4}. Care pathways are also known as clinical pathways, critical pathways, integrated pathways, patient journeys or care maps³. In this study care pathways are defined as logical coherent individual care processes which patient with a specific tumor go through from the first need for care to survivor or death⁵. Introducing care pathways usually leads to structuring health care services to improve the compliance with evidence based guidelines or evidence based medicine⁶. However, implementing care pathways in an organization is a complex intervention³. To support hospitals with developing, implementing and monitoring multidisciplinary cancer pathways as well as implementing evidence based guidelines, the Comprehensive Cancer Centre the Netherlands (IKNL) has introduced the model for Integrated Oncological Care Pathways (IOCP) and a corresponding roadmap^{5,7}. This model is based on principles of process management as well as national (evidence based) guidelines. Central elements of the IOCP model are 'process', 'organization' and 'planning'. These elements lead to a certain 'performance'. E.g. agreements about the moments of transfer (process), a better organization of the multidisciplinary meeting (organization and structure) or a better planning of operations (planning) may improve the performance of the care pathway and results in better quality of care. The IOCP model is frequently used for introducing cancer care pathways of several tumor types in Dutch hospitals.

As pathways are seen as a method within the field of continuous quality improvement, evidence about the effects of implementing cancer care pathways is essential. In 2001 a literature review was published about the impact of clinical practice guidelines and pathways for several tumor types, including breast cancer. The authors concluded that costs and length of stay can be reduced, practice variations can be minimized, and patient quality of care and satisfaction can be maintained⁶. Next, a study about a mastectomy pathway concluded that the consistency in patients' treatment as well as the quality of patient outcome improved, and the costs of care and length of hospital stay reduced⁸. More recently, another study reported the following positive effects of a clinical pathway for breast surgery: patient satisfaction increased, patient anxiety levels decreased, and patient's quality of care improved⁹. To our

knowledge no studies exist about the effects of implementing a multidisciplinary breast cancer pathway by using a systematic method for developing and implementing oncological care pathways in more than one hospital. The aim of this study was to determine whether the implementation of a multidisciplinary breast cancer pathway in three hospitals improved the care for breast cancer patients. As care pathways are strongly related to other methods of quality improvement, such as introducing (new) guidelines and quality criteria, it is important to determine the actual influence of introducing the care pathway on the results. Therefore, data from a national database was combined with the opinion of involved project leaders concerning the impact of the breast cancer pathway.

METHODS

Selection of indicators

The quality of care before and after having implemented the breast cancer pathway was assessed by selecting fourteen indicators. These indicators were chosen because they are all available in the NCR and because of their focus on the compliance national guidelines, these are the evidence based guideline for breast cancer (www.oncoline.nl) and the norms of the National Breast Cancer Organization of the Netherlands (NABON). The NCR, established in 1989, is a nationwide population-based cancer registry and has data of new cancer patients, such as tumor type, incidence data and stage and NABON indicators, based on information from the pathology laboratories and patient files collected by specially trained registrars.

Study population and setting

The quality of breast cancer care was assessed in a retrospective study. Included were breast cancer patients diagnosed with primary breast cancer from three medium-sized hospitals in the Northern Netherlands. For the hospital characteristics, see table 1. Breast cancer patients which were diagnosed with breast cancer in these three hospitals in the period 1 July 2006 until 30 June 2007 were identified from the NCR for the baseline measurement. Another group of breast cancer patients which were diagnosed in the period 1 January 2009 until 31 December 2009 were selected for the post measurement. The implementation of the pathway took place in 2008 according the Integrated Oncological Care Pathways model (IOCP) and identifies five phases^{6,7}. (1) In the awareness and vision phase commitment was created. A baseline measurement was performed and patient's satisfaction was measured. (2) The project plan was written and a kick-off meeting was organized. (3) In the next phase the current situation was described, using the results of the baseline measurement, followed by a description of the desired situation. Both situations were compared to identify the measures and actions to be undertaken. (4) In the implementation phase the actions were systematically implemented according to the action plan and continuously monitored. (5) In the last phase the actions were evaluated through a post measurement.

Statistical analyses were performed to calculate the difference between the total scores of the post and baseline measurement by using Stata (Statistical Software VCS, TX: Stata Corporation). Only patients which followed the pathway were included in the analysis. The chi2 test was used to calculate significant results of all indicators, except indicator 9, 10 and 12. The *t* test was used to compare the mean number of days for indicator 9 and 10. And the Fisher's exact test (two-tailed significance) was used for indicator 12, as the chi2 test was not appropriate because of the low numbers. A *p*-value of <0.05 was considered significant.

Table 1 Hospital information

	Hospital		
	A	B	C
Catchment area ¹	140.000*	100.000	121.602
Number of residents in whole region: 647.214 ²			
Number of breast cancer patients diagnosed with primary breast cancer ³	128	139	160
New diagnosed breast cancer patients ⁴ :			
• whole region: 629			
• the Netherlands: 14.964			
Number of beds ¹	304	221	339
Number of first hospital visits ¹	87.542	77.016	77.208
Number of employees (excl. medical specialists) ¹	1.393 (1.014,0 fte)	1.190 (797,1 fte)	1.404 (767,0 fte)
Number of medical specialist ¹	99 (80,0 fte)	88 (75,7 fte)	89 (74,7 fte)
Treatments: all basis specialisms such as oncology ¹	Yes	Yes	Yes
Radiotherapy: patients are referred to the same specialized regional radio therapeutic centre ¹	Yes	Yes	Yes

¹ based on documents of the participated hospitals 2009; *) 2011 (www.jaarverslagenzorg.nl)

² statline.cbs.nl, 1 January 2012

³ based on Netherlands Cancer Registry (NCR), 2009

⁴ www.cijfersoverkanker.nl, 2009

Determination of the impact of the breast cancer pathway

Once phase 5 was performed, structured interviews with the involved project leaders from each hospital were held to verify whether these results were caused by the implementation of the breast cancer pathway. Prior to the interviews, the project leaders received a questionnaire in which for each result three questions were asked: 1) was this action already well implemented before the introduction of the breast cancer pathway?, 2) was this result caused (or consolidated) by the care pathway?, and 3) when this result was not related to the implementation of the pathway, what other cause gave rise to this result?

RESULTS

Selection of indicators

For this study fourteen indicators were selected: eight providing medical information and six giving information about waiting- and throughput times (process and structure indicators). Data analyses was performed by calculating the difference between the post and baseline measurement. Figure 1 shows in which phase of the care process the indicators are situated.

Figure 1 Indicators in breast cancer

Comparing ‘before’ and ‘after’ data

Of all patients with invasive breast cancer (N=793, see table 2) almost 50% of them were between 50 and 70 years old and 57% had negative lymph nodes. The results of the baseline and post measurement for each hospital are shown in table 3. For the overall comparison between both measurements including results of the statistical tests, see table 4. The results of the interviews are presented in table 5. One indicator was omitted from the interviews (indicator 12, see table 3 & 4); a correct interpretation was not possible due to the low numbers. See the annex with quotes from the interviews which support the results.

Table 2 Patient characteristics

	Hospital A		Hospital B		Hospital C		Total	
	N	%	N	%	N	%	N	%
Measurement								
baseline measurement	126	49,6	104	42,8	136	45,9	366	46,2
post measurement	128	50,4	139	57,2	160	54,1	427	53,8
Gender								
man	2	0,8	0	0,0	2	0,7	4	0,5
woman	252	99,2	243	100,0	294	99,3	789	99,5
Age								
<50	65	25,6	45	18,5	65	22,0	175	22,1
50-59	58	22,8	61	25,1	66	22,3	185	23,3
60-69	63	24,8	64	26,3	74	25,0	201	25,3
70+	68	26,8	73	30,0	91	30,7	232	29,3
Tumor behavior								
in-situ	20	7,9	22	9,1	34	11,5	76	9,6
invasive	234	92,1	221	90,9	262	88,5	717	90,4
T-stadium								
IS	19	7,5	20	8,2	33	11,1	72	9,1
pT1ab	22	8,7	43	17,7	53	17,9	118	14,9
pT1c	99	39,0	69	28,4	88	29,7	256	32,3
pT2	75	29,5	76	31,3	82	27,7	233	29,4
pT3/4	15	5,9	14	5,8	6	2,0	35	4,4
pTx	24	9,4	21	8,6	34	11,5	79	10,0
N-stadium								
pN0	132	52,0	159	65,4	161	54,4	452	57,0
pN1	68	26,8	36	14,8	65	22,0	169	21,3
pN2N3	28	11,0	24	9,9	29	9,8	81	10,2
pNx	26	10,2	24	9,9	41	13,9	91	11,5
Extensive local tumor								
no	193	76,0	193	79,4	242	81,8	628	79,2
yes	61	24,0	50	20,6	54	18,2	165	20,8
Total	254	100,0	243	100,0	296	100,0	793	100,0

Table 3 Results per hospital

		Definition	NABON norm
Indicators with medical information	Number of patients		
	1.	HER2neu determination	invasive tumours
	2.	Sentinel node procedure is performed	
	3a.	Axillary lymph node dissection by pN0(i-)	pT1-2, pN0(i-), excl neo-adj
	3b.	Axillary lymph node dissection by pN0(i+)	pT1-2, pN0(i+), excl neo-adj
	3c.	Sentinel node procedure with >5 nodes, without ALND by pN0(i-)	pT1-2, pN0(i-), excl neo-adj
	3d.	Sentinel node procedure with >5 nodes, without ALND by pN0(i+)	pT1-2, pN0(i+), excl neo-adj
	4.	Number of breast cancer surgeries per year per surgeon	% >30 surgeries in period
	5.	Number of (re-)surgeries	
		initial	
		initial + re-excision	
		initial + 2 re-excisions	
	6.	Breastconserving therapy	T1
	7.	Adjuvant chemotherapy	pT1-2, pN1, < 60 yr, excl neo-adj chemo
Indicators with information about waiting- and throughput times	8.	Radiotherapy and chemotherapy not simultaneously	
	9.	Time between first visit and PA-confirmation	median; mean (days)
	10.	Time between first visit and first surgery	median; mean (days)
	11.	Time between PA-confirmation and first surgery, including direct reconstruction	excl M1, excl neo-adj beh >90% within 5 weeks
	12.	Time between PA-confirmation and neo-adjuvant chemotherapy	invasive, M0 within 5 weeks
	13.	Time between last surgery and first chemotherapy	invasive tumour within 4 weeks
	14.	Time between last surgery and first radiotherapy	within 4 weeks between 4 & 6 weeks

Performance											
Baseline measurement 01 July 2006 - 30 June 2007						Post measurement 01 Jan - 31 Dec 2009					
Hospital A		Hospital B		Hospital C		Hospital A		Hospital B		Hospital C	
N	% patients	N	% patients	N	% patients	N	% patients	N	% patients	N	% patients
126	100%	104	100%	136	100%	128	100%	139	100%	160	100%
117	95%	97	96%	127	87%	117	98%	124	95%	135	96%
115	77%	94	75%	115	73%	118	75%	133	82%	149	77%
50	16%	51	20%	60	17%	52	12%	74	8%	63	6%
5	80%	6	83%	7	71%	4	50%	5	40%	4	25%
42	2%	40	3%	50	2%	46	0%	68	1%	59	2%
105	70%	94	72%	120	78%	112	100%	130	78%	111	100%
115	86%	94	79%	115	83%	118	88%	133	83%	149	85%
115	11%	94	15%	115	14%	118	10%	133	13%	149	10%
115	0%	94	1%	115	1%	118	0%	133	0%	149	2%
57	77%	44	82%	61	75%	64	69%	68	79%	80	81%
13	62%	5	100%	16	100%	20	90%	15	93%	21	86%
32	97%	19	100%	34	71%	49	98%	40	100%	50	100%
117	0 / 5,9	77	0 / 3,3	125	1 / 4,6	103	0 / 3,9	98	0 / 1,0	129	0 / 2,3
112	26 / 36,8	94	18 / 26,1	113	19 / 22,5	117	27 / 33,7	131	18 / 29,3	145	20 / 21,7
110	86%	89	98%	112	97%	115	80%	131	96%	147	93%
1	100%	3	67%	No obs.		3	67%	1	100%	No obs.	
21	33%	14	14%	31	42%	46	59%	36	31%	41	41%
60	48%	49	51%	56	64%	50	64%	71	59%	78	56%
60	28%	49	20%	56	23%	50	18%	71	25%	78	31%

Table 4 Results overall differences

		Performance				
		Baseline measurement 01 July 2006 - 30 June 2007		Post measurement 01 Jan - 31 Dec 2009		Significance
		N	% patients	N	% patients	(p < 0.05)
	Number of patients	366	100%	427	100%	
1.	HER2neu determination	341	92%	376	96%	0.016
2.	Sentinel node procedure is performed	324	75%	400	78%	0.303
3a.	Axillary lymph node dissection by pN0(i-)	161	17%	189	8%	0.012
3b.	Axillary lymph node dissection by pN0(i+)	18	78%	13	38%	0.06
3c.	Sentinel node procedure with >5 nodes, without ALND by pN0(i-)	132	2%	173	1%	0.766
3d.	Sentinel node procedure with >5 nodes, without ALND by pN0(i+)	4	0%	8	0%	
4.	Number of breast cancer surgeries per year per surgeon	319	74%	353	92%	<0.001
5.	Number of (re-)surgeries					
	initial	324	83%	400	85%	0.831
	initial + re-excision	324	13%	400	11%	
	intial + 2 re-excisions	324	1%	400	1%	
6.	Breastconserving therapy	162	78%	212	77%	0.839
7.	Adjuvant chemotherapy	34	85%	56	89%	0.705
8.	Radiotherapy and chemotherapy not simultaneously	85	87%	139	99%	<0.001
9.	Time between first visit and PA- confirmation,median; mean (days)	319	0 / 4,8	330	0 / 2,4	0.019
10.	Time between first visit and first surgery, median; mean (days)	319	21 / 28,6	393	21 / 27,8	0.764
11.	Time between PA-confirmation and first surgery, including direct reconstruction, >90% within 5 weeks	311	92%	393	90%	0.121
12.	Time between PA-confirmation and neo- adjuvant chemotherapy, within 5 weeks	4	75%	4	75%	1.000
13.	Time between last surgery and first chemotherapy, within 4 weeks	66	33%	123	45%	0.129
14.	Time between last surgery and first radiotherapy, within 4 weeks	165	55%	199	59%	0.312
	Time between last surgery and first radiotherapy, between 4 & 6 weeks	165	24%	199	26%	

Table 5 Results structured interviews

	Already implemented well in baseline measurement? (Yes/No)			Result caused by implementing the breast cancer pathway? (Yes/No)		
	Hospital			Hospital		
	A	B	C	A	B	C
1. HER2neu determinations	Yes	No	No	No	No	Yes
2. Sentinel node procedures	Yes	Yes	Yes	Yes	Yes	No
3. Axillary lymph node dissections	No	No	Yes	Yes	No	No
4. Breast cancer surgeries per year per surgeon	No	?	?	Yes	No	No
5. (Re-)excisions	Yes	No	Yes	No	No	No
6. Breast conserving therapy for patients with T1 mamma carcinoma	Yes	Yes	Yes	No	?	Yes
7. Patients receiving adjuvant chemotherapy	Yes	Yes	No	No	No	Yes
8. Radiotherapy and chemotherapy not simultaneously	Yes	No	No	No	Yes	Yes
9. Time between first visit and PA-confirmation	No	No	No	Yes	Yes	Yes
10. Time between first visit and first surgery	Yes	Yes	Yes	Yes	Yes	Yes
11. Time between PA-confirmation and first surgery, including direct reconstruction	Yes	Yes	No	Yes	Yes	Yes
12. Time between last surgery and first chemotherapy	No	No	Yes	Yes	Yes	No
13. Time between last surgery and first radiotherapy	Yes	No	Yes	Yes	Yes	No

? it was not clear whether the result was already implemented well in the baseline measurement or caused by implementing the breast cancer pathway.

Compliance with national guidelines

Medical results

Once the breast cancer pathway was implemented, seven out of eight 'medical' indicators reveal positive results. For four indicators, based on the national guidelines, the following results were found. The percentage of patients for whom a HER2neu test was performed improved from 92% to 96% (+ 4%). This result was statistically significant ($p = 0.016$). The sentinel node procedure was performed in 78% of patients compared to 75% before the introduction of the pathway (+ 3%). Because more sentinel node procedures were performed, less axillary lymph node dissections were necessary. Only 8% for patients T1 and T2 tumors and pN0 (negative isolated cells) and 37% of the patients with T1 and T2 tumors and pN0 (positive isolated cells) needed an axillary lymph node dissection after the pathway was

implemented compared to 17% and 78% respectively to the previous period. More patients received adjuvant chemotherapy (+ 4%): 89% compared to 85%.

The aforementioned results indicate a better compliance with the national guidelines for breast cancer. However, the project leaders mentioned that these results were not all directly caused by the implementation of the breast cancer pathway. These effects were rather consequences of the revised national evidence based guideline for breast cancer, published in 2008. Nevertheless, the project leaders explained that the implementation of the care pathway was of great importance and this actually facilitated the implementation of the new guideline. The organization of a joint multidisciplinary meeting between the three hospital teams, facilitated by videoconferencing since 2007, was implemented because of the pathway. This service supported all relevant disciplines to join the multidisciplinary meeting and to follow the guidelines.

An overall significant difference between the post measurement and the baseline measurement for the number of breast cancer surgeries per year per surgeon was found ($p = 0.019$). After testing the differences for each hospital the results show that for two hospitals the difference was significant (hospital A, $p = 0.05$; hospital C, $p = 0.05$).

However the number of patients who underwent breast conserving therapy decreased did not improve, this treatment procedure was already implemented well before the introduction of the pathway.

Waiting- and throughput times

Four out of five 'time' indicators show positive effects in two or three hospitals. Two indicators in this category were based on the national guidelines. After the implementation of the pathway, 45% of the patients with invasive tumors started their first chemotherapy within 4 weeks after surgery, while it was previously 33% (+ 12%). No significant differences were found among the hospitals when comparing the post measurement and baseline measurement. A similar observation could be made for the start of radiotherapy: 59% compared to 55% started their first session of radiotherapy within 4 weeks after surgery (+4%).

The time between first visit to the hospital and PA-confirmation and the time between first visit and first surgery improved slightly. The overall results in time to PA-confirmation was statistically significant ($p = 0.019$). For one hospital a significant difference was found after comparing the post measurement and baseline measurement (hospital B, $p = 0.012$).

According to the project leaders, these process improvements were caused by the implementation of the care pathway. They gave the following explanations: 1) norms for all waiting- and throughput times were included in the care pathway, 2) a new referral system for all three hospitals was introduced, 3) new agreements about referral with GP's fastened the referral of patients, and 4) the time schedule to discuss the results of the mammography by surgeons and oncology nurses was better respected.

The time between PA-confirmation and first surgery, including direct breast reconstruction did not improve. However, in the post measurement still 90% of the patients were operated within 5 weeks after their first visit to the hospital according to the NABON norm. Furthermore, the project leaders mentioned that direct breast reconstruction, based on the evidence based guideline, was performed more often after the implementation of the care pathway. Knowing that this surgical operation needs to be planned and takes time, a slight reduction of this interval is rather a positive result.

DISCUSSION

After the implementation of the multidisciplinary breast cancer pathway according to the IOCP model improvements were found in process and structure indicators of breast cancer care in all three hospitals. Improvements in the compliance with the evidence based guideline for breast cancer and the NABON norms after care pathway implementation are supported by literature⁵. The pathway was responsible for structuring and organizing all processes in the care for breast cancer patients and therefore a more efficient overall care process was achieved. Contrary to the improvements in waiting- and throughput times, the breast cancer pathway indirectly resulted in improvements of medical results. Due to the implementation of the care pathway, the revised evidence based guideline for breast cancer was easily implemented.

This study shows that the central elements of the IOCP model lead to improvements in the quality of breast cancer care. Better agreements about referral of patients by GP's (process), the introduction of a new GP referral system (organization) as well as better planning of different treatments facilitated by an improved organization of the multidisciplinary meeting (planning). Therefore developing and implementing the breast cancer pathway according to the IOCP model helps to reorganize health care and implement relevant guidelines in order to achieve improvements in the quality of cancer care.

There are a few shortcomings of this study. First, a selection of relevant indicators was used. More structure and outcome indicators might be interesting. A precondition for using more indicators is the availability of reliable data from independent registries, such as the NCR. Unfortunately, other registries are not always available. And even when they exist, they do not always contain relevant and fully completed information. Secondly, this study does not provide results about the effects of care pathways on patients' satisfaction as information from the patients' perspective is essential. It is likely that a high compliance with evidence based guidelines and national norms implicates a better organized 'pathway' for the patient and less discomfort. Future studies about the effects of patients' satisfaction after the implementation of cancer care pathways are necessary to estimate the value of pathways for patients and patients' quality of care. Thirdly, a control group was not added to compare

the results from the three participating hospitals with other hospitals. The most likely control group would be a number of hospitals which do not have a breast cancer pathway. However, all hospitals in the Netherlands are somehow still occupied with the introduction or they already have an implemented care pathway for breast cancer patients.

The reported results are only applicable for the impact of breast cancer pathways. However, the implementation of this breast cancer pathway can be an example for other cancer types. Especially the care for rare tumors, lacking routine, guidelines and local expertise can benefit of a common agreed regional care pathway with a well organized multidisciplinary meeting as key, facilitated by videoconferencing and achieve great impact on quality of care and waiting- and throughput times with transparent agreements about referral. To determine the impact of pathways for other tumor types on the quality of care, more research is necessary.

To increase the quality of these studies, we recommend not only to analyse reliable data from before and after the implementation of the pathway, but to combine this with the opinion of professionals about the impact of the implemented care pathway. This feedback makes a more accurate interpretation of the results possible.

In conclusion, the implementation of the multidisciplinary breast cancer pathway did improve the medical, process, structural and organizational aspects of care. Therefore, introducing the breast cancer pathway according the IOCP model supports reorganization of health care and helps on implementing evidence based guidelines to improve the quality of care.

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CHAPTER 7

Long-term effects of a regional care pathway for patients with rectal cancer

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ABSTRACT

Purpose

Introducing care pathways is seen as method to realize patient-focussed care conform evidence-based guidelines. The goal of this study is to determine the long-term effects of a regional care pathway for patients with rectal cancer.

Patients and methods

Data on almost 400 patients with rectal carcinoma from three hospitals were obtained from the Netherlands Cancer Registry and the Dutch Surgical Colorectal Audit. Results on seven structure and process indicators were analyzed and compared before and at two time points after implementing a regional care pathway over a total period from 2007 to 2012. To determine motivation and interpret the results, relevant professionals of the participating hospitals were interviewed.

Results

After implementing the care pathway, the performance of computed tomography (CT) scans in the diagnostic phase significantly improved ($p=0.007/0.07$). The number of patients discussed in the preoperative multidisciplinary team (MDT) meeting improved significantly ($p<0.001$), and after implementing the care pathway, 94% of the patients were discussed. Further, a significant reduction in time between the first tumor biopsy and the MDT meeting was realized ($p=0.01$). Professionals stated that the regional care pathway has led to more clarity about the patient route and more awareness about complying with evidence-based guidelines.

Conclusions

The regional care pathway provided a solid basis for uniforming care, working according evidence-based guidelines and further cooperation on regional level. For mainly the waiting and throughput times, the guidelines and norms had probably a stronger effect on the results than the care pathway.

INTRODUCTION

Colorectal cancer is a common disease in the Netherlands. In 2013 more than 13,000 new patients were diagnosed of which almost 4,000 with rectal cancer. The mortality rate of patients with rectal cancer was more than 1,000 patients in 2013. The relative 10 year survival of patients diagnosed in 2004 - 2007 was 55%¹.

Multiple specialisms take part in diagnosing and treating rectal cancer patients, therefore a multidisciplinary coordination of all steps in the care process is necessary². A care pathway, also known as clinical pathway, critical pathway, integrated care pathway or care map is a method for patient focussed care based on evidence-based guidelines, best practices and patient experiences by facilitating the communication and coordination within the MDT meeting, with patients and their relatives³. Through continuous improvement, care pathways aim to improve the quality of care, reduce risks, increase patient satisfaction and increase the efficiency in the use of resources³. Preferably the care pathway should cover the complete route of patients from diagnosis to follow-up. Care pathways usually lead to better standardization and more structure in health care services resulting in better compliance with evidence-based guidelines or evidence-based medicine⁴.

In order to deliver the best multidisciplinary care to cancer patients, many health care organizations apply care pathways. However, the effects of care pathways are often inconsistent⁵. The impact of clinical practice guidelines and pathways for several tumor types, including colorectal cancer, was mainly focussed on reduction of costs and length of hospital stay, minimizing practice variations and maintaining patient quality of care and patient satisfaction despite a shorter length of stay⁴. Studies concerning the effects of pathways in rectal cancer are limited. In 2010 a Spanish study showed that the implementation of a clinical pathway for patients with rectal cancer reduced hospital costs and optimized the use of limited resources². Other studies focussed on the impact of limited parts of the complete rectal cancer pathway, such as referral of patients, the diagnostic process or laparoscopic surgery⁶⁻⁸.

In this study we aim to describe the long term effects of a regional care pathway for patients with rectal cancer in the three hospitals in the Netherlands. Further, we describe the motivation of professionals to participate in this project. Moreover, the experienced impact of the care pathway according relevant professionals was determined.

PATIENTS AND METHODS

Care pathway

In 2008, the regional care pathway for patients with rectal cancer was developed and implemented in three hospitals in the East of the Netherlands. These hospitals all refer patients to one radiotherapy center. The radiation oncologists observed variation in the diagnostic procedures and the referral of patients with rectal cancer. This was discussed with the three hospitals and the need for regional agreements on diagnosis, MDT meeting and treatment for this patient group was recognised. The development and implementation of the regional care pathway was initiated by the Netherlands Comprehensive Cancer Organisation (IKNL). Before developing the pathway the involved professionals formulated two joint goals. The main goal of the pathway was to deliver excellent and more uniform care for patients with rectal carcinoma. Another goal was to maintain care and treatment for these patients in the region. The introduction of the care pathway started with a regional kick off for all relevant professionals. After installing the steering group, the current situation in all hospitals was described and joint norms were formulated about the diagnostic process, MDT meeting and waiting- and throughput times. During the implementation of the care pathway several meetings were held in the hospitals as well as on regional level in order to learn from the implementation process in other hospitals.

After implementing the care pathway, a final meeting with the members of the steering group was held in which results of the implementation were presented and an article was published in a Dutch journal for professionals working in the field of oncology⁹. While this Dutch article reported the results before and after implementing the rectal cancer pathway, the study presented in this article focusses on the long term effects of this pathway.

Data sources

Data was derived from the Netherlands Cancer Registry (NCR) and the Dutch Surgical Colorectal Audit (DSCA). The NCR is a nationwide population-based cancer registry and is hosted by IKNL¹. Newly diagnosed cancer patients are notified to the registry by the Dutch Pathology Network (PALGA), to which pathology departments submit their reports on histological, cytological and autopsy examinations. Additional information on patient and tumor characteristics, diagnostics and therapy is collected from hospital records by trained registry personnel of the NCR. Topography and morphology are coded according to the International Classification of Diseases for Oncology (ICD-O).

The DSCA is an audit registry including patients who underwent a resection for colorectal carcinoma and is part of the Dutch Institute for Clinical Auditing¹⁰. All hospitals in the Netherlands fill in data in order to get insight in their quality of the care for colorectal patients and make improvements based on these data. In the DSCA a benchmark is available which makes it possible for medical specialists to compare the care in their own hospital with the national average.

Selection of cases

From the NCR, we selected patients with a primary rectal carcinoma who underwent surgery in three hospitals in the period 1 January until 31 December 2007 before introducing the care pathway (baseline measurement). After implementing the care pathway, patients with rectal cancer in the period 1 June 2008 until 31 May 2009 were selected (1st post measurement). For the baseline measurement and the 1st post measurement extra data on e.g., waiting- and throughput times and MDT meeting, was collected by the registry personnel of the NCR. Data for the 2nd post measurement was collected from the DSCA, selecting patients who underwent surgery in the period 1 January until 31 January 2012, more than three years after implementing the care pathway. The DSCA started in 2009, therefore it was not possible to use this data for the baseline and 1st post measurement.

Interviews

Because care pathways are strongly related to other quality methods, such as the introduction of evidence-based guidelines and audits based on quality criteria, it is important to determine whether the changes which were revealed were due to the implementation of the care pathway. Therefore semi-structured interviews with professionals were held in order to determine the experienced impact of the care pathway and interpret the observed differences in the registered data. In these interviews the professionals were also asked about their motivation to participate in the regional project, the goals before developing the pathway and the experienced (long term) outcome after implementation. In hospital A and C information was received from multiple disciplines in a group interview. In hospital B separate interviews were held because a group interview could unfortunately not be planned (table 1). In the interviews the participants were informed about the results of the baseline and both post measurements. Next they were asked to interpret the data and estimate the impact of the care pathway on the results.

Prior to the interview, the participants received the questionnaire in order to prepare themselves. After the interviews were held, the summary of the interview was checked on correctness by the interviewed professionals.

Table 1 Interviewed professionals

	Hospital		
	A	B	C
Colorectal surgeon	x	x	x
Medical oncologist	x		x
Radiologist	x		x
Specialized nurse	x		x
Radiation oncologist		x	

Statistical analyses

Differences in the total scores of indicators between the baseline and the post measurements were tested using the chi-square test. Analyses were performed using software package Stata version 12.0 (StataCorp, College Station, Texas). A p-value < 0.05 was being considered to be statistically significant.

RESULTS

In this paragraph the motivation to participate in the regional project as well as the goals before introducing the regional pathway and the impact on the outcome after implementation according the professionals are described. Next, the results on diagnostic procedures, MDT meeting and waiting- and throughput times are reported. These quantitative results (table 2) are completed with information from the interviews (table 3).

Table 2 Results NCR and DSCA data

Period	Baseline measurement January - December 2007				1 st post measurement June 2008 - May 2009				2 nd post measurement January - December 2012				Tests, p-value (totals)		
Hospital	A	B	C	Total	A	B	C	Total	A	B	C	Total	Period 1-2	Period 1-3	Period 2-3
Norm															
Number of (operated) patients	65	41	27	133	68	55	15	138	57	41	27	125			
1. Diagnostic procedures [#]															
- chest CT scan or chest x-ray performed					57 (80%)	51 (93%)	15 (100%)	123 (89%)	55 (96%)	40 (98%)	27 (100%)	122 (98%)			0.007*
- pelvis MRI scan performed					58 (82%)	39 (71%)	13 (87%)	110 (80%)	44 (77%)	38 (93%)	20 (74%)	102 (82%)			0.70
- abdominal CT scan or liver CT scan performed					56 (82%)	52 (95%)	15 (100%)	123 (89%)	56 (98%)	41 (100%)	22 (81%)	119 (95%)			0.07*
2. Patients discussed in multi-disciplinary meeting before surgery	18 (28%)	12 (29%)	18 (67%)	48 (36%)	47 (69%)	47 (85%)	15 (100%)	109 (79%)	51 (89%)	40 (98%)	27 (100%)	118 (94%)	<0.001*	<0.001*	<0.001*
3a. Time between the first positive tumor biopsy and MDT meeting ≤ 14 days (days)	10 (56%)	1 (8%)	13 (72%)	24 (50%)	13 (28%)	23 (50%)	8 (53%)	44 (41%)	18 (35%)	21 (64%)	25 (93%)	64 (58%)	0.28	0.37	0.01*
3b. Time between MDT meeting and start radiotherapy (days)	3 (18%)	1 (9%)	8 (47%)	12 (27%)	11 (28%)	5 (16%)	3 (27%)	19 (23%)	15 (32%)	7 (29%)	6 (24%)	28 (29%)	0.69	0.81	0.44

No data available in baseline measurement

* Significant results

Table 3 Results interviews

	Hospital		
	A	B	C
Motivation, goals and results pathway			
1. Motivation for developing the regional care pathway for patients with rectal cancer	<p>Realize uniform processes for all hospitals in the region and synchronize the differences in treatment. Publication of the revised evidence-based guideline stimulated the introduction of the rectal cancer pathway.</p>	<p>Not all patients with colorectal liver metastases were discussed in a multidisciplinary meeting. Agreements with the other hospitals in the region were necessary to deliver the best treatment.</p>	<p>A care pathway for patients with rectal cancer was already available in this hospital. Delivering uniform care and making agreements about treatment were the main reasons to participate in the regional project.</p>
2. Goals of the care pathway	<p>1. more uniformity in care and treatment between hospitals in the region. 2. decrease differences in care and treatment between professionals. 3. introduce diagnostic procedures according the evidence-based guidelines. 4. reduce waiting- and throughput times.</p>	<p>1. more uniformity in the region. 2. better care for patients with colorectal liver metastases. 3. discuss all patients in a MDT meeting. 4. agreements about liver resections. 5. working according the evidence-based guidelines. 6. better pelvis MRI scan reports. 7. offer all patients radiotherapy. 8. reduce waiting- and throughput times.</p>	<p>1. determine regional norms for waiting- and throughput times. 2. faster diagnostic route. 3. uniform radiology reports.</p>
3. Experienced results care pathway for the hospital	<p>1. shorter waiting- and throughput times (faster diagnostic and treatment phase). 2. more uniformity in procedures between professionals and hospitals. 3. MDT meeting for discussing patients with colorectal liver metastases.</p>	<p>1. care and treatment, including radiotherapy, according the evidence-based guidelines. 2. all patients with rectal cancer are discussed in the MDT meeting. 3. an regional colorectal liver metastases MDT meeting was installed. 4. MRI scan reports were standardized. 5. more willingness of professionals to cooperate.</p>	<p>1. Clarity about the route for patients until surgery due to planning ahead. 2. Less interference of professionals after planning. 3. Shorter waiting- and throughput times. 4. Patients are assigned to a casemanager. 5. Less dissatisfied patients.</p>

Indicators		
Diagnostic procedures		
1.1	Diagnostic procedures	
	Improvement in the performance of the chest CT scan/chest x-ray and the abdominal CT scan/liver CT scan was recognized. There is no logical explanation for the reduction of the pelvis MRI scans.	Before the introduction of the regional care pathway the pelvis MRI scans were done only for patients with a lower rectal carcinoma. Nowadays the MRI scan is performed for patients with this tumor.
1.2	Influence of the regional care pathway	Regional agreements were made about the diagnostic procedures. Earlier abdominal ultrasounds were made, after introducing the regional care pathway abdominal CT scans were performed instead.
	Yes, this was based on the agreements about diagnostic procedures in the care pathway. In this hospital these agreements are being monitored by a specialized nurse.	Yes
	Yes, influenced by the care pathway as well as other factors. By discussing patients in the MDT meeting more thorough decisions were made about the necessary diagnostic procedures.	Yes
MDT meeting		
2.1	Patients discussed in a MDT meeting	As the results show, all patients were discussed in the two weekly MDT meeting before treatment. Based on the care pathway patients with a T4 tumor were discussed in the MDT meeting colorectal liver metastases.
	More patients were discussed in the MDT meeting, mainly because the specialized nurses coordinate and monitor the care for patients with rectal cancer.	Yes
	Yes, influenced by the care pathway some patients with less complex tumors were not discussed in the MDT meeting. Afterwards, more attention was given to discuss all patients and to perform all diagnostic procedures before the MDT meeting.	Yes
2.2	Influence of the regional care pathway	Yes, influenced by the care pathway as well as the evidence-based guidelines and DICA registry. Most pressure probably from guidelines.
	Yes, but partly. This result is more influenced by national norms and DICA registry as this provides more pressure to deliver the best treatment.	

Waiting- and throughput times

3.1a Time between tumor biopsy and MDT meeting

An explanation for the data could be that more diagnostic procedures were performed before the MDT meeting and this takes more time. Nevertheless, planning started at the first hospital visit.

This improvement is ongoing because more attention was given to reduction of time to the MDT meeting. For the gastroenterology more policlinic hours were realized.

Improvement for this item was one of the goals for introducing the hospital care pathway years ago. This goal was maintained over the years, however the basis for planning appointments ahead was made in the hospital care pathway.

3.1b Influence of the regional care pathway

Yes, agreements were described in the regional care pathway. Meanwhile the national norms were published and implicated more time. The specialized nurse contributed to this by coordinating this process.

Yes, the care pathway caused more focus on reducing waiting- and throughput times and therefore forced to attend evidence-based guidelines. Guidelines and norms also influenced these results.

No

3.2a Time between MDT meeting and start radiotherapy

More improvement is desirable. Probably there was an dependency with the logistics for radiotherapy.

Nowadays a 5x5 scheme is given in combination with a longer waiting time to surgery. This can explain the presented data.

Improvement is still necessary, however radiotherapy is not part of the hospital and therefore little influence can be taken to change this.

3.2b Influence of the regional care pathway

Yes, see 7b

Yes, see 7b

No

Motivation and goals

The main motivation for all hospitals to participate in the project was to realise the best treatment for patients with rectal carcinoma in the region. Further, the professionals wanted to maintain the care for this patient group in the region. Next, for patients who were referred for radiotherapy, the radiation oncologists observed undesirable differences in procedures, norms and treatment between hospitals. Therefore the professionals formulated goals for developing and implementing the regional care pathway, such as uniform care and treatment, determine joint norms, reduce waiting- and throughput times and work according evidence-based guidelines. Further, there were specific goals which differed for each hospital. For example in hospital A implementing the evidence-based guidelines was important and the professionals mentioned that the publication of the revised evidence-based guideline rectal carcinoma was stimulating for them to participate in the care pathway project. The professionals in hospital B observed that patients with synchronous colorectal liver metastases were not always discussed in the multidisciplinary meeting and they wanted to make agreements about this in the region in order to realize better care for these patients. In hospital C a care pathway for patients with rectal carcinoma already existed for their hospital and they wondered how to improve and expand this on a regional level.

Estimated impact of the pathway

Overall the interviewed professionals stated that the regional care pathway improved clarity in the route for patients and more uniformity in procedures between professionals and between hospitals was reached after implementing the care pathway. Also the introduction of a MDT meeting for discussing patients with colorectal liver metastases was mentioned by professionals in two hospitals as a result. They experienced the profit of discussing with and learning from each other.

Furthermore, this project has led to more willingness of professionals to cooperate on regional level. This willingness is essential because in the care and treatment for patients with rectal cancer none of the medical specialists has a leading role in the care process, emphasizing the importance of a multidisciplinary approach. Below we present the results on the indicators completed with information from the interviews with the involved professionals.

RESULTS OF THE PATHWAY

Diagnostic procedures

The regional agreement for the diagnostic procedures was: perform a chest CT scan or chest x-ray, a pelvis MRI scan and an abdominal CT scan or liver CT scan for every patient.

The overall proportion of patients for who a chest CT scan or chest x-ray and an abdominal CT scan or liver CT scan was performed increased and significantly improved in the 2nd post

measurement compared to the 1st post measurement (chest CT scan/chest x-ray: 98% vs. 89%, $p = 0.007$; abdominal CT scan/liver CT scan: 95% vs. 89%, $p = 0.07$).

In both group interviews it was mentioned that the actual performance of diagnostic procedures was a result of the agreements which were described in the regional care pathway. For example, in the regional pathway an agreement was made to perform an abdominal CT scan. This had consequences for one hospital where all patients with the suspicion of rectal cancer received an abdominal ultrasound. In another hospital a professional said that besides the care pathway, the performance of the diagnostic procedures was also influenced by other factors, such as the regional MDT meeting for patients with liver metastases which facilitates a more thorough choice for the necessary diagnostic procedures.

Multidisciplinary (MDT) meeting

The regional agreement for the MDT meeting was: discuss every patient in the MDT meeting before surgery. The overall proportion of patients discussed in the MDT meeting before surgery improved significantly in both post measurements ($p = <0.001$). In two hospitals the percentage of patients increased from 28% and 29% in the baseline measurement to respectively 89% and 98% in the 2nd post measurement. In hospital C this percentage improved in the 1st post measurement to 100%, in the 2nd post measurement it maintained 100%. According the professionals the implemented care pathway (partly) influenced the findings. Professionals of two hospitals mentioned that besides the pathway, evidence-based guidelines and profession based norms also contributed to the improvements which were observed after implementing the care pathway. Further, the reports based on registered data from the DSCA gave insight in the performance of the care for colorectal patients. Besides, the estimated pressure of these guidelines and norms seems to be stronger than agreements in a regional care pathway. Additional, for patients with a T4 tumor and patients with liver metastases a new regional MDT meeting was established as spin-off of the regional pathway. In doing so, patients who need more complex treatment are discussed and expertise of professionals in the region concerning this care and treatment is united. Nowadays, also patients with esophageal, gastric and pancreatic cancer are discussed in this meeting. In one hospital the specialized nurse has an important role in the coordination of the care for patients with rectal cancer as well as in the planning and monitoring of discussing patients in the MDT meeting.

Waiting- and throughput times

Time between first positive tumor biopsy and MDT meeting

The regional agreement for the time to MDT meeting was: within 14 days. The time between the first positive tumor biopsy and MDT meeting improved in two hospitals after implementing the care pathway. Overall there was a significant difference between the 1st and 2nd post measurement (respectively 41% and 58%, $p = 0.01$). However, in hospital C there was a relapse in the 1st post measurement, but in the 2nd post measurement 93% of the patients

were discussed in the MDT meeting within 14 days. In hospital A less patients were discussed within 14 days in the 1st post measurement comparing to the baseline measurement and little improvement was made in the 2nd post measurement (35%).

Time between MDT meeting and start radiotherapy

The regional agreement for the time to starting radiotherapy was: within 21 days, which was in accordance to the later stated national norms. The time between the MDT meeting and starting radiotherapy improved in two hospitals. However, in hospital A and B resp. 32% and 29% of the patients started radiotherapy within three weeks after the MDT meeting in 2012. In hospital C this time did not improve and in the 2nd post measurement less than a quarter of all patients started radiotherapy within three weeks.

Based on information from the interviews, in two hospitals the care pathway influenced the abovementioned results on the waiting- and throughput times. The professionals mentioned that more attention was given to reducing waiting- and throughput times due to the agreements which were described in the care pathway. These agreements were mainly based the evidence-based guidelines and norms. According to the professionals in another hospital the results were on one hand influenced by the norms in the regional care pathway and on the other by the role of the specialized nurse who contributed to the coordination and monitoring of the waiting- and throughput times in the care process. In the third hospital it was said that, however the hospital visits for patients were planned ahead, the reduction of waiting- and throughput times was a result of their own individual hospital pathway years ago. The regional care pathway did not contributed to the observed results in this study. In two hospitals the department of radiotherapy is not part of their hospital and the professional feel they have little influence on reducing the time before starting the first radiotherapy.

DISCUSSION

The results of this study reveal that in all three hospitals in which the regional care pathway for rectal cancer patients was implemented significant improvements in the performance of diagnostic procedures, the MDT meeting and the waiting time to MDT meeting. Parts of these improvements were maintained over a time period of more than three years and were clearly a result of the implementation of the pathway. Other factors like the introduction of national norms evidence-based guidelines influenced the care for rectal cancer patients during the last time period of this study to a large extent.

The main regional goals, which were formulated before introducing the care pathway, were achieved. Firstly, according to the professionals more uniform care for patients with rectal cancer was realized. Secondly, the percentages of patients which were treated in the participating hospitals in all measurements were more than 90% (resp. 95%, 93% and 93%). Clearly, the care and treatment for this group of patients maintained in the region.

A previous study showed improvements in the care for breast cancer patients after implementing a regional care pathway¹¹. This supports the statement that care pathways can be effective to realise improvements in cancer care, possibly for high volume tumors as well as for low volume tumor types. Our study shows that overall long time improvement was achieved for all indicators, except for one diagnostic procedure (MRI scan) and the time between MDT meeting and starting radiotherapy. For these indicators no significant improvements were observed. A possible explanation could be that following the guidelines in order to increase quality of care is time consuming, because guidelines often recommend a complete diagnostic work up before patients are discussed in the MDT meeting. Therefore it is difficult to achieve a reduction of waiting- and throughput times in the care process. Van der Geest et al¹² analyzed waiting- and throughput times in colorectal care and concluded that a guidelines-based diagnostic process and multidisciplinary collaboration was associated with increased hospital delay in colorectal cancer patients. Based on this conclusion and the results in our study, we can state that evidence-based guidelines probably have an important impact on the care process for different groups of cancer patients but do not always result in shorter waiting- and throughput times.

Further, improvements after the implementation of a care pathway can lead to other, not foreseen, long term improvements as well. For example, the new regional MDT meeting was initially established in order to discuss patients with T4 rectal tumors and patients who had colorectal liver metastases. However, due to the insight that agreements and coordination can also lead to better care for other patient groups, this MDT meeting was extended and nowadays patients with oesophageal, gastric and pancreatic cancer are also discussed on regional level.

The strength of this study is the combination of quantitative data from the NCR and DSCA registries with qualitative data from the interviews with professionals. In the interviews professionals were asked about the motivation to participate in the care pathway project, the goals before the introduction of the regional care pathway and the outcome afterwards. Further, the results of the quantitative analyses were verified in the interviews and professionals were asked to give explanations for the differences. Therefore more detailed information was collected and, in our opinion, a thorough conclusion about the experienced impact of the regional care pathway could be formulated.

This study shows the importance to measure results before and after implementing a care pathway. Caused by various reasons a baseline measurement is often not performed. When this is missing, the results after implementation cannot be related to the situation before and the effort put in the pathway cannot be linked to the benefits achieved after implementation. Besides the importance of a baseline and post measurement, it is important to monitor the improvements over time and to evaluate the care pathway a few years after implementation in order to take actions and improve the care process or make adjustments in the care pathway.

However, inherent to the low incidence of patients with rectal cancer, the number of included patients is limited. Furthermore, a small number of indicators were used. In this study a choice was made for relevant indicators for which data was available.

Future research on the effects of pathways can focus on evaluating the impact of a care pathway at larger scale, for example evaluating a care pathway for patients with one tumor type in more hospitals or evaluating the impact of multiple cancer pathways in one hospital. Studies in the future could also incorporate a control group, like a group of patients in other hospitals without a care pathway.

CONCLUSION

Most improvements, observed after implementation of the regional care pathway for patients with rectal cancer, maintained over a time frame of 3 years. As the MDT meeting is essential for organizing multidisciplinary care for patients with a rectal carcinoma, the overall improvement of the MDT meeting in time is remarkable and promising in this study. Further improvements were made in the performance of diagnostic procedures as well as the waiting time between first tumor biopsy and the MDT meeting.

The involved professionals stated that the improvements mainly were due to the regional care pathway. In the pathway a basis was given for agreements and norms about diagnostic procedures, MDT meeting and waiting- and throughput times. Further the care pathway resulted in more willingness of professionals to cooperate on a regional level.

Although the regional care pathway provided a solid basis for improvement in the care for patients with rectal cancer, the interviews made it clear that there were other factors besides the care pathway influencing the improvements. Clearly, evidence-based guidelines as well as national norms also influenced the outcome. As the interviewed professionals mentioned, for the waiting- and throughput times the guidelines and norms had probably a stronger effect on the results than the care pathway.

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CHAPTER 8

Evaluation of a regional network for esophagogastric cancer care

**Results based on data and from the perspective
of health care professionals and patients**

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ABSTRACT

Background and purpose

In the south-west region of the Netherlands nine health care organizations collaborated in a regional oncology network: EMBRAZE. In 2016 regional care pathways were formalized with agreements for patients with esophagogastric cancer. The aim of this study was to evaluate the regional care pathways and determine the performance of diagnostic procedures, lead time, and patients outcomes, based on data.

Materials and Methods

Patients with esophageal or gastric cancer diagnosed one year before (2015) and after the implementation of the regional pathways (2017) within the EMBRAZE network were selected from the Netherlands Cancer Registry. Additional, interviews were performed with patients and health care professionals to gain insight in their perspectives and experiences with the care pathways.

Results

A total of 941 patients were included. After implementation of the regional care pathways more patients received a PET or PET/CT scan ($p < 0.01$). Moreover, the lead time for all patients from the first diagnostic procedure to the Multidisciplinary (MDT) meeting decreased over time with at least 5 days ($p < 0.007$). The regional MDT meeting was recognized as being of crucial importance in the collaboration. Both patients and health care professionals experienced a more efficient and personalized care process.

Conclusion

This evaluation of care pathways for patients with esophagogastric cancer revealed that diagnostic procedures were performed more according the agreements within shorter lead time after implementation. Although these changes were similar to the national developments, qualitative data showed that regional oncology networks contributes to better structured and efficient care for patients with esophagogastric cancer.

INTRODUCTION

Cancer care has become more complex. This is due to evolving novel diagnostic modalities and curative and palliative treatments^{1,2,3}. The demographics of esophagogastric cancer has changed resulting in increased numbers of patients over the age of 65 years with substantial comorbidity⁴. Care for patients with esophagogastric cancer is now more individualized and provided by a multidisciplinary team of cancer specialists^{5,6}.

To prevent performing complex cancer treatments in low volume hospitals, regionalization and centralization of cancer care was deployed to improve the quality of care. This has led to better outcomes including lower morbidity and mortality rates after surgery for pancreatic and esophageal cancer and improved lymph node harvesting and a successful introduction of laparoscopic gastrectomies for gastric cancer^{7,8,9}. However, regionalization requires communication and coordination between specialists and across centers¹⁰. As a consequence, regional oncology networks were formed to optimize cancer care delivered within a region consisting of several hospitals and a tertiary referral center. These networks could also improve accrual of patients to clinical trials and may provide better resources to ensure standardization, compliance, and documentation of scientific research¹¹.

In 2015, six general hospitals, two radiotherapy institutions and one university hospital in the south-west of the Netherlands formed a regional oncology network called "EMBRAZE" (Erasmus Mc, BRabant, ZEeland). The aim of this network was to deliver high-quality, timely, efficient and evidence-based cancer care as close as possible to where the patient lives. The EMBRAZE network also facilitates the development of regional care standards, pathways and multidisciplinary meetings. The organization of outcome meetings and auditing and regional participation on clinical trials are an essential part of the process to identify areas for further improvement.

For esophagogastric cancer care, the EMBRAZE network standard was developed in 2016 covering the diagnostics, referral patterns, treatments and also nursing care. Gastric resections were centralized in two hospitals, esophageal cancer resections in one hospital, and high complex surgical procedures were only performed in the academic center.

The EMBRAZE network standard met the national guidelines on the diagnostic and (surgical) treatment of esophageal cancer and gastric cancer^{12,13,14}.

We found limited evidence about the added value of oncology networks in which regional agreements were formalized. Therefore, the aim of this study was to evaluate whether care and treatment of patients with esophagogastric cancer was performed according the agreements after implementing regional pathways within the EMBRAZE network, based on data about diagnostic procedures, lead time, and patients outcomes and from the perspective of health care professionals and patients.

MATERIALS AND METHODS

In this study we used a mixed methods explorative retrospective research design. Based on pre-defined outcomes, a quantitative before (1-1-2015 to 31-12-2015) - after (1-1-2017 to 31-12-2017) measurement was performed. To be able to interpret the results on regional level more accurate outcomes of the EMBRAZE network were compared with a national benchmark including all esophageal and gastric cancer patients in the Netherlands. Qualitative interviews were conducted with patients and health care professionals of the participating hospitals to gain more insight in their perspectives and experiences with the regional care pathways.

Data source

Data for the before-after measurement were obtained from the population-based Netherlands Cancer Registry (NCR). This registry covers the complete Dutch population. The NCR is based on a notification of all newly diagnosed malignancies in the Netherlands by the national automated pathological archive (PALGA). Specially trained data managers of the NCR routinely extract information on diagnosis, tumor stage, and treatment from medical records.

Patient selection

For this study we selected all patients diagnosed with primary esophageal or gastric cancer in one of the hospitals (based on hospital of diagnosis) within the EMBRAZE network in 2015 and 2017. For the benchmark we included all patients with primary esophageal or gastric cancer (including the EMBRAZE network) in the Netherlands. To increase the comparability of data between the EMBRAZE network and the national population, data of two hospitals were deleted, because items regarding diagnostic procedures and complications were not registered in these two hospitals. Tumor staging was performed according to the International Union Against Cancer (UICC) TNM classification that was valid at the time of diagnosis. Patients diagnosed in 2015 were staged according to TNM-7¹⁵ and patients diagnosed in 2017 according to TNM-8¹⁶. Patients with gastro-esophageal junction (GOJ) cancer were included in the group of esophageal cancers. Based on the clinical tumor stage, patients were classified in three groups: patients with early esophageal or gastric cancer (cT1,cN0,cM0), curable patients (cT1-4a,cNany,cM0 & cTx,cNany,cM0, without cT1N0cM0, and non-curable patients (cT4b and/or cM1).

Outcome measures

The measures, used to evaluate whether care and treatment of patients with esophagogastric cancer within the EMBRAZE network were performed according the regional care pathways within the EMBRAZE network, were defined and arranged according to the classification developed by Donabedian¹⁷. The Donabedian model is a conceptual model that provides a framework for examining health services and evaluating quality of health care¹⁸ and distinguishes three categories of indicators: "structure", "process", and "outcomes"¹⁹. The indicators used in the EMBRAZE network were based on consensus. See Figure 1 for the regional agreements regarding esophagogastric cancer.

In total three structure, five process and four outcome indicators were specified:

- Structure indicator: hospital volume, number of patients referred for surgical treatment, and the presence of a case manager.
- Process indicators: percentage of diagnostic procedures such as gastroscopy, endoscopic ultrasound, and CT scans and PET or PET/CT scans, time between the first diagnostic procedure and Multidisciplinary (MDT) meeting, time between MDT meeting and start therapy, length of hospital stay, and Intensive Care Unit stay after surgical treatment.
- Outcome indicators: treatment combinations for curable patients (cT1-4a,cNany,cM0 & cTx,cNany,cM0, without cT1N0cM0) or non-curable patients (cT4b and/or cM1), postoperative complications (including anastomotic leakages), postoperative mortality, and 1-year overall survival.

Figure 1 EMBRAZE agreements for esophageal or gastric cancer (in brief)

Statistical analysis

A comparison was made between the before and after measurement by using the chi-squared test. Differences between characteristics were analyzed using chi-squared tests for nominal data and Mann-Whitney U tests for continuous data. In case of small cell sizes (expected values less than 10), the Fisher's Exact test was used to calculate the association between categorical variables. The one year overall survival was estimated using the Kaplan-Meier curve and for calculating the differences between groups the log-rank test was used. The analyses of diagnostic procedures, treatment combinations, lead time, and one year overall survival were based on the hospitals where patients were diagnosed for their cancer. In addition, the analyses of surgical treatment, patient referral for surgery, postoperative complications, length of hospital stay, and postoperative mortality were based on the hospitals where patients underwent surgical treatment. The analyses were conducted using STATA (StataCorp LLC, Texas, USA). In addition, sensitivity analysis were performed to test whether the results of the national benchmark (including the EMBRAZE network) deviated from the national population minus the EMBRAZE network.

Interviews with health care professionals

To collect additional information from health care professionals, the teams of care givers of each hospital and radiotherapy institution of the EMBRAZE network were interviewed using multidisciplinary semi-structured group interviews (see additional file 1). When it was not feasible to interview the whole team, therefore a part of this team represented the interviews, resulting in a sample of at least 2 health care professionals for each hospital. The main topics of these interviews were: utilization and implementation of regional care pathways, the perceived benefits of the agreements and improvements for the future. These interviews were led and analyzed by an independent researcher. After performing the interview, a summary of the interview was returned to the persons interviewed in order to make sure the content was correctly reproduced and no information was missing. The qualitative data was analyzed by clustering and extracting topics from the interview reports.

Interviews with patients

After the regional care pathways were implemented, 20 curable patients with a curable intent were interviewed within a period of a year in order of planned surgery, using a semi-structured questionnaire to collect information about the efficiency of the patient trajectory, the communication between health care professionals, the transfer between hospitals and their satisfaction with the received care and treatment (see questionnaire in additional file 2). All interviewed patients received care and treatment in two or more hospitals to enable the collection of information about referral and communication between hospitals. Patients were informed and asked by their case manager to participate after they finished neo adjuvant chemo(radio)therapy, and an informed consent form was signed by all patients prior to the interview. At the time of the interview, all patients already had one or more appointments with a surgical oncologist and the case manager of the hospital where surgical treatment would take place. The interview contained a question to rate each health care organization using a ten-points scale. The interviews were conducted by the independent researcher by telephone a few weeks before surgery.

RESULTS

The study population of the EMBRAZE network consisted of a total of 941 patients in both 2015 and 2017. Out of these patients, 676 were diagnosed with esophageal cancer (EC) and 265 with gastric cancer (GC). The absolute number of patients with esophageal cancer increased in the EMBRAZE network (3,6%). The number of patients with gastric cancer decreased over time (3,8%). See table 1. The patient characteristics age, sex, tumor stage, type of cancer and comorbidity were comparable between both study groups (2015 and 2017). (table 1).

Table 1 Patient and tumor characteristics according to year of diagnosis for esophageal and gastric cancer

Characteristics	Esophageal cancer EMBRAZE (n=676)			Gastric cancer EMBRAZE (n=265)		
	2015 (n=326)	2017 (n=350)	p	2015 (n=136)	2017 (n=129)	p
Year of diagnosis						
Median age	69 (±10.60)	68 (±10.02)	0.852	72 (±11.75)	74 (±11.13)	0.358
Gender						
Male	231 (71%)	251 (72%)	0.806	87 (64%)	85 (66%)	0.743
Female	95 (29%)	99 (28%)		49 (36%)	44 (34%)	
Tumor staging						
Early esophageal cancer	4 (1%)	3 (0.9%)	0.872	3 (2%)	2 (2%)	0.926
Potentially curable cancer	216 (66%)	230 (66%)		70 (52%)	67 (52%)	
Potentially non-curable cancer	106 (33%)	117 (33%)		63 (46%)	60 (46%)	
Histology						
Adenocarcinoma	241 (74%)	279 (80%)	0.049	NA*	NA*	-
Squamous cell carcinoma	75 (23%)	68 (19%)		NA*	NA*	
Other	10 (3%)	3 (0.9%)		NA*	NA*	
Comorbidity	(n=312)	(n=336)		(n=129)	(n=119)	
0	73 (23%)	79 (24%)	0.626	25 (19%)	29 (24%)	0.419
1	88 (28%)	84 (25%)		34 (26%)	24 (20%)	
≥ 2	151 (49%)	173 (51%)		70 (55%)	66 (56%)	

* NA: Not Applicable

Diagnostic procedures

In 2017 more patients with esophageal or gastric cancer received a PET or a PET/CT scan (EC: +19%, $p < 0.001$; GC: +11%, $p = 0.012$). See table 2 for more detailed information.

Treatment combinations

Potentially curable patients with esophageal cancer in the EMBRAZE network, mainly received neoadjuvant chemoradiotherapy followed by resection (44% in 2015; 39% in 2017) or chemoradiotherapy only (21% in 2015; 20% in 2017). Patients with non-curable esophageal cancer received chemotherapy only (35% in 2015; 40% in 2017) or some other treatment or no treatment at all (38% in both years).

Patients with potentially curable gastric cancer mainly underwent resection with or without (neo)adjuvant chemotherapy (63% in 2015; 66% in 2017). Furthermore, more than half of patients with non-curable gastric cancer received some other treatment or no treatment at all in the EMBRAZE network (table 2).

Lead time

The median lead time between first diagnostic procedure and first MDT meeting in which the patient's treatment plan was discussed, reduced significantly for all patients in the EMBRAZE network (EC: from 14 to 7 days, $p<0.001$; GC: from 12 to 7 days, $p=0.007$). Meanwhile, the median time between MDT meeting and the start of the first treatment did not change significantly. See table 2.

Survival

The one year overall survival did not significantly changed for patients in the EMBRAZE network, see table 2.

Surgical treatment

Esophageal cancer patients most often underwent transthoracic surgery, which increased over time (70% in 2015; 75% in 2017). Meanwhile, transhiatal surgery decreased (15% in 2015; 5% in 2017). Further, minimal invasive surgery was performed frequently for esophageal cancer (83% in 2015; 93% in 2017) and increased significantly over time in the EMBRAZE network. Patients with gastric cancer mainly underwent a partial stomach resection (70% in 2015; 54% in 2017). In 2017 most patients were referred for surgical treatment to hospitals within the EMBRAZE network, and less patients were referred outside the region. For patients with esophageal cancer this result was statistically significant ($p<0.001$). See table 3.

Postoperative outcome

Most postoperative complications (anastomotic leakage, cardiac and thromboembolic complications, chyle leakage, and wound infection) did not change over time for both patient groups. However, more patients with esophageal cancer had to deal with pulmonary complications after surgery (11% in 2015; 32% in 2017, $p<0.001$) (table 3).

The length of hospital stay and Intensive Care Unit stay did not significantly change over time for patients who underwent a surgical treatment. See table 3.

Postoperative mortality for patients did not reduce over time in the EMBRAZE network. See table 3 for more details.

Table 2 Diagnostic procedures & treatment combinations according to year of diagnosis for esophageal and gastric cancer (based on hospital of diagnosis)

Year of diagnosis	Esophageal cancer EMBRAZE (n=676)			Gastric cancer EMBRAZE (n=265)		
	2015 (n=326)	2017 (n=350)	p	2015 (n=136)	2017 (n=129)	p
Diagnostic procedures						
Gastroscopy	317 (97%)	349 (99%)	0.008	128 (94%)	116 (90%)	0.436
Endoscopic ultrasound	124 (38%)	133 (38%)	0.992	22 (16%)	14 (11%)	0.206
CT scan (or PET/CT scan)	302 (93%)	322 (92%)	0.756	120 (88%)	117 (91%)	0.515
PET / PET/CT scan	170 (52%)	249 (71%)	<0.001	15 (11%)	29 (22%)	0.012
PET/CT scan if cT => 2	146 (45%)	205 (59%)	<0.001	9 (7%)	16 (12%)	0.107
Treatment for potentially curable patients						
	(n=216)	(n=230)		(n=70)	(n=67)	
Neoadjuvant CRT* & resection	94 (44%)	89 (39%)	0.301	NA*	NA*	-
Neoadjuvant CT* & resection	5 (2%)	13 (6%)	0.093	NA*	NA*	-
Resection (with or without CT*)	NA*	NA*	-	44 (63%)	44 (65.5%)	0.731
CRT* only	46 (21%)	45 (20%)	0.650	NA*	NA*	-
Resection only	14 (7%)	20 (9%)	0.379	NA*	NA*	-
CT* only	4 (2%)	8 (4%)	0.384	5 (7%)	1 (1.5%)	0.209
RT* only	22 (10%)	21 (9%)	0.706	1 (1.5%)	2 (3%)	0.614
Other/no treatment	31 (14%)	34 (15%)	0.897	20 (28.5%)	20 (30%)	0.869
Treatment for potentially non-curative patients						
	(n=106)	(n=117)		(n=63)	(n=60)	
Resection (with or without C(R)T*)	0 (0%)	6 (5%)	0.030	5 (8%)	4 (7%)	1.000
CRT* only	9 (9%)	4 (4%)	0.152	NA*	NA*	-
CT* only	37 (35%)	47 (40%)	0.418	18 (29%)	23 (38%)	0.251
RT* only	19 (18%)	15 (13%)	0.290	4 (6%)	2 (3%)	0.680
Other/no treatment	41 (38%)	45 (38%)	0.973	36 (57%)	31 (52%)	0.542
Lead time (median in days)						
	(n=244)	(n=242)		(n=87)	(n=100)	
Lead time between first diagnostic procedure and MDT*	14 (IQR:14)	7 (IQR:13)	<0.001	12 (IQR:12)	7 (IQR:11)	0.007
	(n=211)	(n=246)		(n=64)	(n=72)	
Lead time between MDT* and start therapy	23 (IQR:13)	23.5 (IQR:17)	0.975	22 (IQR:19)	23.5 (IQR:18)	0.366
Overall survival						
1 year overall survival (for potentially curative patients)	65.2 (58.4-71.1)	65.7 (59.1-71.4)	0.857	70.0 (57.8-79.3)	70.2 (57.7-79.6)	0.483
1 year overall survival (for potentially non-curative patients)	21.9 (14.6-30.2)	24.8 (17.4-32.9)	0.827	15.9 (8.2-25.9)	21.7 (12.3-32.7)	0.215

* CRT: chemoradiotherapy; CT: chemotherapy; NA: Not Applicable; RT: radiotherapy; MDT: Multidisciplinary team meeting (in which the treatment plan for the patient was discussed).

Table 3 Surgical treatment and clinical outcomes according to year of diagnosis for esophageal and gastric cancer (based on 1st resections)

Number of resections	Esophageal cancer EMBRAZE (n=250)			Gastric cancer EMBRAZE (n=107)		
	2015 (n=119)	2017 (n=131)	P	2015 (n=57)	2017 (n=50)	P
Type of surgery						
TTE*	83 (70%)	100 (75%)		NA*	NA*	
THE*	18 (15%)	6 (5%)		NA*	NA*	
Partial gastrectomy	NA*	NA*	0.042	40 (70%)	27 (54%)	0.200
Total gastrectomy	4 (3%)	5 (4%)		15 (26%)	19 (38%)	
Other	14 (12%)	20 (15%)		2 (4%)	4 (8%)	
Surgical approach	(n=98)	(n=111)		(n=53)	(n=46)	
Open surgery	17 (17%)	8 (7%)	0.024	26 (49%)	18 (39%)	
Minimally invasive surgery	81 (83%)	103 (93%)		27 (51%)	28 (61%)	0.322
Patient referral for surgery	(n=119)	(n=131)		(n=57)	(n=50)	
Patients referred within own network	88 (74%)	121 (92%)	<0.001	50 (88%)	48 (96%)	0.124
Anastomotic leakage	(n=99)	(n=108)		(n=49)	(n=45)	0.092
	24 (24%)	27 (25%)	0.899	3 (6%)	0 (0%)	
Other postoperative complications	(n=102)	(n=109)		(n=51)	(n=45)	
Pulmonary complications	11 (11%)	35 (32%)	<0.001	5 (10%)	6 (13%)	0.588
Cardiac complications	11 (11%)	12 (11%)	0.958	1 (2%)	0 (0%)	1.000
Thromboembolic complication	0 (0%)	1 (1%)	1.000	0 (0%)	0 (0%)	-
Chyle leakage	8 (8%)	7 (6%)	0.791	0 (0%)	0 (0%)	-
Wound infection	11 (11%)	9 (8%)	0.531	7 (14%)	4 (9%)	0.534
	(n=111)	(n=129)		(n=57)	(n=50)	
Length of hospital stay (median in days)	9 (IQR:6)	11 (IQR:11)	0.143	7 (IQR:5)	9 (IQR:8)	0.509
	(n=111)	(n=116)		(n=55)	(n=42)	
ICU* stay (median in days)	1 (IQR:1)	1 (IQR:3.5)	0.258	0 (IQR:1)	1 (IQR:1)	0.429
Postoperative mortality						
30 days	2.5%	3.8%	0.561	3.5%	0%	0.181
60 days	6.7%	5.3%	0.647	5.3%	2%	0.375
90 days	8.4%	6.9%	0.648	7%	4%	0.498

* TTE: Transthoracic surgery; THE: Transhiatal surgery; NA: Not Applicable; ICU: Intensive Care Unit.

Health care professionals experiences

Eight interviews were performed in total. In seven EMBRAZE hospitals multidisciplinary semi-structured group interviews were held, and an interview in one radiotherapeutic institute with a radiation oncologist was carried out. In four of the seven hospital interviews, a team with multiple disciplines was interviewed, including medical oncologists, surgical oncologists, gastro-enterologists, pathologists and clinical nurse specialists or Physician Assistants. In the other hospitals less disciplines were able to attend the group interview, but at least a surgical or medical oncologist together with a clinical nurse specialist were present. See table 4 for the results of the interviews.

Table 4 Experiences of health care professionals with the regional care pathways and collaboration

Utilization and implementation of regional agreements

- The regional pathways and agreements were well known and used in clinical practice.
- Regional pathways implemented mainly through integrating agreements in existing procedures.
- Success factor for implementation pathways: a case manager (CM) in all seven hospitals with tasks: patient's contact person, facilitate pathway implementation, realize efficient care process.

The perceived benefits

- Clear description of tasks and responsibilities which led to more structured care and treatment.
- Nice working setting & efficient patient referrals due to personal contacts between care givers.
- The weekly regional Upper GI MDT meeting via video conferencing is a platform to discuss patients, actual trends, added value of diagnostics, and treatment criteria.
- More uniform and complete reporting, and feedback between health care professionals.

A few improvements for the future were mentioned:

- Develop joint patient information or a patient version of the regional pathway.
- Shorter lead time for patients until the start of (radio)therapy.
- Further agreements e.g. for non-curable patients and patients in the follow-up phase.

Patients experiences

In total 20 telephone interviews were held with patients. All patients were referred from four hospitals to the hospital where the treatment would take place: eight patients were referred to the academic hospital and 11 patients to another hospital for surgical treatment. Out of all patients, 17 patients were diagnosed with esophageal cancer and three patients with gastric cancer. The results of the interviews with patients were listed in table 5.

Table 5 Experiences of patients with the regional pathways and collaboration

Patient satisfaction	
Patient information and respect for patients	'good' or 'very good'
Diagnosis hospital (mean)	8.7 (n=18; range: 7-10)
Surgery hospital (mean)	8.2 (n=15; range: 7-10)
Efficient care process	
<ul style="list-style-type: none">• Adequate information transfer between health care professionals.• No unnecessary diagnostic or treatment procedures.• Overlap in requested health care history and medication information. (3 patients)	
Case management	
<ul style="list-style-type: none">• All patients knew their case manager and how to make contact.• Case managers: oncology nurses, nurse specialists or physician assistants.• Less frequently medical specialists functioned as contact person. (2 patients)	
Improvements for future collaboration within the EMBRAZE network	
<ul style="list-style-type: none">• Better communication about appointment planning, and diagnostic results.• Prevent double actions and questions (especially about medications).• If feasible, receive chemotherapy treatment at home in the future.	

DISCUSSION

In this study we evaluated the staging and treatment of patients with esophagogastric cancer in an oncology network including six general hospitals, two radiotherapy institutions and one university hospital in the Netherlands. One year after the implementation of the regional pathways, statistical significant changes were observed in the utilization of PET or PET/CT scans, lead time from the first diagnostic procedure to the MDT meeting, and esophageal cancer patients referral for surgery. Additional, the results of the EMBRAZE network showed a less increased lead time between the MDT meeting and start of therapy compared to the (significant) changes within the national benchmark. Other outcomes, such as overall survival, postoperative complications (except pulmonary complications for esophageal cancer patients), as well as postoperative mortality did not change significantly over time within the EMBRAZE network. The increased postoperative pulmonary complications after

surgery, which was also observed in the national population, could be due to the increased number of transthoracic surgeries over time.

The results which were observed one year after the implementation of the regional care pathways, could only be attributed to the regional agreements when the national data did not show changes over time. Therefore, the utilization of PET or PET/CT scans, and lead time from the first diagnostic procedure to the MDT meeting, are probably due to national developments. Nevertheless, the regional care pathways in the EMRBAZE network, could have led to a boost towards the level of the national results regarding diagnostics for patients with esophagogastric cancer. Besides, for gastric cancer the changes in diagnostic procedures could also be a result of the revision of the Dutch guideline gastric cancer in 2016, in which the PET/CT scan was recommended for staging only locally advanced gastric cancer (patients with T3-T4 gastric tumor)²⁰.

Besides the results based on data, qualitative data showed that such collaboration and regional pathways in the EMBRAZE oncology network contributes to better deployment of case managers and increased referral of patients leading to better structured care for patients with esophagogastric cancer. Despite, this improved structure subsequently can indicate better regional collaboration without directly leading to better patient outcomes. Additional to improvements on regional level, it should be noticed that improvement processes within separate hospitals and other health care institutions can still be necessary to achieve better outcome on local level. Nevertheless, regional agreements can be helpful to make local improvements feasible.

In this study the collaboration of the EMBRAZE region was reflected in the regional MDT meeting. According to the health care professionals, the regional MDT meeting was of crucial importance for further collaboration and improving care for patients with esophagogastric cancer in the future. A systematic review about the impact of MDT meetings revealed that patients discussed at MDT meetings were more likely to receive more accurate and complete pre-operative staging, and neo-adjuvant/adjuvant treatment²¹. Further, a Dutch study showed that discussion of patients with upper-GI malignancies by a multidisciplinary tumor board led to an altered diagnostic work-up or treatment plan in 1/3 of cases²². Still little evidence is available whether MDT meetings result in improvements in clinical outcomes²¹. Nevertheless, it is recommended to discuss every patient with cancer in a MDT meeting for optimal oncological care. Nowadays this is a time consuming and expensive practice, leading to a growing demand to change the current workflow. Therefore a debate is necessary for a more durable and efficient new MDT meeting strategy²³.

This study has several strengths and limitations. A strength of the study was the fact that the regional patient population was a representative sample of the total national population. Further, the results were based on a rather extensive network of seven hospitals including an

academic center, which made it possible to create larger patient groups and perform statistical testing. Moreover, a national benchmark was included, which helps to interpret the results on regional level more accurate. The additionally performed sensitivity analysis showed no clinical relevant differences between the national benchmark with or without the EMBRAZE network. An important limitation of this study lies within the design of the study as we did not use a controlled study design which is characterized with less risk of bias. Furthermore, the evaluation was limited to only one year after the implementation of the regional pathways. Evaluation of more recent years would have provided a more accurate comparison related to the national benchmark. These research findings are not generalizable to other oncology networks, because there may be differences in the patient population, regional agreements and the organization of care and treatment within participating hospitals and other health care institutions.

CONCLUSION

This evaluation has added value for health care professionals, managers and board of directors by providing insight in the clinical outcomes supplemented with both the perspective of health care professionals and patients receiving their care and treatment in multiple hospitals. Evaluation of oncology networks, such as performed in the EMBRAZE region, provides a base for continuing further collaboration for patients with esophagogastric cancer. Nevertheless, the results of this evaluation after implementing the regional agreements can contain lessons learned for other regions and can contribute to a better understanding of the use of regional agreements in order to realize a better organization of care and treatment for this patient population.

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Additional file 1 Interview with health care professionals about the regional care pathways and collaboration regarding esophageal and gastric cancer in the EMBRAZE network

Date

Interviewer

Health care professionals present	Discipline
•	•
•	•
•	•
•	•
•	•
•	•
•	•
•	•
•	•

Explanation by the interviewer

In 2016, regional agreements about the care and treatment of patients with esophageal and gastric cancer were developed, formalized in regional care pathways and implemented. The tumor group Upper GI of the EMBRAZE network would like to know how the health care professionals use the care pathways in practice and carry out an evaluation. In addition, we want to know the strengths and points of improvement of the care pathways, especially to adapt and/or improve the pathways in the future.

It was chosen to perform an interview with several health care professionals at the same time, because it can be meaningful to discuss issues with each other in the context of the evaluation of the regional care pathways.

The interviews are elaborated in a short report and submitted to the attendees. All interviews are taken into account in the entire evaluation, which also includes a data analysis and interviews with patients. A (scientific) article will be written of this evaluation.

If you have any questions about this study or this interview, please contact Jolanda van Hoeve, j.vanhoeve@iknl.nl, T: +31 6 46139056.

This interview will take around 45 minutes of your time.

1. Agreements about diagnostics and referral after diagnostics

1a. Are you aware of the regional diagnostics agreements? And are these used?

1b. What runs well and what can be improved?

2. Agreements about treatment

2a. Are you aware of the regional appointments for treatment? And are these used?

2b. What runs well and what can be improved?

3. Agreements about follow-up

3a. Are you aware of the regional follow-up agreements? And are these used?

3b. What runs well and what can be improved?

4. Implementation process

4a. How did the process of implementing the regional care pathways go?

4b. What has changed compared to the situation before?

4c. What went well in the implementation process?

4d. What could have been better? What are the points of interest for continuation?

5. Results implementation regional care pathways

5a. What was the purpose and/or reason for the care pathways? What were your expectations prior to the implementation?

5b. Did the care pathways deliver what you expected? Have the goals of the care pathways been achieved?

5c. What have the care pathways achieved for the patient? What improvement in patient care has occurred in your opinion?

5d. What have the care pathways for the hospital achieved? And what has it achieved for you as a health care professional?

5e. What is the impact of the care pathways? How far-reaching has the development of the care pathways been for you as a health care professional(s)?

6. Strengths and opportunities

6a. What are the strengths of current care pathways?

6b. What are the areas for improvement for current care pathways? What could be better regulated in these pathways?

6c. What other areas of improvement and collaboration opportunities do you see for the region? Where do you see opportunities for improvement of care and treatment? Is there a desire to make further appointments?

6d. Which role can the tumor group Upper GI of the EMBRAZE network play in this?

Finally: Do you have any points that have not been addressed but are important?

Additional file 2 Interview with patients about the regional care pathways and collaboration regarding esophageal and gastric cancer in the EMBRAZE network

Date

Interviewer

Explanation by the interviewer

In 2016 agreements were made between the hospitals, the Medical Center and the radiotherapeutic institutes in the EMBRAZE network. The aim to formalize the agreements in regional pathways was to organize the care and treatment for patients with esophageal and gastric cancer better in the future.

With this interview we want to know whether the agreements are being followed in clinical practice and are sufficient enough for the care of patients. Therefore, we want to ask your opinion about the care and treatment you received in the hospitals or radiotherapeutic institutes.

In this interview we will ask you about your opinion of the care and treatment your received, the coordination between health care professionals (within and between hospitals), how the transfer(s) between hospitals or institutions went, and which improvements could be made for the care for patients in the future.

Your answers to these questions will be analyzed anonymous within this study. Your opinion will not influence your care and treatment.

If you have any questions about this study or this interview, please contact Jolanda van Hoeve, j.vanhoeve@iknl.nl, T: +31 6 46139056.

On behalf of the tumor group Upper GI of the EMBRAZE network, thank you very much for sharing your opinion and feedback!

This interview will take around 45 minutes of your time.

1. Agreements about diagnostics and referral after the diagnostics phase

- 1a. Which diagnose did you received? (esophageal or gastric cancer)
- 1b. Which diagnostic procedure did you underwent? In which sequence?
- 1c. How much time did it take from the first appointment in a hospital to the appointment in which the results of the diagnostic procedures and treatment plan were discussed with you? Was this shorter or longer than 3 weeks?
- 1d. Did all diagnostic procedures took place in one hospital, or where there other diagnostic procedures in other hospitals? If yes, how did you experience this? If applicable, were the health care professionals in the other hospital well informed about your situation? And were the agreements clear enough?

2. Agreements about treatment

- 2a. Which treatments did you underwent?
- 2b. Did all treatments took place in one hospital? Or did you received treatment in another hospital or other hospitals? What was your experience with this? Was the hospital which you were referred to well informed about your situation? Were the agreements about care and treatment clear enough in the hospital you were referred to?
- 2c. If you received radiotherapy in a radiotherapeutic institute, how did you experienced the transfer from the hospital to the radiotherapeutic institute? Were the care givers in the radiotherapeutic institution well informed about your situation? And were the agreements about care and treatment clear enough?
- 2d. How long did it take from the discussion about your treatment plan to the start of the treatment? Was this 2 weeks or shorter? How did you experience this?
- 2e. How long did it take from the gastroscopy to the start of treatment? Was this shorter or longer than 5 weeks? How did you experience this?
- 2f. If you underwent a surgical treatment: how long did you stay hospital afterwards? Was this shorter or longer than 10 days? How did you experience this?

3. Agreements about follow-up

- 3a. How did it go in the period after the surgical treatment?
- Ask for: In which hospital did the follow-up and aftercare took place? (the hospital of diagnosis or somewhere else?) If applicable: how did you experience the transfer? Did adequate coordination took place? Were the health care professionals well informed?
- 3b. How often did an appointment after treatment took place? In which hospital?
- 3c. Which diagnostic procedures were performed after treatment took place? If applicable, which procedures?

4. Your opinion on the care in the hospital in which you received diagnostic procedures

4a. What did you think of the information you received in the first hospital you went to?

Good/moderate/bad

Why?

4b. What did you think of the care of doctors and other care workers in this hospital? Was this respectful?

Good/moderate/bad

Why?

4c. How did you experience the care and treatment in your first hospital?

Please choose a number between 1 and 10.

5. If applicable: your opinion on the care in the hospital where you have received surgical treatment

5a. What did you think of the information you received in the hospital of surgery?

Good/moderate/bad

Why?

5b. What did you think of the care of the doctors and other care workers in this hospital? Was this respectful?

Good/moderate/bad

Why?

5c. How did you experience the care in the hospital where you have received surgical treatment? Please choose a number between 1 and 10.

6. If applicable: your opinion on the care in the radiotherapeutic institute where you have received radiotherapy

6a. What do you think of the information you have received in the radiotherapeutic institute?

Good/moderate/bad

Why?

6b. What did you think of the care of the doctors and other care workers in this institute? Was this respectful?

Good/moderate/bad

Why?

6c. How did you experience the care in the radiotherapeutic institute?

Please choose a number between 1 and 10.

7. If applicable: your opinion on the transfer between hospitals

7a. What did you think of the transfer or transition between hospitals (or hospital to radiotherapeutic institute and vice versa)? Can the transition be performed even faster and better? If so, how?

7b. If applicable: Do you think things have been done twice in different hospitals/institutes? If so, what?

7c. Was it clear at all times who your first contact person or case manager was? And was it clear who your medical responsible was?

8. Strengths and opportunities

8a. Because the hospitals in your region collaborate, agreements have been made and formalized about the care of patients with esophageal and gastric cancer. Have you noticed any of that in any way? What do you think about the collaboration between the hospitals and radiotherapeutic institutes in the region?

8b. What are the strengths of care? What are the advantages of the collaboration between the hospitals and radiotherapeutic institutes in the EMBRAZE network?

8c. What should be better regulated in the region between hospitals and/or radiotherapeutic institutes? Where do you see opportunities for improvement of care and treatment?

Finally: Do you have any points that have not been addressed but are important?

Additional file 3 Patient and tumor characteristics according to year of diagnosis for esophageal and gastric cancer in the Netherlands

Characteristics	Esophageal cancer Netherlands (n=5444)			Gastric cancer Netherlands (n=2090)		
	2015 (n=2700)	2017 (n=2744)	p	2015 (n= 1085)	2017 (n=1005)	p
Year of diagnosis						
Median age	68 (± 10.78)	69 (± 10.48)	0.034	73 (± 12.63)	74 (± 12.35)	0.032
Gender						
Male	2018 (75%)	2013 (73%)	0.245	652 (60%)	630 (63%)	0.224
Female	682 (25%)	731 (27%)		433 (40%)	375 (37%)	
Tumor staging						
Early cancer	30 (1%)	32 (1%)	0.382	13 (1%)	9 (0.9%)	0.782
Potentially curable cancer	1631 (60%)	1706 (62%)		550 (50%)	507 (50%)	
Potentially non-curable cancer	1039 (39%)	1006 (37%)		522 (48%)	489 (49%)	
Histology						
Adenocarcinoma	1974 (73%)	2070 (75%)	0.135	NA*	NA*	-
Squamous cell carcinoma	652 (24%)	601 (22%)		NA*	NA*	
Other	74 (3%)	73 (3%)		NA*	NA*	
Comorbidity	(n=2571)	(n=2559)		(n=1015)	(n=913)	
0	632 (24%)	623 (24%)	0.955	250 (25%)	196 (22%)	0.110
1	713 (28%)	705 (28%)		282 (28%)	241 (26%)	
≥ 2	1226 (48%)	1231 (48%)		483 (47%)	476 (2%)	

* NA: Not Applicable.

Additional file 4 Diagnostic procedures & treatment combinations according to year of diagnosis for esophageal and gastric cancer in the Netherlands (based on hospital of diagnosis)

Year of diagnosis	Esophageal cancer Netherlands (n=5444)			Gastric cancer Netherlands (n=2090)		
	2015 (n=2700)	2017 (n=2744)	p	2015 (n=1085)	2017 (n=1005)	p
Diagnostic procedures						
Gastroscopy	2659 (98%)	2645 (96%)	<0.001	1028 (95%)	862 (86%)	<0.001
Endoscopic ultrasound	884 (33%)	817 (30%)	0.018	97 (9%)	87 (9%)	0.819
CT scan (or PET/CT scan)	2477 (92%)	2467 (90%)	0.019	973 (90%)	869 (86%)	0.023
PET / PET/CT scan	1371 (51%)	1763 (64%)	<0.001	124 (11%)	264 (26%)	<0.001
PET/CT scan if cT => 2	1194 (44%)	1502 (55%)	<0.001	76 (7%)	194 (19%)	<0.001
Treatment for potentially curable patients	(n=1631)	(n=1706)		(n=550)	(n=507)	
Neoadjuvant CRT* & resection	682 (41%)	669 (39%)	0.126	NA*	NA*	-
Neoadjuvant CT* & resection	65 (4%)	71 (4%)	0.797	NA*	NA*	-
Resection (with or without CT*)	NA*	NA*	-	345 (63%)	303 (60%)	0.323
CRT* only	336 (21%)	367 (22%)	0.519	NA*	NA*	-
Resection only	122 (8%)	140 (8%)	0.436	NA*	NA*	-
CT* only	14 (0.9%)	30 (2%)	0.023	29 (5%)	20 (4%)	0.305
RT* only	180 (11%)	183 (11%)	0.774	21 (4%)	22 (4%)	0.668
Other/no treatment	232 (14%)	246 (14%)	0.872	155 (28%)	162 (32%)	0.181
Treatment for potentially non-curative patients	(n=1039)	(n=1006)		(n=522)	(n=489)	
Resection (with or without C(R)T*)	16 (2%)	27 (3%)	0.071	41 (8%)	30 (6%)	0.285
CRT* only	171 (17%)	150 (15%)	0.336	NA*	NA*	-
CT* only	249 (24%)	275 (27%)	0.081	156 (30%)	151 (31%)	0.731
RT* only	238 (23%)	204 (20%)	0.149	33 (6%)	15 (3%)	0.015
Other/no treatment	365 (34%)	350 (35%)	0.872	292 (56%)	293 (60%)	0.200
Lead time (median in days)	(n=1987)	(n=1902)		(n=723)	(n=710)	
Lead time between first diagnostic procedure and MDT*	13 (IQR:14)	7 (IQR:10)	<0.001	12 (IQR:13)	9 (IQR:13)	0.003
	(n=1713)	(n=1883)		(n=546)	(n=490)	
Lead time between MDT* and start therapy	21 (IQR:17)	24 (IQR:18)	0.002	20 (IQR:19)	27 (IQR:22)	<0.001
Overall survival						
1 year overall survival (for potentially curative patients)	67.0(64.7-69.2)	66.5(64.2-68.7)	0.323	62.5(58.3-66.4)	63.0(58.7-67.1)	0.670
1 year overall survival (for potentially non-curative patients)	20.2(17.9-22.7)	22.5(19.9-25.1)	0.389	15.0(12.1-18.2)	19.8(16.4-23.5)	0.097

* CRT: chemoradiotherapy; CT: chemotherapy; NA: Not Applicable; RT: radiotherapy; MDT: Multidisciplinary team meeting (in which the treatment plan for the patient was discussed).

Additional file 5 Surgical treatment and clinical outcomes according to year of diagnosis for esophageal and gastric cancer in the Netherlands (based on 1st resections)

Number of resections	Esophageal cancer Netherlands (n=1862)			Gastric cancer Netherlands (n=807)		
	2015 (n=919)	2017 (n=943)	P	2015 (n=440)	2017 (n=367)	P
Type of surgery						
TTE*	577 (63%)	657 (70%)		NA*	NA*	
THE*	187 (20%)	98 (10%)	<0.001	NA*	NA*	0.207
Partial gastrectomy	NA*	NA*		255 (58%)	199 (54%)	
Total gastrectomy	54 (6%)	48 (5%)		161 (36%)	137 (37%)	
Other	101 (11%)	140 (15%)		24 (6%)	31 (9%)	
Surgical approach	(n=789)	(n=759)		(n=384)	(n=297)	
Open surgery	216 (27%)	75 (10%)	<0.001	167 (43%)	115 (39%)	
Minimally invasive surgery	573 (73%)	684 (90%)		217 (57%)	182 (61%)	0.210
	(n=716)	(n=726)		(n=338)	(n=271)	
Anastomotic leakage	158 (22%)	173 (24%)	0.426	39 (12%)	23 (8%)	0.216
Other postoperative complications	(n=734)	(n=731)		(n=343)	(n=274)	
Pulmonary complications	193 (26%)	233 (32%)	0.009	47 (14%)	33 (12%)	0.542
Cardiac complications	61 (8%)	68 (9%)	0.503	15 (4%)	3 (1%)	0.016
Thromboembolic complication	9 (1%)	9 (1%)	1.000	3 (1%)	1 (0.4%)	0.633
Chyle leakage	59 (8%)	44 (6%)	0.200	9 (2.6%)	4 (1.5%)	0.404
Wound infection	68 (9%)	50 (7%)	0.088	41 (12%)	30 (11%)	0.698
Length of hospital stay (median in days)	(n=904) 11(IQR:10)	(n=930) 10 (IQR:9)	0.004	(n=429) 8 (IQR:6)	(n=363) 7 (IQR:6)	0.001
ICU* stay (median in days)	(n=866) 2 (IQR:4)	(n=804) 2 (IQR:3)	0.932	(n=411) 0 (IQR:1)	(n=307) 0 (IQR:1)	0.466
Postoperative mortality						
30 days	2.5%	1.5%	0.116	5.2%	2.7%	0.074
60 days	4.5%	2.7%	0.035	7.7%	3.8%	0.019
90 days	6.1%	3.4%	0.006	9.8%	5.5%	0.023

* TTE: Transthoracic surgery; THE: Transhiatal surgery; NA: Not Applicable; ICU: Intensive Care Unit.

CHAPTER 9

Variation in esophageal cancer care within a Managed Clinical Network

Trends in treatment strategies, lead time, and 2-year survival

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ABSTRACT

Objective

Despite evidence-based guidelines, variation in esophageal cancer care exists in daily practice. Many oncology networks deployed regional agreements to standardize the patient care pathway and reduce unwarranted clinical variation. The aim of this study was to explore the trends in variation of esophageal cancer care between participating hospitals of the Managed Clinical Network (MCN) in the Netherlands.

Methods

Patients with esophageal cancer diagnosed from 2012 to 2016 were selected from the Netherlands Cancer Registry. Variation on treatment strategies, lead time to start of treatment, and 2-year survival, were calculated and compared between five clusters of hospitals within the network.

Results

A total of 1763 patients, diagnosed in 17 hospitals, were included. 71% of all patients received treatment with a curative intent, which ranged from 69% to 77% between the clusters of hospitals in 2015-2016. Although variation in treatment modalities between the clusters was observed in 2012-2014, no significant variation existed in 2015-2016, except for patients receiving no treatment at all. The 2-year overall survival of patients receiving treatment with a curative intent did not vary significantly between the clusters of hospitals (range: 56% to 63%). Nevertheless, the median lead time before patients started treatment with a curative intent varied between clusters of hospitals in 2015-2016 (range: 34 to 47 days; $p < 0.001$).

Conclusion

Limited variation in esophageal cancer treatment between clusters of hospitals in the MCN existed. This study shows that providing insight in variation of care fits into a continuous learning process within an oncology network.

BACKGROUND

Esophageal cancer is the seventh most common cancer worldwide. Around 572,000 new cases of esophageal cancer were diagnosed globally in 2018, accounting for 3.2% of all new cases of cancer¹. The incidence of esophageal cancer has risen in the Netherlands over the last years, approximately 2500 new cases of esophageal cancer were diagnosed in 2018². Survival rates are poor, mainly because esophageal cancer is usually diagnosed at a late stage^{1,3}.

Variation in care and treatment of patients with esophageal cancer exists. A previous study showed a large variation in the probability to undergo treatment with a curative intent for esophageal cancer which depended on the hospitals of diagnosis and which also affected the survival of these patients. In this study regional expert MDT meetings with involvement of experienced specialists were recommended for all patients with esophageal cancer³.

The complexity of cancer care is increasing requiring expertise, skills and availability of technologies as well as (expensive) diagnostics and treatments. Moreover, hospitals are facing demands from external parties, such as volume norms and the increasing trend to publish results based on indicators and quality of care more transparently. Therefore, regional oncology networks were formed to maintain approachable access to care in all hospitals, to guarantee the quality of care regardless of the hospital of diagnosis, to refer patients to specialized center if needed, to improve accrual to clinical trials and to provide a platform for quality improvement⁴.

Networks refer to a group of three or more organizations consciously formed, organized, and directed in ways to achieve a common goal⁵. Cancer services delivery is considered as a good example of network-based working because patients receive care from multiple health care teams located in different settings^{6,7}. Nevertheless, little evidence is available about the effects of networks in cancer care.

In the Netherlands many oncology networks have been established in recent years. In the North East region of the Netherlands a Managed Clinical Network (MCN) for patients with esophagogastric cancer was already founded in 2008. In this network 17 hospitals are collaborating, including teaching and non-teaching hospitals and one academic hospital. The aim of the MCN is to provide all esophagogastric cancer in the network easily accessible and equal care conform high quality standards and (inter)national guidelines. Within the MCN five regional multidisciplinary team (MDT) meetings occur, in which patients diagnosed with esophageal cancer from one or more hospitals, including a surgical treatment center, are jointly being discussed. All participating hospitals gave their commitment to formalized agreements leading to a standardized care pathway and treatment protocols, according to the Dutch Guidelines⁸. Five years after the establishment of the MCN differences between hospitals were observed, and the MCN members wondered whether these differences persisted in the following years.

In order to learn from the best practices and improve the care and treatment for patients with esophageal cancer care, the primary aim of this study was to gain insight in the variation of care between the clusters of hospitals within the MCN.

METHODS

In this study we used a retrospective research design. Patients with esophageal cancer receiving care from 2012-2014 within the MCN, were compared to 2015-2016. In addition, outcomes of the MCN were compared with a national benchmark including all esophageal cancer patients in the Netherlands (including the MCN), to interpret the results of the regional network more accurate. The same patient selection criteria were applied for both the MCN and the national benchmark.

Data source

Data registered in the Netherlands Cancer Registry (NCR) were used to perform the analyses. This population-based registry covers the complete Dutch population (79 hospitals) and is based on a notification of all newly diagnosed malignancies in the Netherlands by a national automated pathological archive (PALGA). Additional notification sources are the national registry of hospital discharge and radiotherapy institutions. Specially trained data managers of the NCR routinely extract information on diagnosis, tumor stage, and treatment directly from the medical records.

Patient selection criteria

All patients with invasive potentially curable esophageal cancer (cT1-4a ,cNany,cM0 & cTx,cNany,cM0, without cT1N0cM0) from 2012 to 2016 were selected from the NCR. The outcome lead time between diagnosis and start of the first treatment (chemoradiotherapy or resection) was restricted to patients with potentially curable esophageal cancer, who received treatment with a curative intent. All patients with early stage esophageal cancer (cT1 cN0 cM0) who mostly underwent an endoscopic mucosal resection (EMR) or an endoscopic submucosal dissection (ESD), which are referred to as endoscopic treatment and therefore differed from other surgical treatments, were excluded from the dataset.

Outcome measures

Variation between 2012-2014 and 2015-2016 was analyzed for treatment modalities with and without a curative intent and lead time to start of treatment. Based on the Donabedian model the following indicators were arranged⁹:

Process indicator:

- Lead time from diagnosis to start of treatment with a curative intent.

Outcome indicators:

- For treatment with curative intent strategies: patients receiving surgical treatment alone;

patients receiving chemoradiotherapy without surgery; patients receiving surgery after neoadjuvant chemo(radio)therapy with or without adjuvant therapy.

- For treatment strategies without a curative intent: patients receiving treatments other than those mentioned above; patients receiving no treatment.
- 2-year overall survival.

Statistical analysis

For statistical testing between both periods the chi-squared test was used. Differences between characteristics were analyzed using chi-squared tests for nominal data and Mann-Whitney U tests for continuous data (based on median lead time and IQR). In case of small cell sizes (expected values less than 5), the Fisher's Exact test was used to calculate the association between categorical variables.

Statistical significant differences were calculated between: 1) the period 2012 to 2014 versus 2015 to 2016, 2) between the clusters of hospitals/surgical treatment centers within the MCN who discussed patients in a joint MDT meeting. In total five clusters of hospitals, ranging from one to six hospitals, were formed based on the existing regional MDT meetings.

The differences between treatment modalities over time and between the cluster of hospitals with the lowest and highest percentage of patients receiving treatment with or without a curative intent, were calculated by using the chi-squared test. The log-rank test was used to test the variation of median lead time to start of treatment within the clusters over time and between the cluster of hospitals with the shortest and longest lead time to start of treatment with a curative intent.

In addition, Kaplan-Meier curves were generated to examine the overall survival over time. Survival curves were compared using the log-rank test. $P < 0.050$ was considered statistically significant. Besides, sensitivity analyses were performed to test whether the results of the MCN deviated from the national benchmark (including MCN). All analyses were conducted using STATA (StataCorp LLC, Texas, USA).

RESULTS

A total of 1763 potentially curable esophageal cancer patients, diagnosed in the total period 2012 to 2016, were included. The median age of patients was 69 years. Apart from the shift in clinical stage over time ($p = 0.008$), no clinically relevant differences were observed for patients in the MCN (table 1).

Table 1 Patient and tumor characteristics according to year of diagnosis for esophageal cancer

Characteristics	Esophageal cancer MCN (n=1763)		
	MCN 2012-2014 (n=1022)	MCN 2015-2016 (n=741)	p
Median age	69 (± 10.81)	69 (± 10.58)	0.306
Gender			
Male	749 (73%)	548 (74%)	0.754
Female	273 (27%)	193 (26%)	
Clinical TNM			
I	217 (21%)	143 (19%)	0.008
II	263 (26%)	196 (26%)	
III	402 (39%)	334 (45%)	
X	140 (14%)	68 (9%)	
Histology			
Adenocarcinoma	752 (74%)	542 (73%)	0.705
Squamous cell carcinoma	250 (24%)	188 (25%)	
Other	20 (2%)	11 (2%)	

Differences in treatment modalities and lead time to start treatment

Out of 1763 patients, 68% of them received treatment with a curative intent in 2012-2014 and 71% in 2015-2016 (table 2). In 2015-2016 less patients underwent surgical treatment alone (-4%; $p < 0.001$) and more patients received neoadjuvant chemo(radio)therapy and surgery with or without adjuvant therapy (+7%; $p = 0.005$) compared to 2012-2014. The latter group consisted of patients with two different treatment modalities, of which the largest group of patients received neoadjuvant chemoradiotherapy and surgery. Further, about 18% of all patients received chemoradiotherapy without surgery.

Treatment without a curative intent was given to 32% of all patients with potentially curable esophageal cancer in 2012-2014 and 29% in 2015-2016. Almost half of these patients received treatment for symptom relieve (i.e. non-curative radiotherapy or stent) and half of these patients did not receive any treatment at all.

The median lead time to the start of treatment with a curative intent reduced from 42 days in 2012-2014 to 41 days in 2015-2016 ($p = 0.040$) for patients with potentially curable esophageal cancer. See table 2.

Table 2 Treatment modalities and lead time to start treatment according to year of diagnosis for esophageal cancer

	MCN 2012-2014 (n=1022)	MCN 2015-2016 (n=741)	p
Treatment with curative intent	697 (68%)	527 (71%)	0.189
Surgery only	72 (7%)	19 (3%)	<0.001
CRT* without surgery	177 (17%)	133 (18%)	0.732
Neoadjuvant C(R)T* & surgery with/without adjuvant therapy	448 (44%)	375 (51%)	0.005
Neoadjuvant C(R)T* & surgery	442	370	0.005
Neoadjuvant C(R)T* & surgery & adjuvant therapy	6	5	0.817
Treatment without curative intent	325 (32%)	214 (29%)	0.189
Other treatment	151 (15%)	108 (15%)	0.907
No treatment	174 (17%)	106 (14%)	0.123
Lead time to start of treatment with curative intent (median)	(n= 696) 42 (IQR:21.5)	(n=527) 41 (IQR:17)	0.040

* CRT: Chemoradiotherapy; CT: Chemotherapy.

Sensitivity analyses

In comparison to the national population, the regional patient population appears to be a representative sample (see additional file 1). Additionally, in 2015-2016 more patients in the national population received treatment with a curative intent, compared to 2012-2014 (66% versus 70%, $p<0.001$), which is comparable to the MCN region (68% and 71%). Nationwide trends in surgery only (-3%, $p<0.001$), and neoadjuvant chemo(radio)therapy and surgery with or without adjuvant therapy (+5%, $p<0.001$) were comparable to the MCN region. In comparison with the results of the MCN cohort which showed no differences over time for treatment with chemoradiotherapy without surgery, in the national benchmark significantly more patients received this treatment in 2015-2016 (+2%, $p=0.008$).

The median lead time of patients to the start of treatment with curative intent reduced in the national cohort from 41 days in 2012-2014 to 40 days in 2015-2016 ($p<0.001$) for patients with potentially curable esophageal cancer. This trend was comparable with the MCN region. See additional file 2.

Variation between clusters of hospitals

Significant variation, ranging from 63% to 78% between the clusters of hospitals, was observed for all patients receiving treatment with a curative intent in 2012-2014. In 2015-2016 these differences reduced with a range of 69% and 77% ($p=0.11$). See table 3. In addition, no variation existed between the clusters for patients receiving surgery only (0% to 7%), chemoradiotherapy without surgery (15% to 21%) and chemo(radio)therapy and surgery with or without adjuvant therapy (48% to 53%) in 2015-2016. The proportion of patients receiving surgery only reduced significantly over time in cluster 2 (14% in 2012-2014 to 5% in 2015-2016,

$p=0.004$), cluster 3 (6% in 2012-2014 to 0% in 2015-2016, $p=0.033$), and cluster 4 (8% in 2012-2014 to 3% in 2015-2016, $p=0.049$). In cluster 2 significant more patients received neoadjuvant chemo(radio)therapy and surgery with or without adjuvant therapy in 2015-2016 (37% in 2014-2014 to 48% in 2015-2016, $p=0.033$). See additional file 3.

Differences between the clusters for patients receiving other treatments varied from 14% to 16% in 2015-2016. In addition, for patients who did not receive any treatment at all, variation ranged from 9% to 17% in 2015-2016, which was a significant difference in both periods. The proportion of patients not receiving any treatment reduced significantly in cluster 5 (16% in 2012-2014 to 9% in 2015-2016, $p=0.040$). For more information, see additional file 3.

Furthermore, significant differences between the clusters of hospitals were found in the median lead time to start of treatment with a curative intent in both study periods (34 versus 54 days in 2012-2014, $p<0.001$; 34 versus 47 days in 2015 to 2016; $p<0.001$). Meanwhile, when focusing on the separate clusters, reduction in median lead time to the start of treatment with a curative intent was observed between 2014-2014 and 2015-2016 for hospital cluster 2 (54 to 47 days; $p=0.020$), cluster 3 (40 to 34 days, $p=0.034$), and cluster 4 (47 to 41 days; $p=0.010$). For more details, see table 3.

Table 3 Treatment modalities and lead time to start of treatment according to year of diagnosis for esophageal cancer

Curative treatment esophageal cancer MCN (n=1763)				
	2012-2014 (P1*) (n=1022)	2015-2016 (P2*) (n=741)	p**	p ↓ versus ↑***
Total treatment with curative intent				
Cluster 1	(n=222) 148 (67%)	(n=196) 136 (69%)↓*	0.552	
Cluster 2	(n=197) 124 (63%)↓*	(n= 155) 107 (69%)	0.233	
Cluster 3	(n=98) 76 (78%)↑*	(n=72) 50 (69%)	0.233	0.011 (P1)
Cluster 4	(n= 251) 172 (69%)	(n=145) 101 (70%)	0.815	0.106 (P2)
Cluster 5	(n= 254) 177 (70%)	(n=173) 133 (77%)↑*	0.102	
Total treatment without curative intent				
Cluster 1	74 (33%)	60 (31%)↑*	0.552	
Cluster 2	73 (37%)↑*	48 (31%)	0.233	
Cluster 3	22 (22%)↓*	22 (31%)	0.233	0.011 (P1*)
Cluster 4	79 (31%)	44 (30%)	0.815	0.106 (P2*)
Cluster 5	77 (30%)	40 (23%)↓*	0.102	
Lead time to start of treatment with curative intent				
	(n=696)	(n=527)		
Cluster 1	(n=148) 42.5 (IQR:18)	(n=136) 43.5 (IQR:18.5)	0.612	
Cluster 2	(n=124) 54 (IQR:22)↑*	(n=107) 47 (IQR:18)↑*	0.020	
Cluster 3	(n=76) 40 (IQR:15.5)	(n=50) 34 (IQR:12)	0.034	<0.001 (P1*) <0.001 (P2*)
Cluster 4	(n=171) 47 (IQR:21)	(n=101) 41 (IQR:14)	0.010	
Cluster 5	(n=177) 34 (IQR:16)↓*	(n=133) 34 (IQR:14)↓*	0.984	

* P1: 2012-2014; P2: 2015-2016; ↓: cluster of hospitals with the lowest percentage of patients receiving treatment with/without curative intent or the shortest median lead time to start of treatment with curative intent; ↑: cluster of hospitals with the highest percentage of patients receiving treatment with/without curative intent or the longest median lead time to start of treatment with curative intent.

** Statistical difference between P1 and P2.

*** Statistical difference between ↓ versus ↑, calculated for P1 and P2 separately.

Variation in survival

The 2-year overall survival of patients receiving treatment with a curative intent ranged from 56% (cluster 2) to 63% (cluster 1 and 5) between the clusters of hospitals (additional file 4).

No significant differences between the 2-year overall survival were found between the hospital clusters. See figure 1.

Figure 1 Overall survival of patients receiving treatment with a curative intent between the hospital clusters (p=0.143).

The same applies for the 2-year overall survival of patients who received treatment without curative intent between the hospital clusters, these differences were not significant. See figure 2.

Figure 2 Overall survival of patients receiving treatment without a curative intent between the hospital clusters ($p=0.318$).

DISCUSSION

Ten years after the foundation of the MCN esophagogastric cancer, we evaluated regional agreements regarding patients with esophageal cancer resulting in a standardized care pathway and treatment protocols, according to the Dutch Guidelines. The results showed no differences in the proportion curative versus non-curative treatment over time. However, for patients who received treatment with a curative intent, less patients underwent surgical treatment only and more patients received neoadjuvant chemoradiotherapy and surgery over time. This observed trend in both the selected study years of 2012-2016 as well as in the national population, was conform the new standard of optimal treatment in the Netherlands based on the results of the CROSS trial¹⁰ and therefore since 2010 formalized in the Dutch Guidelines.

Although significant differences between all treatment modalities for potentially curable patients in the clusters of hospitals existed in the years 2012-2014, in the following years these differences reduced and no significant results were observed. The only exception to this was seen for patients who did not receive any treatment at all. In addition, neither significant

differences between the 2-year survival occurred for patients receiving treatment with a curative intent nor for patients receiving treatment without a curative intent. In a previous study a large variation in the probability to undergo treatment with a curative intent for esophageal cancer between individual hospitals was revealed³. The present study showed that within the MCN potentially curable patients received treatment with a curative intent equally regardless of the hospital of diagnosis, suggesting that having clusters of hospitals around a regional MDT meeting has a positive effect on decreasing variation.

Within oncology networks the use of standardized pathways, quality improvement programs, and clinical trial resources are similarly increased¹¹. Data provides enhanced analytic capabilities to facilitate greater understanding of care delivery outcomes¹². In this study the MCN had a stimulating role in the regionalization of esophagogastric cancer care, and facilitated frequent insight in variation between (clusters of) hospitals which led to discussion about topics about the observed variation in previous years. In addition, literature confirms that sharing measurement of quality performance within an oncology network can be useful to assess the effectiveness of improvement initiatives¹³. Discussing data and variation has arose an awareness of standardization of care and discussing patients is a MDT meeting for exchange of expertise among the participants of the MCN. The formalization of regional agreements into a standardized care pathway was consisted with the goal of the network: to guarantee equal access and high quality of care in each hospital. Based on the results of this study, we assume that regionalization and standardization of care can lead to limited clinical variation and more equal care for esophageal cancer patients. Moreover, a continuous learning process serves as a platform for future collaboration and improvements.

Meanwhile, the observed variation in lead time to start of treatment can be a signal for improving the efficiency of care. However, three hospital clusters achieved a significant reduction of median days to treatment. Nevertheless, longer waiting times can be the result of suboptimal access to standard diagnostics, suboptimal coordination between the multidisciplinary team, or due to a more extensive diagnostic process, or suboptimal access to treatment facilities. Moreover, in clinical practice variation exists in diagnostics trajectories not fastened in guidelines. For instance, some hospitals used endoscopic ultrasonography, as a routine in the workup, others perform these tool on demand. Similarly, current guidelines do not routinely advice geriatric assessment and cardiopulmonary exercise tests. Moreover, waiting times are frequently cited as a cause of patient dissatisfaction with the health care system¹⁴ and reduction can be valuable from the patient's perspective. Besides, the relation waiting times before start treatment and patients' survival are controversial. Studies exists in which the influence of the delay of oncological therapy on cure and overall survival was confirmed^{15,16}. In other studies, no evidence about this relation was available^{17,18}.

This study has several strengths and limitations. A strength of the study was the extensive dataset of the MCN which made it possible to perform statistical testing with larger patient groups. Moreover, a national benchmark was included, which helps to interpret the results on

regional level more accurate. Based on this benchmark, the additionally performed sensitivity analysis showed no clinically relevant differences between the national benchmark and the MCN.

A limitation of this study was the selection of the limited number of two years which was used for follow-up. Using data covering more years would have given more insight in trends and variation over a longer period. Furthermore, the results presented in this study are not generalizable to other oncology networks, due to differences in patient population, regional agreements and organization of care processes.

CONCLUSION

This variation analysis provides insight in the reduction of variation between treatment modalities and patients' survival between clusters of hospitals within an oncology network over time. This study shows that reporting data and providing insight in variation can lead to awareness of the health care professionals and contribute to achieve and the best optimal care for cancer patients, without unwarranted variation. Providing insight in variation of care fits into a continuous learning process within an oncology network. Further opportunities to reduce variation between the clusters of hospitals were pointed out and provided a basis for further collaboration and knowledge sharing about best practices between hospitals.

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Additional file 1 Patient and tumor characteristics according to year of diagnosis for esophageal cancer; national benchmark

Characteristics	Esophageal cancer NL (n=7634)		p
	NL 2012-2014 (n=4395)	NL 2015-2016 (n=3239)	
Median age	69 (± 11.10)	69 (± 10.97)	0.221
Gender			
Male	3228 (73%)	2341 (72%)	0.255
Female	1167 (27%)	898 (28%)	
Clinical TNM			
I	775 (18%)	630 (19%)	0.000
II	1140 (26%)	911 (28%)	
III	1805 (41%)	1356 (42%)	
X	675 (15%)	342 (11%)	
Histology			
Adenocarcinoma	3043 (69%)	2255 (70%)	0.701
Squamous cell carcinoma	1264 (29%)	912 (28%)	
Other	88 (2%)	72 (2%)	

Additional file 2 Treatment modalities and lead time to start treatment according to year of diagnosis for esophageal cancer; national benchmark

	Esophageal cancer NL (n=7634)		p
	NL 2012-2014 (n=4395)	NL 2015-2016 (n=3239)	
Treatment with curative intent	2884 (66%)	2278 (70%)	<0.001
Surgery only	250 (6%)	96 (3%)	<0.001
CRT* without surgery	775 (18%)	649 (20%)	0.008
Neoadjuvant C(R)T* & surgery with/without adjuvant therapy	1859 (42%)	1533 (47%)	<0.001
Neoadjuvant C(R)T* & surgery	1797	1459	<0.001
Neoadjuvant C(R)T* & surgery & adjuvant therapy	62	74	0.004
Treatment without curative intent	1511 (35%)	961 (30%)	<0.001
Other treatment	732 (17%)	482 (15%)	0.036
No treatment	779 (18%)	479 (15%)	0.001
	(n=2881)	(n=2278)	
Lead time to start of treatment with curative intent (median)	41 (IQR:20)	40 (IQR:16)	<0.001

* CRT: ChemoRadioTherapy; CT: ChemoTherapy.

Additional file 3 Treatment modalities with and without curative intent according to year of diagnosis for esophageal cancer

Curative treatment esophageal cancer MCN		(n=1763)		
	2012-2014 (P1*) (n=1022)	2015-2016 (P2*) (n=741)	p**	p ↓ versus ↑***
Total treatment with curative intent				
Cluster 1	(n=222)	(n=196)		
Cluster 2	(n=197)	(n= 155)		
Cluster 3	(n=98)	(n=72)		
Cluster 4	(n= 251)	(n=145)		
Cluster 5	(n= 254)	(n=173)		
Surgery onlyCluster 1	9 (4%)	2 (1%)	0.053	
Cluster 2	27 (14%)↑*	7 (5%)↑*	0.004	
Cluster 3	6 (6%)	0 (0%)↓*	0.033	<0.001 (P1)
Cluster 4	19 (8%)	4 (3%)	0.049	0.067 (P2)
Cluster 5	11 (4%)↓*	6 (3%)	0.655	
CRT* without surgery				
Cluster 1	48 (22%)	37 (19%)	0.487	
Cluster 2	24 (12%)	25 (15%)↓*	0.288	
Cluster 3	23 (24%)↑*	13 (18%)	0.393	0.023 (P1)
Cluster 4	30 (12%)↓*	22 (15%)	0.361	0.513 (P2)
Cluster 5	52 (20%)	36 (21%)↑*	0.933	
Neoadjuvant C(R)T* & surgery with/without adjuvant therapy				
Cluster 1	91 (41%)	97 (49%)	0.081	
Cluster 2	73 (37%)↓*	75 (48%)↓*	0.033	
Cluster 3	47 (48%)	37 (51%)	0.659	0.011 (P1)
Cluster 4	123 (49%)↑*	75 (52%)	0.602	0.446 (P2)
Cluster 5	114 (45%)	91 (53%)↑*	0.117	
Total treatment without curative intent				
Other treatment				
Cluster 1	41 (18%)↑*	29 (15%)	0.316	
Cluster 2	29 (15%)	22 (14%)	0.889	
Cluster 3	6 (6%)↓*	10 (14%)	0.087	0.003 (P1*)
Cluster 4	39 (16%)	23 (16%)↑*	0.932	0.619 (P2*)
Cluster 5	36 (14%)	24 (14%)↓*	0.930	
No treatment				
Cluster 1	33 (15%)↓*	31 (16%)	0.787	
Cluster 2	44 (22%)↑*	26 (17%)↑*	0.194	
Cluster 3	16 (16%)	12 (17%)	0.953	0.049 (P1*)
Cluster 4	40 (16%)	21 (14%)	0.699	0.042 (P2*)
Cluster 5	41 (16%)	16 (9%)↓*	0.040	

* CRT: ChemoRadioTherapy; CT: ChemoTherapy; P1: 2012-2014; P2: 2015-2016; ↓: cluster of hospitals with the lowest percentage of patients receiving (a specific) treatment with/without curative intent; ↑: cluster of hospitals with the highest percentage of patients receiving (a specific) treatment with/without curative intent.

** Statistical difference between P1 and P2.

*** Statistical difference between the cluster of hospitals with the lowest percentage of patients receiving (a specific) treatment with/without curative intent versus the cluster of hospitals with the highest percentage of patients receiving (a specific) treatment with/without curative intent, calculated for P1 and P2 separately.

Additional file 4 Overall survival for patients with potentially curable esophageal cancer

	Esophageal cancer MCN	2-year OS*
2012-2016: treatment with curative intent	1224	
Cluster 1	284	0.63 (0.57-0.68)
Cluster 2	231	0.56 (0.49-0.62)
Cluster 3	126	0.58 (0.49-0.67)
Cluster 4	273	0.60 (0.54-0.66)
Cluster 5	310	0.63 (0.57-0.68)
2015-2016: treatment without curative intent	539	
Cluster 1	134	0.16 (0.10-0.23)
Cluster 2	121	0.10 (0.05-0.17)
Cluster 3	44	0.05 (0.01-0.15)
Cluster 4	123	0.11 (0.06-0.17)
Cluster 5	117	0.09 (0.05-0.16)

* OS: overall survival.

CHAPTER 10

Discussion and future perspectives

DISCUSSION

In the first part of this thesis the evidence for developing and implementing care pathways in cancer care were presented, which was the first aim of this thesis. As shown in **Chapter 2** and **Chapter 3** the evidence base for the added value of pathways in cancer care in the international literature is rather limited. However, there was evidence for a reduced length of stay in favor of care pathways for some tumor types. Unfortunately, conclusions about readmissions and complications of patients after the implementation of care pathways were not conclusive enough, mainly because the number of included studies was low. Nevertheless, for this review we restricted the study design inclusion criteria to RCT's and controlled study design, leaving out the uncontrolled studies, case studies, and descriptive studies focusing on implementation of care pathways without control groups to compare the results with. Probably we would find more studies after a literature search with less restrictions. Consequently, the evidence would be far more questionable. In addition, because cancer care is known as highly multidisciplinary care in which many health care professionals are involved, we added to part I of this thesis a review about the transitions of cancer care related to care pathways. Based on this review which was presented in **Chapter 4** we can conclude that transitions of the cancer patient in primary and secondary/tertiary health care settings involve various time intervals. Shorter intervals were associated with implemented guidelines in clinical pathways and enhanced coordination of care between settings/professionals. In **Chapter 5** an assessment showed that variation in clinical practice of follow-up was considerable for the organization of aftercare, especially regarding the involved health care professionals and coordination of care. Further, the need for improving guidelines and tools to support personalization had been stressed.

The added value of regional care pathways within an oncology network of collaborating (academic) hospitals and other health care institutions from the professional's and patients' perspective, were studied in the chapters in part II. The papers in **Chapter 6** and **Chapter 7** investigate the effects of regional pathways of respectively three and four hospitals. Based on these results we observed improvements in diagnostics and treatment after the implementation of the regional care pathway. In the study about the regional care pathway for patients with rectal cancer in four hospitals (**Chapter 7**) it was shown that, based on clinical and process indicators, improvements were achieved after one year which maintained for three years after implementation of the pathway. According to the health care professionals the regional care pathway has led to working according evidence-based guidelines, and the pathway provided a solid basis for standardization of care and further regional cooperation. In **Chapter 8** regional pathways were evaluated which were implemented in a larger oncology network including seven hospitals and two radiotherapeutic institutions. Based on these outcomes evidence was found for better compliance to the guidelines as well as the regional agreements for diagnostic procedures, and the waiting times to the MDT meeting decreased. However, we did not find evidence about effect of these regional care pathways on patients

outcomes, such as postoperative mortality and survival. Qualitative data based on interviews with health care professionals and patients, showed that regional care pathways contributed to better structured and efficient care for patients with esophagogastric cancer within a more adequate collaborated team. In **Chapter 9** a retrospective variance analysis was performed over five years for patients with esophageal cancer regarding the treatment and waiting times before start of treatment within a network of 17 hospitals. Variation was calculated for treatment modalities and lead time to the start of treatment and 2-year survival, between clusters of hospitals discussing patients in regional MDT meetings. The results showed limited variation between clusters of hospitals within the oncology network for different treatment modalities. In addition, opportunities for future improvement lie in reducing the lead times to start of treatment between the clusters of hospitals.

Collaboration between health care organizations within oncology networks

Based on the interviews with health care professionals which are presented in **Chapter 6**, **Chapter 7** and **Chapter 8** the process of developing a regional care pathway has led to the acquaintance between health care professionals and more personal contacts regarding the care for patients in different hospitals and other health care organizations. Moreover, a reinforcement of these contacts, leading to smoother patient transfers between health care organizations, was a result of implementing the pathway. Furthermore, the increased personal contacts between health care professionals influenced a more adequate (regional) MDT meeting with more focus on the total care process leading to better treatment advices. Literature showed effective decision-making in the MDT meeting was found to be mediated by having a clear purpose, agreed processes and a team atmosphere that facilitates inclusion and improvement¹. The importance of the team atmosphere was confirmed in the study presented in **Chapter 8**. This study showed that also a more effective MDT meeting was mainly due to the pleasant working environment created by the involved health care professionals making it easier to provide each other feedback based on guidelines, developments and the regional agreements. Job satisfaction of health workers is referred to as important for motivating employees and improving efficiency, because higher job satisfaction is known to improve employee performance and patient satisfaction². In addition, patients stated they experienced more efficient and personal care within the region when health care professionals knew each other better and the interaction between them was characterized as more personal. Probably, patients who do not exactly fit in the care pathway and were monitored otherwise, also benefit from these improved personal communication structures.

Multidisciplinary Team (MDT) meetings

As a central part of the care pathway, MDT meetings in cancer care are a clinically valued resource allowing a diverse range of health care experts, necessary for increasingly complex cancer care, to come together and discuss treatment options for patients³. MDT meetings have widely been

implemented in cancer care based on the principle that interdisciplinary case discussions lead to improved treatment recommendations based on updated and evidence-based knowledge or expert opinion. The MDT meeting structure is broadly considered to improve communication, coordination and decision making⁴. The importance of a (regional) MDT meeting was confirmed in the studies presented in **Chapter 6** and **Chapter 8**, in which participants of the network mentioned the MDT meeting as an important basis for the collaboration within the oncology network. Core MDT meeting expertise varies between diagnoses, but typically includes surgeons, medical oncologists, organ specialists, radiation oncologists, radiologists and pathologists. More recently, experts in nuclear medicine and molecular pathology, contact nurses, research nurses and cancer care coordinators have been added to the multidisciplinary team¹. When nurses are actively involved in care planning in these meetings, the team is perceived as performing at a higher level. Similarly, teams reported that presence of nursing staff and more diverse teams were associated with increased effectiveness^{5,6}. This correlates to the findings in **Chapter 8**, in which health care professionals emphasized the tasks and responsibilities of the case managers, which was mainly fulfilled by nurses or nurse specialists. Furthermore, nurses tend to involve patients' views in the decision-making process more than medical staff does. This is important because only 4% of MDT meeting discussions involve holistic information of patients directly in the decision-making process⁶.

Transmural character of regional care pathways

The MDT meeting, as a central connection for multidisciplinary knowledge exchange and decision making, brings health care professionals involved in the care and treatment for cancer patients together. However, care and treatment is more and more taking place in multiple hospitals and health care institutions and, sometimes, simultaneously in primary, secondary and tertiary care. This sets requirements for an adequate exchange of information between health care organizations, concentration and dissemination of clinical expertise and agreements about financing expensive drugs and technologies as well as hospitals visits and consultation. Therefore, pathways should have a transmural character and focus on the whole patient process from the first symptom through the diagnostic and treatment process to survival or palliative care. Transmural care has been defined as: 'care, attuned to the needs of the patient, provided on the basis of co-operation and co-ordination between general and specialized caregivers with shared overall responsibility and the specification of delegated responsibilities'⁷. However, in literature and clinical practice care pathways are not always defined as transmural care pathways, in which the total care and treatment is included. Cancer care pathways in clinical practice mainly focus on the diagnostic and treatment process, some pathways are particularly focused on the care process for potentially curable patients, but less attention is given to care for patients with non-curable cancer as well as follow-up, aftercare and palliative care. In addition, cancer care has been shifting from a disease-focused to a holistic approach, in which more attention is paid to psychosocial aspects, quality of life, patients' rights and empowerment and survivorship⁸. Therefore, a transmural approach

of care supported by transmural care pathways including all health care organizations and other health care professionals within primary, secondary and tertiary care is necessary. An opportunity to guarantee the continuity within the transmural care pathway, could be the expansion of the role of the GP realizing continuous support for the cancer patient throughout the whole pathway. Lang and colleagues studied the role of the general practitioner in cancer care and found that patients want their GP to take an active part in the cancer therapy. Early integration of the GP may also enhance early integration of palliative care and also help family members and caregivers. A strategy to integrate GPs is the establishment of shared care models, in which GPs are supported by specialists and get additional training in cancer care⁹.

Methodology used to deal with context dependent factors

As care pathways seem to influence patients outcomes, the context in which care pathways were developed and implemented could not be seen separately from other developments within health care in general and cancer care in specific. Care pathways are often based on (evidence-based) guideline, the development and revisions of relevant guidelines will affect (regional) care pathways directly. Other context factors which can influence care pathways are new developments in health care, such as new available drugs, new standards and norms and indicators from the government or professionals associations, new technologies, eHealth, and modern communication technology, such as video consultation, which is now rapid evolving after the COVID-19 pandemic.

Differences in patients outcomes or variation in cancer care can be caused by variations in health care structures, and organizational aspects within health care organizations, such as the availability of diagnostic resources and treatment facilities. Furthermore, the absence or presence of certain health care disciplines within a health care organization can be decisive, such as specialized nurses, who can have a coordinating role within the care process and can keep an overview on the total care pathway. Therefore, in this thesis the studies presented in **Chapter 6**, **Chapter 7** and **Chapter 8** were performed using a mixed methods study design. A mixed methods design is characterized by the combination of at least one qualitative and one quantitative research component¹⁰ and can be defined as 'a type of research in which a researcher or a team of researchers combines elements of qualitative and quantitative research approaches (e.g. use of qualitative and quantitative viewpoints, data collection, analysis, inference techniques) for the broad purposes of breadth and depth of understanding and corroboration'¹¹. The overall goal of mixed methods research, of combining qualitative and quantitative research components, is to expand and strengthen a study's conclusions and, therefore, contribute to the published literature¹⁰. By using a mixed methods study design in the studies described in **Chapter 6**, **Chapter 7** and **Chapter 8** the quantitative data could be combined with qualitative information and explanation from health care professionals and patients. In addition, the conclusions were strengthened based on the additional qualitative data. Moreover, added value of the care pathway on improvements in collaboration and communication were revealed, which otherwise would not have been included in the study results.

FUTURE PERSPECTIVES

Care pathways have been implemented in Dutch health care since 1970 and were introduced in oncological care to deal with the coordination of multidisciplinary actions for care and treatment. In the last decade, more and more oncology networks have been formed due to changing demographics, new developments, revised guidelines, and external demands. These oncology networks intend to provide the best quality of care and treatment for all patients with cancer within a region. When networks enable an open environment for health care professionals, where knowledge can be shared and mutual feedback can be expressed, the results of this thesis show that this could lead to better personalized care and treatment for cancer patients. Likewise, Haire and colleagues stated that integration of cancer, when organizations work through a network or alliance to deliver services, has the potential to change the traditional model of service provision moving away from the clear demarcations between primary, secondary and tertiary care to one which is designed around the needs of the patient¹².

Nevertheless, a challenge for oncology networks concerns the possible differences in interest regarding collaboration between the managing directors of hospitals versus the medical and nursing specialists who are working with patients. While the board of directors focus on quality and safety of care, whereby the financial implications of the (concentration) agreements will also be important, the health care professionals mainly focus on their own working field and optimizing the quality of care for patients. A system of integral financing of care and treatment transcending health care settings could provide a certain basis for transmurall collaboration and realize (regional) agreements.

Primary and secondary health care

The multidisciplinary character of cancer care, the increased complexity of care, and the specialization of treatment in multiple hospitals, will require care pathways in which coordination of cancer care and treatment is facilitated. Coordination of care can be defined as: the deliberate organization of patient care activities between two or more participants involved in a patients' care to facilitate the appropriate delivery of health care services."¹³. In this definition, all providers working with a particular patient share important clinical information and have clear, shared expectations about their roles. Equally important, they work together to keep patients and their families informed and to ensure that effective referrals and transitions take place. In case when patients receive treatment in different hospitals at different locations within a region, coordination of patients care and treatment is of great importance. Often the coordination of care within one organization/hospital is concentrated in one person: the so called case manager. Transmurally seen, the role of 'case manager' could be fulfilled by the GP. This would require a higher level of integration between primary and secondary health care. In the light of reducing the health care costs, it would be worthwhile to investigate whether more expensive care and treatment provided to patients

in secondary care, can be transferred to the cheaper primary health care setting. Initiatives to transfer secondary cancer care and survivorship care from secondary health care to primary or intermediate care, have been undertaken particularly due to improved cancer survival, and considering the anticipated shortage of oncology providers¹⁴. However, there are many barriers to be overcome regarding the financial consequences, workload, organization, communication and expertise. An important condition to transfer secondary health care to primary care seems to be the involvement of the primary health care professionals in the all phases of the care process. Chaput and colleagues reported obstacles for the provision of comprehensive care to cancer survivors by primary care providers, such as adequate information from oncology providers to primary care providers¹⁵.

Technologies

Another condition for the integration of cancer services is shared informatics systems by using mutual exchangeable IT systems and Electronic Health Records (EHR)¹². Clearly, communication failures between physicians and nurses are one of the most common causes of adverse events for hospitalized patients, as well as a major root cause of all sentinel events¹⁶. In most network hospitals and other health care organizations health care professionals have to deal with different systems for the patients EHRs provided by different suppliers. To facilitate oncology networks and their communication even more, uniform health information technology may optimize the communication technology (i.e., the electronic medical record, computerized provider order entry, email, and pagers)¹⁶. This can provide uniform and safe communication transfers of text and imaging between different health care organizations within the collaboration to realize efficient and personalized care and treatment for cancer patients.

Another technology which can be relevant in the future is video consultation. Video consultation is a communication technology that allows two or more locations to connect in real-time two-way video and audio transmission¹⁷. This type of technology enables patients to access health care services, by using the internet, without the burden of distant travel. Eliminating health disparities such as advanced age, physical disability, and isolated geographic location are possible through this technology. Video consultation could be particularly relevant in improving health, care management, access and cost in the care of chronic illnesses. While video consultation has been found to be feasible and effective, a low number of randomized controlled trials limit evidence¹⁸. During the COVID-19 pandemic alternative communication possibilities, such as video consultations evolved rapidly and might be expanded in future health care. Consequently, the use of communication via telephone, video and other online consultations, can lead to broader possibilities to provide (coordinated) care regarding specific needs of patients and better access to health care providers.

The role of the patient

Patient participation is increasingly recognized as a key component in the redesign of health care processes and is advocated as a means to improve patient safety¹⁹. Literature is available about the non-negligible role of patient participation in enhancing health care service, including the nurse-patient relationship, shared decision making, chronic disease treatment, and a redesign of health care systems²⁰. Past research has widely shown the positive influence of patient participation on patients, most notably on patient satisfaction, patient safety, quality of health care, patient psychological well-being, and clinical outcomes^{19,21,22,23,24}. Implementation research has shown that patient involvement is a crucial factor for the success or failure of care pathway interventions in terms of the quality of care and clinical efficiency²⁵. A plain language version of a care pathway for guidance of the patient and shared decision-making could lead to increasing compliance and patient safety²⁶.

Following the trend of concentration of treatment and collaboration in cancer care may have implications for patients, such as receiving treatment in another hospital than the hospital of diagnosis. Therefore, patients should be informed well about treatment choices and the quality of care to realize shared decision making on health care organizations or health care professionals. Participants of oncology networks should provide adequate information about which care is delivered in which hospital, based on the network agreements, and the choices patients can make for their own care process. Also patients organizations can help to provide solid and conceivably patient information. Another challenge for health care professionals within this trend of network collaboration is to deliver personalized care to patients, because more health care professionals are involved and care pathways are aiming to standardize care, and reduce unnecessary practice variation²⁷. Patients can take advantage of a coordinating health care professional, such as a case manager in the hospital and/or a GP who has personal contacts with the patient, which leads to a focus on the whole care pathway from the first symptoms throughout cancer treatment up to follow-up and aftercare, including cancer survivorship or palliative care. Therefore, the health care professional with this coordinating role, should be involved in all phases of the patients' cancer care pathway. Optimal added value of care pathways can only be achieved by a multidisciplinary transmurial approach including patients.

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Summary

SUMMARY

Cancer is the second leading cause of death globally, accounting for an estimated 9.6 million deaths, or one in six deaths, in 2018. The main reasons for the increased incidence of cancer are aging, growth of the population, and changes in the prevalence and distribution of the main risk factors for cancer. Because cancer care is multidisciplinary and complex, it requires close collaboration among care professionals, based on the latest evidence, pooling their expertise and exchanging information.

Care pathways are used worldwide as methods for patient-care management of a well-defined group of patients during a well-defined period of time. They are based on guidelines, best practices and patient expectations by facilitating the communication, and coordinating roles. Care pathway enable sequencing the activities of the multidisciplinary care team, patients and their relatives, by documenting, monitoring and evaluating variances, and by providing the necessary resources and outcomes. Furthermore, care pathways may serve as useful and evidence-based tools to improve quality and outcomes of health care interventions, reduce variation in clinical practice, promote teamwork on a multidisciplinary team, facilitate the use of guidelines, and they may act as a basis for a payment system.

Care pathways were first developed in the 1980s in the United States and the United Kingdom. During the 1990s nursing pathways were developed, in which all aspects of patients care were incorporated, including medical and psychosocial care. Care pathways are widely used in cancer care.

Based on all developments of pathways in health care the main aims of pathways are: improve the multidisciplinary quality of care, reduce risks, increase patient satisfaction, and increase the efficiency in the use of resources.

The aim of this thesis was to determine whether the above mentioned goals for oncological care pathways were achieved. The effects of cancer care pathways were described, focusing on the quality of care, the added value for health care professionals and patients, and the applicability within oncology networks.

Part I

In the first part of this thesis the available literature about care pathways in cancer care was synthesized.

Chapter 2 describes a protocol which was written prior to the systematic review of effects on cancer care pathways. The main goal of this systematic review was to identify, assess, and synthesize high-quality evidence on the effects of cancer care pathways, meeting the Cochrane Effective Practice and Organisation of Care (EPOC) design criteria. The results of the systematic review were presented in **Chapter 3**. Out of more than 13,000 search results, eight studies were included in the review. Most of these studies were performed in secondary or

tertiary care. Length of Stay (LOS) was the most common used indicator, and was reported in five studies. Subgroup meta-analysis showed an overall shorter LOS for patients with gastric cancer and gynecological cancer. Two studies reported measured effects in terms of complications and one study reported effects regarding readmissions. Costs were reported in six studies, and most studies reported significant lower costs in favor of cancer care pathways. Despite the low number of included studies and the differences between these studies, the systematic review provides an evidence base for the subgroup effects of LOS. The effects on complications, readmissions, and costs as well as implications of differences in implementation of cancer care pathways were not conclusive enough. This indicates the need for further well-designed research to provide insight in the effects of cancer care pathways.

As the systematic review focuses on the cancer care pathway, **Chapter 4** examines the availability of evidence regarding transitions in cancer care pathways. This mixed methods review was based on a search conducted in the previous systematic review and aimed to provide a more complete picture of care pathways on transitions of care between primary, secondary and tertiary cancer care. Data analysis was performed using induction (data-driven generalization) and deduction (theory-driven exploration of hypothesis), and three descriptive themes were identified which guided the framework analysis: transition outcomes, coordination between settings and translation of guidelines. In this mixed methods review a total of 16 studies were included. Most studies covered the diagnostic phase, and some studies described transitions in treatment and follow-up. The included studies showed that shorter time intervals were associated with implemented guidelines in care pathways and enhanced coordination of care between settings or professionals.

To get more insight in the organization and personalization of care for patients with breast cancer, **Chapter 5** presents the results of an inventory of aftercare for breast cancer patients. The aim of the study was to gain insight in the similarities and differences in the organization of follow-up and identify best practices and opportunities for the future. After performing semi-structured in-depth interviews with health care professionals in seven Dutch hospitals, variation was found in the organization of aftercare (identifying and managing side and late effects of cancer), especially in timing and frequency and in disciplines of involved health care professionals. Less variation was found for follow-up (aimed at detection of recurrences), which is based on the national guideline. Opportunities for the future focus on improving monitoring of patients' needs, developing a comprehensive guideline for the organization and content of aftercare, and further integration and personalization of follow-up.

Part II

The second part of this thesis investigates the added value of (regional) care pathways for patients with a low-complex high-volume tumor types (breast cancer) as well as a high-complex low-volume tumor types (esophageal and gastric cancer).

Chapter 6 shows the results of an evaluation of a regional care pathway for breast cancer patients in three hospitals. In this study quantitative data was supplemented with qualitative data based on interviews with health care professionals. Fourteen indicators were used to assess the quality of care before and after implementation of the pathway. In order to estimate the impact of the care pathway, related to evidence-based guidelines and profession-based norms, the involved project leaders of the hospitals were interviewed. The main results showed that more patients received a HER2neu test after implementation of the breast cancer pathway. Furthermore, more patients started the first chemotherapy or first radiotherapy within four weeks after surgery. Based on the interviews, the joint multidisciplinary meeting was seen as the key in the breast cancer pathway and was implemented in response to the development and implementation of the care pathway.

In **Chapter 7** the effects of a regional care pathway for patients with rectal cancer were described. This study applied a mixed methods research design and focusses on the long term results after implementation of this rectal cancer care pathway within the four participating hospitals. Data on almost 400 patients were collected from two national databases. Results of seven structure and process indicators were analyzed and compared before and at two time points, over a total period from 2007 and 2012, after implementing a regional care pathway for patients with rectal cancer. Interviews were performed with relevant health care professionals of the participating hospitals to determine the motivation for developing and implementing the care pathway and to interpret the results. The results after implementing the care pathway were: an improved performance of computed tomography (CT) scans in the diagnostic phase, a higher number of patients discussed in the preoperative multidisciplinary meeting, and a reduction in lead time between the first tumor biopsy and the multidisciplinary meeting. Interviews with health care professionals indicated that the regional care pathway led to more clarity about the patient route and more awareness of complying with evidence-based guidelines. In conclusion, the regional care pathway provided a solid base to uniform care, working according evidence-based guidelines and further cooperation within the region. Nevertheless, the waiting and throughput times were affected by the guidelines and norms rather than the care pathway.

In **Chapter 8** an evaluation of a regional collaboration for esophagogastric cancer in seven hospitals and two radiotherapeutic institutions was presented. The aim of this study was to evaluate the regional care pathways and determine the performance of diagnostic procedures, lead time, and patients outcomes, based on data from the Netherland Cancer Registry. In this study quantitative data was combined with qualitative data from health care professionals and patients. To interpret the outcomes more adequate, a national benchmark was included. The results of this study revealed that patients who were treated after the implementation of the care pathways, received more positron emission tomography (PET) scans or PET/CT scans. Furthermore, the lead time from the first diagnostic procedure to the multidisciplinary meeting decreased with at least five days. In addition, patients as

well as health care professionals mentioned a more efficient and personalized care process after implementation of the care pathways. Based on the interviews with health care professionals, the multidisciplinary meeting was mentioned as being of crucial importance in the collaboration. Although the presented changes in this study were similar to the national developments, qualitative data supports the contribution of a regional oncology network to better structured and efficient care for patients with esophagogastric cancer.

Variation of care and the impact of an oncology network to standardize the patient care pathway and reduce unwarranted clinical variation, was the focus of **Chapter 9**. In this study more insight was provided in the variation of care for patients with esophageal cancer care within a network of 17 hospitals, including a national benchmark. The aim of this study was to explore trends in variation of esophageal cancer care between clusters of hospitals discussing patients in a joint multidisciplinary meeting. The results of this study showed that although variation in treatment modalities existed between the clusters of hospitals in 2012-2014, no variation was present in 2015-2016, except for patients who received no treatment at all. In addition, the 2-year overall survival of patients receiving treatment with a curative intent did not vary between the clusters of hospitals. Meanwhile, the median lead time before patients started their treatment with a curative intent did vary between the hospital clusters. This study showed that providing insight in variation of care fits into a continuous learning process within an oncology network.

In conclusion, this thesis showed that cancer care pathways can contribute to better patient outcomes. Besides, the development and implementation cannot be isolated from other developments in health care, in fact care pathway should be based on actual evidence-based guidelines and profession-based norms, and therefore outcomes cannot always be assigned to the care pathway alone. This thesis revealed not only effects of care pathways for patients, but also for health care professionals for whom the process of developing and implementing a care pathway contributed to a more pleasant working environment with personal contacts between colleagues within an oncology network. This thesis also underlines the importance of an effective and goal oriented development of cancer care pathways, including the implementation and continuously monitoring using quantitative and qualitative data to provide high-quality and personalized care, based on the needs of patients.

Nederlandse samenvatting

SAMENVATTING

Wereldwijd is kanker de tweede grootste doodsoorzaak, verantwoordelijk voor ongeveer 9,6 miljoen sterfgevallen, ofwel 1 op de 6, in 2018. De belangrijkste redenen van de toename van het voorkomen van kanker zijn de groei van de populatie, de vergrijzing en de verspreiding van de belangrijkste risicofactoren van kanker. Omdat de zorg voor mensen met kanker multidisciplinair en complex is, is nauwe samenwerking tussen de betrokken zorgprofessionals, gebaseerd op het meest recente onderzoek, waarbinnen kennis en ervaring wordt gebundeld en informatie adequaat wordt uitgewisseld, van groot belang.

Zorgpaden worden veelvuldig ingezet als een methode voor het besturen, organiseren en beheren van de zorg en behandeling van een specifieke groep patiënten gedurende een specifieke tijdsperiode. Zij zijn gebaseerd op richtlijnen, goede voorbeelden en verwachtingen van patiënten. De inzet van zorgpaden faciliteert communicatie, coördinatie en de opeenvolging van activiteiten van het multidisciplinaire team, patiënten en hun naasten. Dit gebeurt enerzijds via het documenteren, beheren en evalueren van verschillen, en anderzijds door te zorgen voor de noodzakelijke middelen en uitkomsten. Ook kunnen zorgpaden dienen als, op wetenschappelijk bewijs gestoelde, instrumenten om de kwaliteit en uitkomsten van interventies in de gezondheidszorg te verbeteren, de variatie in de klinische praktijk te verminderen, de samenwerking binnen een multidisciplinair team te stimuleren, het gebruik van richtlijnen te stimuleren. Ook kunnen zorgpaden fungeren als basis voor een betaalsysteem in de zorg.

Zorgpaden zijn in de jaren 80 ontwikkeld in Amerika en Engeland. Gedurende de jaren 90 zijn verpleegkundige zorgpaden ontwikkeld, waarin alle aspecten van de zorg, inclusief medische en psychosociale zorg, voor patiënten zijn opgenomen. Ook binnen de zorg voor kankerpatiënten worden zorgpaden veelvuldig ingezet.

Concluderend zijn de belangrijkste doelen van zorgpaden: verbeteren van de multidisciplinaire kwaliteit van zorg, verminderen van risico's, verhogen van patiënttevredenheid, verbeteren van de inzet en het gebruik van beschikbare middelen.

Het doel van dit proefschrift is om te bepalen of bovengenoemde doelen voor zorgpaden in de oncologie zijn bereikt. De effecten van zorgpaden worden beschreven, waarbij de focus ligt op de kwaliteit van zorg, de toegevoegde waarde voor zorgprofessionals en patiënten en de toepasbaarheid binnen oncologische netwerken.

Deel I

In het eerste deel van dit proefschrift is de beschikbare literatuur over zorgpaden in de oncologische zorg ondergebracht.

Hoofdstuk 2 beschrijft een protocol dat is geschreven voorafgaand aan de uitvoering van de systematische review over de effecten van zorgpaden in de oncologische zorg. Het belangrijkste doel van deze systematische review was om wetenschappelijk bewijs van hoog

niveau te identificeren, te beoordelen, met elkaar in verband te brengen en samen te vatten. Hierbij is voldaan aan de Cochrane Effective Practice and Organisation of Care (EPOC) criteria. De resultaten van deze systematische review zijn gepresenteerd in **Hoofdstuk 3**. Vanuit meer dan 13.000 zoekresultaten zijn uiteindelijk acht studies geïncludeerd in deze review. De meeste van deze studies zijn uitgevoerd in de 2^{de} of 3^{de} lijns zorg (ziekenhuizen of expertise centra). De uitkomst 'duur van het verblijf in het ziekenhuis' was de meest gebruikte indicator en werd gerapporteerd in vijf studies. De uitgevoerde meta-analyses voor subgroepen van patiënten toonde een kortere verblijfsduur aan voor patiënten met maagkanker en gynaecologische kanker. Twee geïncludeerde studies rapporteerden de gemeten effecten betreffende complicaties en in één studie werd het effect van heropnames beschreven. De kosten werden gerapporteerd in zes studies en de meeste studies lieten significant minder kosten zien voor de zorg die volgens een zorgpad aan patiënten met kanker was verleend. Ondanks het beperkt aantal geïncludeerde studies en de verschillen tussen deze studies voorziet deze systematische review in een wetenschappelijke basis voor de effecten van zorgpaden in de oncologische zorg voor de verblijfsduur in het ziekenhuis voor subgroepen van patiënten. De effecten van complicaties, heropnames en kosten, alsook de implicaties van de verschillen in de implementatie van oncologische zorgpaden, waren niet doorslaggevend genoeg om hieruit conclusies te kunnen trekken. Dit geeft aan dat er behoefte is aan gedegen vervolgonderzoek, om inzicht te verschaffen in deze effecten van zorgpaden in de oncologie.

Waar in de systematische review de focus werd gelegd op het oncologische zorgpad, is in **Hoofdstuk 4** naar beschikbare wetenschappelijk bewijs in de literatuur gezocht over zorgpaden waarbij transitie in de kankerzorg een rol spelen. Deze review is gebaseerd op de zoekresultaten vanuit de eerdere systematische review met als doel om een meer compleet beeld te verkrijgen van zorgpaden en de hieraan gerelateerde transitie tussen eerste, tweede en derde lijns gezondheidszorg. De data werd geanalyseerd via het principe van inductie (data gedreven generalisatie) en met behulp van deductie (theorie gedreven exploratie van hypothesen). Drie beschrijvende thema's zijn geïdentificeerd die leidend zijn voor het raamwerk van de analyse: transitie uitkomsten, coördinatie tussen zorginstellingen en vertaling van richtlijnen. In deze review zijn in totaal 16 studies geïncludeerd. De meeste studies betreffen de diagnostische fase, enkele studies beschrijven de transitie van zorg in de fases van behandeling en follow-up. De resultaten van deze review laten zien dat kortere tijdsintervallen zijn geassocieerd met geïmplementeerde richtlijnen in zorgpaden en verbeterde coördinatie van zorg tussen zorgorganisaties en zorgprofessionals.

Voor het verkrijgen van meer inzicht in de organisatie en personalisatie van zorg voor patiënten met borstkanker zijn in **Hoofdstuk 5** de resultaten van een inventarisatie van de follow-up en nazorg voor borstkanker patiënten beschreven. Het doel van deze studie was om inzicht te krijgen in de overeenkomsten en verschillen in de organisatie van de follow-up alsook om de goede voorbeelden en mogelijkheden voor de toekomst te identificeren. In zeven Nederlandse ziekenhuizen zijn semigestructureerde diepte interviews met zorgprofessionals uitgevoerd. Variatie bleek te bestaan in de organisatie van nazorg (identificeren en aandacht

voor bijwerkingen en late gevolgen van kanker of de behandeling), specifiek in de timing en frequentie van nazorg en de disciplines van betrokken zorgprofessionals. Minder variatie was gevonden voor de follow-up (detectie van terugkeer van kanker of nieuwe tumoren), mede omdat dit is gebaseerd op de landelijke richtlijn. Mogelijkheden voor de toekomst worden gezien in verbeteren van de monitoring van behoeften van patiënten, het ontwikkelen van een veelomvattende richtlijn voor de organisatie en de inhoud van nazorg en verdere integratie en personalisatie van de follow-up.

Deel II

Het tweede deel van dit proefschrift richt zich op de toegevoegde waarde van (regionale) zorgpaden voor enerzijds patiënten met een laag-complex hoog-volume tumortype (borstkanker) en anderzijds patiënten met een hoog-complex laag-volume tumortype (slokdarm- en maagkanker).

Hoofdstuk 6 presenteert de evaluatie van een regionaal zorgpad voor borstkanker patiënten in drie ziekenhuizen. In deze studie zijn de kwantitatieve data aangevuld met kwalitatieve data vanuit interviews met zorgprofessionals. Patiënten die voorafgaand aan de implementatie van het gezamenlijke borstkanker zorgpad zijn behandeld, werden vergeleken met patiënten die na de implementatie zijn behandeld. In totaal zijn 14 indicatoren gebruikt om de kwaliteit van zorg te beoordelen. Om de impact te bepalen van het zorgpad in relatie tot richtlijnen en beroepsnormen, zijn de projectleiders van de ziekenhuizen geïnterviewd. De belangrijkste resultaten laten zien dat een HER2neu test bij meer patiënten is toegepast na implementatie van het borstkanker zorgpad. Verder zijn na implementatie meer patiënten binnen vier weken nadat de chirurgische behandeling heeft plaatsgevonden, gestart met de eerste chemotherapie of de eerste radiotherapie. Vanuit de interviews bleek dat het gezamenlijke multidisciplinaire overleg werd gezien als het centrale punt in het borstkanker zorgpad, welke was geïmplementeerd als vervolg op de ontwikkeling en implementatie van het zorgpad. Het zorgpad was daarom faciliterend voor de implementatie van de landelijke richtlijn.

In **Hoofdstuk 7** zijn de effecten van een regionaal zorgpad voor patiënten met endeldarmkanker beschreven. Voor deze studie is een combinatie van kwantitatieve en kwalitatieve onderzoeksmethoden toegepast met als focus de lange termijn resultaten na implementatie van het endeldarmkanker zorgpad in vier deelnemende ziekenhuizen. Data vanuit twee landelijke databases werden verzameld. De resultaten van zeven structuur- en proces indicatoren werden voorafgaand en op twee tijdstipmomenten, na de implementatie van het regionale zorgpad voor patiënten met endeldarmkanker, over een totale periode van vijf jaar geanalyseerd en met elkaar vergeleken. Interviews werden uitgevoerd met zorgprofessionals van de deelnemende ziekenhuizen om de motivatie voor de ontwikkeling en implementatie van het zorgpad te bepalen en om de resultaten te interpreteren. De belangrijkste resultaten na de implementatie van het zorgpad waren: een verbeterde uitvoering van computer tomografie (CT) scans in de diagnostische fase, een hoger aantal

patiënten dat werd besproken in het preoperatieve multidisciplinaire overleg en een vermindering van de tijd tussen de eerste tumor biopsie en het multidisciplinaire overleg. Interviews met zorgprofessionals geven aan dat het regionale zorgpad heeft geleid tot meer duidelijkheid over de route die de patiënt doorloopt. Ook heeft het zorgpad geleid tot meer bewustzijn van de zorgverlening in relatie tot de landelijke richtlijnen. De conclusie van deze studie is dat het regionale zorgpad heeft voorzien in een basis voor uniforme zorg, voor het werken volgens de landelijke richtlijnen en voor verdere samenwerking binnen de regio. Desondanks bleek dat de wacht- en doorlooptijden niet zozeer beïnvloed zijn door het zorgpad, maar met name door richtlijnen en normen.

In **Hoofdstuk 8** is een evaluatie van een regionale samenwerking voor patiënten met maag- of slokdarmkanker in zeven ziekenhuizen en twee radiotherapeutische instituten beschreven. Het doel van deze studie was om de regionale zorgpaden te evalueren en de uitvoering van diagnostische procedures, doorlooptijden, en patiënt uitkomsten te bepalen op basis van geregistreerde data. Deze data zijn gecombineerd met informatie vanuit interviews met patiënten en zorgprofessionals. Om de regionale uitkomsten meer adequaat te interpreteren, is een landelijke benchmark geïncorporeerd. De resultaten van deze studie laten zien dat patiënten die behandeld waren na de implementatie van het zorgpad vaker positron emissie tomografie (PET) scans of PET/CT scans hebben ontvangen, zoals ook de richtlijn adviseert. Verder daalde de doorlooptijd tussen de eerste diagnostische procedure tot het multidisciplinaire overleg met tenminste vijf dagen. Na de implementatie van het zorgpad benoemden patiënten en zorgprofessionals het zorgproces efficiënt en gepersonaliseerd. Gebaseerd op de interviews met zorgprofessionals, bleek dat het multidisciplinaire overleg van cruciaal belang is in de samenwerking. Hoewel de gepresenteerde veranderingen vergelijkbaar zijn met de landelijke ontwikkelingen, blijkt uit de kwalitatieve data dat het regionale oncologische netwerk bijdraagt aan betere gestructureerde en efficiëntere zorg voor patiënten met maag- of slokdarmkanker.

Het standaardiseren van het zorgpad voor de patiënt en verminderen van ongewenste klinische variatie was de focus van de studie die beschreven is in **Hoofdstuk 9**. In deze studie werd inzicht verkregen in de variatie van zorg voor patiënten met slokdarmkanker in een oncologisch netwerk van 17 ziekenhuizen. Hierbij werd ook een landelijke benchmark toegevoegd. Het doel van deze studie was trends te ontdekken in de variatie van de zorg voor patiënten met slokdarmkanker tussen clusters van ziekenhuizen die gezamenlijk patiënten in een multidisciplinair overleg bespreken. De resultaten van deze studie laten zien dat, ondanks dat er variatie was geconstateerd in de behandelingsmodaliteiten tussen de ziekenhuisclusters tussen 2012 en 2014, deze niet aanwezig was in de daaropvolgende periode tussen 2015 en 2016, behalve voor patiënten die geen behandeling hebben ontvangen. Ook bleek dat de 2-jaars overleving voor patiënten die een behandeling met curatieve intentie hebben ontvangen, niet verschilde tussen de clusters van ziekenhuizen. Wat wel verschilde tussen de ziekenhuisclusters was de mediane doorlooptijd voordat patiënten starten met

een behandeling met curatieve intentie. Deze studie laat zien dat inzicht in de variatie van zorg past in een continue leerproces van een oncologisch netwerk.

Concluderend laat dit proefschrift zien dat zorgpaden voor mensen met kanker bijdragen aan betere kwaliteit van zorg en uitkomsten voor patiënten. Daarbij kan de ontwikkeling en implementatie van zorgpaden niet los gezien worden van andere ontwikkelingen in de gezondheidszorg, sterker nog: in feite dient een zorgpad juist gebaseerd te zijn op actuele landelijke richtlijnen en beroepsnormen. Daarom kunnen uitkomsten die we hebben gevonden niet altijd alleen aan het zorgpad worden toegeschreven. Dit proefschrift onthult niet alleen effecten van zorgpaden voor patiënten, maar ook voor zorgprofessionals voor wie het proces van de ontwikkeling en implementatie van een zorgpad bijdraagt aan een prettiger werkomgeving met persoonlijke contacten tussen collega's werkzaam binnen een oncologisch netwerk. Ook wordt in dit proefschrift het belang onderstreept van een effectieve en doelgerichte ontwikkeling van zorgpaden. Hierbij is aandacht voor implementatie en continue monitoring met behulp van kwantitatieve en kwalitatieve data van belang, om patiënten gepersonaliseerde zorg en kwalitatief hoogwaardige zorg en behandeling te bieden, gebaseerd op de behoeften van patiënten.

Dankwoord

DANKWOORD

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Curriculum Vitae

CURRICULUM VITAE

Jolanda Christina van Hoeve was born on May 18th, 1973 in Zuidhorn, the Netherlands. She completed secondary school at Augustinus College in Groningen in 1991. Thereafter, she followed higher professional education for nursing at Hanzehogeschool in Groningen, and obtained her bachelor's degree in Health Science, study route Nursing Science in 1998. After her first job at a mental health hospital where she worked as a quality employee, she started working at the Cancer Organisation in the Eastern part of the Netherlands (IKST) in 2006. Her activities focused on the organization of oncological care. In particular coordinating the

development and implementation of care programs, self-evaluations and audits/site visits, as well as supporting regional and national health care working groups, networks and patient representative groups. After starting as an external PhD student at the University of Twente, she continued working as advisor in oncology at the Netherlands Comprehensive Cancer Organisation (IKNL), which hosts the Netherlands Cancer Registry. She is participating in projects and research on breast cancer and esophagogastric cancer. In addition, she support multiple multidisciplinary working groups, for the revision of the evidence-based breast cancer guidelines in the Netherlands and regional tumor working groups. Besides her work for IKNL, she works since June 2020 for the Organisation of European Cancer Institutes (OECI) to contribute to (benchmark)projects and organize peer review visits in European cancer centers.

List of publications

LIST OF PUBLICATIONS

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