

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 synthesise existing literature on the effects of pathways in oncological care.

Methods

All patients diagnosed with cancer in primary and secondary 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 "patient outcomes" and "costs" were extracted from each study.

Results

Out of 12,689 search results, we selected 158 articles eligible for full text assessment. The remaining 10 studies represented 4,786 patients. Most studies were conducted in secondary care. LOS was the most common used indicator for patients outcomes, and was reported in five studies. Meta-analysis based on subgroups showed an overall shorter LOS regarding gastric cancer (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 care regarding the positive effects of LOS in favour 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 healthcare and have been implemented since the 1980s [2]. Care pathways provide a means to improve multidisciplinary communication and care planning, including primary and secondary care. Further, pathways aim to improve communication between clinicians and patients as well as patient satisfaction [3]. In addition, care pathways are described to have a positive impact on quality of care, efficiency and teamwork [4,5]. Rotter et al [6] 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 costs. 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 available [7].

Cancer care is complex and relies upon careful coordination between multiple healthcare 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 needed [8]. Therefore, care pathways are often used in cancer care and are seen as a method to provide patient-centred care, reduce waiting times and improve quality of cancer care [9,10].

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 "patient outcomes" and "costs" will be presented. Because cancer care is characterized by coordination and multidisciplinary communication within and between healthcare organizations, we

searched for literature in primary as well as secondary healthcare. 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 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 utilisation studies), where available. Retrospective cohort studies, prospective cohort studies, cross-sectional studies, and case-control studies were excluded.

Types of participants

Eligible participants for inclusion in this systematic review were patients in primary, secondary care, and transitional care which includes the coordination and continuity of healthcare 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.

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 healthcare 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 care [11]. 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 objectively 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. An additional file shows an overview of the inclusion criteria for this systematic review [see additional file 1].

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 June 1, 2019. The search strategy is shown in an additional [see additional file 2]. Two reviewers independently screened all titles and abstracts (JvH,RV), using Covidence [12]. 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.

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” [13]. 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 year [13].

For calculating the pooled effects estimate, called Weighted Mean Difference (WMD), we used Review Manager from the Cochrane Collaboration [14]. To assess the comparability of the results from individual studies and included subgroups, we used the statistic for quantifying inconsistency: $I^2 = [(Q \text{ df})/Q] \times 100\%$ [15]. We considered an overall test-value greater than 60% to serve as evidence of substantial heterogeneity of a magnitude were statistical pooling is not appropriate [15].

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.

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) [16]. A third reviewer was available for consultation in case of disagreements between the two reviewers (TR).

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 Calculator [17]. 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 Calculator [18].

Results

Search results

The specialized search strategy led to 12,689 results. After removing duplicates, all of the 12,675 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, 148 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 or the intervention did not meet our definition of cancer care pathways (23 studies). Finally, 10 studies matched our methodological requirements. In an additional file the PRISMA flow diagram is presented [see Additional file 3]. In Table 1 the key characteristics of the included primary studies included are presented. 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 which were conducted in the secondary healthcare setting separate from the study conducted within both primary and secondary healthcare, because these settings differ, for instance in location, patient population and organization.

Please insert Table 1

Results of studies conducted in the secondary healthcare (hospital care) setting

Intervention characteristics

The majority of the included studies (nine studies) were conducted in the setting of secondary healthcare, within hospitals or in oncology centres [19–27]. These studies represented 1,494 patients. The evidence base of pathway interventions in two studies remained “not sure”, these studies are pending review because the authors did not reply to our emails and phone calls [19,25].

The specific interventions regarding the pathways described in the included studies, showed considerable variation. In three studies a description of the pathway as well as a figure of the pathway was provided [20,23,26]. In six studies the care pathway focused on the perioperative phase in order to guide surgical management [20–24,26]. One study presented a pathway for the hospital staff as well as a pathway for patients [23].

In most studies focussing on pathways for the surgical care, key components which were addressed in these pathways were described. The following components were mentioned most frequently: nutrition and diet [20,22–24,26], diagnostic modalities and laboratory tests [20,22,23,26], medication [20,23,24,26], patient education [22,24,26], preoperative consultation and visits [20,23,26], drains [21,23], activity [20,26], clinical procedures and treatment [20,26], discharge planning or -instruction [20,26], assessment and preadmission testing and evaluation [20,23], and psychosocial support and education [20,26]. Other components which were mentioned in one study only: performance status, outcome criteria, follow-up criteria, and follow up care [20], pain management and pain control, and deep vein thrombosis prophylaxis [22], preoperative bowel preparation and fasting, and removal of nasogastric tube [23], removal of a catheter and mobility [24].

One study included in this review was not focused on surgical care and investigated pain management, including an initial consultation with a control pain doctor and weekly follow up sessions [27].

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) Group [28].

Randomised controlled study (NRS) designs

We included two studies which applied randomized study designs [24,27]. In these studies patients were randomized to either a pathway group or a non-pathway group.

Interrupted time series studies

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 [21,22]. In one study pathway groups at 12 and 36 months after implementation were compared to a pre-pathway group [21], and in the other study a pre-pathway group and pathway groups at six, 12, and 18 months after implementation were used [22].

Non-randomized controlled trials

In three studies a non-randomized controlled trial study design was applied [20,23,26]. In these studies patients in the non-pathway group received general care, and simultaneously patient 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 group [20].

Tumor location

In the articles patients with different tumors were studied: three studies described the effects of pathways for head and neck cancer [20,21,27]. Other studies presented the results of pathways for gastric cancer [23,24], gynaecological cancer [22], and breast cancer [26].

Sample size

The number of included participants varied, and ranged from less than 70 patients to more than 600 patients [20–24,26,27].

Country

Three studies were conducted in Asia [23,24,26]. In addition, two studies were performed in the United States of America (USA) [21,22], and one in Europe [27].

Setting

Three studies were conducted in general and non-academic hospitals or oncology centres [24,26,27]. Other studies were performed in an academic hospital [20,21,22]. In one study the setting was not clearly reported [23].

Outcomes

Length of stay was the most common used indicator and was reported in five studies [20–24]. The most frequently used quality indicators were complications [20,21,24] and readmission [20–22]. Other outcomes which were reported in the included studies, were: patient satisfaction [26,27], patient anxiety [26,27], morbidity [24], and quality of life [26]. However, these quality outcomes measures were not comparable between the studies.

Costs and hospital charges were described in six studies [20–24,27], but these studies showed considerable differences in definitions and results. Nevertheless, in most studies the actual costs instead of charges were reported [20,22–24,27], because costs are set constant over time. In one study the median total charges per patient was used as the primary outcome [21]. 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 [20,22,24,27]. Medication was included in five studies [20,21,22,24,27]. Facilities, like inpatient ward costs, operation room, medical and surgical supplies were reported in two studies [21,22]. One study included professionals fees [20]. And in another study the costs for patient monitoring and patient education were included [22].

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 time [20] 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 pay [27].

For the outcome measure "length of stay (LOS)" we were able to carry out a meta-analysis.

Quality assessment

Based on the validated criteria suggested by the Effective Organisation of Care Group (EPOC) [15], all studies were assessed as "high risk of bias", except for one study. In an additional file the results of the risk of bias assessment are shown [see Additional file 6]. To appraise the methodological quality of the included cost evaluations the Evers checklist was used, which is recommended for Cochrane Reviews [14]. See Additional file 7.

Effects on LOS

The effects of cancer care pathways on LOS were reported in five studies [20–24]. All included studies that measured LOS, reported results in favour of cancer pathways. However, in only two studies both mean and standard deviation were reported [22,24]. One study reported the mean LOS, and the SD was calculated by using the Revman Calculator [23]. In another study the median and range was reported and the mean as well as the standard deviation were estimated [21] (see 'dealing with missing data' in the methods section). In one study the median was reported only [20], therefore we were not able to calculate the mean and standard deviation. Two studies consisted of two subgroups which were separately studied [22,23].

After conducting a meta-analysis with data of four studies [21–24], which represented a study population of 1079 patients, substantial heterogeneity between the studies was observed ($I^2 = 72\%$). Therefore a forest plot with the pooled effects of all included studies reporting on LOS was not presented. The results of the meta-analysis of subgroups is presented in the section 'subgroup analysis'.

Effects on patient outcomes

Quality outcome measures were reported in four studies [20–22,24]. However, only two studies reported the measured effects in terms of complications [21,24], and one study reported outcomes measures in terms of readmissions [21]. Therefore, statistical pooling of quality outcomes could not be performed. Both studies reporting effects of complications described less observed complications among the pathway groups [21,24]. The study reporting effects of readmissions described less readmissions for the pathway group within 30 days after surgery [21].

Effects on costs

Out of nine studies, six studies reported on costs effects [20–24,27]. In four studies, including two studies with each two subgroups, lower costs were reported for pathway groups [20–22,24], and three of these studies reported a significant reduction of costs related to cancer care pathways [20,23,24]. 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 group [23]. Another study reported lower total and medication costs, but higher total daily costs in the pathway group [24].

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. For more information about the included and excluded costs or charges, see 'interventions characteristics' in the results section. In Table 2 the costs differences are presented. In addition, we have provided the un-discounted cost data in a separate table shown in Additional file 8, to allow readers recalculate the results using any discount rate.

Please insert Table 2

Implementation of cancer care pathways

Information about the implementation of pathways was reported in five studies [20–23,26]. To categorize the detailed information about the reported implementation process of the pathways, we used the refined taxonomy for guideline implementation of Mazza and colleagues [29]. 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 (healthcare professionals, patients), organizational (healthcare professionals, patients, structural) and regulatory.

Professional domain

Present materials at meetings: in two studies healthcare professionals were given information regarding the pathway in order to implement the pathway adequately [20,26]. Also several conferences and seminars were organized for outpatient and inpatient healthcare teams working with a disease site working group. Further, physicians were briefed on the pathway [20]. 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 it [26].

Organizational domain

Creation of an implementation team: in three studies a multidisciplinary group was involved in the development of the pathway [20,21,23]. In one study a core group determined which pathways were developed and a disease site working group was organized to draft the pathway [20]. In another study the pathway was developed and continued to be modified by a multidisciplinary team which included surgeons, nurses, and allied healthcare representatives [21]. In addition, in one

other study the involvement of the multidisciplinary team was less clear [22]. 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 anaesthesia pain service and a pharmacist reviewed the recommendations. Moreover, the nursing team played an active role in developing these pathways [22].

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 used [23].

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 cancer [22] and studies including patients with gastric cancer [23,24]. 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 1 with the subgroup analyses of the effects on LOS.

Insert here: Figure 1 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 (both in the USA) versus the studies performed in Asia (Korea and Japan) were analyzed. However, no association between the 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.

Other subgroups

Subgroup analysis based on differences in the setting in which the studies were conducted could not be performed, because one study was performed an academic hospital setting, one study in a non-academic setting and the setting of the other study was unclear. In addition, subgroups based on the risk of bias of the included studies could not be

performed also, because all studies were assessed as "high risk of bias" except for one. Furthermore, subgroups based on the age of the population were not possible, due to the fact that the mean age of the included studies was not distinctive enough to form different subgroups.

Sensitivity analysis

First, 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 ($\text{WMD: } -2.75; \text{ } I^2 = 59\%$).

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 healthcare (hospital care) setting

Intervention characteristics

The study about cancer pathways for patients with colorectal cancer, lung cancer, breast cancer, prostate cancer, melanoma and other types of tumor covers both the primary setting as well as the secondary setting [30]. This study represented 3,292 patients.

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 healthcare 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 pathways [30].

More detailed information about the specific pathway which was studied, was found in an article included in the list of references [31]. 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 healthcare 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 phases [31]. 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 is presented [31].

Study design

The included 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 [30].

Types of tumor

Pathways for multiple types of tumor were studied: colorectal cancer, lung cancer, breast cancer, prostate cancer, melanoma and other types of tumors [30].

Country

This study was performed in Europe [30].

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 data [30].

Quality assessment

To assess the quality of this study conducted in both primary and secondary care, we adhered to the validated criteria suggested by the Effective Organisation of Care Group (EPOC), see 'results studies in the secondary care setting, quality assessment' in the result section. See for the results of the risk of bias assessment 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 healthcare professionals. But it remains unclear which role the regional representatives and other relevant healthcare professionals had in the implementation process of the pathway.

Using the taxonomy for guideline implementation [29], 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, healthcare 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, healthcare 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 process [31].

Discussion

We screened and analyzed more than 12,000 published studies to assess the effects of cancer care pathways in both primary and secondary care. Finally, 10 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 healthcare setting.

Most studies were conducted in secondary 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 favour 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 healthcare 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 favour 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. However, 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.

Although we searched for studies in primary, secondary and intersectional healthcare, we mainly found studies performed within secondary cancer care and only one study was related to both primary care and secondary healthcare. 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 care, but their potential benefit in primary care is largely unclear [11].

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 readmissions [32]. 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.

Abbreviations

NRCTs, non-randomized trial; RCTs, randomized controlled trial; CBA, controlled before-after study; ITS, interrupted time series; EPOC, effective practice and organisation of care; LOS, length of stay; WMD: Weighted Mean Difference; OR: Odds Ratio.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and material

The protocol for the systematic review is available from: https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=57592

The protocol for the systematic review was published and available from:
<https://systematicreviewsjournal.biomedcentral.com/articles/10.1186/s13643-018-0693-x>

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

All review authors have contributed to the production of the manuscript. All authors read and approved the final manuscript. JvH and TR led the writing of the manuscript; all other review authors provided comments and suggestions. MF has developed the search strategy and conducted the literature searches. JvH and RV screened all titles and abstracts for eligibility and assessed all primary studies. JvH and RV abstracted data and undertook analysis. TR and SS gave advice on the methodological issues and the statistical analysis. TR acted as arbitrator in the case of disagreement. JvH and TR led the writing of the full review. TR, SS and PN critically appraised the review findings and conclusions to assess the practical relevance and the transferability of the international evidence.

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Tables

Table 1 Key Characteristics of Included Primary Studies

Study ID	CPW	Study groups	Intervention	Setting	Care	Sample	Study design	Country	Outcomes	
								pathway*	Size	
1	Bao et al.	Breast, colon and rectal	Separate groups for breast, colon and rectal cancer:	Implementation started in July 2012 to guide surgical management. The pathways were published by the NHFPC of China.	Specialized cancer	Unclear, poor	1768	Interrupted time series study**	China	Length of hospital stay (median, IQR)
			<ul style="list-style-type: none"> · Pre-pathway group (Jan-Jun 2012) · Post pathway group 1 (2013) · Post pathway group 2 (2014) 	No detailed information about the pathway was reported.	Hospital, secondary care			Complications Quality indicators about the compliance with the care process		
2	Chen et al.	Unilateral neck dissection	<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) 	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, Patients in the preoperative visit and same day admit surgery. during the time of implementation, but were not managed based on the pathway. The treated physician decided solely to place patients on the pathway.	Academic cancer Center, - 4	Meets criteria 1	190	Non-randomized controlled trial** (with a historical control group)	USA	Length of hospital stay (median) Complications Readmission Costs of care

Study ID	CPW	Study groups	Intervention	Setting	Care	Sample	Study design	Country	Outcomes
								pathway*	Size
3 Dahl et al. 2017	Cancer	<ul style="list-style-type: none"> · Before · After implementation (Sep pathways includes three different (colorectal, lung, melanoma, breast, prostate & other)) · After implementation 	<p>The framework of the Danish cancer implementation (Sep pathways includes three different (colorectal, lung, melanoma, breast, prostate & other))</p> <p>descriptions of the pathway: a total (May-Aug 2010) A pathway in the Danish context is a pathway referred (May-Aug 2010)</p> <p>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 shown [Probst et al. 2012].</p>	Danish hospitals, primary care	Meets criteria 1 - 4	3292	Non-randomized controlled trial** (with a historical control group)	Denmark	Patient dissatisfaction with long term waiting times

Study ID	CPW	Study groups	Intervention	Setting	Care	Sample	Study design	Country	Outcomes	
								pathway*	Size	
4	Gendron et al. 2002	Head and neck cancer surgery	<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) 	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.	Tertiary care	Meets criteria 1 - 4	212	Interrupted time series study**	USA	Length of stay (median, range)
5	Ghosh et al. 2001	Hysterectomy cervical or endometrial cancer	<p>Separate groups for cervical and endometrial cancer:</p> <ul style="list-style-type: none"> - Preintervention - Postintervention - Postintervention - Postintervention - Postintervention - Postintervention 	Care pathways for patients with gynecologic malignancies were developed based on the results of clinical trials and on the consensus group (Jan 1997-June 1998), a pharmacists were involved. The nursing team played an active role in group (July 1998-Dec 1998) 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.	Academic Medical Center, secondary care	Meets criteria 1 - 4	151	Interrupted time series study**	USA	Length of hospital stay (mean, SD)

Study ID	CPW	Study groups	Intervention	Setting	Care	Sample	Study design	Country	Outcomes	
								pathway*	Size	
6	Jeong et al. 2011	Treatment of gastric cancer (early vs advanced; non-CP vs CP)	Separate groups for early gastric cancer and advanced gastric cancer: · Non care pathway (general care) group · Pathway group	The pathway was first implemented in September 2004. The pathway for patients with gastric cancer following gastrectomy were developed in 2006	Unclear, secondary care	Meets criteria 1 - 4	631	Non-randomized controlled trial**	Korea	Length of hospital stay (pre, post and total) (mean) Costs (pre, post and total)
7	Kiyama et al. 2003	Gastric cancer	· Traditional care group (control) · Clinical pathway group	The CP employed standardised 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.	Nippon Medical School	Meets criteria 1 - 4	85	Randomized Controlled Trial	Japan	Length of hospital stay: pre- and postoperative (mean, SD) Morbidity rate Postoperative complications

Study ID	CPW	Study groups	Intervention	Setting	Care	Sample	Study	Country	Outcomes
		condition			pathway*	Size	design		
8	Muehling et al. 2008°	Fast track lung resections	<ul style="list-style-type: none"> · Conservative treatment group · Fast track treatment group <p>No period of time is reported.</p>	<p>In order to reduce postoperative pulmonary complications, a perioperative treatment (fast track) protocol for lung surgery has been developed and optimized.</p> <p>A detailed overview of the conservative and fast track regimen was given in table 1 with the following aspects: preoperative patient education, fasting, preoperative, pain control, intraoperative normothermia, start of enteral feeding, intravenous fluids postoperative and ambulation.</p>	<p>University Hospital, secondary care</p>	<p>Unclear, poor reporting</p>	<p>58</p> <p>randomized controlled pilot study</p>	<p>Prospective Germany</p> <p>(pulmonary, cardiovascular, technical)</p> <p>Reoperation Morbidity Mortality Length of stay at the ICU (median) Day of discharge (median)</p>	<p>Complications</p>

Study ID	CPW	Study groups	Intervention	Setting	Care	Sample	Study design	Country	Outcomes	
								pathway*	Size	
9	Tastan et al. 2012	Breast cancer	<ul style="list-style-type: none"> · Control group (clinical pathway was not used) · Clinical pathway <p>Both groups: March 2004-April 2005</p>	<p>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.</p>	Military	Meets criteria 1 - 4	69	Non-randomized controlled trial**	Turkey	Patient anxiety satisfaction Quality of life

Study ID	CPW	Study groups	Intervention	Setting	Care	Sample	Study design	Country	Outcomes
condition					pathway*	Size			
10	Williams Pain et al. 2015	<ul style="list-style-type: none"> · Usual care group · Intervention group 	<p>Pain assessment and treatment was conducted by two pain clinic doctors and two nurses who were independent of the research team.</p> <p>The usual care treatment is based on the Royal Marsden Hospital Pain and Palliative Care treatment guidelines.</p> <p>The intervention group received combined screening, treatment and educational approach.</p> <p>Patients in the usual care group were not proactively assessed at baseline, nor did they receive a timetabled weekly pain assessment conducted by their pain physician. They also did not receive the pain education brochure.</p>	<p>Hospital, secondary care</p> <p>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. 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.</p>	<p>Meets criteria 1 - 4</p>	156	RCT	UK	Pain severity, Patient satisfaction, Anxiety, Depression, Treatment costs

Abbreviations: RCT: Randomized Controlled Trial; USA: United States of America; UK: United Kingdom; ICU: Intensive Care Unit.

* Pending studies

* the described pathway was defined using the working 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.

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

Table 2 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	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	HCG vs (historical pathway: control group, -\$3028.31 HCG) NPG vs \$9341.37 pathway: (non-pathway -\$892.75 group, NPG)
Gendron et al. 2002	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)	\$137769.62	Control vs pathway group 1: -\$34609.05 Control vs pathway group 2: -\$51614.27
Ghosh et al. 2001 (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).	\$5204.43	\$7361.88	-\$2157.45 (-29%)
Ghosh et al. 2001 (endometrial cancer)	USA	US\$	Total hospital costs	\$5031.83	\$6327.63	-\$1295.80 (-32%)
Jeong et al. 2011 (advanced gastric cancer)	Korea	US\$	Total hospital costs There is no description available of which costs are included.	\$9297.65	\$9329.28	-\$31,63
			Preoperative costs	\$1330.75	\$1651.92	-\$321.17
			Postoperative costs	\$7966.90	\$7681.14	+\$285.76
Jeong et al. 2011 (early gastric cancer)	Korea	US\$	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

Postoperative costs							\$8522.61	\$9143.07	-\$620.46
Kiyama et al.	Japan	US\$	The total costs						
2003			The total direct costs reported were the total medical costs (including medication and examinations).						
			Medication costs only						
			Daily total costs						
Williams et al.	UK	US\$	Costs included: analgesic drug costs, pain clinic visits, use of physiotherapy, psychology and other resources.						
2015									

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

Supplementary Files Legend

Additional file 1: Overview of inclusion criteria for this systematic review

Additional file 2: Search strategy

Additional file 3: Systematic review cancer care pathways PRISMA flow diagram

Additional file 4: Excluded full text studies with the reason for exclusion

Additional file 5: References of all excluded full text studies

Additional file 6: Risk of bias of included studies

Additional file 7: Quality assessment of cost evaluation studies

Additional file 8: Original reported costs / charges data

Figures

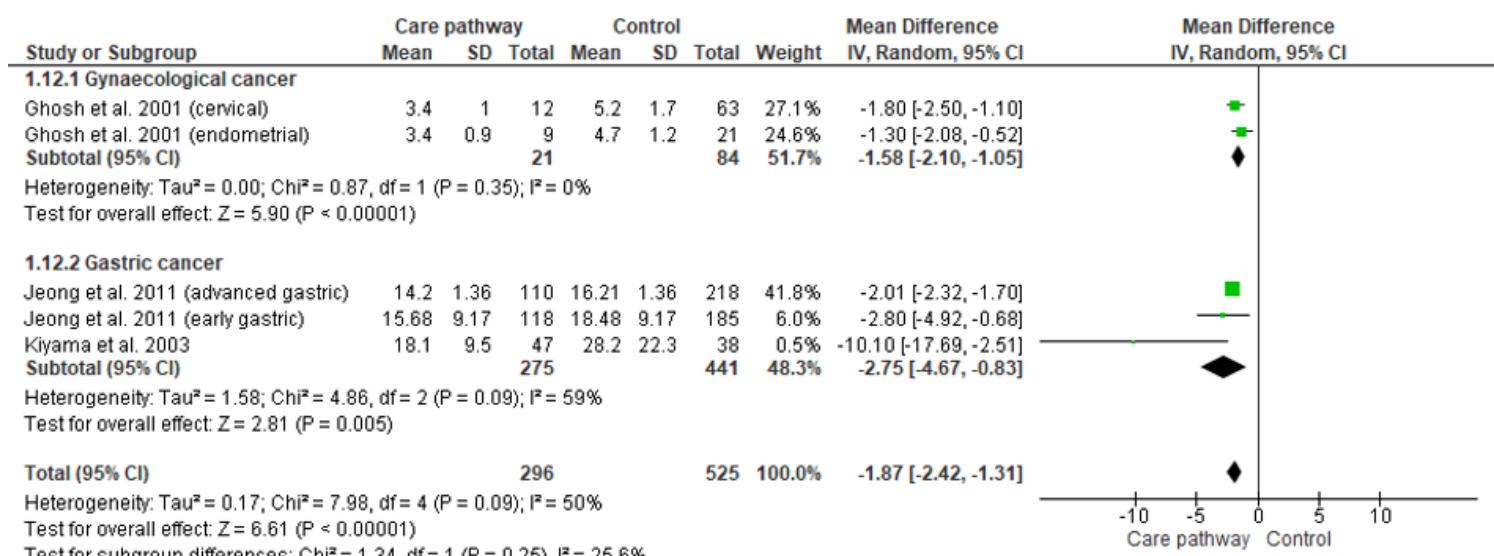


Figure 1

Subgroup analyses of the effects on LOS

Supplementary Files

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