RESEARCH ARTICLE

Could Clinical Pathways Improve the Quality of Care in Patients with Gastrointestinal Cancer? A Meta-analysis

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Abstract

This meta-analysis was performed to assess the implementation effects of clinical pathways in patients with gastrointestinal cancer. A comprehensive search was conducted in the Cochrane Library, PubMed, EMBASE, Web of Science and Chinese Biomedical Literature Database (from inception to May 2014). Selection of studies, assessing risk of bias and extracting data were performed by two reviewers independently. Outcomes were analyzed by fixed-effects and random-effects model meta-analysis and reported as mean difference (MD), standardized mean difference (SMD) and odds ratio (OR) with 95% confidence intervals (CI). The Jadad methodological approach was used to assess the quality of included studies and the meta-analysis was conducted with RevMan 5.1 software. Nine citations (eight trials) involving 642 patients were included. The aggregate results showed that a shorter average length of stay [MD = -4.0; 95% CI (-5.1, -2.8); *P* < 0.00001] was observed with the clinical pathways as compared with the usual care. A reduction in inpatient expenditure [SMD = -1.5; 95% CI (-2.3, -0.7); P = 0.0001] was also associated with clinical pathways, along with higher patient satisfaction [OR = 4.9; 95% CI (2.2, 10.6); *P* < 0.0001]. Clinical pathways could improve the quality of care in patients with gastrointestinal cancer, as evidenced by a significant reduction in average length of stay, a decrease in inpatient expenditure and an improvement in patient satisfaction. Therefore, indicators and mechanisms within clinical pathways should be a focus in the future.

Keywords: Clinical pathways - gastrointestinal cancer - length of stay - expenditure - satifaction

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Introduction

As the second leading cause of death in developing countries and the leading cause of death in developed countries (Mathers et al., 2008), cancers have become a predominantly healthy problem worldwide. There were approximately 12.7 million cancer patients and 7.6 million died in 2008 (Jemal et al., 2011). In addition, International Agency for Research on Cancer (IARC) indicated that the top five cancer caused death are lung cancer (1.4 million deaths), stomach cancer (740,000 deaths), liver cancer (700,000 deaths), colorectal cancer (610,000 deaths), and breast cancer (460,000 deaths) (Globocan 2008 fact sheet, 2013), of which stomach cancer and colorectal cancer accounted for 34.5%. Moreover, the elderly are more likely to suffer gastrointestinal malignancies, especially in their 60s or 70s (Wo et al., 2012). With the arrival of aging population, gastrointestinal cancer is becoming a serious threaten to people' health.

Clinical pathways (CPW), also called as critical pathways, critical paths or care paths (Every et al., 2000), were first introduced to standardize treatment in USA (Coffey et al., 1992; Pearson et al., 1995). CPW are multidisciplinary care plans that outline the sequence and timing of actions necessary for achieving expected patient outcomes and organizational goals regarding quality, costs, patient satisfaction and efficiency (El Baz et al., 2007). The aim of CPW is to link evidence to practice for specific health conditions (Rotter et al., 2012). In the past few years, the implementation of CPW in clinical practices has increased significantly (Zander 2002; Vanhaecht et al., 2006; Zhu et al., 2014).

However, the implementation effect of CPW varies among individual studies. Several ambiguous statements exist on it (Saint et al., 2003). Additionally, there is not high quality evidence to evaluate the effect of CPW used in gastrointestinal cancer. Therefore, this meta-analysis was performed to assess the effect of CPW in gastrointestinal cancer compared with usual care.

Materials and Methods

The Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) were used to conduct data

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extraction.

Search methods for identification of studies

Seven databases were searched comprehensively, including the Cochrane Library (Issue 5, 2014), PubMed (1966-5/2014), EMBASE (1974-5/2014), Web of Science (1974-5/2014), Chinese Biomedical Literature Database (1978-5/2014) et, al. Search strategy was medical subject headings (MeSH) terms combined with free text terms, which was translated into appropriate vocabularies in different databases. MeSH search was performed based on the following search string: Stomach Neoplasms, Esophageal Neoplasms, Intestinal Neoplasms, Colorectal Neoplasms, and Gastrointestinal Stromal Tumors et al. Details of search strategy in PubMed were showed in Table1. The languages were not restricted during the document retrieval. In addition, the reference lists of included articles were also searched, and these relevant studies were checked manually to identify other literature related to our article topic. In order to avoid missing articles, we conducted both online and manual retrieval.

Data collection and analysis

Selection of studies: Two reviewers (Song XP and Cui Q) independently assessed every retrieved study. The studies which cannot be determined by titles and abstracts were subjected to full text assessment. Disagreements during the process were resolved by consulting the third reviewer (Tian JH). When two or more studies were from the same trial, the study which could provide the most comprehensive data was included. If these studies report different indicators, all of them were included.

Inclusion criterion

RCTs compared CPW with usual care in patients with gastrointestinal cancers were included. Histology or cytology was used to diagnose gastrointestinal cancers. The following cancers are included: Esophageal Neoplasms, Stomach Neoplasms, Intestinal Neoplasms, Zllinger-Elison Syndrome, Gastrointestinal Stromal Tumors, Cecal Neoplasms, Colorectal Neoplasms, Duodenal Neoplasms, Ileal Neoplasms, Jejunal Neoplasms, Immunoproliferative Small Intestinal Disease, Appendiceal Neoplasms, Colonic Neoplasms, Adenomatous Polyposis Coli, Gardner Syndrome, Sigmoid Neoplasms, Colorectal Neoplasms, Hereditary Nonpolyposis, Rectal Neoplasms, Anus Neoplasms, and Anal Gland Neoplasms.

Exclusion criterion

Patients with previous or coexisting cancer; Patients with severe underlying disease, such as serious circulatory or respiratory disorders, renal or liver dysfunction.

Data extraction and management

Two reviewers (Song XP and Cui Q) independently extracted data from the included studies. If any disagreement was found, we had planed to discuss with each other and overseen by a third reviewer (Tian JH). We contacted with original authors via email or phone when additional information were needed. The following data were extracted from each study: the first author year of publication, disease, study period, sample size, age of participants, therapeutic method, reported indicators, and country.

Assessment of risk of bias in included studies

The modified Jadad 7-point scale was used to assess the risk of bias of included studies. This scale was derived from Jadad 5-point scale (Jadad et al., 1996), adding the item of allocation concealment (Schulz et al., 1995). Risk of bias was assessed by two reviewers (Song XP and Cui Q) independently. Any disagreements were resolved by consensus and the third reviewer (Tian JH) acted as an arbiter. The scale address five specific aspects: randomization generation (0-2 points), blinding (0-2 points), description of withdrawals and dropouts (0-1 point), and allocation concealment (0-2 points). A total score of 4 or more points is high quality study.

Statistical analysis

Statistical analysis was performed with Review Manager 5.1 software. Statistical heterogeneity among studies was evaluated by the Chi-square test and the extent of inconsistency was assessed by the I^2 statistic. The mean difference (MD) is recommend for continuous data when all studies use the same scale to report their outcomes, while standardized mean difference (SMD) is more appropriate for studies using different scales. Odds ratio (OR) with 95% confidence intervals (CI) was suitable for dichotomous data. Funnel plot was not created in this study because Higgins and Green indicated that it is appropriate only when at least 10 trials are included (Higgins et al., 2011). Meta analysis was performed using a fixed-effects model (p>0.1) or a randomized-effects model (P≤0.1) according to the degree of heterogeneity.

Results

Details of selection process from the initial results of publication searches to the final inclusion were presented in Figure 1. Ultimately, 9 citations (8 trials) (Jiang et al., 2003; Kiyama et al., 2003; Jiang et al., 2004; Hu et al., 2004; Wang et al., 2004; Liang et al., 2008; Xiong, 2010; Tian, 2011; Li, 2012) involving 642 patients met our criteria and were included in the meta-analysis. Two studies (Jiang et al., 2003; Wang et al., 2004) were published based on the same trial, but reported indicators are different. All studies were verified for comparability of

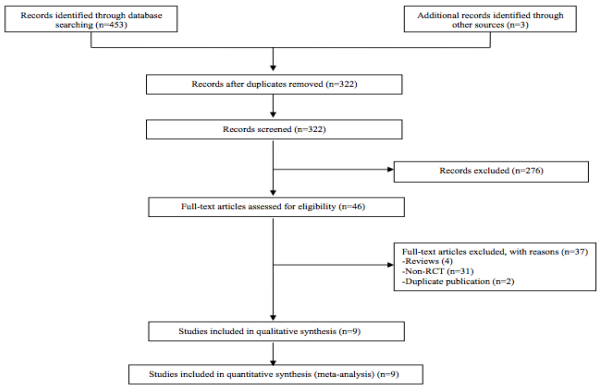

Figure 1. Chart of the Literature Screening Process

Table 1. Search Strategy for PubMed

No.	Search Strategy
#1	gastric cancer/or gastric neoplasm/or gastric tumor/or stomach cancer/or stomach neoplasm/or stomach tumor.ti,ab.
#2	esophageal cancer/or esophageal neoplasm/or esophageal tumor/or oesophageal cancer/or oesophageal neoplasm/or oesophageal tumor.ti,ab.
#3	gastrointestinal stromal cancer/or gastrointestinal stromal neoplasm/or gastrointestinal stromal tumor/ or GIST*/or MGIST*.ti,ab.
#4	zollinger-ellison syndrome/ or ZES*.ti,ab.
#5	intestinal cancer /or intestinal neoplasm/or intestinal tumor.ti,ab
#6	cecal Neoplasms/cecal cancer/cecal tumor.ti,ab.
#7	appendiceal neoplasms/appendiceal cancer/ appendiceal tumor.ti,ab.
#8	colorectal cancer/or colorectal neoplasm/or colorectal tumor.ti,ab.
#9	colon cancer/or colon neoplasm/or colon tumor/or colonic cancer/or colonic neoplasm/or colonic tumor.ti,ab.
#10	adenomatous polyposis coli/APC.ti,ab.
#11	gardner syndrome/familial colorectal polyposis/FAP. ti,ab.
#12	sigmoid cancer/ sigmoid colon neoplasm/ sigmoidal cancer/ sigmoidal colon neoplasm/sigmoid neoplasm /sigmoid tumor /sigmoidal neoplasm /sigmoidal tumor.ti,ab.
#13	colorectal neoplasms, hereditary nonpolyposis/lynch syndrome/HNPCC.ti,ab.
#14	rectal cancer/or rectal neoplasm/or rectal tumor/or rectum cancer/or rectum neoplasm/or rectum tumor.ti,ab.
#15	anus cancer/anus neoplasm/anus tumor.ti,ab.
#16	anal gland neoplasms/anal gland tumor/anal gland cancer.ti,ab.
#17	duodenal Neoplasms/duodenal cancer/duodenal tumor.ti,ab.
#18	ileal neoplasms/ileal cancer /ileal tumor.ti,ab.
#19	immunoproliferative small intestinal disease/IPSID.ti,ab.
#20	jejunal neoplasms/jejunal cancer/jejunal tumor.ti,ab.
#21	Stomach Neoplasms/Esophageal Neoplasms/ Gastrointestinal Stromal Tumors/Zollinger-Ellison Syndrome/Intestinal Neoplasms.sh.
#22	Cecal Neoplasms/Colorectal Neoplasms/ Duodenal Neoplasms/Ileal Neoplasms/Jejunal Neoplasms/Immunoproliferative Small Intestinal Disease.sh
#23	Appendiceal Neoplasms/Colonic Neoplasms/ Colorectal Neoplasms, Hereditary Nonpolyposis/ Rectal Neoplasms.sh
#24	Adenomatous Polyposis Coli/Gardner Syndrome/ Sigmoid Neoplasms/Anus Neoplasms/Anal Gland Neoplasms.sh
#25	or/1-24
#26	Critical Pathways.sh.
#27	clinical pathway/or clinical pathways/or clinical path / or clinical paths.ti,ab.
#28	critical pathway/or critical pathways/or critical path / or critical paths.ti,ab.
#29	care pathway/or care pathways/or care path/or care paths.ti,ab.
#30	care map/or care maps.ti,ab.
#31	care protocol/or care protocols.ti,ab.
#32	or/26-31
#33	random*.ti,ab.
#34	and/25,32,33.

baseline data between CPW and usual care. The PubMed search strategy was presented in Table1. Characteristics of included studies were showed in Table 2. Table 3 demonstrated the assessment of risk of bias in included studies.

Average length of stay (ALOS)

Data of seven trials (Kiyama et al., 2003; Jiang et al., 2004; Hu et al., 2004; Wang et al., 2004; Liang et al., 2008; Xiong, 2010; Tian, 2011) were pooled in ALOS. There was significant heterogeneity existed in included studies (I^2=88%, p<0.00001). CPW was superior to usual care on ALOS (MD=-4.0 d, 95%CI [-5.2, -2.9], p<0.00001) (Figure 2).

Inpatient expenditures

Aggregate overall results of six trials (Jiang et al., 2003; Kiyama et al., 2003; Jiang et al., 2004; Hu et al., 2004; Liang et al., 2008; Tian, 2011) showed that significant heterogeneity existed in included studies (I^2 =93%, p<0.00001). CPW was associated with lower inpatient expenditures [SMD=-1.5; 95%CI (-2.3, -0.7); p=0.0001] (Figure 3).

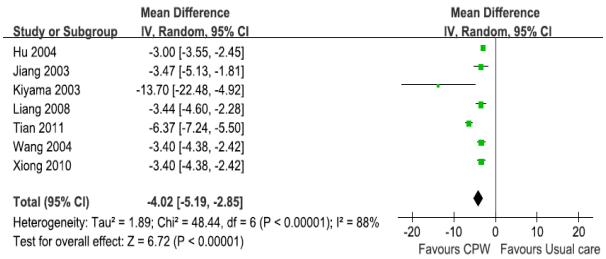

Figure 2. Forest Plot of Meta-Analysis: Average Length of stay (ALOS), Mean Difference (MD) with 95% Confidence Interval (CI)

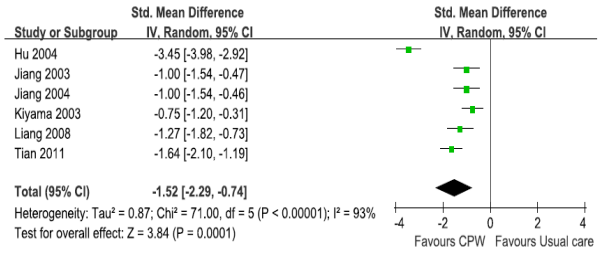

Figure 3. Forest Plot of Meta-Analysis: Inpatient Expenditures, Standardized Mean Difference (SMD) with 95% Confidence Interval (CI)

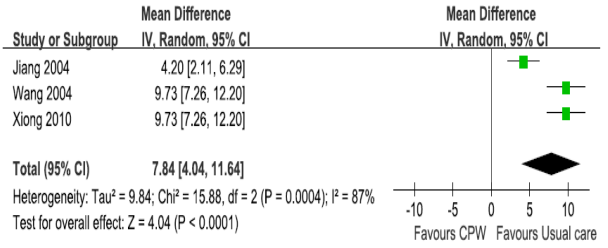

Figure 5. Forest Plot of Meta-Analysis: Postoperative Self-Care Behaviors, Mean Difference (MD) with 95% ConfidenceInterval (CI)

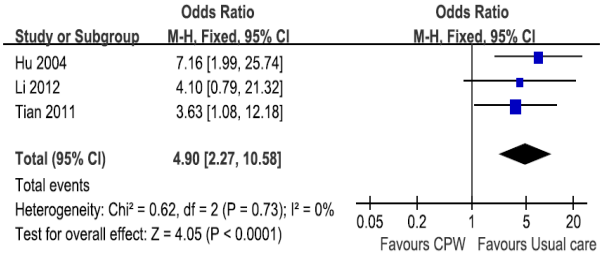

Figure 4. Forest Plot of Meta-Analysis: Patient Satisfaction (%), Odds Ratio (OR) with 95% Confidience Interval (CI)

Table 2. Characteristics of Included Studies

Study	Year	Disease	Study Period	Sample Size		Age		Reported Indicators
				CPW	Usual care	CPW	Usual care	
Wang et al	2004	GC	2001, 9~2002, 8	30	30	38.73±6.36	41.13±8.39	ALOS, PRI, GHK, PRI
Xiong et al	2010	GC	2007, 9~2008, 9	30	30	50.32	48.93	ALOS, GHK, PSCB, PRI
Kiyama et al	2003	GC, GST	2011, 1~2011, 12	49	38	63.0±12.9	66.8±12.1	ALOS, IE, PC, DWS
Jiang et al	2004	CC	2002, 10~2003, 9	30	30	47.13±6.84	44.60±8.13	ALOS, IE, GHK, PSCB
Li et al	2012	EC	2009, 1~2012, 6	36	36	56.1 (42-72)	58.3 (46-75)	ALOS, IE, PS, PRI
Tian et al	2011	EC	2008, 2~2009, 12	50	50	—	—	ALOS, IE, GHK, PS, PRI
Jiang et al	2003	GC	2001, 9~2002, 8	30	30	38.73±6.36	41.13±8.39	ALOS, IE, GHK, PRI
Liang et al	2008	RC	2005, 2~2007, 12	32	31	51.56 (38-78)	51.56 (38-78)	ALOS, IE, GHK, PS
Hu et al	2004	GC, CC, RC	2002, 1~2003, 4	70	70	47.2(18-83)	47.2(18-83)	ALOS, IE, PS, QC

*: mean; +: median; #: rangeALOS, IE, PS, QC; GC: Gastric Cancer; WS: Days of Waiting for Surgery; ALOS: Average Length of Stay; EC: Esophageal Cancer.; CC: Colon Cancer; PC: Postoperative Complications; IE: Inpatient Expenditures; QC: Quality of Care; RC: Rectal Cancer; PRI: Postoperative Recovery Indicators; PS: Patient Satisfaction; GHK: Grasp of Health Knowledge; GST: Gastrointestinal Stromal Tumors

Table 3. Methodological Quality of Included Studies

Study	Randomization	Blinding	Withdrawals and dropouts	Allocation Concealment	Total
Wang 2004	Numerical order	Assessors blind	No	Not reported	4
Xiong 2010	Numerical order	Not reported	No	Not reported	4
Kiyama 2003	Not reported	Not reported	Yes / 2 patients	Not reported	4
Jiang 2004	Computer generated	Not reported	No	Not reported	5
Li 2012	Hospital number	Not reported	No	Not reported	3
Tian 2011	Hospital number	Assessors blind	No	Not reported	3
Jiang 2003	Numerical order	Assessors blind	No	Not reported	4
Liang 2008	Hospital number	Not reported	No	Not reported	3
Hu 2004	Hospital number	Not reported	No	Not reported	3

Patient satisfaction

Meta-analysis was conducted in the three trials (Hu et al., 2004; Tian, 2011; Li, 2012) for patient satisfaction. No heterogeneity existed among trials (I^2=0%, p=0.7). The overall results showed that a significantly higher patient satisfaction in the CPW compared with usual care [OR=4.9; 95%CI (2.3, 10.6); p<0.0001] (Figure 4).

Postoperative self-care behaviors

There were three trials (Jiang et al., 2004; Wang et al., 2004; Xiong, 2010) reported postoperative self-care behaviors. The pooled results demonstrated that heterogeneity among three studies was significant (I^2 =87%, p=0.0004). Better postoperative self-care behaviors were observed in CPW [MD=7.8, 95%CI (4.0, 11.6), p<0.0001) (Figure 5).

Discussion

Since CPW were initially been employed in 1980s, it has been implemented globally. It was reported that 80% of hospitals in United States of America had used the CPW by 2003 (Deng et al., 2010). As a country has the largest population in the world, China has improved its influences significantly in the past years. Chinese government conducted pilot works in some hospitals since 2009 and promoted it nationwide gradually. National health and family planning commission of the people's republic of China had promulgated 380 items of CPW by 2012 (Ministry of Health of the People's Republic of China, 2013). Therefore, as an efficient method to improve the quality of care, CPW will still be an important topic in the field of health care in the future.

The current studies on the implementation of CPW in gastrointestinal cancer are limited. Ultimately, nine citations (eight trials) (Jiang et al., 2003; Kiyama et al., 2003; Jiang et al., 2004; Hu et al., 2004; Wang et al., 2004; Liang et al., 2008; Xiong, 2010; Tian, 2011; Li, 2012) involving 642 patients were included in the meta-analysis, one (Kiyama et al., 2003) of which arose from Japan and others were conducted in China. The bias of 5 included studies was assessed as low risks. Included studies reported specific indicators differently on postoperative recovery indicators (ambulation time, postoperative in-bed time et, al.). Grasp of health knowledge in different studies reported different evaluation items. However, good effects were associated with CPW in studies reported postoperative recovery indicators and grasp of health knowledge. Surgical treatment was used in eight studies, five of which performed radical operations (Jiang et al., 2003; Jiang et al., 2004; Liang et al., 2008; Tian, 2011; Li, 2012). However, specific surgical method was unclear in three studies (Kiyama et al., 2003; Wang et al., 2004; Xiong, 2010). Moreover, a study (Hu et al., 2004) performed chemotherapy.

ALOS and inpatient expenditures not only reflect the utilization of health resources, but also are important indicators to evaluate health care quality. ALOS and inpatient expenditures are widely used in health care outcome measurement, which belong to financial domain.

All trials reported ALOS, while one study (Li, 2012) did not report it in the standard form of Mean Standard Deviation (SD). Therefore, seven trials (Kiyama et al., 2003; Jiang et al., 2004; Hu et al., 2004; Wang et al., 2004; Liang et al., 2008; Xiong, 2010; Tian, 2011) involving 570 patients were pooled. Seven trials (Jiang et al., 2003; Kiyama et al., 2003; Hu et al., 2004; Jiang et al., 2004; Liang et al., 2008; Tian, 2011; Li, 2012) reported inpatient expenditures, the units of which were RMB Yuan and JPY Yen. Data of one study (Li, 2012) was not been pooled

due to the same reason above. Under the consideration of exchange rate and interest rate, the result would be more realistic if the inpatient expenditures could be converted into the same currency in the same year. The raw data was not available although we contacted with authors. Therefore, SMD and random-effects models were applied in the meta-analysis of inpatient expenditures. The results of the meta-analysis presented that a significant reduction in ALOS and inpatient expenditures were observed in CPW.

As the country with the highest gastric cancer risk in the world (Yamamoto, 2001), Japan' study (So, et al., 2008) resented that reduction in ALOS and inpatient expenditures were associated to CPW for gastric cancer. In addition, a cohort study in Japan also showed CPW can decrease ALOS considerably for colorectal cancer (Ishiguro et al., 2008). Our study comprehensively summarized and analyzed the RCTs in the field of CPW implemented in gastrointestinal cancer. Therefore, it is reasonable to conclude that CPW have good effects on gastrointestinal cancer.

Patient-centered care is one of core values in health at present. The indicator of patient satisfaction may be particularly important to cancer patients because cancer is tough and hard to cure. Five trials (Hu et al., 2004; Jiang et al., 2004; Liang et al., 2008; Tian, 2011; Li, 2012) were identified to reported patient satisfaction, one (Liang et al., 2008) of which reported it in the form of Mean SD. The remaining four trials reported it in percentage, one (Jiang et al., 2004) of which reported an overall patient satisfaction of colon cancer and ventricular septal defect. Thus, three trails were included in the meta-analysis. Overall results of the study showed that CPW can significantly improved patient satisfaction.

There were three studies (Jiang et al., 2003; Wang et al., 2004; Tian, 2011) reported postoperative self-care behaviors, which were evaluated by the following aspects: washing, activities, eating, and toileting. The scale of postoperative activities cited the primary items of Katz index of independence in activities of daily living (ADL). Three studies all reported that blinding was applied to outcome assessors in this indicator. The overall results showed that better postoperative self-care behaviors were associated to CPW.

There are several limitations existed in this meta-analysis. First, most included studies researched gastric cancer, colorectal cancer, and esophageal cancer. It maybe caused by the incidence of these cancers in gastrointestinal tract is higher than other cancers. In addition, CPW for these cancers are generic interventions which could be copied to other gastrointestinal cancers. Therefore, these cancers are representative on implementation of CPW in gastrointestinal cancer. Second, there were high heterogeneity existed in several pooled results, which maybe caused by the following reasons. The level of hospitals among included studies was different. While LOS and postoperative self-care behaviors have a close relation with institution context. In addition, specific inpatient expenditures method used to generate the data was unclear, which is also different between Japan and China. Therefore, a random effects analysis was performed to control the heterogeneity and increase the strength of the results. Third, sample sizes of some included studies were small, which may led to patient selection bias.

Some uncertainties about CPW need to be researched further. First, the definition of CPW is still unclear (Harkleroad et al., 2000; De et al., 2006). It was reported that there are 17 different terms expressed the concept of CPW (De, 2001). Relatively acceptable definition of CPW at present is a standard formulated by Leigh K (Kinsman et al., 2010), which contained five criteria. The accuracy and precision of which should be examined by practice. Second, mechanism of how the pathway work is still not clear (Rotter et al., 2008). In this meta-analysis, the results demonstrated that CPW have positive impact on ALOS, inpatient expenditures, patient satisfaction and postoperative self-care behaviors. We could only infer that the results may be caused by the standardization of the process of care. It is suggested that which component of CPW works should be researched fatherly. Third, Indicators are crucial in assessing the effects of CPW. The Indicators for CPW were classified into five domains to evaluate the effects of CPW: the 'clinical', 'service', 'team', 'process', and 'financial' domains (Lemmens et al., 2008). 'clinical' and 'financial' domains were the most widely used indicators. As a integrated care pathways, indicators in the domains of 'service', 'team', and 'process' should be pay more attention in the future.

In conclusion, this meta-analysis showed that CPW could improve the quality of care in patients with gastrointestinal cancer, which was associated with a significant reduction in ALOS, a decrease in inpatient expenditures and an improvement in patient satisfaction. As an effective method to improve health quality care, CPW should be promoted in the management of gastrointestinal cancer. Further studies should pay more attention to the indicators and mechanisms within CPW..

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