

R E V I E W

Clinical pathways and patient-related outcomes in hospital-based settings: a systematic review and meta-analysis of randomized controlled trials

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Abstract. Clinical pathways represent a multi-disciplinary approach to translate clinical practice guidelines into practical interventions. The literature from 2010 onward regarding the efficacy of adopting a clinical pathway on patient-related outcomes within the in-hospital setting has not been synthesized yet. For this reason, this systematic review and meta-analysis of randomized controlled trials aimed to critically synthesize the literature from 2010 onward about the efficacy of clinical pathways, compared with standard of care, on patient-related outcomes in different populations and to determine the effects of clinical pathways on patient outcomes. We searched PubMed, Scopus, CINAHL, and reference lists of the included studies. Two independent reviewers screened the 360 identified articles and selected fifteen eligible articles, which were evaluated for content and risk of bias. Eleven studies were finally included. Given the commonalities of the measured outcomes, a meta-analysis including eight studies was performed to evaluate the effect size of the associations between clinical pathways and quality of life (OR=1.472 [0.483–4.486]; $p=0.496$), and two meta-analyses, including four studies, were performed to evaluate the effect sizes of the associations between clinical pathways with satisfaction (OR=2.226 [0.868–5.708]; $p=0.096$) and length of stay (OR=0,585 [0.349–0.982]; $p=0.042$). Reduced length of stay appeared to be associated with clinical pathways, while it remains unclear whether adopting clinical pathways could improve levels of quality of life and satisfaction. More primary research is required to determine in specific populations the efficacy of clinical pathways on patient-related outcomes. (www.actabiomedica.it)

Keywords: care pathways; clinical pathways; meta-analysis; multi-interventions; outcomes; systematic review

Introduction

The need to tailor care delivery and take complex decisions boosted the shift from opinion-based practice to the current evidence-based approach (1). As such, clinical decision-making is required to be evidence-based and supported by tools aimed to facilitate clinical practice (2). At the end of the 1980s, some document-based tools, referred to as clinical pathways, started to be developed and published to optimize

patient outcomes and clinical efficiency (3). In those years, clinical pathways were considered as the organizational response to the challenging patient-focused care, as they were developed to improve patient safety, quality of care, and efficiency of healthcare procedures (4).

Clinical pathways inherited the industrial process approach, but they were focused on facilitating the match between evidence and practice within a person-centered framework (5). More precisely, clinical

pathways were conceptualized to link the most updated evidence to practice for specific clinical conditions (6). For this reason, clinical pathways should be periodically updated in the clinical contexts. Overall, clinical pathways define structured multi-disciplinary care plans for specific clinical conditions, which breakdown the care process into its essential steps (7). Thus far, the literature presents numerous terminologies referred to as clinical pathways, such as care plans, clinical paths, care maps, care pathways.

Numerous studies focused on describing the implementation of clinical pathways in different hospital-based contexts (8), and, from 2000 onwards, some authors started to describe the efficacy of the implementation of clinical pathways on several clinical outcomes with experimental or quasi-experimental (pre-/post- studies) designs (9). For this reason, Rotter and colleagues (3) published in 2010 the first systematic review (Cochrane systematic review), after the one published in 2004, focused on the effects of clinical pathways, compared with standard of care, among patients with acute stroke (10). Rotter and colleagues (3) aimed to assess the efficacy of clinical pathways, compared with standard of care, in different clinical settings. They found that clinical pathways reduced in-hospital complications, improving documentation without negatively impacting the length of stay and hospital costs (3). However, some authors remained skeptical about the adequacy of the performed systematic reviews until 2010, as these reviews seemed to be poorly adequate to capture complex interventions, as per the characteristics of clinical pathways (11).

As a consequence of the debate, it was proposed a refinement of the operational definition of clinical pathways to identify studies for systematic reviews (12). Accordingly, clinical pathways have to reflect the described four main elements (12). First, they have to adopt a multi-disciplinary approach to translate guidelines into practical interventions. Second, the evidence underpinning clinical pathways has to be adapted considering the local context. Third, clinical pathways have to include precise time-frames or criteria-based progression algorithms. Four, clinical pathways have to be focused on specific populations.

Although the literature regarding clinical pathways has increased over the last decade, the studies

aimed to synthesize the evidence referred to the efficacy of clinical pathways, compared with standard of care, are still lacking (13,14). The lack of systematic reviews on this topic could undermine the current knowledge about the efficacy of clinical pathways, as defined by Lawal and colleagues (12), on specific patient-related outcomes. For this reason, this study aimed to critically synthesize the literature about the efficacy of clinical pathways, compared with standard of care, on patient-related outcomes in different populations and to determine the effects of clinical pathways on patient outcomes.

Methods

Design

This study is a systematic review with meta-analysis, reported following the Preferred Reporting System for Systematic Reviews (PRISMA) statement (15).

Search strategy

We performed on July 2019 an extensive search of the literature, consulting PubMed, CINAHL, and Scopus databases. Further, we additionally examined the reference lists of all retrieved full-text articles to obtain additional articles previously not identified by consulting the databases directly. Two authors performed the search process independently, following the four phases described by the PRISMA flowchart: identification, screening, eligibility, and inclusion (16). Overall, identification is based on developing the queries for performing the electronic searches in the different databases. After having identified all the potential articles, the screening is based on the reading of each title/abstract for excluding records that did not meet the inclusion/exclusion criteria of the systematic review. The remained articles were referred to be eligible records, which have to be retrieved in full-text and evaluated in accordance with the pre-identify strategy of quality appraisal (see paragraph on quality appraisal). Finally, the articles with moderate/good quality were included in the systematic review.

The queries for the systematic searches (identification) were developed, combining entry terms referred to problem/population, intervention, comparison, and outcome (PICO) with Boolean operators (17). We identified to main queries for PubMed, CINAHL, and Scopus: (a) Query one (PubMed) (b) query two (PubMed). For all the databases, we also developed queries combining the entry term of clinical pathway* (with synonyms) and patient outcome* (with synonyms). Two authors had a consensus discussion for each phase of the PRISMA flowchart.

The following inclusion criteria were adopted: (a) primary research in adult populations, (b) with experimental design, (c) published in English, (d) between January 2010 and September 2019 (when the review was performed), (e) containing an indexed abstract, (f) with an operational definition of clinical pathway consistent with the requirements indicated by Lawal and colleagues (12), and (g) aimed to assess the effects (or efficacy) of clinical pathways on the measured patient-related outcome(s). We considered the low-quality appraisal as the exclusion criteria that required to be applied in the eligibility phase of the PRISMA flow diagram.

Study selection process

As described in **Figure 1**, our electronic searches identified 355 records from utilizing the developed queries (n=140 in PubMed; n=96 in Scopus; n=119 in CINAHL) and five additional records derived from the manual search performed to examine the reference lists of all retrieved full-text articles in the eligibility phase. After removing the duplicates, two authors screened 278 titles and abstracts. In this phase, 228 records were excluded as these articles' main topic was not referred to as clinical pathways. From the remaining 50 articles, two authors verified the abstract if inclusion criteria were met, and 35 articles were excluded because they did not present an experimental arm. The 15 eligible articles were then retrieved in full-text and evaluated for their content and quality by following the criteria described in the section "quality appraisal." Before evaluating the quality and risk of bias of the eligible articles, four additional articles were excluded as they did not meet some inclusion criteria,

precisely: one was referred to the pediatric setting, three did not measure any possible patient-related outcomes. Accordingly, 11 studies were included in this systematic review. Considering the evaluation of the contents of the included studies, the length of stay (LoS) was a patient-related outcome common to four studies, the quality of life (QoL) was common in eight studies, and the satisfaction was common in four studies. Only three studies reported the hospital readmission after discharge as an outcome, and one study that has the LoS as the only outcome was not included in the meta-analysis, as performing a meta-analysis with less than four studies could not add information to the narrative synthesis.

Quality appraisal

The "Cochrane Effective Practice and Organisation of Care Review Group" (EPOC) checklist was used for evaluating the included studies, considering the seven standard criteria for evaluating the randomized controlled trials (RCT) (18). EPOC risk of bias tool is able to appraise the methodological quality and risk of bias of the included articles. The seven standard criteria were: random sequence generation (selection bias), allocation concealment, blinding of participants/personnel (performance bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), other bias (18).

Data extraction

Two investigators (LT and RC) independently conducted data extraction. Initially, data from the 11 included articles were synthesized using the following format: (a) authors and publication year, (b) population, (c) main aim & method, (d) results, and (e) measured outcome(s). Measures of associations were extracted from multivariable analyses (where available). Any discrepancy between the two investigators was solved by consensus discussion.

Statistical analysis

The outcomes considered for applying meta-analysis were LoS (four studies), QoL (eight studies), and

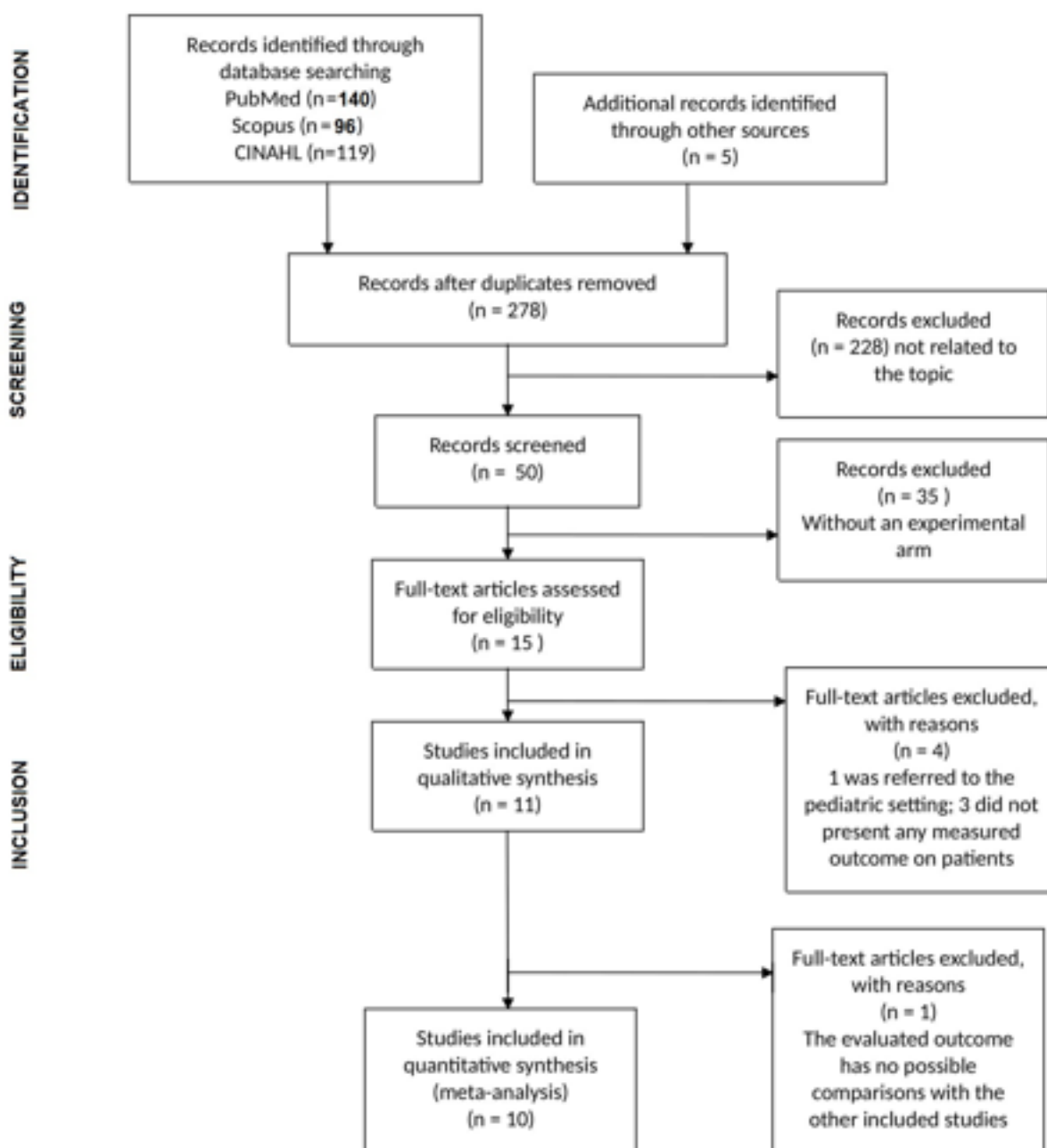


Figure 1. PRISMA 2009 Flow Diagram

satisfaction (four studies). We aimed at estimating the strength of associations between clinical pathways with LoS, QoL, and satisfaction. Considering that clinical pathways encompassed different multi-disciplinary interventions and the populations of the included studies were diverse, we adopted the random-effect

modeling approach, as the fixed-effect models assume the presence of a single common parameter to all studies (19). As there are no covariates that contend with explaining the heterogeneity, random-effect models are appropriate. The proportion of heterogeneity (percentage of total variation across studies due to

heterogeneity rather than chance) was evaluated using the I^2 measure, considering low ($I^2 < 25\%$), moderate ($25\% < I^2 < 75\%$), and high ($I^2 > 75\%$) heterogeneity (20). The associations were represented by adopting odds ratios (ORs) with 95% confidence intervals (95% CIs) extracted for each study and pooled for each outcome. We dichotomized the populations of the included studies in *chronic obstructive pulmonary disease* (COPD) versus “diverse” due to four studies were referred to COPD patients, and the other studies were referred to different types of population (stroke=1 article, hospitalized adults=2 articles, fecal incontinency=1 article, breast cancer=1 article, lung cancer=1 article). This approach allowed a sub-group analysis according to the population (COPD versus “diverse”) in evaluating the associations between clinical pathways and QoL. As all the performed meta-analyses did not include at least ten studies, the comparison-adjusted funnel plot was used to evaluate small-study effects for outcomes (21). Analyses were run using the Comprehensive Meta-Analysis software (version 2.2.057, Biostat, Englewood, USA).

Results

Description of the included studies

This systematic review included 11 RCTs (22–32). Four studies were conducted in the United States of America (USA) (23,24,31,32), five studies in Europe [two in the Netherlands (25,26), two in the United Kingdom (28,29), and one in Italy (22)], one study in Australia (30), and one study in Asia (Hong Kong) (27). Specifically, **Table 1** shows a summary of the main findings of the included studies. As noticed, the patient-related outcomes described in the studies were diverse. Overall, the QoL was described in eight studies (22,25–30,32), both satisfaction towards care (26,30–32) and LoS (24,27,29,31) were measured in four studies, while other outcomes (e.g., readmission, mortality, clinical outcomes) were specific to few studies.

This systematic review utilized the data of 2224 patients for determining associations between the model of care (clinical pathways versus standard of

care) and QoL (22,25–30,32); 524 patients were encompassed in the analysis for determining the associations between the care practice (clinical pathways versus standard of care) and satisfaction (26,30–32); 10897 patients were included in the analysis for describing the associations between the model of care (clinical pathways versus standard of care) and LoS (24,27,29,31).

Risk of bias in included studies

Figure 2 shows the overall evaluation referred to the risk of bias, and **Table 2** describes the detailed evaluation. The random sequence generation was adequately explained in eight RCTs (23,25–32); in one study, we found that some information regarding the random sequence generation would require a more in-depth explanation (22), and in one study, we did not find sufficient information to evaluate the selection bias adequately in terms of sequence generation for randomization (24). The allocation concealment was easily evaluable in nine RCTs (23–32), and one would benefit from some additional information (22). Considering the nature of the included RCTs (utilization of clinical pathways versus usual care), the blinding of participants/personnel was not possible; however, we considered the blinding of the statistician as the criteria to evaluate the performance bias, and its overall evaluation was adequate. We also evaluated from the description of the procedure of the implantation of the clinical pathway how the detection bias was managed in the studies, assigning a rating that considered the fact that blinding the procedure was not feasible. The statements regarding the management of missing outcome data (attrition bias) were also clear in five studies (24,26–28,30). We did not find selective reporting in all the included RCTs. Other biases were referred to as the limited sample size of three studies (26,29,30).

Clinical pathways versus standard of care and QoL

The overall model presented moderate heterogeneity ($I^2=44\%$), low heterogeneity ($I^2=0\%$) was reported for the sub-group of studies related to COPD (25,27,29,32), and moderate heterogeneity

Table 1. Characteristics of the included studies (n = 11)

Authors and publication year	Population	Main aim (method)	Results	Measured main outcomes
De Luca et al. (2016)	Adults with multiple morbidities	To assess the effectiveness of a telehealth-care multi-interventions on mental health (RCT).	Sample: fifty-nine patients [19 males and 40 females; mean age 79.1 (± 9.2), allocation 1:1]. Patients in the experimental arm reported lower levels of depression and higher levels of quality of life.	QoL; depression; other outcomes.
Dykes et al. (2010)	Adults with multiple morbidities	To determine the effects of structured multi-interventions on hospital falls (Cluster RCT).	Sample: 5160 patients in the experimental group and 5104 in the control group. Falls differed between the group related to usual care (n=87), and intervention (n=67) were different ($P= .02$). No differences were detected on LoS.	Patient falls; LoS.
Fan et al. (2012)	COPD	To determine the efficacy of structured multi-interventions in reducing the risk for COPD Hospitalization (RCT).	Sample: 209 were randomly assigned to the experimental group and 217 to the control group. The mean follow-up was 250 days. The 1-year cumulative incidence of COPD-related hospitalization was 27% in the experimental group and 24% in the control group. At 1-year follow-up, no significant improvements in the experimental group were found in relation to QoL and satisfaction, while le levels of self-efficacy were improved.	Hospitalization; QoL; satisfaction; other outcomes.
Field et al. (2018)	Stroke	To test the efficacy (and feasibility) of clinical pathways on reducing the incidence of pneumonia within three months after an acute stroke (Pragmatic RCT).	Sample: 192 patients in the experimental group and 190 in the control group. There was a non-significant reduction in pneumonia rates in the two groups. There was a non-significant difference in length of stay. However, significant differences were found in relation to secondary outcomes, such as satisfaction.	Pneumonia; LoS; satisfaction; other outcomes.
Hussain et al. (2017)	Fecal incontinence	To assess the impact of the implementation of standardized multi-program on patients' care (RCT).	Sample: 15 patients per arm. No significant difference in the quality of life and incontinence scores were found.	QoL; satisfaction; incontinence.
Kirshbaum et al. (2016)	Breast cancer	To assess the effects of structured multi-interventions on QoL (RCT).	Sample: 56 patients per arm. Age was found to be a determinant of QoL in both arms. Increasing age was negatively associated with sexual functioning, systematic therapy side effects, and physical functioning, and positively associated with future perspective.	QoL

Ko et al. (2017)	COPD	To evaluate whether a clinical pathway would decrease hospital readmissions and LoS for patients with COPD (RCT) within 12 months (RCT).	Sample: 90 patients per arm. The risk of readmission was lower in the experimental arm. Secondary outcomes, such as QoL, LoS seemed to be improved in the experimental arm.	Hospitalization; QoL; LoS; other outcomes.
Kreber et al. (2016)	Lung cancer & head/neck cancer	To assess the efficacy of the implementation of a standardized multi-program on the psychological distress in head and neck cancer and lung cancer patients (RCT).	Sample: At the end of the trial (12 months follow-up), 66 patients in the experimental arm, 62 patients in the control group. The measured outcomes related to psychological distress were found improved in the experimental arm.	Depression and anxiety; QoL; satisfaction
Kruis et al. (2014)	COPD	To assess the long-term effectiveness of a standardized multi-program on the QoL in adults with COPD (pragmatic RCT)	Sample: At the end of the trial (24 months follow-up), 554 patients in the experimental arm, 552 patients in the control group. No particular differences were found between groups.	QoL and clinical outcomes
Linden et al. (2014)	Chronic patients (heart failure and COPD)	To assess the effects of a standardized multi-program on the readmission for disease exacerbation in adults with COPD or chronic heart failure (RCT).	Sample: 129 patients to the experimental arm, 128 patients to the control group. At 90 days of follow-up, patients of the experimental arm experienced lower rates of readmission for disease exacerbation.	Readmission for disease exacerbation
Johnson-Warrington et al. (2016)	COPD	To assess the effects of a standardized multi-program on the respiratory in adults with COPD (RCT). LoS and QoL were secondary outcomes.	Sample: 35 patients in the experimental arm, 36 patients in the control group. Patients of the experimental group reported greater improvements in tolerating physical exercises compared with controls and decreased LoS. No differences were detected in relation to QoL.	Readmission; LoS; QoL; mortality; clinical outcomes

Legend: COPD = *Chronic obstructive pulmonary disease*; QoL = quality of life; LoS = length of stay; RCT = randomized controlled trial.

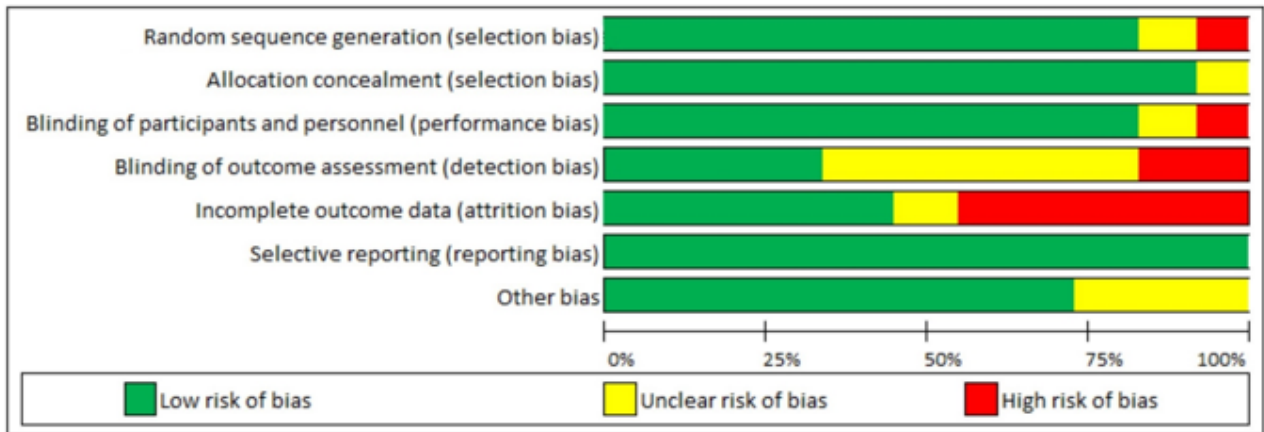


Figure 2. Risk of bias generated using Cochrane Risk of Bias Assessment Tool

Table 2. Risk of bias evaluation

Study	Criteria 1	Criteria 2	Criteria 3	Criteria 4	Criteria 5	Criteria 6	Criteria 7
De Luca et al. (2016)	?	?	+	?	-	+	?
Dykes P. et al. (2010)	-	+	-	?	+	+	+
Fan V.S. (2012)	+	+	+	-	?	+	+
Field M. et al. (2018)	+	+	+	?	?	+	+
Hussain Z. et al. (2017)	+	+	+	-	+	+	?
Kirshbaum et al. (2016)	+	+	+	+	+	+	+
Ko F. et al (2017)	+	+	?	?	+	+	+
Krebber et al. (2016)	+	+	+	+	+	+	?
Kruis et al. (2014)	+	+	+	+	?	+	+
Linden et al. (2014)	+	+	+	?	?	+	+
Johnson-Warrington et al. (2016)	+	+	+	+	?	+	+

Legend: 1= Random sequence generation (selection bias); 2 = Allocation concealment (selection bias); 3 = Blinding of outcome assessment; 4 = Blinding of personnel/participates (performance bias); 5 = Incomplete data (attrition bias); 6 = Selective Reporting (reporting bias); 7 = other sources of bias

($I^2=49%$) was detected in the effects of the studies encompassing diverse clinical conditions [lung cancer (30), older adults with multiple chronic conditions (22), breast cancer (28), and head & neck or lung cancer (26)]. The forest plot of the model is depicted in **Figure 3**. Study-level significant associations between groups (clinical pathways *versus* control) and QoL were detected in three studies (22,27,30). The overall effect size of the meta-analysis showed that no differences were detected in the relationships between the model of care (clinical pathways *versus* control) and

QoL (OR=1.472 [0.483–4.486]; $p=0.496$). However, the overall effect size of the specific sub-group of studies encompassing diverse clinical conditions (mainly cancers) showed that patients belonging to the groups of clinical pathways reported higher levels of QoL (OR=2.629 [1.016–6.803]; $p=0.046$).

Clinical pathways versus standard of care and satisfaction

The overall model presented low heterogeneity ($I^2=0%$). The forest plot of the model is depicted in

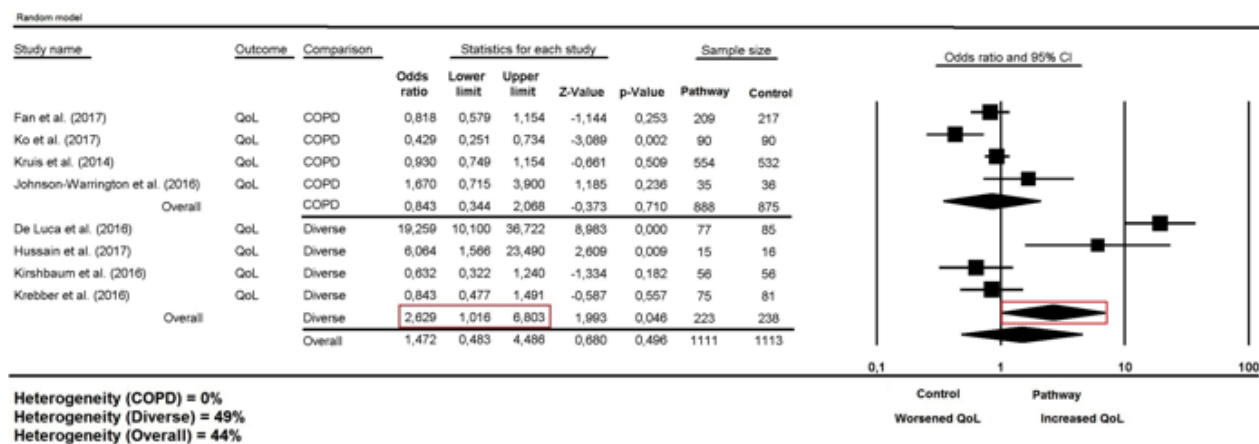


Figure 3. Clinical pathways and QoL

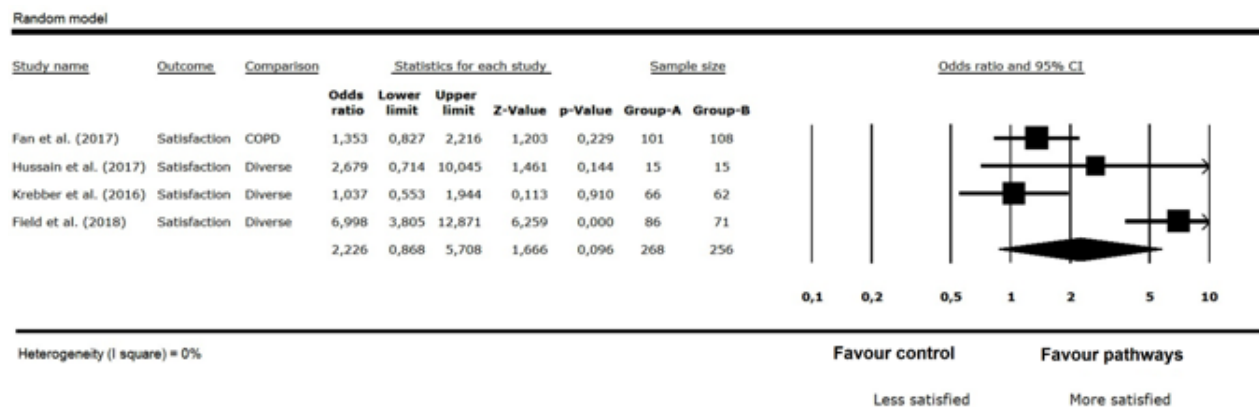


Figure 4. Clinical pathways and satisfaction

Figure 4. The overall effect size of the model showed that levels of satisfaction did not differ significantly between patients belonging to the group of clinical pathways and those belonging to the group of usual care (OR=2.226 [0.868–5.708]; $p=0.096$). A study-level significant association between the model of care (clinical pathways *versus* control) and satisfaction was detected in one study (31).

Clinical pathways versus standard of care and LoS

The overall model presented moderate heterogeneity ($I^2=45%$). The forest plot of the model is depicted in **Figure 5**. The overall effect size of the model showed that LoS decreased significantly among patients belonging to the group of clinical pathways

(OR=0,585 [0.349–0.982]; $p=0.042$). Study-level significant associations between the model of care (clinical pathways *versus* control) and LoS were detected in three studies out of four (24,27,29,31).

Discussion

This study provided a systematic review and meta-analysis of randomized controlled trials of evidence regarding the efficacy of adopting clinical pathways on patient-related outcomes. The descriptive synthesis of the included studies (Table 1) showed that the clinical fields where the adoption of clinical pathways was tested were diverse. As such, the included studies enrolled patients with different types of cancer (26,28),

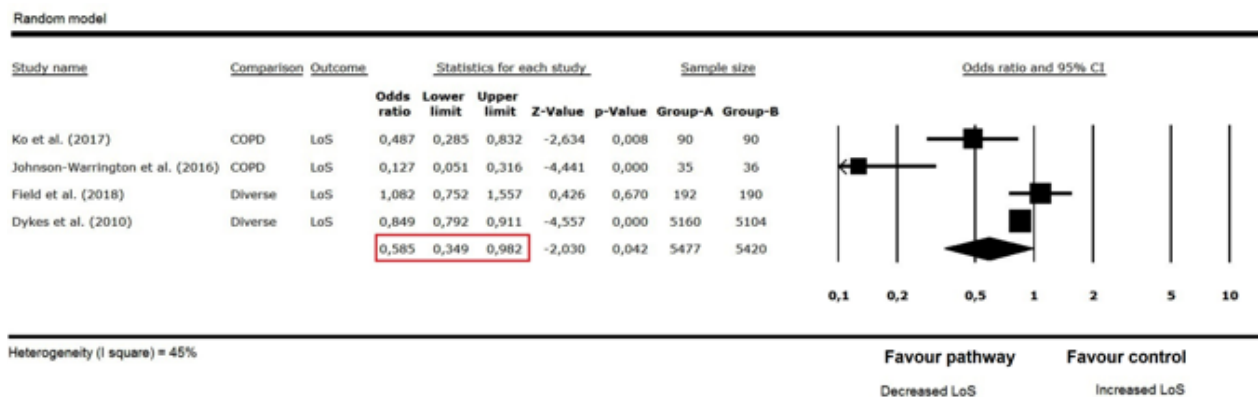


Figure 5. Clinical pathways and LoS

with COPD (23,25,27,29,32), and with multiple chronic conditions (22–24,30,31).

The QoL was the most described patient-related outcome in the included studies (22,25–30,32). The overall effect size of the meta-analysis on QoL did not support the associations between clinical pathways and QoL, but the sub-group analysis provided some insights into this regard. The QoL among patients with COPD was not significantly different in patients enrolled in clinical pathways and those treated by usual care; in fact, study-level associations showed improved patients who followed a clinical pathway only in one study (27). This result is consistent with the systematic review performed in 2016 for determining whether telemedical interventions could improve QoL in patients with COPD (33), where authors concluded that studying QoL in these patients is complex considering the clinical features of COPD. For this reason, it is plausible that significant changes in QoL of patients with COPD are challenging to be determined (33). Likewise, determining changes in the levels of QoL related to the effects of clinical pathways could be difficult in patients with COPD, owing to the features of the disease; accordingly, the comprehensive use of COPD-specific and general tools for measuring QoL represents the most appropriate strategy when it is needed measuring QoL in these patients (34).

Besides, the four articles focused on patients with diverse clinical conditions (mainly cancers or chronic morbidities, such as heart failure) showed that patients in the experimental groups (clinical pathways) reported

over time higher level of QoL, compared with those reported by patients in the usual care (22,26,28,30). In our subgroup analysis, this effect might reflect the high presence of patients with cancer (breast, lung, and head & neck) who could theoretically receive more benefit from the multi-disciplinarity of the multi-interventions embedded into clinical pathways (35–37). Considering the characteristics of people living with cancer, some authors recently stressed the importance of developing clinical pathways that embody interventions aimed at improving individual’s QoL and their psycho-social wellbeing (38). Future robust RCTs testing the effectiveness of clinical pathways on patient-related outcomes are needed to consolidate the available evidence.

Another overall effect size that showed statistically non-significant results was related to the association between the model of care (clinical pathways *versus* control) and satisfaction. As only four studies were meta-analyzed (26,30–32), a sub-group analysis was not feasible. The tools used to assess satisfaction in the included RCTs were heterogeneous, and considering that each tool has specific validity features for targeted populations (sensitivity, specificity, psychometric characteristics), it is plausible that the different used tools could have contributed to underestimating the observed pooled effect size. Further research aimed at evaluating the effects of clinical pathways on patient satisfaction is pivotal, as the satisfaction in the health-care context reflects the quality of the patient-provider relationship, technical competence accessibility, and

efficacy (39). Other aspects that contribute to determining satisfaction are individual-level characteristics, such as expectation, patient demographics, and personality (39). For this reason, studying patient satisfaction as an outcome is challenging: it should be analytically controlled for several determinants; however, it is crucial for its associations with patient compliance and clinical outcomes (39).

Finally, the pooled effect size of associations between the care model (clinical pathways *versus* control) and LoS was significant. Likely, this result could reflect the characteristics of the implemented clinical pathways (24,27,29,31): it is reasonable to think that the standardization of the multi-intervents required to develop and implement a clinical pathway has contributed to smooth the practical activities of the several professionals involved in the care process, resulting in a reduced LoS for patients.

During the early 2000s, the evidence suggested that clinical pathways were more likely to improve clinical outcomes when applied to clinical conditions with lower severity/complexity features (10). However, our study highlighted that in the last ten years, there is a tendency to develop and implement clinical pathways also for moderate and complex clinical conditions, such as including in the studies patients with different complexity (22,23,26,27,31,32) or performing pragmatic studies for defining the effectiveness of clinical pathways (25). This approach requires to be adopted by future research to demonstrate the feasibility and the efficacy of the implementation of clinical pathways to improve the practice. In recent years, the studies focused on testing clinical pathways for patients in the context of primary care are increasing, acknowledging the possibility to adopt digital solutions to intervene in education and remotely monitoring patients at home (40).

This study presents several limitations that require to be acknowledged. Firstly, the samples for each population (COPD, cancer, and other conditions) were limited and diverse, undermining the possibility to perform further in-depth analysis (e.g., sub-group analysis for each outcome): the generalization of our results is intended to be limited to those conditions consistent with those presented in the included studies. Furthermore, the low number of included studies represents

another limitation. Although we tried to identify all relevant studies to summarize the evidence regarding the efficacy of clinical pathways on patient-related outcomes within in-hospital settings, the search terms we used might not have found all the relevant studies because of the numerous terms adopted in the literature to describe a clinical pathway. Another limitation could be related to the choice of being not conservative in evaluating performance and detection biases (blinding) in our critical appraisal. However, considering that the blinding of patients and healthcare providers was not feasible for the characteristics of studies testing clinical pathways, we evaluated the blinding of data analysts and outcome assessment in the included RCTs. Finally, the limited number of included RCTs undermined the possibility of performing meta-analysis for determining the effect size of the associations between clinical pathways and other outcomes measured in the included studies, such as readmission, mortality, and several disease-specific clinical outcomes.

Conclusion

This systematic review and meta-analysis of RCTs synthesized the recent evidence regarding the efficacy of adopting clinical pathways on patient-level outcomes. Reduced LoS seemed to be associated with clinical pathways, while it is unclear whether adopting clinical pathways could improve QoL and satisfaction in patients with COPD, cancer, and multi-chronic conditions. For this reason, more primary research is needed to clarify how clinical pathways influence patient-related outcomes. Acknowledging that developing and implementing clinical pathways require high organizational commitment, we believe that higher levels of engagement towards these aspects among managers and multi-professional researchers would be desirable for continuously improving the research quality and effectively translating into the practice the available evidence.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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