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Clinical pathways for secondary care and the effects on professional practice, patient outcomes, length of stay and hospital costs (Review)

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[Intervention Review]

Clinical pathways for secondary care and the effects on professional practice, patient outcomes, length of stay and hospital costs

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ABSTRACT

Background

Clinical pathways (CPWs) are structured multidisciplinary care plans. They aim to translate evidence into practice and optimize clinical outcomes. This is the first update of the previous systematic review.

Objectives

To investigate the effect of CPWs on patient outcomes, length of stay, costs and charges, adherence to recommended practice, and to measure the impact of different approaches to implementation of CPWs.

Search methods

For this update, CENTRAL, MEDLINE, and Embase were searched on 25 July 2024. Two trial registries were searched on 26 July 2024, along with reference checking, citation searching and contacting authors to identify additional studies.

Selection criteria

We considered two groups of participants: health professionals involved in CPW utilization, including (but not limited to) physicians, nurses, physiotherapists, pharmacists, occupational therapists and social workers; and patients managed using a CPW. We included randomized trials, non-randomized trials, controlled before-after (CBA) studies, and interrupted time-series (ITS) studies comparing (1) stand-alone clinical pathways with usual care, and (2) clinical pathways as part of a multifaceted intervention with usual care.

Data collection and analysis

Two authors independently screened all titles, abstracts and full-text manuscripts to assess eligibility and the methodological quality of included studies using the Cochrane Effective Practice and Organization of Care 'Risk of Bias' tool. Certainty of evidence was assessed by two authors independently. Interventions were scored as 'high', 'moderate' or 'low' for the evidence-based implementation process.

Main results

The update provided 31 additional studies for a total of 58 included studies (24,841 patients and 2027 healthcare professionals). Forty-one (71%) were randomized trials, four (7%) non-randomized trials, four (7%) CBA studies and nine (16%) ITS studies. Forty-nine studies compared stand-alone CPWs to usual care and nine compared multifaceted interventions including a CPW to usual care. Collectively, the risk of bias was high due to potential contamination by healthcare professionals, lack of blinding of patients and personnel, lack of allocation concealment and selective reporting in ITS studies.

Stand-alone clinical pathway interventions

It is uncertain whether stand-alone CPWs reduce inhospital mortality (13% v 16%: OR 0.79, 95% CI 0.53 to 1.20; P = 0.27; I^2 = 65%; 7 randomized trials; n = 4603; low-certainty evidence due to serious imprecision and inconsistency) or mortality (up to 6 months) (4% v 3%: OR 1.37, 95% CI 0.72 to 2.60; P = 0.34; I^2 = 20%; 3 randomized trials, n = 805; low-certainty evidence due to serious risk of bias and imprecision). Stand-alone CPWs likely reduce inhospital complications (10% v 17%: OR 0.57, 95% CI 0.41 to 0.80; P = 0.001; I^2 = 52%; 11 randomized trials, n = 3668; moderate-certainty evidence due to serious risk of bias). It is very uncertain whether stand-alone CPWs reduce hospital readmissions (up to 6 months) (9% v 13%: OR 0.67, 95% CI 0.44 to 1.03; P = 0.07; I^2 = 11%; 9 randomized trials, n = 1578; very low-certainty evidence due to serious risk of bias and very serious imprecision). Stand-alone CPWs likely reduce the length of hospital stay compared to usual care (MD -1.12 days, 95% CI -1.60 to -0.65; P < 0.00001; I^2 = 64%; 21 studies; n = 5201; moderate-certainty evidence due to serious inconsistency). Costs and charges were generally lower in CPWs as indicated by negative MDs in nine studies (10 studies, n = 2113, data not pooled; very low-certainty evidence due to serious indirectness and very serious inconsistency). Stand-alone CPWs may slightly increase adherence to recommended practice compared with usual care (3 randomized studies, n = 573; data not pooled; low-certainty evidence due to serious risk of bias and serious inconsistency).

Multifaceted clinical pathway interventions

It is uncertain whether multifaceted CPWs reduce inhospital mortality (2 randomized studies, n = 6304, data not pooled; low-certainty evidence due to very serious inconsistency). Multifaceted CPWs may make little or no difference to mortality (up to 6 months) (9% v 8%: OR 1.05, 95% CI 0.88 to 1.25; P = 0.61; I^2 = 0%; 3 randomized studies; n = 6531; low-certainty evidence due to serious imprecision and serious risk of bias). It is uncertain whether multifaceted CPWs reduce inhospital complications (9% v 23%: OR 0.32, 95% CI 0.12 to 0.87; 1 study, n = 140; low-certainty evidence due to very serious imprecision).

It is uncertain whether multifaceted CPWs reduce hospital readmission (up to 6 months) (2 randomized studies, n =1569, data not pooled; low-certainty evidence due to very serious inconsistency), or length of stay (4 randomized studies, n = 1936, data not pooled; low-certainty evidence due to very serious inconsistency), or hospital costs and charges (4 randomized studies, n = 2015, data not pooled; very low-certainty evidence due to very serious imprecision and serious indirectness in outcome measures). It is uncertain whether multifaceted CPWs increase adherence to recommended practice (2 randomized studies, n = 6304, data not pooled, low-certainty evidence due to very serious inconsistency).

Key study characteristics

The highest proportion of included studies were from the USA (36%), followed by Australia (10%), China (10%), Japan (5%), the UK (5%), Canada (5%), Italy (5%), and Germany (5%). More than half of the included studies tested CPW in general acute wards (53%), followed by emergency departments (17%), intensive care (14%), and extended-stay facilities (10%). The most common clinical conditions were asthma (16%), stroke (10%), mechanical ventilation (9%) and myocardial infarction (7%).

Authors' conclusions

Stand-alone CPWs are likely to reduce inhospital complications and length of hospital stay and may slightly increase adherence to recommended practice. There was little conclusive evidence for multifaceted CPWs due to mixed results from a limited number of included studies. It is uncertain whether stand-alone CPWs or CPWs, as part of a multifaceted approach, reduce inhospital mortality, mortality (up to 6 months), hospital readmission (up to 6 months) or costs and charges.

PLAIN LANGUAGE SUMMARY

Effects of clinical pathways in hospitals on patient outcomes, length of hospital stay, hospital costs and charges, and adherence to recommended practice.

What is the aim of this review?

Clinical pathways (CPW) are document-based tools that provide a link between the best available evidence and clinical practice. They provide recommendations, processes and time frames for the management of specific medical conditions or interventions. This review update aimed to summarize the evidence and assess the effect of clinical pathways on patient outcomes (inhospital mortality, mortality (up to 6 months), inhospital complications, and hospital readmissions (up to 6 months)), length of hospital stay, hospital costs and charges, and professional practice (i.e. healthcare professionals adhering to recommended practice), compared to hospital care as usual. Also, we identified and compared different implementation strategies. We included patients in hospitals that were treated according to (1) the recommendations of a CPW, or (2) a CPW that has been implemented together with other interventions, such as a case manager or quality improvement initiatives. We analyzed 58 studies (24,841 patients and 2027 healthcare professionals), of which 27 were included in a previously published review (Rotter 2010) and 31 were retrieved for this update. This is the first update of the previous review.

Key messages

CPWs might have the potential to improve patient outcomes, and they may reduce length of hospital stay, hospital costs, and improve adherence to recommended practice. But we still need more high-quality studies that report on implementation strategies used during the pathway development and implementation.

What was studied in the review?

Decision-making in hospitals has evolved from being opinion-based to being based on sound scientific evidence (i.e. evidence-based practice). Hospitals incorporate evidence into clinical pathways for health professionals to follow. They have been implemented worldwide but the evidence about their impact from single trials is contradictory. Perpetual publication of new evidence combined with the demands of everyday practice makes it difficult for health professionals to keep up to date.

Included study designs were individual and cluster-randomized studies, non-randomized studies, controlled before-after studies (CBA), and interrupted time-series studies (ITS). In individual randomized trials, study participants were allocated to the CPW or usual care group by chance, called random allocation. Cluster-randomized trials divided all study participants into smaller groups known as clusters. These clusters were then allocated by chance to the CPW or usual care group. For non-randomized trials, participants were allocated to different groups by investigators in a quasi-random fashion. Quasi-random allocation means that study participants were allocated to the CPW or usual care group based on criteria such as their date of birth or the day of the week. CBA studies are experimental studies without a random or quasi-random allocation process. Data are collected from the CPW and usual care group before the CPW was implemented, and then further data were collected after the CPW was introduced. ITS studies represent a robust method of measuring the effect of a CPW as a trend over time.

All included studies tested the impact of clinical pathways used in hospitals on one or more of the prespecified outcomes: inhospital mortality, mortality (up to 6 months), inhospital complications, hospital readmissions (up to 6 months), length of hospital stay, hospital costs and charges, and adherence to recommended practice. Studies focused on the change in outcome measures following the implementation of a stand-alone clinical pathway or a multifaceted clinical pathway combined with other interventions compared to usual care.

What are the main results of the review?

We found 58 studies that measured the effects of clinical pathways on included outcomes. The main results are that, compared to usual care, it is uncertain if the implementation of a stand-alone clinical pathway has any effect on in-hospital mortality and mortality (up to 6 months) (low certainty). Stand-alone CPWs are likely to reduce inhospital complications (moderate certainty) but it is very uncertain if they make any difference to hospital readmissions (up to 6 months) (very low certainty). Stand-alone CPWs are likely to reduce length of hospital stay (moderate certainty). Costs and charges were generally lower in CPWs in nine out of ten studies included in this comparison (very low certainty). Stand-alone CPWs may also slightly increase adherence to recommended practice (low certainty).

For multifaceted clinical pathways compared to usual care, it is uncertain whether there is a reduction in inhospital mortality (low certainty) and they may make little or no difference to mortality (up to 6 months) (low certainty). It is uncertain whether CPWs that have been combined with other interventions reduce inhospital complications (low certainty) or hospital readmissions (up to 6 months) (low certainty). It is also uncertain if they reduce length of hospital stay (low certainty), hospital costs and charges (very low certainty), and adherence to recommended practice (low certainty), compared to usual care.

How up-to-date is this review?

This review update searched for new studies up to July 26, 2024.

SUMMARY OF FINDINGS

Summary of findings 1. Summary of findings

Stand-alone clinical pathway compared to usual care in secondary care

People: Hospitalized patients with conditions managed using a CPW, irrespective of diagnosis

Settings: Inpatient, outpatient, medical, surgical, critical care, emergency, rehabilitation, aged care

Intervention: Stand-alone clinical pathway

Comparison: Usual care

Outcomes	Absolute Effect*		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Usual care	With stand-alone clinical pathway				
Inhospital mortality	156 per 1000	127 per 1000 (89 to 181)	OR 0.79 (0.53 to 1.20)	4603 (7 RCTs)	⊕⊕⊖⊖ **Low**[a,b]	It is uncertain whether stand-alone CPWs reduce in-hospital mortality compared to usual care because the certainty of the evidence from RCTs is low. Similar effects were apparent in an nRCT and a CBA study.
Mortality (up to 6 months)	32 per 1000	43 per 1000 (23 to 79)	OR 1.37 (0.72 to 2.60)	805 (3 RCTs)	⊕⊕⊖⊖ **Low**[c,d]	It is uncertain whether stand-alone CPWs reduce 6-month mortality compared to usual care because the certainty of the evidence is low.
Inhospital complications (e.g. rate of infections, pressure injuries, pain, uncontrolled bleeding)	169 per 1000	104 per 1000 (77 to 140)	OR 0.57 (0.41 to 0.80)	3668 (11 RCTs)	⊕⊕⊕⊖ **Moderate** [c]	Stand-alone CPWs likely reduce inhospital complications, including infections, pressure injuries, pain and uncontrolled bleeding, compared to usual care. Similar effects were apparent in an nRCT.
Hospital readmission (up to 6 months)	131 per 1000	92 per 1000 (62 to 134)	OR 0.67 (0.44 to 1.03)	1578 (9 RCTs)	⊕⊖⊖⊖ **Very low** [c,e]	The evidence is very uncertain about the effect of stand-alone CPWs on hospital readmission. Effects varied between an nRCT and a CBA study.

Length of hospital stay (days) from admission until discharge	Not calculated due to an absence of baseline data in a number of RCTs.	MD 1.12 days lower (1.6 lower to 0.65 lower)	-	5201 (21 RCTs)	⊕⊕⊕⊖ **Moderate**[a]	Stand-alone CPWs likely reduce the arithmetic mean length of hospital stay compared to usual care. Similar effects were apparent in one of two nRCTs. Three additional studies (two RCTs and one nRCT) reported similar effects and lower geometric mean length of hospital stay compared to usual care.
Hospital costs and charges	The costs and charges varied widely between studies reflecting the different patient populations; for example, usual care ranged from $1806 to $40,445 and CPW ranged from $1180 to $40,801. For 10 RCTs, costs and charges were generally lower in CPWs as indicated by negative MDs in nine studies. The MDs ranged from -$6682 (95% CIs -$12,840 to -$523) to $355 (95% CIs -$7703 to $8414).			2113 (10 RCTs)	⊕⊖⊖⊖ **Very low**[f]	The evidence is very uncertain about the effect of stand-alone CPWs on hospital costs and charges. Costs ranged from a mean of $1180 for patients with atrial fibrillation on a CPW in the emergency department to $40,800 for mechanically ventilated intensive care unit patients. Results were too heterogeneous to combine in a meta-analysis.
Adherence to recommended practice	Two studies reported that CPWs increase adherence (ORs were 18.6 (95% CIs 8.1 to 42.7) and 26.7 (95% CIs 3.5 to 206)). One study reported no evidence of a difference (OR 1.9, 95% CIs 0.6 to 6.2).			573 (3 RCTs)	⊕⊕⊖⊖ **Low**[a,c]	Stand-alone CPWs may slightly increase adherence to recommended practice in treating geriatric hip fracture and stroke patients compared to usual care. Results from RCTs were too heterogeneous to combine in a meta-analysis. Similar effects were apparent in an nRCT.

*CI: Confidence interval; MD: Mean difference; OR: Odds ratio; RCTs: Randomized controlled trials; nRCTs: Non-randomized controlled trials; CBA: Controlled before-after

* The risk WITHOUT the intervention is based on the prevalence of the outcome in the control population. The corresponding risk WITH the intervention (and the 95% confidence interval for the difference) is based on the overall relative effect (and its 95% confidence interval).

GRADE Working Group grades of evidence

High = This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different‡ is low.

Moderate = This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different‡ is moderate.

Low = This research provides some indication of the likely effect. However, the likelihood that it will be substantially different‡ is high.

Very low = This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different‡ is very high.

‡ Substantially different = a large enough difference that it might affect a decision

[a] Downgraded one level due to serious inconsistency (substantial unexplained heterogeneity)
[b] Downgraded one level due to serious imprecision; despite optimal information size [n~4000] being met, CIs cannot exclude appreciable benefit or harm
[c] Downgraded one level due to serious risk of bias in included studies
[d] Downgraded one level due to serious imprecision (optimal information size was not met)

[e] Downgraded two levels due to very serious imprecision (CIs cannot exclude appreciable benefit or harm)
[f] Downgraded two levels due to very serious inconsistency (substantial unexplained heterogeneity) and one level due to serious indirectness in outcome measures

Summary of findings 2. Summary of findings

Multifaceted clinical pathway compared to usual care in secondary care

People: Hospitalized patients with conditions managed using a CPW, irrespective of diagnosis

Settings: Inpatient, outpatient, medical, acute care, emergency, aged care

Intervention: Multifaceted clinical pathway

Comparison: Usual care

Outcomes	Absolute Effect*		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Usual care	With multifaceted clinical pathway				
Inhospital mortality	One study (n = 4800) reported significantly lower inhospital mortality under a multifaceted CPW (0.46%) compared to usual care (0.96%) (OR 0.48, 95% CI 0.23 to 0.99). Another study (n = 1504) reported no difference in inhospital mortality between CPW (5.2%) and usual care (3.7%) (OR 1.41, 95% CI 0.86 to 2.32).			6304 (2 RCTs)	⊕⊕⊖⊖ **Low** [a]	It is uncertain whether multifaceted CPWs reduce inhospital mortality compared to usual care. Only two studies were included, and the results were too heterogeneous to combine in a meta-analysis.
Mortality (up to 6 months)	82 per 1000	86 per 1000 (73 to 101)	OR 1.05 (0.88 to 1.25)	6531 (3 RCTs)	⊕⊕⊖⊖ **Low** [b]	Multifaceted CPWs may make little to no difference to mortality (up to 6 months) compared to usual care.
Inhospital complications (rate of irregular bleeding or infection)	229 per 1000	87 per 1000 (34 to 205)	OR 0.32 (0.12 to 0.87)	140 (1 RCT)	⊕⊕⊖⊖ **Low** [c]	It is uncertain whether multifaceted CPWs reduce inhospital complications compared to usual care. Results were only available for one study of cirrhosis patients.
Hospital readmission (up to 6 months)	One study (n = 65) reported significantly lower readmissions for hypoglycemia in diabetic patients under a multifaceted CPW (6%) compared to usual care (34%) (OR 0.12, 95% CI 0.02 to 0.60). Another study (n = 1504) reported no difference in all cause hos-			1569 (2 RCTs)	⊕⊕⊖⊖ **Low** [a]	It is uncertain whether multifaceted CPWs reduce hospital readmission (up to 6 months) compared to usual care.

	pital readmissions between CPW (43%) and usual care (44%) (OR 0.93, 95% CI 0.72 to 1.20).			Only two studies were included, and the results were too heterogeneous to combine in a meta-analysis.
Length of hospital stay (days) from admission until discharge	Of four studies, two reported a reduction in length of hospital stay (MDs were -3.98 and -2.44 days, respectively), and two studies reported no evidence of a difference between groups in length of hospital stay between CPW and usual care (MDs were 0.60 and -0.80, respectively).	1936 (4 RCTs)	⊕⊕⊖⊖ **Low** [a]	It is uncertain whether multifaceted CPWs reduce the length of stay compared to usual care. Results were too heterogeneous to combine in a meta-analysis.
Hospital costs and charges	Of four studies, one reported reduced costs and charges (the MD was -$535.10) and three studies reported no evidence of a difference between groups in costs and charges between CPW and usual care (MDs were -$3316.19, -$52.63 and -$887.03).	2015 (4 RCTs)	⊕⊖⊖⊖ **Very low** [d]	The evidence is very uncertain about the effect of multifaceted CPWs on hospital costs and charges. Costs ranged from a mean of $153 for admitted patients with diabetes on a CPW to $37,100 for treatment of bipolar disorder over 3 years. Results were too heterogeneous to combine in a meta-analysis.
Adherence to recommended practice	One study (n = 1504) reported no significant difference in each of three process of care outcome measures between a multifaceted CPW and usual care. Another study (n = 4800) reported slightly greater adherence to recommended practice among patients receiving care under a multifaceted CPW (53.8%) compared to usual care (47.8%) (OR = 1.3, 95% CI 1.1 to 1.4).	6304 (2 RCTs)	⊕⊕⊖⊖ **Low** [e]	It is uncertain whether multifaceted CPWs increase adherence to recommended practice compared to usual care. Only two studies were included and the results were too heterogeneous to combine in a meta-analysis. A CBA study reported greater symptom assessment in multifaceted CPWs.

*CI: Confidence interval; OR: Odds ratio; RCTs: Randomized controlled trials; nRCTs: Non-randomized controlled trials; CBA: Controlled before-after

* The risk WITHOUT the intervention is based on the prevalence of the outcome in the control population. The corresponding risk WITH the intervention (and the 95% confidence interval for the difference) is based on the overall relative effect (and its 95% confidence interval).

GRADE Working Group grades of evidence

High = This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different‡ is low.

Moderate = This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different‡ is moderate.

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Very low = This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different‡ is very high.

‡ Substantially different = a large enough difference that it might affect a decision

[a] Downgraded two levels due to very serious inconsistency (meta-analysis not possible due to significant heterogeneity and lack of overlap between confidence intervals)
[b] Downgraded two levels due to serious risk of bias and serious imprecision; despite optimal information size [n~4000] being met, CIs cannot exclude appreciable harm or benefit
[c] Downgraded two levels due to very serious imprecision: only one study with small sample size
[d] Downgraded three levels due to very serious imprecision (meta-analysis not possible due to significant heterogeneity and lack of overlap between CIs) and serious indirectness in outcome measures
[e] Downgraded two levels due to very serious inconsistency (meta-analysis not possible due to risks of duplicate counting)

BACKGROUND

This is the first update of the original review (Rotter 2010).

Description of the condition

With continuous advocacy for patient-centered care by the public, health systems are continually faced with the task of delivering safe and high-quality services to patients (Parand 2014). The adoption of clinical pathways (CPWs) worldwide is gradually on the increase and substantial resources have been expended on pathway development, implementation, and sustainability in hospitals (Van de Klundert 2010). However, individual studies investigating the impact of CPWs have reported conflicting outcomes (Rotter 2010). For instance, some studies found that the introduction of CPWs for different types of clinical conditions such as myocardial infarction (Li 2018), transient ischemic attack (Deng 2014 (TIA)) or intracerebral hemorrhage (Deng 2014 (ICH)), can reduce the length of hospital stay, while others such as Trombetti 2013 and Bernard 2011 found increased or equal length of hospital stay for malnourished and diabetic patients, respectively.

Description of the intervention

Clinical pathways aim to link evidence to practice for specific health conditions or treatments and, therefore, optimize patient outcomes and maximize clinical efficiency (Plishka 2016). For this review, CPWs are defined as structured multidisciplinary care plans which detail essential steps in the care of patients with a specific clinical problem (Rotter 2010). They support the translation of clinical guidelines into local protocols and clinical practice (Campbell 1998). Whilst clinical guidelines provide generic recommendations, CPWs detail the local structures, systems, and time frames to address these recommendations. Note that a myriad of terms has been used to describe CPW, such as 'integrated care pathways', 'critical pathways', 'care plans', 'care paths', 'algorithms' and 'care maps' (Kinsman 2010; Lawal 2016). In addition to evidence-based practice, CPWs have been proposed as a strategy to optimize resource allocation in a climate of rising healthcare costs, as they may improve the efficiency with which healthcare is delivered (Kimberly 2009).

Clinical pathway definition

We undertook a three-stage process to develop an operational definition for a CPW. This process was described in the previous version of this review (Rotter 2010). Recently, we refined the operational definition following the rigorous approach suggested by (Kinsman 2010) and (Wieland 2011) to accommodate relevant literature on CPWs, spanning across a broader context of healthcare settings, including primary care (Lawal 2016). The following four criteria for a CPW operational definition, derived from the refinement process described above, are: (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 the 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); and (4) the intervention aimed to standardize care for a specific population. We considered an intervention meeting all four criteria to be a CPW.

How the intervention might work

CPWs may serve as strategies to reduce variation in hospital practice by providing evidence-based care recommendations. CPWs have the potential to reduce inhospital complications, improve patient outcomes, and enhance efficiency in the health system (Rotter 2010). They are most commonly developed at local levels via consensus and/or adapting clinical practice guidelines, and they interact with other contextual and behavioral factors where implemented to achieve desirable outcomes.

Even though CPWs are used as knowledge translation tools to provide the best available evidence during an episode of care, there has been limited research focused on understanding which components contribute to the success of CPW interventions (Dalkin 2012). Because CPWs are multidisciplinary and may have multiple components, contextual factors must be considered during their implementation (Jabbour 2013). Several theories to explain the incorporation of new knowledge into practice have been identified in the literature (Grol 2013; Kastner 2015). These have been broadly classified by Grol 2007 into (1) individual-related theories: cognitive theories, educational theories, and motivational theories; and (2) social interaction and context theories: theories of communication, social learning theory, teamwork theories, leadership theories, theories of organizational learning and culture, complexity theory, and economic theories.

Behavioral change theories emphasize the incorporation of patient and healthcare professionals' perspectives on existing care standards in order to facilitate optimum adherence to the pathways (Grol 2007). Positive outcomes of CPW implementation may be most easily observed when prior compliance to clinical standards has been poor, as this leaves the potential for substantial improvements. In contrast, CPW implementation in settings demonstrating already high compliance to clinical standards has shown little or no improvement (Deneckere 2012). CPWs may help to overcome the barrier of updating clinical standards in a practice area that is not feasible for individual healthcare professionals. CPWs aim to support the decision-making process of physicians and other healthcare professionals in hospitals, but they do not directly target patients and their families. How to better involve patients in their own care process with the support of CPW is an important gap in the literature. Organizational theories may provide insights into critical elements from a macro health systems perspective that are required for change and sustainability processes (e.g. barriers to change, organizational culture, vision, and focus).

Why it is important to do this review

This review is part of a series of Cochrane Reviews on CPWs to investigate their effects on professional practice, patient outcomes, length of hospital stay, and hospital costs (Rotter 2007; Rotter 2013). This review focuses on the effects of CPWs in hospitals and updates a previous Cochrane Review (Rotter 2010). The previous version of this Cochrane Review included 27 studies that met the inclusion criteria at that time from eight countries (Australia, Canada, Japan, Norway, Taiwan, Thailand, UK, and USA). The review in 2010 concluded that CPWs are associated with reduced inhospital complications and improved adherence to recommended practice without negatively impacting on length of hospital stay and hospital costs.

The review on CPWs in hospitals published in 2010 (Rotter 2010) has been highly cited, and the findings have been used in clinical practice guideline development. Since the original review was published, there has been a gradual rise in the uptake of CPWs in hospitals (Rotter 2019). Maintaining a high-quality, up-to-date, and relevant database of pathway effectiveness is crucial to meaningfully and objectively assessing the impact of CPWs in hospitals.

OBJECTIVES

To investigate the effects of clinical pathways on patient outcomes, length of hospital stay, costs and charges, and professional practice (i.e. adherence to recommended practice) compared to usual care in hospital settings, and assess the impact of different approaches to implementation of CPWs.

METHODS

Criteria for considering studies for this review

Types of studies

For this review update, we included randomized trials and non-randomized trials. Our original review protocol (Rotter 2007) included non-randomized studies as there were few randomized trials at that time. This update revealed there has been a substantial increase in randomized trials that meet inclusion criteria since the protocol was published in 2007. While we have included non-randomized trials in this update, we will reconsider their contribution to review outcomes in future updates.

Following the Effective Practice and Organization of Care (EPOC) methodological design criteria, we included: individual and cluster-randomized trials, non-randomized trials, controlled before-after (CBA) studies, and interrupted time-series (ITS) studies (EPOC 2017a).

In individual randomized trials, participants are allocated to the intervention or control groups in a random fashion. Cluster-randomized trials were required to meet the EPOC minimum inclusion criteria of at least two intervention and two control sites.

For non-randomized trials, participants are allocated to different groups by investigators in a non-random fashion. They pose a greater risk of bias compared to randomized trials.

CBA studies are experimental studies with at least two intervention sites and two control sites without randomization during the allocation process. Data are collected from the control and intervention groups before the intervention is introduced and then further data are collected after the intervention has been introduced. We reassessed all CBA studies from Rotter 2010 to ensure they met the current EPOC standards for CBA studies for this updated review.

ITS studies represent a robust method of measuring the effect of an intervention as a trend over time; it is a useful design when recruitment of a control cohort is impractical, for example, change in hospital policy. Three or more data points are collected before and after the intervention as a minimum standard (EPOC 2017a). The intervention effect is measured against the pre-intervention trend.

There was no restriction on the language of studies or date of publication.

Types of participants

We considered two groups of participants relevant for this review.

- Health professionals, including physicians, nurses, physiotherapists, pharmacists, occupational therapists, social workers, dietitians, psychologists, psychiatrists, speech pathologists, and dentists involved in CPW utilization in the hospital setting;
- Hospitalized patients (inpatient and outpatient settings) with conditions managed using a CPW, irrespective of diagnosis.

Setting

We included studies conducted in hospitals evaluating the impact of CPWs.

Types of interventions

We included two comparisons.

- Stand-alone CPW versus usual care;
- Multifaceted interventions that include CPW versus usual care.

The interventions included in this review fall under the EPOC taxonomy 'delivery arrangements' and the category 'co-ordination of care and management of care processes' (EPOC 2017b).

We excluded dissemination of clinical practice guidelines alone, unless the guidelines were translated into a CPW. We expected that most studies would compare a CPW intervention with usual care in the same setting. We included studies of multifaceted interventions if the CPW could be separately assessed from other elements of the intervention. For example, a multifaceted intervention that included the introduction of a case management model, professional education, introduction of a CPW and structural change, such as the introduction of information technology support, with the aim being to enhance evidence-based practice. In such an instance, we included studies in which a multifaceted intervention incorporating CPW was compared to usual care.

The four criteria for the definition of a CPW were:

- The intervention was a structured multidisciplinary plan of care;
- The intervention was used to channel the translation of guidelines or evidence into local structures;
- The intervention detailed the 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); and
- The intervention aimed to standardize care for a specific clinical problem, procedure or episode of healthcare in a specific population.

Please see Appendix 1 for our working definition (checklist) on CPWs.

Types of outcome measures

Based on our experience with the previous review (Rotter 2010), we expected to find variation in the range of follow-up and criteria used for assessing outcomes in the included studies.

Primary outcomes

- Inhospital mortality, defined as death (from all causes) occurring during hospitalization (from admission to discharge);
- Mortality (up to 6 months);
- Inhospital complications;
- Hospital readmission (up to 6 months).

Secondary outcomes

- Length of hospital stay (days);
- Hospital costs and charges;
- Adherence to recommended practice;
- ICU admissions;
- Discharge destination.

Search methods for identification of studies

Electronic searches

We topped up the searches in the following databases with no language restrictions on 25 July 2024, restricting the most recent search to articles with a creation date between 5 April 2022 and 26 July 2024.

- The Cochrane Central Register of Controlled Trials (CENTRAL; 2024, Issue 4, 2024) in the Cochrane Library;
- MEDLINE Ovid (1946 to 25 July 2024);
- Embase Ovid (1974 to 25 July 2024).

We searched electronic sources using a strategy incorporating the methodological component of the EPOC search strategy combined with selected MeSH terms and free-text terms relating to clinical or critical pathways. We translated this search strategy into the other databases using the appropriate controlled vocabulary, as applicable. The full search strategies for all databases are provided in Appendix 2.

Searching other resources

Grey literature

On 29 September 2020, we conducted the most recent grey literature search to identify studies not indexed in the databases listed above. Sources included the sites listed below. We documented additional sources, if any, in the review (Appendix 3). Please note, the grey literature searches were not updated in 2024, because our previous searches did not identify additional studies to be included in this review update.

- Web of Science (www.webofknowledge.com);
- OpenGrey (www.opengrey.eu);
- Google (www.google.com).

Trial registries

We searched the following trial registries on 26 July 2024.

- The World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) search portal (https://trialsearch.who.int/);
- ClinicalTrials.gov (clinicaltrials.gov).

In addition to databases, we searched other resources for published and unpublished studies.

- We handsearched high-yield journals and conference proceedings which had not already been hand searched on behalf of Cochrane (Appendix 4);
- We reviewed reference lists of all papers and relevant reviews identified;
- We contacted authors of relevant articles regarding any further published or unpublished work;
- We contacted researchers with expertise relevant to the review topic for other studies.

Data collection and analysis

Selection of studies

We imported the search results into reference management software and removed duplicate records. Three pairs of review authors (TR, LK, CC, GG, LA, PW) independently screened all titles and abstracts for manuscripts eligible for full-text assessment, including criteria for the definition of a CPW. We resolved any disagreement by verbal or written discussion or through a third review author who served as an arbitrator (LB, UR, AA). We retrieved the full-text copies of all potentially relevant papers identified during the titles and abstract screening phase, and we sent non-English studies for translation to examine eligibility for inclusion in the final stage of review. Two review authors (TR and LK) independently assessed all full-text studies with the review inclusion criteria and resolved disagreements by discussion or with the use of an arbitrator (AA). We documented the selection process in sufficient detail to complete a PRISMA flow chart (Liberati 2009; Page 2021).

Data extraction and management

We extracted data using a modified standardized data extraction form based on Cochrane EPOC's data collection checklist (EPOC 2017c), and extracted directly from trial reports. Three pairs of review authors (TR, AA, LK, SS, TS, CP) independently extracted information. LB and AM served as arbitrators in case of disagreement. When necessary, we sought additional information on study characteristics, study design, intervention types, and outcomes reported by the authors of primary studies. For all the included studies, we extracted study characteristics (see data collection form in Appendix 5) and implementation features reported in the studies.

We extracted the following main sets of data from each included study.

Methods: study design (randomized trials, non-randomized trials, CBA, ITS):

- For randomized trials, non-randomized trials or CBA: level of randomization/allocation, level of analysis;
- For CBA: timing of data collection, number, and characteristics of control sites;
- For ITS: defined point in time when the intervention occurred and number of data points before and after the intervention;
- Power calculation for sample size.

Setting and participants:

- Geographic location and section of the hospital, country, number and characteristics of health professionals, number and characteristics of included patients.

CPW intervention characteristics:

- Type of CPW intervention (single CPW or multifaceted CPW intervention), CPW condition targeted, purpose of the CPW, format of the CPW intervention (paper-based or electronic), and CPW implementation process reported (see section on implementation features below).

Outcome measures, primary outcomes:

- Inhospital mortality, defined as death from all causes occurring during hospitalization (from admission to discharge);
- Mortality (up to 6 months);
- Inhospital complications;
- Hospital readmission (up to 6 months).

Secondary outcomes:

- Length of hospital stay (days);
- Hospital costs and charges;
- Adherence to recommended practice;
- ICU admissions;
- Discharge destination.

Notes:

- Trial registration, trial funding, declarations of interest of authors.

For this updated review, we applied a 10-criteria checklist for implementation features of complex interventions to all included studies. Previous studies (including EPOC reviews) have demonstrated that implementation of interventions to improve professional practice benefits from being multifaceted and includes the following features: 1) evidence-based content; 2) adaption for local use; 3) clinician involvement in CPW development; 4) use of an implementation team; 5) evidence-practice gap identification prior to implementation; 6) identification of potential barriers to change; 7) incorporation of reminder systems; 8) incorporation of audit and feedback into implementation; 9) use of education sessions; and 10) use of local opinion leaders as part of the process (Cluzeau 1999; Doherty 2006b; Grimshaw 1998; Grimshaw 2001; Stone 2002). We ranked each study based on an overall implementation score with an equal weight applied to each criterion on the checklist. We could not estimate from previous studies the relative weightings for each of the ten implementation features. We ranked a study as 'high' if seven or more implementation features were used, 'moderate' if four to six implementation features were used, and 'low' for up to three implementation features.

For studies reporting on costs and charges, we extracted information on the costing method.

For ITS data presented in a graphical format, we extracted data using the Plotdigitizer software recommended by EPOC (Sourceforge 2020). We saved each graph as a JPEG file, opened it via the Plotdigitizer software and the raw data were extracted by dragging the cursor over each data point.

Continuous and dichotomous data reported in the included studies were extracted, transformed if necessary and imported into Review Manager 5 for further analysis (Review Manager 2025).

Assessment of risk of bias in included studies

Two reviewers (KS and TS) independently assessed the risk of bias for each study outcome. Reasons for any disagreements were explored and resolved by an independent third reviewer if needed (LK). The risk of bias tool was piloted prior to use on five papers.

We assessed the following domains for randomized trials, non-randomized trials and CBA studies: sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective outcome reporting (reporting bias), baseline imbalance (other bias) and protection against contamination (other bias) (EPOC 2017d).

For other sources of bias, we considered studies that had not controlled for study variables that could impact the findings. These types of included studies reported potential confounders in the CPW implementation, such as different unit culture and leadership in the CPW and control groups, parallel exposure to other educational offerings by healthcare professionals, wide variations in the processes of care, and lack of information about participants. We used funnel plots to check for the existence of funding and/or publication bias.

For ITS studies we assessed the following seven domains: intervention independent of other changes, prespecified effect shape, intervention unlikely to affect data collection, blinding, incomplete outcome data, selective outcome reporting, and other bias (EPOC 2017d).

We rated each domain and categorized it in a 'Risk of bias' table as 'low risk', 'unclear risk', or 'high risk', as described in the Cochrane Handbook for Systematic Reviews of Interventions (Boutron 2019; Higgins 2011). We did not exclude any study based on risk of bias. We earmarked studies given an overall rating of 'high risk' (see below) for sensitivity analysis, in order to examine their influence on the pooled effect estimates.

Overall risk of bias

We assigned an overall risk of bias judgment by following the Cochrane handbook to map risk of bias judgments within domains to an overall judgment for the outcome (Higgins 2011):

- Low risk of bias: The study was assessed at low risk of bias for all domains;
- Unclear risk of bias (some concerns): The study was assessed at unclear risk of bias (some concerns), but not at high risk of bias for any domain;
- High risk of bias: The study was assessed at high risk of bias in at least one domain.

We used the ‘overall’ risk of bias judgment for conducting the sensitivity analysis and for the SoF tables.

Measures of treatment effect

Measures of treatment effect reported for randomized trials

Cluster-randomized trials

We critically appraised all included cluster-randomized trials if they reported on measures of treatment effects for continuous and dichotomous data that had been adjusted for cluster (design) effects. Also, if it remained unclear that a specific study outcome had been adjusted for cluster effects, we reported this outcome in the section on 'Unit of analysis issuest' below.

Dichotomous data

We extracted the total number of events (N) from the primary studies that were included and calculated a percentage (%) for each study group (CPW group versus control group) for inhospital mortality, mortality (up to 6 months), inhospital complications, hospital readmissions (up to 6 months), and adherence to recommended practice.

Continuous data

We used the mean values (mean) and standard deviations (SD) reported for each study group (CPW group versus control group), including P values and 95% CIs (as far as reported) for the hospital length of stay and hospital costs and charges data.

Measures of treatment effect reported for CBA studies, non-randomized studies, and ITS studies

For the 17 non-randomized individual studies included in this review update (four CBA studies, four non-randomized studies, and nine ITS studies), the reported treatment effects are based on unadjusted study results.

We performed all analyses using Review Manager 5 (Review Manager 2025). We estimated the effect of the intervention on continuous outcome measures by calculating the mean difference (MD) with the corresponding 95% confidence interval (CI). We estimated the effect of the intervention on dichotomous outcomes using odds ratio (OR), together with the associated 95% CI, or risk difference (RD) with 95% CI.

Hospital cost measures

We extracted and reported the cost measures (hospital costs and charges) and the approach used to estimate costs (e.g. direct costs, indirect costs, or full costing approach) in additional Table 1. Also, we planned to include full economic evaluations (e.g. cost-effectiveness and cost-benefit analysis), but this was not possible as the data were not reported. We updated the effects of CPWs on costs and charges (cost/charges analysis), for all studies that reported on cost measures. We presented cost/charges data in USD for the common price year 2016 (see additional Table 2) by using the 'CCEMG-EPPI-Centre Cost Converter' (Version 1.5), a web-based tool that can adjust an estimate of cost expressed in one currency and price year to a target currency and/or price year, or both (Shemilt 2008; Shemilt 2010). We adjusted costs/charges for inflation by applying Gross Domestic Product deflators ('GDPD values') or using government recommended rates (Drummond 1996). Additionally, we provided the undiscounted cost data (additional Table 3) to allow readers to recalculate the results using any discount rate.

Unit of analysis issues

The majority of the cluster-randomized trials properly accounted for design effects in their analysis (Costantini 2014; Doig 2008; Kinsman 2012; Panella 2009; Panella 2012; Panella 2018; Philbin 2000 Seys 2019; Vanhaecht 2016; Wang 2018), except for two studies that reported on continuous outcomes (Marrie 2000, Cunningham 2008). Also, it remained unclear if the continuous outcomes (e.g. length of stay) in the pathway investigation by Panella and colleagues (2009) had been adjusted for cluster effects (Panella 2009). Those studies that accounted for design effects provided adjusted ORs for dichotomous data, and thus we were able to combine data from the cluster-randomized trials and individual-randomized trials (i.e. in the inhospital mortality, inhospital complications, hospital readmission, adherence to recommended practice outcomes).

For continuous outcomes, we used the intra-cluster correlation coefficient (ICC) to recalculate an effective sample size that accounted for design effects (Higgins 2011a). For studies that did not provide the ICC, we selected a similar intervention with comparable study characteristics reporting an ICC (ICC-database 2017).

Dealing with missing data

If a primary study did not provide information about standard deviation and P values, we used the approximate or direct algebraic connection between the stated confidence intervals, or P values, and the standard deviation and calculated the inverse transformation to the individual or pooled standard deviation (Deeks 2019). In other instances, we attempted to contact the primary author for additional information.

Results arising from included ITS studies (Bartlett 2017; Brattebø 2002; Brennan 2018; Tilden 1987) were provided graphically only. The raw data were not available. Graphs of results were converted to raw numbers using the following process:

- Each graph was saved as a Micrososoft Paint file;
- In Plotdigizer (Sourceforge 2020), the number of pixels per unit measure was calculated by dragging the cursor over each graph's scale. The height of the scale was displayed in a total number of pixels using this approach. Pixels per unit of measure were then calculated by dividing the number of pixels by the corresponding scale number;
- Raw numbers for each data point were then calculated by dragging the cursor over each data point to display the number of pixels and converting the number of pixels to raw numbers using the previously calculated conversion figure (Grimshaw 2005).

Assessment of heterogeneity

Please see 'Assessment of heterogeneity' section below.

Assessment of reporting biases

We assessed the potential for publication bias in the results of each meta-analysis in which ten or more studies were included by visual inspection of funnel plots for asymmetry. In the event of an asymmetry, we planned to re-assess the characteristics of the included trials to better understand whether the asymmetry was due to publication bias or other reasons such as heterogeneity.

Data synthesis

We followed the Cochrane and Cochrane EPOC recommendations regarding re-analysis of individual studies and data synthesis (EPOC 2017e; Higgins 2019a.)

We reported results from different types of study designs (i.e. randomized trials, non-randomized trials, CBA studies and ITS studies) separately. We pooled results in a meta-analysis when it was meaningful to do so, i.e. when interventions, participants and outcomes were sufficiently similar and reported for two or more outcomes. We used a random-effects model to combine the data across studies. In order to combine dichotomous outcomes from cluster-randomized studies and individual randomized studies (i.e. for inhospital mortality, inhospital complications, hospital readmission, adherence to recommended practice outcomes), we used the generic inverse variance method (note that all cluster-randomized studies reporting these outcomes provided ORs that had been adjusted by design effects). Where meta-analysis was not appropriate due to the clinical and methodological diversity of individual studies, we presented a structured summary of effects and described the results narratively in the results section of the review. The structured summary of effects presented summary data for intervention and control arms, the intervention effect estimates, 95% CIs, P values and statistical tests used.

Assessment of heterogeneity

We assessed statistical heterogeneity by visual inspection of the forest plots and by using the Chi^2 and I^2 tests. We interpreted the Chi^2 test so that $P < 0.10$ indicated evidence of statistical heterogeneity. The Cochrane Handbook indicates that an I^2 statistic of > 75% indicates considerable heterogeneity, and necessitates further exploration of the possible causes and may preclude meta-analysis (Deeks 2019). Where I^2 was above 75%, we did not calculate a pooled estimate of effect. We had planned to explore clinical heterogeneity via the subgroup analyses listed below if there were an adequate number of studies to justify subgroup analyses. The Cochrane Handbook suggests that at least ten observations (i.e. ten studies in a meta-analysis) should be available for each subgroup analysis (Deeks 2019).

Subgroup analysis and investigation of heterogeneity

- Type of study (randomized studies versus non-randomized studies);
- Country(s) where the study was carried out (to identify potential country-specific effect modifiers);
- The date of study/year of publication (e.g. studies grouped and effects compared in 5-year intervals);
- Hospital area (intensive care versus acute care);
- Type of procedure (invasive versus non-invasive);
- Implementation score (high versus moderate versus low).

We had hypothesized that non-randomized trials might report on larger effect sizes as opposed to randomized trials. We had hypothesized that country-specific mortality rates might be an effect modifier. We had hypothesized that studies conducted up to 2002, between 2003 and 2008, and those after 2009 might report on different effect sizes due to temporal trends. We had hypothesized that different levels of care (intensive care versus acute care) might report on context-specific effect sizes. We had hypothesized that the type of procedure (invasive versus non-invasive) might explain the larger effect sizes reported for invasive CPW interventions. We had hypothesized that the evidence-based implementation score might be linked to the size of effect reported (e.g. larger effects reported for studies with high implementation scores).

Sensitivity analysis

In order to examine the robustness of the pooled effect estimates, we conducted a sensitivity analysis by removing studies rated at high risk of bias from the analysis.

Summary of findings and assessment of the certainty of the evidence

We assessed the certainty of the evidence (Appendix 6; high, moderate, low and very low) using the five GRADE considerations (risk of bias, consistency of effect, imprecision, indirectness, and publication bias) as described in (Guyatt 2008). Two authors (TS and TR) independently assessed the certainty of the evidence. We created two 'Summary of findings' tables for the two main comparisons examined in this review (stand-alone CPWs versus usual care and multifaceted CPWs versus usual care) and, included: inhospital mortality, mortality (up to 6 months), inhospital complications, hospital readmission (up to 6 months), length of hospital stay, hospital costs and charges, and adherence to recommended practice.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies;

Results of the search

This review update searched for new studies up to July 26, 2024. The database searches in this review update yielded 24,737 search records. After de-duplication, titles and abstracts of 20,474 records were screened and 20,053 were excluded. We screened the remaining records by reviewing 421 full-text records and 377 were excluded. See 'Characteristics of excluded studies' for detailed information about the most relevant full-text papers excluded. This left 45 records. One of the included records presents independent results for two clinical populations and thus is presented as two separate studies in the results section (i.e. Deng 2014 (ICH); Deng 2014 (TIA)). Thus, there were 31 new studies included in this review update, and 14 studies listed as 'awaiting classification'. Along with the 27 studies included in Rotter 2010, 58 studies are included in this review update. See Figure 1 for the PRISMA diagram.

Figure 1. Prisma diagram: update review

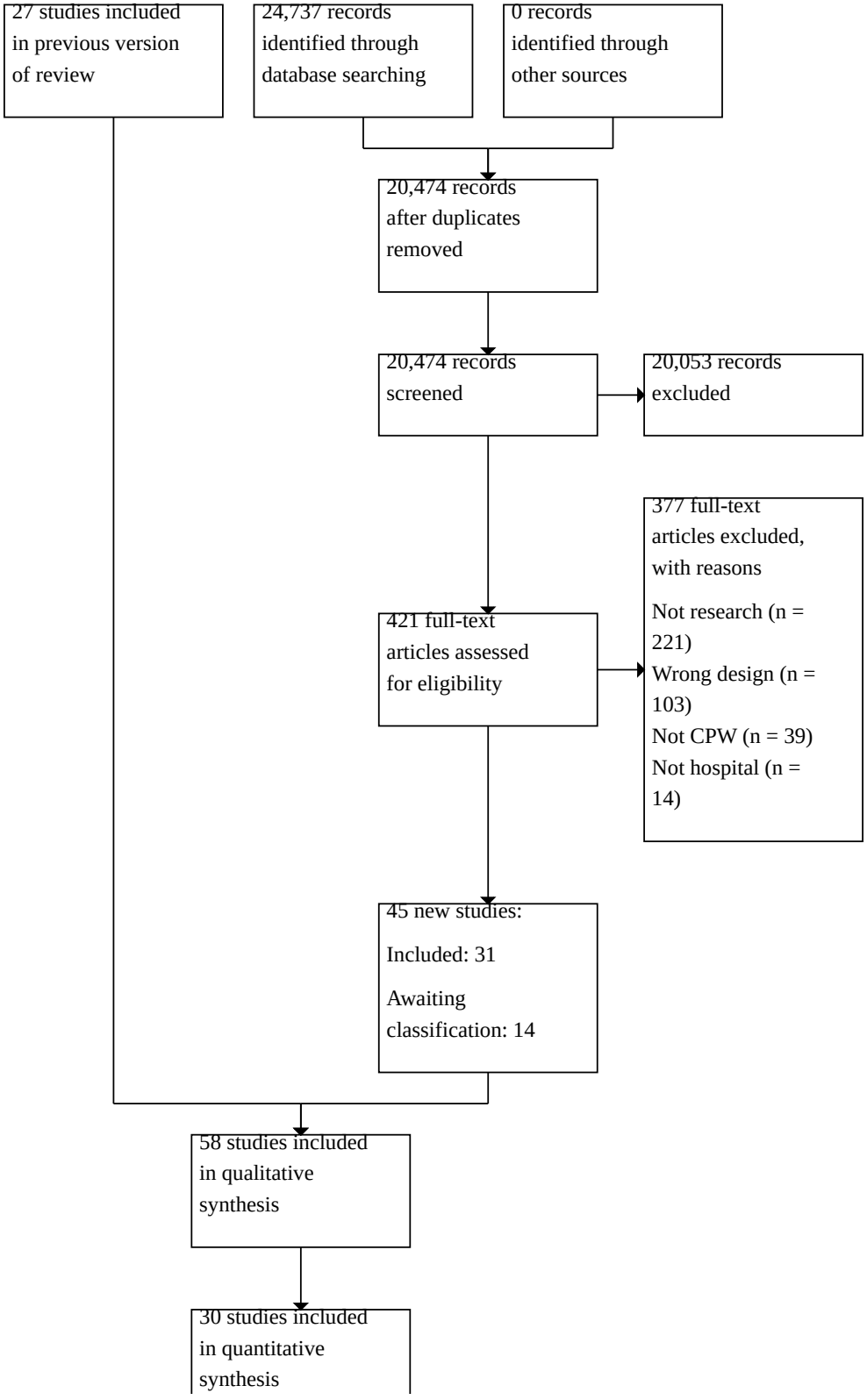


Figure 1. (Continued)

in qualitative synthesis (meta-analysis)

Included studies

The 58 studies represent a combined sample size of 24,841 patients and 2027 healthcare professionals across approximately 200 hospitals from 20 countries for a wide range of conditions described below. A description of the 58 studies is provided in the Characteristics of included studies tables. See also additional Table 4 for a summary of population and study design characteristics for all included studies.

Study designs

Forty-one (71%) included studies were randomized trials (Aizawa 2002; Almalki 2017; Bauer 2006; Bernard 2011; Bittinger 1995; Brook 1999; Chen 2004; Chen 2019; Cole 2002; Costantini 2014; Cunningham 2008; Delaney 2003; Deng 2014 (ICH); Deng 2014 (TIA); Doig 2008; Dowsey 1999; Falconer 1993; Gomez 1996; Gooch 2012; Homagk 2016; Jalil 2017; Johnson 2000; Ju 2019; Kampan 2006; Kim 2002; Kinsman 2012; Kiyama 2003a; Kollef 1997; Li 2018; Marelich 2000; Marrie 2000; Muehling 2008; Panella 2009; Panella 2012; Panella 2018; Philbin 2000; Roberts 1997; Seys 2019; Sulch 2002; Vanhaecht 2016; Wang 2018). Out of the 41 randomized trials, 12 were cluster-randomized trials (Costantini 2014; Cunningham 2008; Doig 2008; Kinsman 2012; Marrie 2000; Panella 2009; Panella 2012; Panella 2018; Philbin 2000; Seys 2019; Vanhaecht 2016; Wang 2018).

Four (7%) studies were non-randomized trials (Choong 2000; Fakhr-Movahedi 2015; Trombetti 2013; Usui 2004), four studies (7%) were CBA studies (Bookbinder 2005; Chadha 2000; Doherty 2006a; Smith 2004), and nine (15%) studies utilized ITS design or reported outcomes in ITS form (Bartlett 2017; Brattebø 2002; Brennan 2018; Phillips 2017; Rotter 2014; Rutman 2017; Smith 2019; Tilden 1987; Kaiser 2020).

Country

Twenty-one (36%) studies were conducted in the USA (Bartlett 2017; Bauer 2006; Bernard 2011; Bittinger 1995; Bookbinder 2005; Brennan 2018; Brook 1999; Delaney 2003; Falconer 1993; Gomez 1996; Johnson 2000; Kaiser 2020; Kim 2002; Kollef 1997; Marelich 2000; Philbin 2000; Phillips 2017; Roberts 1997; Rutman 2017; Smith 2019; Tilden 1987), six (10%) in Australia (Choong 2000; Doherty 2006a; Doig 2008; Dowsey 1999; Kinsman 2012; Smith 2004; note that Doig 2008 was conducted in New Zealand and Australia), six (10%) in China (Chen 2019; Deng 2014 (ICH); Deng 2014 (TIA); Ju 2019; Li 2018; Wang 2018), three (5%) in Japan (Aizawa 2002; Kiyama 2003a; Usui 2004), three (5%) in the UK (Chadha 2000; Cunningham 2008; Sulch 2002), three (5%) in Canada (Cole 2002; Gooch 2012; Marrie 2000), three (5%) in Italy (Costantini 2014; Panella 2009, Panella 2012), three (5%) in Germany (Homagk 2016; Muehling 2008; Rotter 2014), and three (5%) are multi-country studies (Italy, Portugal, Belgium; Panella 2018; Seys 2019; Vanhaecht 2016). The remaining seven studies were implemented in one country each (2%); Thailand (Kampan 2006), Taiwan (Chen 2004), Norway (Brattebø 2002), Switzerland (Trombetti 2013), Saudi Arabia (Almalki 2017), Iran (Fakhr-Movahedi 2015) and Chile (Jalil 2017)).

Setting

Thirty-one (53%) studies were conducted in a general acute ward (for example, medical, surgical, pediatrics, gynecology (Aizawa 2002; Bartlett 2017; Bittinger 1995; Chadha 2000; Chen 2004; Choong 2000; Cole 2002; Deng 2014 (ICH); Deng 2014 (TIA); Doherty 2006a; Dowsey 1999; Fakhr-Movahedi 2015; Gomez 1996; Gooch 2012; Johnson 2000; Kampan 2006; Kiyama 2003a; Li 2018; Marrie 2000; Muehling 2008; Panella 2009; Panella 2012; Panella 2018; Philbin 2000; Rotter 2014; Seys 2019; Smith 2004; Trombetti 2013; Usui 2004; Vanhaecht 2016; Wang 2018), five (9%) in an extended stay facility (for example, rehabilitation or palliative care, end of life) (Bookbinder 2005; Costantini 2014; Delaney 2003; Falconer 1993; Sulch 2002), nine (16%) in an intensive care unit (ICU) (Bittinger 1995; Brattebø 2002; Brennan 2018; Brook 1999; Doig 2008; Homagk 2016; Kollef 1997; Marelich 2000; Phillips 2017), ten (17%) studies were conducted in or commenced in the emergency department (ED) (Almalki 2017; Bernard 2011; Cunningham 2008; Jalil 2017; Kim 2002; Kinsman 2012; Roberts 1997; Rutman 2017; Tilden 1987; Wang 2018), and one (2%) in a mental health outpatient hospital (Bauer 2006). It was unclear where two (3%) studies were conducted (Chen 2019; Kaiser 2020).

Forty-three (74%) studies described CPWs for a non-invasive diagnosis (for example, diabetes, stroke, asthma, deep vein thrombosis, sepsis) (Almalki 2017; Bartlett 2017; Bauer 2006; Bernard 2011; Bittinger 1995; Bookbinder 2005; Brennan 2018; Chen 2004; Chen 2019; Cole 2002; Costantini 2014; Cunningham 2008; Deng 2014 (ICH); Deng 2014 (TIA); Doherty 2006a; Doig 2008; Fakhr-Movahedi 2015; Falconer 1993; Jalil 2017; Johnson 2000; Ju 2019; Kaiser 2020; Kampan 2006; Kim 2002; Kinsman 2012; Li 2018; Marrie 2000; Panella 2009; Panella 2012; Panella 2018; Philbin 2000; Phillips 2017; Roberts 1997; Rutman 2017; Seys 2019; Smith 2004; Smith 2019; Sulch 2002; Tilden 1987; Trombetti 2013; Usui 2004; Vanhaecht 2016; Wang 2018). In 13 (22%) studies, the CPW was designed for an invasive procedure (Aizawa 2002; Brattebø 2002; Brook 1999; Choong 2000; Homagk 2016; Delaney 2003; Dowsey 1999; Gooch 2012; Kiyama 2003a; Kollef 1997; Marelich 2000; Muehling 2008; Rotter 2014). Two (3%) studies described CPWs for combined invasive/non-invasive procedures (for example, suspected myocardial infarction with or without percutaneous transluminal coronary angioplasty) (Chadha 2000; Gomez 1996).

Participants

Two thousand and twenty-seven health professionals were included in nine studies (Bookbinder 2005; Brattebø 2002; Cole 2002; Costantini 2014; Gooch 2012; Panella 2012; Panella 2018; Seys 2019; Sulch 2002). Health professionals reported in each study

were: psychiatrists, geriatricians, nurses (Cole 2002); orthopedic surgeons (Gooch 2012); doctors, nurses, physiotherapists, speech therapists, discharge planners and educators (Sulch 2002); anesthetists, doctors and nurses (Brattebø 2002); surgeons, physicians, anesthetists, nurses, physiotherapists, social workers, occupational therapists, dietitians and speech therapists (Panella 2018); nurses (Bookbinder 2005); general practitioners (Costantini 2014); physicians, nurses, physiotherapists and speech therapists (Panella 2012); and doctors, nurses, physiotherapists, social workers, occupational therapists, dietitians, speech therapists and psychologists (Seys 2019). The number of included health professionals ranged from five (Cole 2002) to 984 (Seys 2019). The remaining 49 studies did not report the number of health professionals included (Aizawa 2002; Almalki 2017; Bartlett 2017; Bauer 2006; Bernard 2011; Bittinger 1995; Brennan 2018; Brook 1999; Chadha 2000; Chen 2004; Chen 2019; Choong 2000; Cunningham 2008; Delaney 2003; Deng 2014 (ICH); Deng 2014 (TIA); Doherty 2006a; Doig 2008; Dowsey 1999; Fakhr-Movahedi 2015; Falconer 1993; Gomez 1996; Homagk 2016; Jalil 2017; Johnson 2000; Ju 2019; Kaiser 2020; Kampan 2006; Kim 2002; Kinsman 2012; Kiyama 2003a; Kollef 1997; Li 2018; Marelich 2000; Marrie 2000; Muehling 2008; Panella 2009; Philbin 2000; Phillips 2017; Roberts 1997; Rotter 2014; Rutman 2017; Smith 2004; Smith 2019; Tilden 1987; Trombetti 2013; Usui 2004; Vanhaecht 2016; Wang 2018)

In total, 24,841 hospitalized patients were included. The number of patients per study ranged from 15 patients (Bittinger 1995) to 4800 patients (Wang 2018). The mean age ranged from 5.7 years (Cunningham 2008) to 85.0 years (Trombetti 2013).

Intervention and comparators

Detailed descriptions of the interventions delivered in each study are summarized in the Characteristics of included studies tables.

Overall, 49 (84%) studies compared a stand-alone CPW to usual care (Aizawa 2002; Almalki 2017; Bartlett 2017; Bernard 2011; Bittinger 1995; Brennan 2018; Brook 1999; Chadha 2000; Chen 2019; Choong 2000; Costantini 2014; Cunningham 2008; Delaney 2003; Deng 2014 (ICH); Deng 2014 (TIA); Doherty 2006a; Doig 2008; Dowsey 1999; Fakhr-Movahedi 2015; Falconer 1993; Gomez 1996; Gooch 2012; Homagk 2016; Jalil 2017; Johnson 2000; Kaiser 2020; Kim 2002; Kinsman 2012; Kiyama 2003a; Kollef 1997; Li 2018; Marelich 2000; Marrie 2000; Muehling 2008; Panella 2009; Panella 2012; Panella 2018; Phillips 2017; Roberts 1997; Rotter 2014; Rutman 2017; Seys 2019; Smith 2004; Smith 2019; Sulch 2002; Tilden 1987; Trombetti 2013; Usui 2004; Vanhaecht 2016), and nine (16%) compared a multifaceted intervention (including a CPW) to usual care (Bauer 2006; Bookbinder 2005; Brattebø 2002; Chen 2004; Cole 2002; Ju 2019; Kampan 2006; Philbin 2000; Wang 2018).

Of the nine studies investigating multifaceted interventions (Bauer 2006; Bookbinder 2005; Brattebø 2002; Chen 2004; Cole 2002; Ju 2019; Kampan 2006; Philbin 2000; Wang 2018), four studies combined a CPW with quality improvement approaches (Bookbinder 2005; Brattebø 2002; Philbin 2000; Wang 2018), such as quality improvement teams, local champions, audit and feedback, medical grand rounds, quality co-ordinators, and performance measure monitoring. Three studies combined a CPW with counseling methods (Chen 2004; Cole 2002; Kampan 2006), and two studies (Bauer 2006; Ju 2019) combined a CPW with case management elements, including patient self-management groups, or a health literacy program for patients.

Clinical conditions targeted

The included studies targeted a wide range of conditions. Nine (16%) studies used CPWs to manage asthma (Bartlett 2017; Brennan 2018; Chen 2004; Cunningham 2008; Doherty 2006a; Johnson 2000; Kaiser 2020; Phillips 2017; Smith 2019), six (10%) studies explored CPW for patients with stroke (Chen 2019; Deng 2014 (ICH); Falconer 1993; Panella 2012; Sulch 2002; Wang 2018), five (9%) studies explore pathways for mechanical ventilation (Brattebø 2002; Brook 1999; Jalil 2017; Kollef 1997; Marelich 2000) four (7%) studies for myocardial infarction (Gomez 1996; Kinsman 2012; Li 2018; Roberts 1997) and three (5%) studies for heart failure (Bittinger 1995; Panella 2009; Philbin 2000), three (5%) for chronic obstructive pulmonary disease (COPD) (Seys 2019; Smith 2019; Vanhaecht 2016), three (5%) studies for pneumonia (Marrie 2000; Rutman 2017; Usui 2004) and three studies (5%) for mental illness (Bauer 2006; Cole 2002; Fakhr-Movahedi 2015). Other patient conditions targeted in the studies included: transient ischemic attack (TIA), acute lower respiratory infection, cirrhosis, proximal femur fracture, hip and knee arthroplasty, diabetes, and palliative care, among others. See 'Characteristics of included studies' and additional (Table 4) for detailed information about all the included pathway conditions or clinical indications.

Study funding

Twenty-eight studies (48%) reported receiving research funding (Almalki 2017; Bauer 2006; Brattebø 2002; Choong 2000; Cole 2002; Costantini 2014; Cunningham 2008; Deng 2014 (ICH); Deng 2014 (TIA); Doherty 2006a; Doig 2008; Falconer 1993; Gomez 1996; Gooch 2012; Johnson 2000; Kim 2002; Kinsman 2012; Marelich 2000; Panella 2009; Panella 2012; Panella 2018; Philbin 2000; Seys 2019; Smith 2004; Sulch 2002; Trombetti 2013; Vanhaecht 2016; Wang 2018) while the remaining 30 (52%) studies did not explicitly report whether they received funding or not (Aizawa 2002; Bartlett 2017; Bernard 2011; Bittinger 1995; Bookbinder 2005; Brennan 2018; Brook 1999; Chadha 2000; Chen 2004; Chen 2019; Delaney 2003; Dowsey 1999; Fakhr-Movahedi 2015; Homagk 2016; Jalil 2017; Ju 2019; Kaiser 2020; Kampan 2006; Kiyama 2003a; Kollef 1997; Li 2018; Marrie 2000; Muehling 2008; Phillips 2017; Roberts 1997; Rotter 2014; Rutman 2017; Smith 2019; Tilden 1987; Usui 2004). Declarations of interest were provided by the authors of six studies (Cole 2002; Doig 2008; Gooch 2012; Marrie 2000; Vanhaecht 2016; Wang 2018).

Primary outcomes

All prespecified primary study outcomes are described narratively in the results section, and we pooled results in meta-analysis for two or more comparable outcomes (Effects of interventions). We also presented all prespecified primary outcomes in additional Table 5, additional Table 6, and additional Table 7.

Inhospital mortality

We defined 'inhospital mortality' as death (from all causes) occurring during hospitalization (from admission to discharge). Inhospital mortality was an objectively measured patient outcome in 12 studies (Almalki 2017; Brook 1999; Deng 2014 (ICH); Doig 2008; Gooch 2012; Kollef 1997; Panella 2009; Panella 2012; Philbin 2000; Smith 2004; Trombetti 2013; Wang 2018).

We decided that the 'inhospital death rate within 30 days of admission to hospital' reported by Panella and colleagues (Panella 2012) was comparable with inhospital mortality outcomes reported

in similar studies, as all the included patients died during hospitalization. Thus, we grouped this mortality outcome with other inhospital mortality outcomes reported.

Mortality (up to six months)

Mortality up to six months from discharge was measured in six studies (Cole 2002; Panella 2018; Philbin 2000; Sulch 2002; Vanhaecht 2016; Wang 2018).

Inhospital complications

The rate of complications during hospitalization was measured in 14 studies (Aizawa 2002; Almalki 2017; Choong 2000; Delaney 2003; Deng 2014 (ICH); Deng 2014 (TIA); Dowsey 1999; Gooch 2012; Ju 2019; Kiyama 2003a; Li 2018; Marelich 2000; Muehling 2008; Panella 2012).

Hospital readmission (up to six months)

Hospital readmissions up to six months from discharge was measured in 14 studies (Aizawa 2002; Almalki 2017; Choong 2000; Delaney 2003; Dowsey 1999; Gomez 1996; Kampan 2006; Panella 2009; Panella 2012; Panella 2018; Philbin 2000; Roberts 1997; Smith 2004; Vanhaecht 2016).

Secondary outcomes

All prespecified secondary study outcomes are described narratively in the results section, and we pooled results in meta-analysis for two or more comparable outcomes (Effects of interventions). We also presented all prespecified secondary outcomes in additional Table 2, additional Table 3 additional Table 5, additional Table 6, additional Table 7, additional Table 8, and additional Table 9.

Please note that because of the high number of adherence measures to recommended practice measures reported in the 16 included studies, we presented the first three adherence measures that have been reported in each of the primary studies in additional Table 8 and additional Table 9.

Length of hospital stay (days)

Length of hospital stay in days was measured by 37 studies (Aizawa 2002; Bartlett 2017; Bernard 2011; Brattebø 2002; Brennan 2018; Brook 1999; Choong 2000; Cole 2002; Cunningham 2008; Delaney 2003; Deng 2014 (ICH); Deng 2014 (TIA); Doig 2008; Dowsey 1999; Falconer 1993; Gomez 1996; Homagk 2016; Jalil 2017; Ju 2019; Johnson 2000; Kampan 2006; Kim 2002; Kiyama 2003a; Li 2018; Marrie 2000; Panella 2009; Panella 2012; Panella 2018; Philbin 2000; Roberts 1997; Rotter 2014; Smith 2004; Smith 2019; Sulch 2002; Trombetti 2013; Usui 2004; Vanhaecht 2016). Length of hospital stay was calculated as total length of hospital stay in days from admission until discharge. However, (Kiyama 2003a) calculated the length of hospital stay from the day of surgery to the day of discharge.

Hospital costs and charges

Hospital costs, hospital charges, and country-specific insurance points were measured in 19 studies (Aizawa 2002; Bauer 2006; Deng 2014 (ICH); Deng 2014 (TIA); Falconer 1993; Gomez 1996; Homagk 2016; Johnson 2000; Ju 2019; Kampan 2006; Kim 2002; Kiyama 2003a; Kollef 1997; Li 2018; Panella 2009; Philbin 2000; Roberts 1997; Rutman 2017; Usui 2004).

Hospital costs data were reported as direct or indirect hospital costs in USD, Japanese YEN, EUROS, Thailand's BAHT, and Chinese yuan. Hospital charges were reported in USD or country-specific insurance points. Within this highly variable set of cost measures reported, a direct costing approach (i.e. treatment costs as direct costs were included in the cost estimates whereas time cost or lost wages and other indirect costs were not included) was used by Bauer 2006 and Kim 2002, excluding professional fees in both USA settings. Kiyama 2003a included direct costs and professional fees. Direct and indirect costs were included in the cost estimates reported in two studies (Kampan 2006; Roberts 1997), although it was unclear which costing method was used and which costs were included (i.e. professional costs) in Kampan 2006 and Kollef 1997. Hospital charges in USD were reported as median hospital charges by Falconer 1993 and as mean hospital charges by Gomez 1996, Johnson 2000 and Philbin 2000. A surrogate for hospital charges in the form of insurance points was reported in two Japanese investigations (Aizawa 2002; Usui 2004). For this update, hospital costs were reported in seven studies (Deng 2014 (ICH); Deng 2014 (TIA); Homagk 2016; Ju 2019; Li 2018; Panella 2009; Rutman 2017). Panella 2009 used an activity-based costing approach, including direct and indirect (e.g. overhead cost) hospital costs, and Homagk 2016 reported on direct and indirect hospital costs. It was unclear which costs have been used for calculating estimates in the five remaining studies (Deng 2014 (ICH); Deng 2014 (TIA); Ju 2019; Li 2018; Rutman 2017).

Because of the different methods used for calculating hospital costs and the highly differing cost outcomes included in this review update (hospital costs, charges, and insurance data), we presented an overview of the costing methods used in the 19 studies included in this comparison in additional Table 1.

Adherence to recommended practice

Adherence to recommended practice measures was reported in 16 studies (Bookbinder 2005; Chadha 2000; Cunningham 2008; Doherty 2006a; Kaiser 2020; Kinsman 2012; Panella 2012; Panella 2018; Philbin 2000; Phillips 2017; Seys 2019; Sulch 2002; Tilden 1987; Trombetti 2013; Vanhaecht 2016; Wang 2018).

ICU admissions

No studies reported this outcome.

Discharge destination

No studies reported this outcome.

Other outcomes

Implementation process

We extracted and recorded the process for developing and implementing the CPW according to whether evidence-informed features had been utilized (note that, for some studies, implementation features might have been present, but not reported). Overall, we scored 25 (43%) studies as having a 'high' implementation score (i.e. seven or more implementation features used (Bartlett 2017; Bauer 2006; Bookbinder 2005; Brattebø 2002; Chadha 2000; Chen 2004; Cole 2002; Costantini 2014; Cunningham 2008; Doherty 2006a; Doig 2008; Gooch 2012; Kaiser 2020; Kinsman 2012; Li 2018; Panella 2009; Panella 2012; Panella 2018; Phillips 2017; Rutman 2017; Seys 2019; Smith 2004; Sulch 2002; Vanhaecht 2016; Wang 2018), 21 (36%) studies as having a 'moderate' implementation score (four to six implementation features used

(Almalki 2017; Bernard 2011; Bittinger 1995; Brennan 2018; Brook 1999; Delaney 2003; Deng 2014 (ICH); Deng 2014 (TIA); Dowsey 1999; Falconer 1993; Gomez 1996; Jalil 2017; Johnson 2000; Kampan 2006; Kollef 1997; Marelich 2000; Philbin 2000; Roberts 1997; Rotter 2014; Smith 2019; Tilden 1987), and 12 (21%) as having a 'low' implementation score (three or less implementation features used (Almalki 2017; Chen 2019; Choong 2000; Fakhr-Movahedi 2015; Homagk 2016; Ju 2019; Kim 2002; Kiyama 2003a; Marrie 2000; Muehling 2008; Trombetti 2013; Usui 2004).

The most frequent implementation feature utilized was clinician involvement during the CPW development (52 studies; 90%). The use of an implementation team was reported in 36 studies (62%), identification of evidence-practice gaps prior to implementation in 31 (53%), identification of potential barriers to change in 10 (17%), incorporation of reminder systems was reported in 18 studies (31%), audit and feedback in 28 (48%), use of educational sessions in 34 (59%) and use of local opinion leaders in 27 (47%). Full details of all implementation features reported in the included studies are presented in additional Table 10.

Excluded studies

As noted above, 377 studies were excluded at the full-text screening phase in this update. The majority were excluded because they did not meet the Cochrane EPOC minimal inclusion criteria for study designs (e.g. Ban 2012; Bapat 2017; Mo 2010; Moller 2011). Some excluded studies did not meet the CPW content criteria used in this review (see 'Types of interventions' for additional information), either because the pathway did not involve a multidisciplinary team (e.g. Carratala 2012; Li 2016; Lu 2019) or just provided generic recommendations without adapting the protocol to local structures, systems and time frames (e.g. Process 2014). In this regard, it is important to note that studies exploring Enhanced Recovery After Surgery (ERAS) pathways have been excluded from the review (e.g. Arrick 2019; Li 2018b). Published by the ERAS society (ERAS Society 2022), ERAS guidelines specify protocols for patient care designed to achieve early recovery after surgical procedures in different specialties. Whereas the ERAS program provides a multimodal, multidisciplinary and evidence-based approach to patient care, the guidelines aim at standardizing care across healthcare sites, and thus are not necessarily tailored to local structures.

The exact reasons for exclusion during full-text assessment for the most relevant studies are detailed in Characteristics of excluded studies.

Risk of bias in included studies

The risk of bias in included studies is presented in the 'Risk of bias' tables within the Characteristics of included studies. We also presented the risk of bias results in a graphical form in Figure 2; Figure 3; Figure 4; Figure 5.

Figure 2. Risk of Bias: RCTs, CRCTs, NRCTs, CBAs

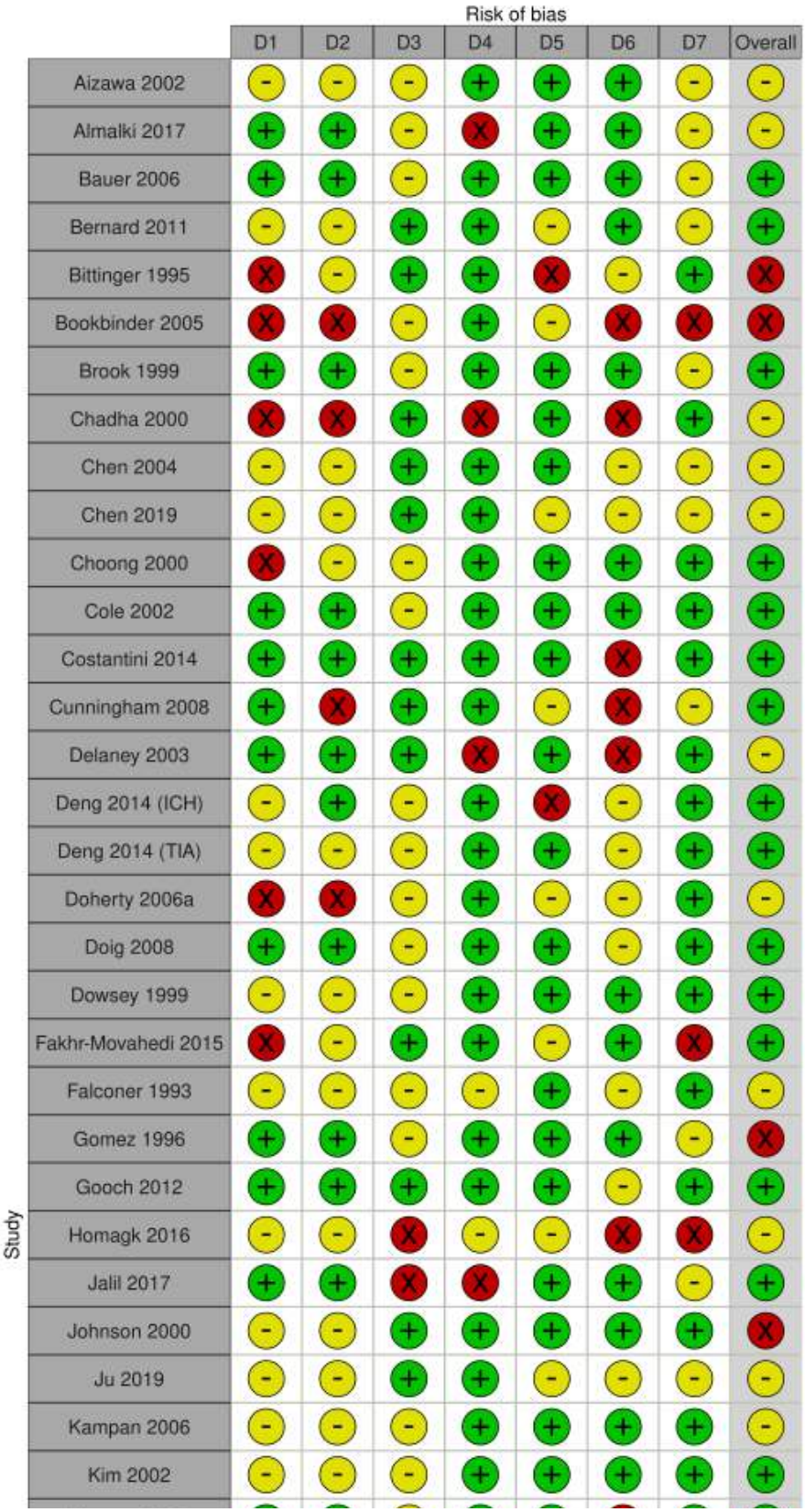


Figure 2. (Continued)

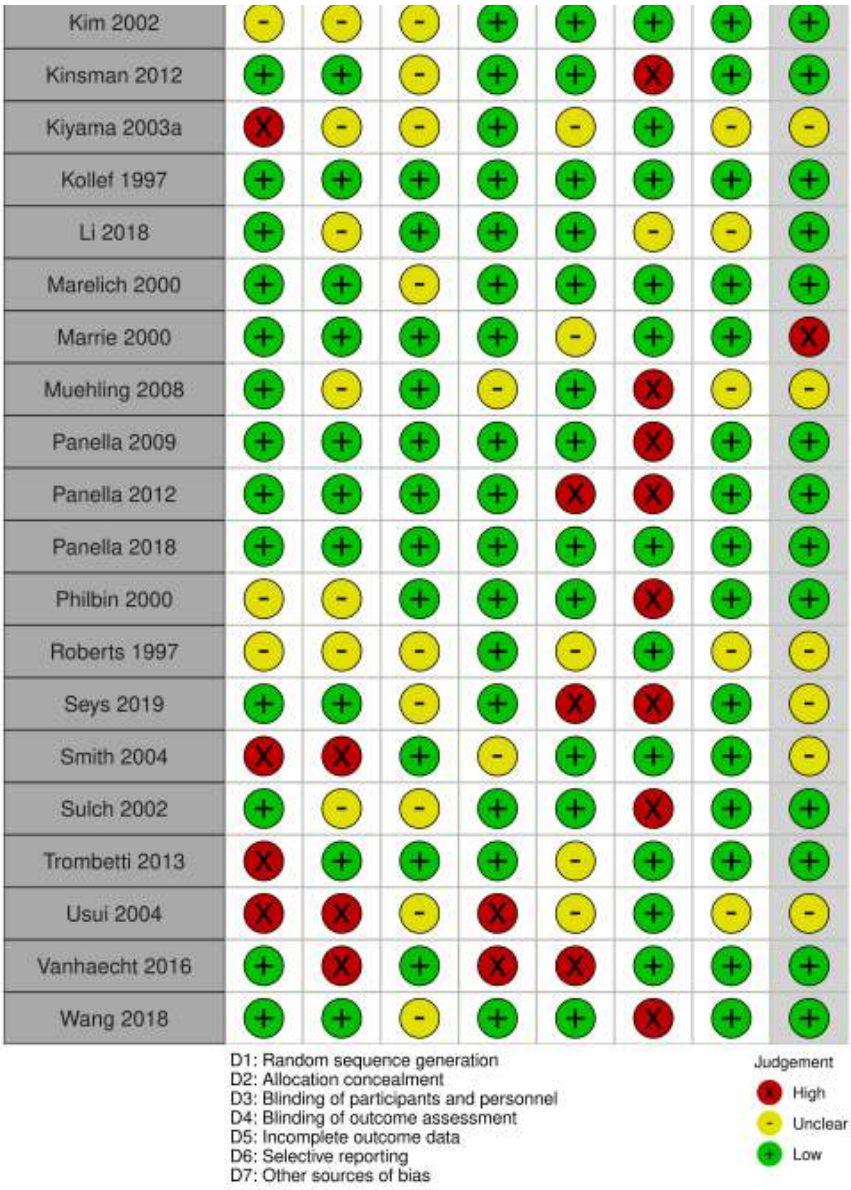


Figure 3. ROB summary: RCTs, CRCTs, NRCTs, CBAs

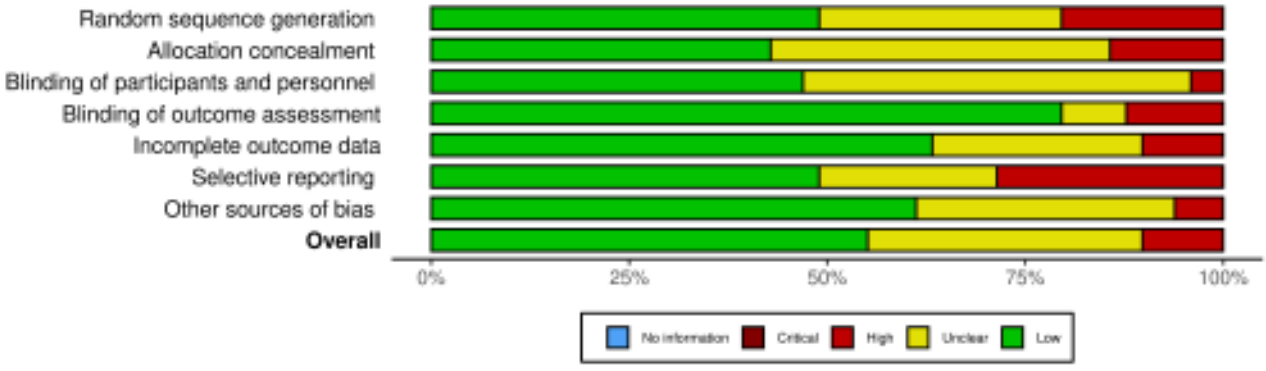


Figure 4. Risk of Bias: ITS studies

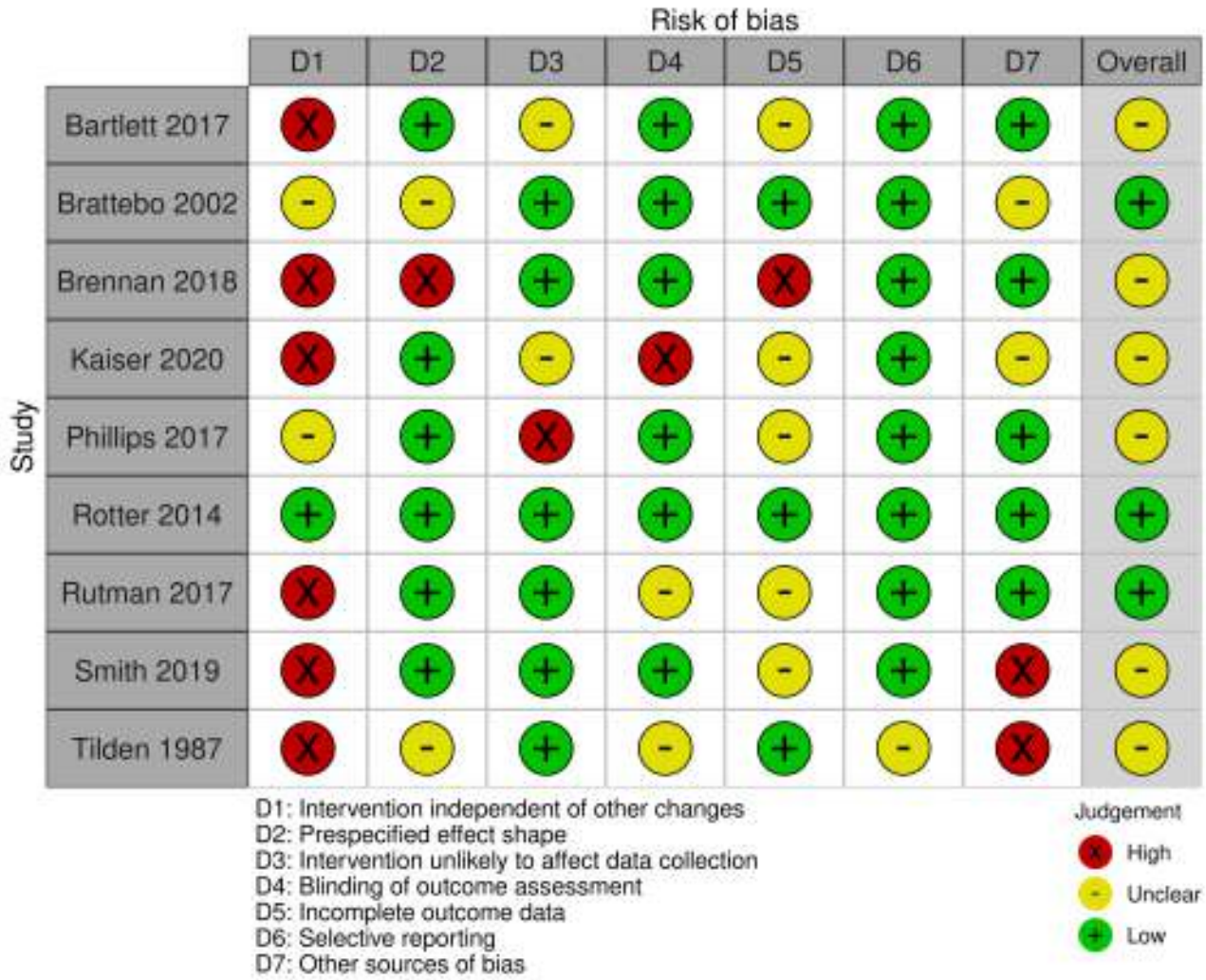
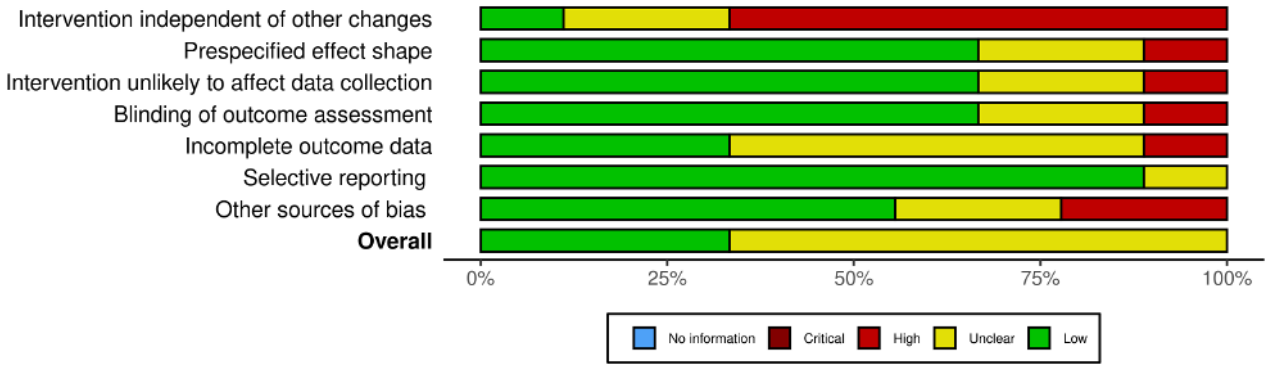


Figure 5. Risk of Bias summary: ITS studies



Allocation

Sequence generation (selection bias) (randomized trials, non-randomized trials, CBA studies)

An adequate method for random sequence generation was reported in 23 studies which we judged as being at low risk (Almalki 2017; Bauer 2006; Bittinger 1995; Brook 1999; Cole 2002; Cunningham 2008; Delaney 2003; Doig 2008; Gomez 1996; Gooch 2012; Jalil 2017; Kinsman 2012; Kollef 1997; Li 2018; Marelich 2000; Marrie 2000; Muehling 2008; Panella 2009; Panella 2012; Panella 2018; Seys 2019; Vanhaecht 2016; Wang 2018). We judged nine studies as being at high risk because a non-random sequence generation was used (Bookbinder 2005; Chadha 2000; Choong 2000; Doherty 2006a; Fakhr-Movahedi 2015; Kiyama 2003a; Smith 2004; Trombetti 2013; Usui 2004). Risk was unclear in 17 studies because the random component was not reported or specified (Aizawa 2002; Bernard 2011; Chen 2004; Chen 2019; Costantini 2014; Deng 2014 (ICH); Deng 2014 (TIA); Dowsey 1999; Falconer 1993; Homagk 2016; Johnson 2000; Ju 2019; Kampan 2006; Kim 2002; Philbin 2000; Roberts 1997; Sulch 2002).

Allocation concealment (selection bias) (randomized trials, non-randomized trials, CBA studies)

Allocation was concealed in 22 studies which we judged as being at low risk (Almalki 2017; Bauer 2006; Brook 1999; Cole 2002; Costantini 2014; Delaney 2003; Deng 2014 (ICH); Doig 2008; Gomez 1996; Gooch 2012; Jalil 2017; Kinsman 2012; Kollef 1997; Marelich 2000; Marrie 2000; Panella 2009; Panella 2012; Panella 2018; Seys 2019; Trombetti 2013; Vanhaecht 2016; Wang 2018). We judged six studies as being at high risk because allocation was not concealed (Bookbinder 2005; Chadha 2000; Cunningham 2008; Doherty 2006a; Smith 2019; Usui 2004). We judged 21 studies as being unclear because the allocation process was not reported (Aizawa 2002; Bernard 2011; Bittinger 1995; Chen 2004; Chen 2019; Choong 2000; Deng 2014 (TIA); Dowsey 1999; Fakhr-Movahedi 2015; Falconer 1993; Homagk 2016; Johnson 2000; Ju 2019; Kampan 2006; Kim 2002; Kiyama 2003a; Li 2018; Muehling 2008; Philbin 2000; Roberts 1997; Sulch 2002).

Protection against contamination (randomized trials, non-randomized trials, CBA studies)

Protection against contamination was adequate in 20 studies which we judged as being at low risk (Chadha 2000; Cole 2002; Costantini 2014; Delaney 2003; Doherty 2006a; Doig 2008; Gooch 2012; Johnson 2000; Kinsman 2012; Marelich 2000; Marrie 2000; Panella 2009; Panella 2012; Panella 2018; Philbin 2000; Seys 2019; Smith 2004; Sulch 2002; Sulch 2002; Vanhaecht 2016). We judged 12 studies as being at high risk because it was considered likely that the control group received the intervention (Almalki 2017; Aizawa 2002; Bauer 2006; Bernard 2011; Bookbinder 2005; Cunningham 2008; Dowsey 1999; Fakhr-Movahedi 2015; Gomez 1996; Jalil 2017; Li 2018; Muehling 2008). We judged 17 studies as being unclear because details regarding potential contamination could not be identified (Bittinger 1995; Chen 2004; Chen 2019; Choong 2000; Deng 2014 (ICH); Deng 2014 (TIA); Falconer 1993; Homagk 2016; Ju 2019; Kampan 2006; Kim 2002; Kiyama 2003a; Kollef 1997; Roberts 1997; Trombetti 2013; Usui 2004; Wang 2018).

Baseline imbalances (randomized trials, non-randomized trials, CBA studies)

Baseline participant characteristics were balanced between groups in 40 studies which we judged as being at low risk (Aizawa 2002; Bauer 2006; Bernard 2011; Bittinger 1995; Bookbinder 2005; Brook 1999; Chen 2004; Chen 2019; Choong 2000; Cole 2002; Costantini 2014; Cunningham 2008; Deng 2014 (ICH); Deng 2014 (TIA); Doherty 2006a; Doig 2008; Dowsey 1999; Fakhr-Movahedi 2015; Falconer 1993; Gomez 1996; Gooch 2012; Johnson 2000; Ju 2019; Kampan 2006; Kim 2002; Kinsman 2012; Kiyama 2003a; Kollef 1997; Li 2018; Marelich 2000; Marrie 2000; Panella 2009; Panella 2012; Panella 2018; Philbin 2000; Roberts 1997; Seys 2019; Sulch 2002; Trombetti 2013; Wang 2018). We judged seven studies as being at high risk because of significant differences between groups (Almalki 2017; Chadha 2000; Delaney 2003; Homagk 2016; Jalil 2017; Usui 2004; Vanhaecht 2016). We judged two studies as being unclear because differences could not be determined (Muehling 2008; Smith 2004).

Blinding

Blinding of participants and personnel (performance bias) (randomized trials, non-randomized trials, CBA studies, ITS studies)

Blinding of participants and personnel to allocated interventions occurred in 24 studies which were judged at low risk of performance bias (Aizawa 2002; Bernard 2011; Brook 1999; Choong 2000; Dowsey 1999; Gomez 1996; Kiyama 2003a; Marelich 2000; Panella 2018; Trombetti 2013; Usui 2004; Vanhaecht 2016; ; Almalki 2017; Bauer 2006; Cole 2002; Fakhr-Movahedi 2015; Jalil 2017; Johnson 2000; Kampan 2006; Kim 2002; Kollef 1997; Marrie 2000; Roberts 1997; Smith 2004). We judged 14 studies as being at high risk because allocated interventions were not concealed from personnel (Cunningham 2008; Delaney 2003; Muehling 2008; Wang 2018, Bookbinder 2005; Chadha 2000; Costantini 2014; Falconer 1993; Homagk 2016; Kinsman 2012; Panella 2009; Philbin 2000; Seys 2019; Sulch 2002). We judged 20 studies as being unclear because blinding could not be determined (Bartlett 2017; Bittinger 1995; Brattebø 2002; Brennan 2018; Chen 2004; Chen 2019; Deng 2014 (ICH); Deng 2014 (TIA); Doherty 2006a; Doig 2008; Gooch 2012; Ju 2019; Kaiser 2020; Li 2018; Phillips 2017; Rotter 2014; Rutman 2017; Smith 2019; Sulch 2002; Tilden 1987).

Objective outcome measures were used or outcomes were assessed blindly in 34 studies which were judged at low risk (Aizawa 2002; Bernard 2011; Bittinger 1995; Chen 2004; Chen 2019; Delaney 2003; Doherty 2006a; Doig 2008; Homagk 2016; Ju 2019; Kaiser 2020; Li 2018; Almalki 2017; Bauer 2006; Brook 1999; Cole 2002; Deng 2014 (ICH); Deng 2014 (TIA); Dowsey 1999; Falconer 1993; Gomez 1996; Gooch 2012; Jalil 2017; Johnson 2000; Kampan 2006; Kim 2002; Kiyama 2003a; Kollef 1997; Marelich 2000; Marrie 2000; Panella 2018; Roberts 1997; Sulch 2002; Vanhaecht 2016), We judged nine studies as being at high risk because outcome measures were not objective or blinded (Bookbinder 2005; Chadha 2000; Costantini 2014; Cunningham 2008; Kinsman 2012; Panella 2009; Panella 2012; Philbin 2000; Seys 2019). We judged 15 studies as being unclear as blinding could not be determined (Bartlett 2017; Brattebø 2002; Brennan 2018; Choong 2000; Fakhr-Movahedi 2015; Muehling 2008; Rotter 2014; Rutman 2017; Smith 2004; Smith 2019; Tilden 1987; Trombetti 2013; Usui 2004; Wang 2018).

Incomplete outcome data

Incomplete outcome data (attrition bias) (randomized trials, non-randomized trials, CBA studies, ITS studies)

Incomplete outcome data were adequately addressed and we judged 32 studies as being at low risk (Aizawa 2002; Almalki 2017; Bauer 2006; Brattebø 2002; Brook 1999; Chadha 2000; Chen 2004; Choong 2000; Costantini 2014; Delaney 2003; Deng 2014 (TIA); Doig 2008; Dowsey 1999; Falconer 1993; Gomez 1996; Gooch 2012; Jalil 2017; Johnson 2000; Kaiser 2020; Kampan 2006; Kim 2002; Kollef 1997; Li 2018; Marelich 2000; Muehling 2008; Panella 2009; Panella 2018; Philbin 2000; Smith 2004; Sulch 2002; Tilden 1987; Wang 2018). We judged six studies as being at high risk because missing data were considered likely to bias results (Bittinger 1995; Cole 2002; Deng 2014 (ICH); Panella 2012; Seys 2019; Vanhaecht 2016). We judged 20 studies as being unclear because incomplete or missing data were not specified (Bartlett 2017; Bernard 2011; Brennan 2018; Bookbinder 2005; Chen 2019; Cunningham 2008; Doherty 2006a; Fakhr-Movahedi 2015; Homagk 2016; Ju 2019; Kinsman 2012; Kiyama 2003a; Marrie 2000; Phillips 2017; Roberts 1997; Rotter 2014; Rutman 2017; Smith 2019; Trombetti 2013; Usui 2004).

Selective reporting

Selective outcome reporting (reporting bias)(randomized trials, non-randomized trials, CBA studies)

There was no evidence of selective reporting in 39 studies which were judged low risk (Aizawa 2002; Almalki 2017; Bauer 2006; Bernard 2011; Bittinger 1995; Brook 1999; Chadha 2000; Choong 2000; Cole 2002; Costantini 2014; Cunningham 2008; Delaney 2003; Deng 2014 (ICH); Deng 2014 (TIA); Doig 2008; Dowsey 1999; Fakhr-Movahedi 2015; Falconer 1993; Gomez 1996; Gooch 2012; Jalil 2017; Johnson 2000; Kampan 2006; Kim 2002; Kinsman 2012; Kollef 1997; Li 2018; Marelich 2000; Muehling 2008; Panella 2009; Panella 2012; Panella 2018; Philbin 2000; Seys 2019; Smith 2004; Sulch 2002; Trombetti 2013; Vanhaecht 2016; Wang 2018). We judged one study as being at high risk because a number of outcomes were omitted from the results (Homagk 2016). We judged nine studies as being unclear because we could not identify whether outcomes were omitted (Bookbinder 2005; Chen 2004; Chen 2019; Doherty 2006a; Ju 2019; Kiyama 2003a; Marrie 2000; Roberts 1997; Usui 2004).

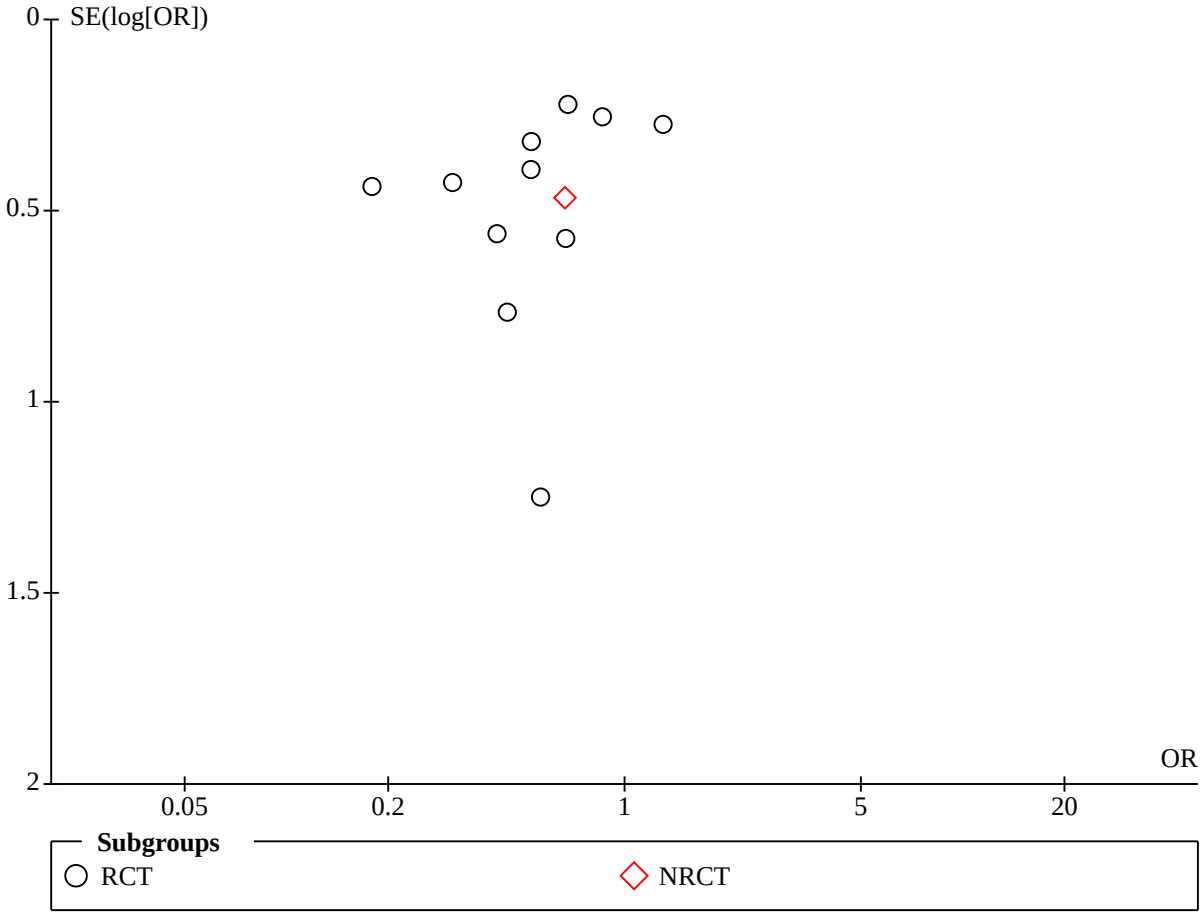
Other potential sources of bias

Other sources

For other sources of bias, we considered papers that had not controlled for study variables that could impact the findings, such as unit culture, leadership, exposure to other educational offerings, wide variations in the processes of care, and lack of information about participants. We found that 15 studies were at high risk of bias (Almalki 2017; Bittinger 1995; Bookbinder 2005; Chadha 2000; Costantini 2014; Cunningham 2008; Delaney 2003; Deng 2014 (ICH); Deng 2014 (TIA); Doherty 2006a; Gomez 1996; Homagk 2016; Johnson 2000; Smith 2004; Usui 2004), 24 were unclear (Aizawa 2002; Bartlett 2017; Bernard 2011; Brattebø 2002; Chen 2019; Chen 2004; Choong 2000; Dowsey 1999; Falconer 1993;Ju 2019; Kaiser 2020; Kampan 2006; Kim 2002; Kiyama 2003a; Marrie 2000; Muehling 2008; Panella 2012; Philbin 2000; Roberts 1997; Rutman 2017; Smith 2019; Sulch 2002; Tilden 1987; Trombetti 2013) and 19 were low risk (Bauer 2006; Brennan 2018; Brook 1999; Cole 2002; Doig 2008; Fakhr-Movahedi 2015; Gooch 2012; Jalil 2017; Kinsman 2012; Kollef 1997; Li 2018; Marelich 2000; Panella 2009; Panella 2018; Phillips 2017; Rotter 2014; Seys 2019; Vanhaecht 2016; Wang 2018).

There was no evidence of funding leading to bias, with research teams reporting complete oversight of research. Also, inspection of the funnel plots in the results of meta-analysis in which ten or more studies were included did not suggest the presence of publication bias (Figure 6).

Figure 6.



Intervention independent of other changes (ITS studies)

None of the ITS studies demonstrated that outcomes from the intervention were independent of other changes and, therefore, none were judged at low risk. We judged seven studies as being at high risk because of other changes (e.g. publicity, hospital policies and procedures changes, quality improvement programs) during the study period (Bartlett 2017; Brennan 2018; Kaiser 2020; Phillips 2017; Rutman 2017; Smith 2019; Tilden 1987). We judged two studies as being unclear because it could not be demonstrated that the intervention was independent of other changes (Brattebø 2002; Rotter 2014).

Shape of intervention effect prespecified (ITS studies)

Prespecification of the intervention effect was provided in six studies which were judged as being at low risk (Bartlett 2017; Kaiser 2020; Phillips 2017; Rotter 2014; Rutman 2017; Smith 2019). We judged three studies as being at high risk because the shape of the intervention was not prespecified (Brattebø 2002; Brennan 2018; Tilden 1987). No studies were judged as being unclear.

Intervention unlikely to affect data collection (ITS studies)

Sources and methods of data collection were the same before and after the intervention in seven ITS studies, and they were judged to be at low risk (Bartlett 2017; Brattebø 2002; Kaiser 2020; Rotter 2014; Rutman 2017; Smith 2019; Tilden 1987). We judged two studies as being at high risk because the pathway intervention was likely to affect data collection (Brennan 2018; Phillips 2017). No studies were judged as being unclear.

Effects of interventions

See: **Summary of findings 1** Summary of findings; **Summary of findings 2** Summary of findings

Stand-alone clinical pathways compared to usual care

Of 49 studies that compared stand-alone CPWs with usual care, 45 studies reported on one or more of the outcomes specified in this review: inhospital mortality, mortality (up to 6 months), inhospital complications, hospital readmission (up to 6 months), length of hospital stay, hospital costs and charges, and adherence to recommended practice (Aizawa 2002; Almalki 2017; Bartlett 2017; Bernard 2011; Brennan 2018; Brook 1999; Chadha 2000; Choong 2000; Cunningham 2008; Delaney 2003; Deng 2014 (ICH); Deng 2014 (TIA); Doherty 2006a; Doig 2008; Dowsey 1999; Falconer 1993; Gomez 1996; Gooch 2012; Homagk 2016; Jalil 2017; Johnson 2000; Kaiser 2020; Kim 2002; Kinsman 2012; Kiyama 2003a; Kollef 1997; Li 2018; Marelich 2000; Marrie 2000; Muehling 2008; Panella 2009; Panella 2012; Panella 2018; Phillips 2017; Roberts 1997; Rotter 2014; Rutman 2017; Seys 2019; Smith 2004; Smith 2019; Sulch

2002; Tilden 1987; Trombetti 2013; Usui 2004; Vanhaecht 2016). See Summary of findings 1.

The remaining four studies (Bittinger 1995; Chen 2019; Costantini 2014; Fakhr-Movahedi 2015) did not report on one of our specified primary or secondary outcomes.

Of the 49 studies that compared stand-alone CPWs with usual care, 34 studies were randomized trials (Aizawa 2002; Almalki 2017; Bernard 2011; Bittinger 1995; Brook 1999; Chen 2019; Costantini 2014; Cunningham 2008; Delaney 2003; Deng 2014 (ICH); Deng 2014 (TIA); Doig 2008; Dowsey 1999; Falconer 1993; Gomez 1996; Gooch 2012; Homagk 2016; Jalil 2017; Johnson 2000; Kim 2002; Kinsman 2012; Kiyama 2003a; Kollef 1997; Li 2018; Marelich 2000; Marrie 2000; Muehling 2008; Panella 2009; Panella 2012; Panella 2018; Roberts 1997; Seys 2019; Sulch 2002; Vanhaecht 2016), and 15 studies were non-randomized trials, CBAs, and ITS studies (Chadha 2000; Choong 2000; Doherty 2006a; Fakhr-Movahedi 2015; Smith 2004; Smith 2019; Trombetti 2013; Usui 2004, Bartlett 2017; Brennan 2018; Phillips 2017; Rotter 2014; Rutman 2017; Tilden 1987; Kaiser 2020).

1.1 Inhospital mortality

Ten studies (n = 5844 participants) reported on inhospital mortality. Eight were randomized trials (Almalki 2017; Brook 1999; Deng 2014 (ICH); Doig 2008; Gooch 2012; Kollef 1997; Panella 2009; Panella 2012), one was a non-randomized trial (Trombetti 2013), and one was a CBA study (Smith 2004). One randomized trial (Almalki 2017) did not observe any events in the intervention and control groups, so did not contribute any information to the meta-analysis.

Based on meta-analysis of data from seven randomized trials, it is uncertain whether stand-alone CPWs make any difference to inhospital mortality compared to usual care because the certainty of the evidence is low (OR 0.79, 95% CI 0.53 to 1.20; P = 0.27; I^2 = 65%; 7 studies; 4603 participants; low-certainty evidence; Analysis 1.1). The certainty of the evidence was downgraded to low certainty due to serious inconsistency (substantial unexplained heterogeneity) and serious imprecision (CI for overall effect could not exclude appreciable benefit or harm) (Summary of findings 1). Six of the randomized trials reported no difference in inhospital mortality between stand-alone CPWs and usual care (Brook 1999; Deng 2014 (ICH); Doig 2008; Gooch 2012; Kollef 1997; Panella 2012). One randomized trial found decreased inhospital mortality for patients with heart failure treated with CPW compared with usual care (5.6% mortality with CPW and 15.4% with usual care, P = 0.001; Panella 2009). There was substantial heterogeneity between studies, with the focus of the CPW ranging from feeding and weaning from mechanical ventilation to knee replacement and stroke, while the hospital wards varied from ICU to surgical and general medical wards.

One non-randomized study (Trombetti 2013, OR 0.63, 95% CI 0.35 to 1.14; P = 0.274) and one CBA study (Smith 2004, OR 0.83, CI 95% 0.51 to 1.36; P = 0.186) found no difference in inhospital mortality between CPW and usual care groups (2 studies; 1203 participants; Analysis 1.1).

Subgroup analyses based on our primary outcome, inhospital mortality, were not possible due to an inadequate number of studies (fewer than ten observations).

Sensitivity analysis based on excluding randomized trials at high risk of bias (Deng 2014 (ICH); Panella 2012) did not substantially alter the pooled effect estimate (OR 0.77, 95% CI 0.45 to 1.29; P = 0.32; I^2 = 75%; 5 studies; 3795 participants; Analysis 1.8).

1.2 Mortality (up to 6 months)

Three randomized trials (n = 805 participants) reported mortality (up to 6 months) (Panella 2018; Sulch 2002; Vanhaecht 2016). It is uncertain whether stand-alone CPWs make any difference to mortality (up to 6 months) compared to usual care as the certainty of the evidence is low (OR 1.37, 95% CI 0.72 to 2.60; P = 0.34, I^2 = 20%; 3 studies, 805 participants; low-certainty evidence; Analysis 1.2). The certainty of evidence was downgraded by two levels due to serious risk of bias (one study at high risk, another with some concerns) and serious imprecision (optimal information size was not met) (Summary of findings 1).

Sensitivity analysis based on excluding randomized trials at high risk of bias (Vanhaecht 2016) did not substantially alter the result (OR 1.80, 95% CI 0.95 to 3.43; P = 0.07; I^2 = 0%; 2 studies, 514 participants (Analysis 1.9).

1.3 Inhospital complications

Thirteen studies (n = 3817 participants) reported on inhospital complications. Twelve were randomized trials (n = 3706; Aizawa 2002; Almalki 2017; Delaney 2003; Deng 2014 (ICH); Deng 2014 (TIA); Dowsey 1999; Gooch 2012; Kiyama 2003a; Li 2018; Marelich 2000; Muehling 2008; Panella 2012) and one was a non-randomized trial (n = 111); Choong 2000).

Almalki 2017 could not be included in the meta-analysis as this study did not observe any events in either the CPW or the usual care groups. Meta-analysis of data from 11 randomized trials showed that stand-alone CPWs likely reduce in-hospital complications compared with usual care (OR 0.57, 95% CI 0.41 to 0.80; P = 0.001, I^2 = 52%; 11 studies; 3668 participants; moderate-certainty evidence; Analysis 1.3). The certainty of the evidence was downgraded due to serious risk of bias (a number of studies at some risk of bias) (Summary of findings 1).

There was variation in the type of complications assessed following the use of a CPW. Three studies reported improvements associated with the use of a CPW (Deng 2014 (ICH); Dowsey 1999; Li 2018). Dowsey 1999 listed wound infection, chest infection, deep vein thrombosis, joint dislocation, pressure areas, failure to cope at home and decreased range of motion post-discharge as complications for patients following knee or hip arthroplasty up to 3 months post-surgery and reported 10 events for 92 patients (10.8%) in the intervention group, versus 20 events for 71 (28.1%) patients in the control group (P = 0.01). Li 2018 reported three outcomes related to postoperative complications (changes in psychological status, abdominal pain and bleeding, and subcutaneous hemorrhage) after a percutaneous coronary intervention, and recorded 10 complications for 62 patients in the CPW group (16%) versus 29 complications for 56 patients (52%) in the usual care group (changes in psychological status (P = 0.10); abdominal pain and bleeding (P = 0.01); and subcutaneous hemorrhage (P = 0.04)). Finally, Deng 2014 (ICH) measured infection as a complication in patients with intracerebral hemorrhage and reported 18 cases for 166 patients (11%) in the CPW group versus 31 cases for 166 patients (19%) in the usual care group (P = 0.07).

Aizawa 2002 reported one generic complication event for 32 patients (3%) in the CPW group versus two events in 37 patients (5%) in the usual care group (no P value provided) for patients following transurethral resection of the prostate. Delaney 2003 listed postoperative infection and uncontrolled bleeding as complications for patients following intestinal resection and reported seven events for 31 patients (23%) in the CPW group versus 10 events for 33 patients (30%) in the usual care group (P = 0.58). Deng 2014 (TIA) reported on the incidence of stroke in patients with TIA and found 35 events for 213 patients in the CPW group (16%) versus 28 events for 213 patients (13%) in the usual care group (P = 0.16). Gooch 2012 listed 46 complications (e.g. deep vein thrombosis, fracture related to site, deep infection) 30 days post-surgery for 1066 patients (4%) undergoing primary hip and knee joint replacement in the CPW group and 25 complications for 504 patients (5%) in the usual care group (no overall P value reported). Kiyama 2003a listed surgery site problems as complications for patients following gastrectomy and reported three events for 47 patients (6%) in the intervention group versus five events for 38 patients (13%) in the control group (no P value reported). Marelich 2000 listed ventilator-associated pneumonia as a complication for patients requiring mechanical ventilation and reported 11 events for 166 patients (7%) in the CPW group versus 20 events for 169 patients (12%) in the usual group (P = 0.06). Muehling 2008 measured two postoperative pulmonary complications in 30 patients (7%) undergoing lung resections in the CPW group versus 10 postoperative pulmonary complications in 28 patients (36%) in the usual care group (P = 0.009), but no differences between groups were observed when accounting for all possible complications. Panella 2012 showed similar rates of inhospital complications for patients with stroke treated with a CPW as compared to the usual care group (53 events for 229 patients (23 %) in the CPW group and 67 events for 219 patients (31%) in the usual care group; P = 0.09).

One non-randomized trial (n = 111) (Choong 2000) did not find a difference in inhospital complications between CPW and usual care. Choong 2000 listed postoperative confusion, infection and deep vein thrombosis as complications for patients with a fractured neck of femur and reported 10 events for 55 patients (18%) in the CPW group versus 14 events for 56 patients (25%) in the usual care (OR 0.67, 95% CI 0.27 to 1.66; P = 0.40; Analysis 1.3.2).

Sensitivity analysis based on excluding randomized trials at high risk of bias (Delaney 2003; Deng 2014 (ICH); Deng 2014 (TIA); Li 2018; Muehling 2008; Panella 2012) did not substantially alter the result (OR 0.62, 95% CI 0.44 to 0.86; P = 0.01; I^2 = 0%; 6 studies; 2222 participants;Analysis 1.10). Inspection of the funnel plot did not suggest the presence of publication bias (Figure 6).

1.4 Hospital readmission (up to 6 months)

Twelve studies (2198 patients) reported on hospital readmissions, of which ten were randomized trials, one was a non-randomized trial (Choong 2000), and one was a CBA study (Smith 2004).

Ten randomized studies (1578 patients; Aizawa 2002; Almalki 2017; Delaney 2003; Dowsey 1999; Gomez 1996; Panella 2009; Panella 2012; Panella 2018; Roberts 1997; Vanhaecht 2016) reported on hospital readmissions for all causes, with follow-up periods up to six months. Panella 2012 was not included in the meta-analysis as it did not provide any usable data. Based on meta-analysis of data from nine randomized trials, it is very uncertain whether stand-alone CPWs make any difference to hospital readmission (OR 0.67, 95% CI 0.44 to 1.03; P = 0.07, I^2 = 11%; 9 studies, n = 1578, very low-certainty evidence; Analysis 1.4) (Summary of findings 1). The evidence was downgraded to very low certainty due to serious risk of bias (majority of studies with some concerns) and very serious imprecision (CIs could not exclude appreciable benefit or harm).

Sensitivity analysis based on excluding trials at high risk of bias (Almalki 2017; Delaney 2003; Gomez 1996; Vanhaecht 2016) did not substantially alter the result (OR 0.77, 95% CI 0.33 to 1.82; P = 0.55; I^2 = 46%; 5 studies, 1122 participants; Analysis 1.11). Note, however, that Vanhaecht 2016 (high risk of bias) had an impact on the overall effect estimate, questioning the robustness of the pooled estimates.

Aizawa 2002 reported one readmission event among 32 patients on the CPW versus no readmissions among 37 patients in the usual care group within six months (no P value reported). Almalki 2017 reported on 30-day readmission rates for patients with acute kidney injury and acute kidney failure and found three readmissions among 18 patients on the CPW versus two readmissions from 20 patients in the usual care group (P = 0.60). In the study from Dowsey 1999, four out of 92 (4.3%) CPW patients were readmitted within a follow-up period of three months versus nine out of 71 (12.7%) patients following usual care (P = 0.06). Delaney 2003 found three readmissions from 31 participants (9.7%) for the CPW group versus six readmissions from 33 (18.2%) for usual care, while managing patients with laparotomy and intestinal resection (P = 0.48). In a period of 30 days, Gomez 1996 reported three readmissions for both 50 (6%) intervention CPW patients and for 50 patients in the usual care group (non-significant). Panella 2009 found 17 rehospitalization events from 214 (7.9%) patients following a CPW compared to 30 events for 215 (14.0%) patients managed with usual care (short follow-up; P = 0.05). Panella 2018 measured both 30-day and six-month readmission for geriatric hip fracture patients (note that only the 6-month readmission rate was used in the meta-analysis, as it provides more comprehensive information for this outcome). No differences between groups in readmission rates were observed either at 30 days or six-month follow-up (P = 0.62 and P = 0.35, respectively). Roberts 1997 observed five rehospitalizations of 82 (6.1%) CPW patients versus four readmission events from 83 (4.8%) individuals managed with usual care within an eight-week period (non-significant). Similarly, Vanhaecht 2016 measured both 30-day and six-month readmission rates, and found no differences between CPW and usual care groups at six months (P = 0.16), but effects (favoring CPW) at three months (P = 0.04; note that only 6-month readmission rate was used in the meta analysis, as it provides more comprehensive information for this outcome).

One non-randomized trial (Choong 2000; 111 patients) measured readmissions for a follow-up period of 28 days and found no difference with two readmissions from 55 (3.6%) patients in the CPW group versus six readmissions from 56 (10.7%) patients in the usual care group. (Analysis 1.4.2; Summary of findings 1; OR 0.31; 95% CI 0.06 to 1.63; P = 0.17). One CBA study (Smith 2004; 509 patients post-intervention) measured readmissions for the study period and found a difference in readmissions from 279 readmissions in the CPW group as opposed to 123 readmissions in the usual care group, favoring usual care (Analysis 1.4.3; Summary of findings 1; OR 2.14; 95% CI 1.39 to 3.30; P =0.0006).

1.5 Length of hospital stay (days)

Thirty-two studies (7944 patients) reported on length of hospital stay (Aizawa 2002;Bartlett 2017; Bernard 2011; Brennan 2018; Brook 1999; Choong 2000; Cunningham 2008; Delaney 2003; Deng 2014 (ICH); Deng 2014 (TIA); Doig 2008; Dowsey 1999; Falconer 1993; Gomez 1996; Homagk 2016; Jalil 2017; Johnson 2000; Kim 2002; Kiyama 2003a; Li 2018; Marrie 2000; Panella 2009; Panella 2012; Panella 2018; Roberts 1997; Rotter 2014; Smith 2004; Smith 2019; Sulch 2002; Trombetti 2013; Usui 2004; Vanhaecht 2016) (Analysis 1.5, Summary of findings 1).

Twenty-four were randomized studies (5643 participants) (Aizawa 2002; Bernard 2011; Brook 1999; Cunningham 2008; Delaney 2003; Deng 2014 (ICH); Deng 2014 (TIA); Doig 2008; Dowsey 1999; Falconer 1993; Gomez 1996; Homagk 2016; Jalil 2017; Johnson 2000; Kim 2002; Kiyama 2003a; Li 2018; Marrie 2000; Panella 2009; Panella 2012; Panella 2018; Roberts 1997; Sulch 2002; Vanhaecht 2016), three were non-randomized trials (Choong 2000; Trombetti 2013; Usui 2004; 866 participants), one was a CBA study (Smith 2004; 509 participants) and four were ITS studies (Bartlett 2017; Brennan 2018; Rotter 2014; Smith 2019; 926 participants). Fourteen randomized trials reported reductions in length of hospital stay (Aizawa 2002; Brook 1999; Deng 2014 (ICH); Deng 2014 (TIA); Dowsey 1999; Gomez 1996; Homagk 2016; Johnson 2000; Kim 2002; Kiyama 2003a; Li 2018; Marrie 2000; Panella 2009; Roberts 1997), and 10 randomized trials found no difference in length of hospital stay between the groups after the use of a CPW (Bernard 2011; Cunningham 2008; Delaney 2003; Doig 2008; Falconer 1993; Jalil 2017; Panella 2012; Panella 2018; Sulch 2002; Vanhaecht 2016).

Meta-analysis of data from 21 randomized trials showed that stand-alone CPWs likely reduce length of hospital stay compared with usual care (MD -1.13, 95% CI -1.60 to -0.65; P < 0.00001; I^2 = 64%; 21 studies; 5201 participants; moderate level of certainty; Analysis 1.5; Summary of findings 1). The certainty of evidence was moderate due to serious inconsistency (substantial unexplained heterogeneity). One randomized study (Homagk 2016; n = 32) tested a CPW for the surgical treatment of spondylodiscitis, but the authors did not provide usable published data for lengths of hospital stay, and we narratively described the reported study outcomes in this comparison. Homagk 2016 reported a length of hospital stay of 17.2 days for 17 participants in the CPW group as opposed to 26 days for 15 participants in the usual care group (authors reported that the difference in length of stay was statistically significant, without providing a P value).

Meta-analysis of data from 2 non-randomized trials (Trombetti 2013; Usui 2004) (n = 755) showed that stand-alone CPWs may have little to no effect on length of hospital stay compared with usual care (MD -1.65, 95% CI -4.98 to 1.69; P = 0.33; I^2 = 42%; 2 studies; 755 participants; very low level of certainty; Analysis 1.5.2; Summary of findings 1). The certainty of evidence was very low due to very serious risk of bias (non-randomized trials), and serious inconsistency (substantial unexplained heterogeneity).

One CBA study (Smith 2004; 509 participants) found no difference in length of hospital stay between the CPW and usual care groups. Due to poor reporting, all the length of stay data were missing (Smith 2004), whilst the investigators only reported the level of significance (not significant) without any other information.

Four included studies (n = 926) used an ITS approach. No change in length of stay after the use of a CPW was observed for prostate patients undergoing laparoscopic radical prostatectomy (Rotter 2014), and patients with asthma (Smith 2019). Studies also explored length of stay for pediatric patients with asthma; Bartlett 2017 reported values of 2.3 to 2.9 days (P value not reported) and Brennan 2018 reported reductions in length of stay (48.5 to 50.8 hours; P = 0.02).

Sensitivity analysis based on excluding randomized trials at high risk of bias (Delaney 2003; Deng 2014 (ICH); Deng 2014 (TIA); Gomez 1996; Jalil 2017; Johnson 2000; Li 2018; Panella 2012; Vanhaecht 2016) did not substantially alter the result (MD -1.05, 95% CI -1.66 to -0.44; P = 0.0007; I^2 = 62%; 12 studies; 3275 participants; Analysis 1.12).

Studies reporting length of hospital stay as a geometric mean

Of the thirty-two studies that reported on the length of hospital stay, three studies reported on a geometric mean for the CPW and the usual care group (Cunningham 2008; Dowsey 1999; Choong 2000). Two were randomized studies (Cunningham 2008; Dowsey 1999) and one was a non-randomized trial (Choong 2000).

Of the two randomized studies (Cunningham 2008; Dowsey 1999; n = 410) that reported a geometric mean, one study (n = 163) found a difference in length of stay between the CPW and the usual care group (Dowsey 1999) and one study (n = 247) found no difference in length of stay (Cunningham 2008). Dowsey 1999 reported a length of hospital stay of 7.10 days for 92 participants in the CPW group as opposed to 8.60 days for 71 participants in the usual care group (95% CI 1.03 to 1.30). Cunningham 2008 reported a length of hospital stay of 1.56 days (SD 1.1) for 134 participants in the CPW group, compared to 1.70 days (SD 1.15) for 113 participants in the usual care group (P = 0.36).

One non-randomized trial reported on a geometric mean (n = 111) and found a decrease in length of hospital stay between the CPW (6.60 days for 55 participants) and usual care group (8 days for 56 participants) (P = 0.03) (Choong 2000). See: Summary of findings 1).

1.6 Hospital costs and charges

Fifteen studies (n = 3028 participants) reported on cost/charge measures (e.g. hospital costs, hospital charges, and hospital charges reported as insurance points) (Aizawa 2002; Deng 2014 (ICH); Deng 2014 (TIA); Falconer 1993; Gomez 1996; Homagk 2016; Johnson 2000; Kim 2002; Kiyama 2003a; Kollef 1997; Li 2018; Panella 2009; Roberts 1997; Rutman 2017; Usui 2004). Thirteen were randomized trials (Aizawa 2002; Deng 2014 (ICH); Deng 2014 (TIA); Falconer 1993; Gomez 1996; Homagk 2016; Johnson 2000; Kim 2002; Kiyama 2003a; Kollef 1997; Li 2018; Panella 2009; Roberts 1997), one was a non-randomized trial (Usui 2004), and one study used an ITS approach (Rutman 2017).

Of the thirteen randomized trials (n = 2335 participants), ten randomized studies (n = 2113 participants) reported on comparable hospital costs and charges (Deng 2014 (ICH); Deng 2014 (TIA); Gomez 1996; Johnson 2000; Kim 2002; Kiyama 2003a; Kollef 1997; Li 2018; Panella 2009; Roberts 1997) but, due to the high level of statistical heterogeneity (I^2 = 99%), we did not report on the pooled estimate (Analysis 1.6; Summary of findings 1). The certainty of evidence is very low due to very serious inconsistency (meta-analysis not possible due to significant heterogeneity despite the

inclusion of ten studies) and serious indirectness in outcome measures. It is thus very uncertain whether stand-alone CPWs reduce hospital costs and charges. We provided a narrative summary of all included studies that reported on hospital costs and charges.

Nine of ten randomized studies reported reductions in hospital costs and charges (Deng 2014 (ICH); Deng 2014 (TIA); Gomez 1996; Johnson 2000; Kim 2002; Kiyama 2003a; Li 2018; Panella 2009; Roberts 1997) and one study reported increased hospital costs for the CPW group (Kollef 1997). Deng 2014 (TIA) reported on hospitalization costs for 213 TIA patients managed in the CPW group of USD 1569.64 (SD 788.97) compared to USD 1805.82 (SD 880.53) for 213 patients in the usual care group (P = 0.02). Deng 2014 (ICH) also reported on the hospitalization cost for 166 stroke patients in the CPW group of USD 2002.56 (SD 1110.63) versus USD 2305.68 (SD 723.12) for 166 stroke patients in the usual care group (P = 0.01). Homagk 2016 reported USD 16,215.21 (SD not reported) as total hospitalization costs for 17 participants in the CPW group as opposed to USD 28,655.91 for 15 participants in the usual care group (authors reported that the difference in hospitalization costs was statistically significant, without providing an SD or P value). Also, it remains unclear if the reported cost values were mean or median values.

Kollef 1997 reported an increase in hospital costs for 179 patients in the CPW group (USD 40,800.54 (SD 39,537.31)) compared to 178 patients in the usual care group (USD 40,445.30 (SD 38,137.0)). Kim 2002 reported direct costs of USD 1180.39 (SD 534.57) for nine patients in the CPW group compared to USD 2314.65 (SD 2051.44) for nine patients in the usual care group (P = 0.18). Kiyama 2003a reported hospital costs (direct and indirect costs) of USD 13,380.86 (SD 2515.63) for 47 patients undergoing gastrectomy in the CPW group as opposed to USD 17,206.63 (SD 7001.15) for 38 patients in the usual care group (P < 0.001). Li 2018 reported on total hospitalization costs of USD 5730.05 (SD 287.34) for 62 participants in the CPW group, as opposed to USD 8039.1 (SD 303.99) for 56 participants in the control group (P = 0.001). Panella 2009 reported USD 3356.72 (SD 843.52) for 201 patients with heart failure in the CPW group as opposed to USD 3492.57 (SD 916.19) for 201 patients in the usual care group (P = 0.11). Roberts 1997 reported hospital costs of USD 2348.62 (SD 1555.50) for 82 patients in the CPW group as opposed to USD 3220.14 (SD 920) for 83 patients in the usual care group (P < 0.01).

Three randomized studies (n = 331 participants) reported on hospital charges (Falconer 1993; Gomez 1996; Johnson 2000). Two studies (n = 210 participants) reported on comparable mean hospital charges and both studies reported reductions (Gomez 1996; Johnson 2000). Gomez 1996 reported USD 1924.79 (SD 2523.74) as mean hospital charges for 50 participants in the CPW group, compared to USD 8606.61 (SD 22,074.10) for 50 participants in the usual care group (P = 0.0001). Johnson 2000 reported USD 3425.12 (SD 1563.86) as mean hospital charges (room charge) for 55 participants in the CPW group as opposed to USD 4434.02 (SD 1563.88) for 55 participants in the usual care group (P < 0.001).

One study conducted by (Rutman 2017) and colleagues (n = 226 participants) used an ITS approach and the investigators found no change in hospital cost between the reported baseline and post-intervention periods. Please see additional Table 7 for the ITS hospital cost data reported. Additional Table 3 provides cost data as reported in the primary studies, whereas additional Table 2 provides price data adjusted to US dollars and translated into the year 2016.

Three randomized studies (n= 222) reported on hospital cost/charge measures that could not be used for our data synthesis (Aizawa 2002; Falconer 1993; Homagk 2016). One randomized study reported on Japanese insurance points (Aizawa 2002). The authors reported 48,424.2 (SD 4437.5) insurance points for patients (n = 32) managed with a CPW and 55,365.5 (SD 16,805.1) insurance points for patients (n = 37) managed with usual care (no P value reported). The second randomized study (Falconer 1993) found no difference in median hospital charges per bed-days and reported USD 24,924.02 (SD not reported) for 53 participants in the CPW group as opposed to USD 24,889.50 (SD not reported) for 68 participants in the usual care group (P = 0.16). Other reported median hospital charges were drugs and other services (Falconer 1993; additional Table 1, additional Table 2, and additional Table 3). The third randomized study (Homagk 2016; n = 32) did not provide usable published data (additional Table 2 and additional Table 3) for our data synthesis on cost/charge measures, and we narratively described these reported hospital cost outcomes from this study below. This leaves us with ten randomized studies that reported on comparable hospital costs and charge measures. One non-randomized trial (Usui 2004) reported 24,338 insurance points for 30 patients in the CPW group, compared to 34,048 insurance points for 31 patients in the usual care group (P = 0.003).

1.7 Adherence to recommended practice

Thirteen studies (n = 5405 participants) measured the impact of stand-alone CPWs on the adherence to recommended practice (guidelines or protocols) by healthcare professionals using a CPW (Chadha 2000; Cunningham 2008; Doherty 2006a; Kaiser 2020; Kinsman 2012; Panella 2012; Panella 2018; Phillips 2017; Seys 2019; Sulch 2002; Tilden 1987; Trombetti 2013; Vanhaecht 2016).

Seven studies were randomized trials (n = 2874 participants) (Cunningham 2008; Kinsman 2012; Panella 2012; Panella 2018; Seys 2019; Sulch 2002; Vanhaecht 2016), one was a non-randomized trial (n = 694 participants) (Trombetti 2013), two were CBA studies (n = 1133 participants) (Chadha 2000; Doherty 2006a), and three were ITS studies (n = 12,289 participants) (Kaiser 2020; Phillips 2017; Tilden 1987).

Three randomized trials (n = 573 participants post-intervention) measured adherence to recommended practice (Panella 2012; Seys 2019; Sulch 2002) and were assessed for statistical pooling but demonstrated significant heterogeneity (I^2 = 81%; Analysis 1.7;Summary of findings 1), precluding meta-analysis. The certainty of evidence is low (downgraded two levels) due to serious risk of bias (all three studies at some risk of bias) and serious inconsistency (meta-analysis not possible due to significant heterogeneity). Stand-alone CPWs may slightly increase adherence to recommended practice compared with usual care (data not pooled; low-certainty evidence). The remaining four randomized trials (n = 1262 participants) that reported adherence to recommended practice as an outcome could not be pooled in the meta-analysis as they provided various measures for adherence (Cunningham 2008; Kinsman 2012; Panella 2018; Vanhaecht 2016) (see additional Table 8 and additional Table 9), without providing a combined or an all-or-nothing performance measure (e.g. proportion of patients who received all the performance measures for which the patient was eligible).

Of the seven randomized studies, six randomized trials (n = 2817) reported increases between CPW and usual care groups in adherence to recommended practice for some or all of the measures of adherence (Cunningham 2008; Panella 2012; Panella 2018; Seys 2019; Sulch 2002; Vanhaecht 2016) and one randomized study (Kinsman 2012) found no difference between CPW and usual care groups for adherence to the reported recommended practice measures.

Panella 2012 (n = 476) reported an increase in adherence to recommended practice for stroke patients associated with CPWs versus usual practice (221/229 [97%] versus 83/139 [60%]; P < 0.001). Indicators of adherence to recommended practice for stroke patients included: provision of information, swallow screen tests on the day of admission, blood pressure assessment, continuous cardiac monitoring within 48 hours of admission, use of a discharge plan, and pre-discharge functional independence measures.

Sulch 2002 (n = 152) measured adherence to recommended practice for seven outcomes. Three measures of adherence were increased in the CPW group versus usual care: nutritional assessment (49/66 [74%] versus 14/64 [22%]; P < 0.001); documentation of goals (75/76 [99%] versus 56/76 [74%]; (P < 0.001); and GP notified of death/discharge with 24 hours (61/76 [80%] versus 34/76 [45%]; P < 0.001). Adherence to recommended practice was decreased in the CPW group versus usual care for written goals for higher functioning (7/61 [11%] versus 25/59 [42%]; P < 0.001). There were no differences between measures of adherence for the three remaining outcomes: assessed caregiver needs, performed caregiver training, and documented death/follow-up arrangements.

Seys 2019 reported adherence to recommended practice for 22 out of 29 (76%) CPW teams as opposed to 15 out of 24 (63%) usual care teams (not significant).

Cunningham 2008 (n = 180) reported on two measures of adherence to recommended practice for CPWs for childhood asthma versus usual care and found increases for: documentation of education for hospitalized children (86/94 [91%] versus 29/86 [34%]; P < 0.001); and documented discharge plans (84/94 [89%] versus 35/86 [41%]; P < 0.001).

Kinsman 2012 (n = 57) included three outcome indicators for adherence to recommended practice for the management of acute myocardial infarction in rural emergency departments. There was no difference between CPW and usual care groups for: eligible participants receiving thrombolysis (25/32 [78%] versus 21/25 [84%]; P = 0.191); participants receiving thrombolytic agents within 30 minutes (12/32 [37%] versus 15/25 [62%]; P = 0.072); and participants having an ECG within ten minutes of arrival (23/32 [72%] versus 20/25 [83%]; P = 0.571).

Panella 2018 reported on 24 outcome measures for adherence to recommended practice and found increases for the CPW group versus usual care for two measures: assessment of pre-fracture status (267/301 [88.7%] versus 71/213 [33.3%]; P < 0.001); and adequate postoperative pain assessment (49/301 [16.3%] versus 20/213 [9.4%]; P < 0.001). There was no evidence of a difference in any of the 22 measures for adherence to recommended practice.

Vanhaecht 2016 also reported on 24 process indicators related to adherence to recommended practice for COPD and found increases for the CPW group versus usual care for nine of these measures. They were: systemic corticosteroids during hospitalization (152/174 [87.4%] versus 93/135 [68.9%]; P = 0.022); recommended dose (30-40 mg) of corticosteroids during the first seven days of hospitalization (134/152 [88.2%] versus 93/135 [68.9%]; P = 0.022); provision of information about quitting strategies for active smokers at admission (23/42 [54.8%] versus 10/40 [25%]; P = 0.03); active smokers receiving a cessation leaflet (15/42 [35.7%] versus 1/40 [2.5%]; P = 0.049); education regarding inhaler therapy (61/173 [35.3%] versus 15/165 [9.1%]; P = 0.037); specific education regarding inhaler technique (114/173 [65.9%] versus 33/165 [20%]; P = 0.049); nutritional assessment conducted (111/174 [63.8%] versus 30/168 [17.9%]; P = 0.002); referral to a dietitian in underweight patients (27/57 [47.4%] versus 5/38 [13.2%]; P = 0.015); and underweight participants receiving nutritional advice (21/57 [36.8%] versus 4/38 [10.5%]; P = 0.04).

One non-randomized trial, Trombetti 2013 (n = 694), reported on three measures of adherence to recommended practice for elderly patients with malnutrition and found improvements in all three for the CPW group versus usual care. These measures were: nutrition counseling requests (200/465 [43%] versus 73/229 [32%]; P < 0.05); prescription of nutritional supplements (177/465 [38%] versus (69/229 [30%]; P < 0.05); receiving an enriched meal (93/465 [20%] versus 18/229 [8%]; P = 0.0001).

Two CBA studies (Chadha 2000;Doherty 2006a) reported on adherence to recommended practice. Chadha 2000 (n = 888) reported on adherence to recommended practice for menorrhagia and urinary incontinence. Using a five-point scale, Chadha and colleagues found no change in adherence for menorrhagia (3.7 versus 3.8; 0.1 change, 95% CI -0.41 to 0.28) and an increase in adherence to recommended practice for urinary incontinence (3.1 versus 3.8; 0.7 change, 95% CI 0.47 to 0.93). Doherty 2006a (n = 187 participants) reported on improvements in the assessment of severity of asthma for the CPW group. Twenty-nine out of 47 patients (62%) were assessed for severity of asthma in the CPW group compared to six out of 42 patients (14%) in the usual care group (P < 0.0001).

Three ITS studies reported on adherence to recommended practice (Kaiser 2020; Phillips 2017; Tilden 1987; additional Table 7; n = 12,289).

Kaiser 2020 (n = 12,013 patients, 68 hospitals) reported on three adherence measures of asthma care: (1) percentage of early administration of bronchodilators, (2) percentage of documented screening for secondhand tobacco smoke exposure, and (3) percentage of documented referral of caregivers to smoking cessation resources. While pathway implementation was associated with increased odds of caretaker referral to smoking cessation resources (OR: 2.22; 95% CI: 1.38 to 3.57), and with increases in the odds of early administration of bronchodilators (OR 3.94; 95% CI: 2.85 to 5.44), CPW implementation was not associated with an increase in documented screening for second-hand tobacco smoke exposure (OR 1.00; 95% CI 0.94 to 1.04).

Tilden 1987 (n = 892 participants) measured adherence to documented identification of female victims of domestic violence in the emergency department before and after the implementation of a clinical pathway. The investigators reported an increase in documented identification from 7/72 (9.72%)

before implementation to 17/74 (22.97%) documented cases after implementation (P = 0.03).

Phillips 2017 (n = 130 participants) measured adherence to recommended practice for inhaled bronchodilator therapy transition time and reported a 4.9-hour decrease in the mean transition time from continuous to intermittent bronchodilator use (31.9 versus 27.0, P = 0.033).

Multifaceted clinical pathways compared to usual care

Out of nine studies (n = 8218) that compared multifaceted interventions (including a CPW) with usual care (Bauer 2006; Bookbinder 2005; Brattebø 2002; Chen 2004; Cole 2002; Ju 2019; Kampan 2006; Philbin 2000; Wang 2018), seven were randomized trials (Bauer 2006; Chen 2004; Cole 2002; Ju 2019; Kampan 2006; Philbin 2000; Wang 2018), one was a CBA study (Bookbinder 2005), and one was an ITS study (Brattebø 2002).

Of the nine studies that compared multifaceted interventions (including CPW) with usual care, six randomized studies (n = 7624) reported on comparable outcomes/effects of multifaceted CPW on one or more outcomes of this review (Bauer 2006; Cole 2002; Ju 2019; Kampan 2006; Philbin 2000; Wang 2018) (Summary of findings 2). One randomized study (Chen 2004; 42 participants) reported on hospital readmissions, but the authors only reported on the level of significance and this outcome could not be included in our meta-analysis on hospital readmissions (Analysis 2.3 hospital readmissions up to 6 months). One of the nine included studies (Bookbinder 2005) reported on adherence to recommended practice but not other prespecified outcomes.

2.1 Inhospital mortality

Two randomized studies (n = 6304) in the multifaceted intervention group reported on inhospital mortality (Philbin 2000; Wang 2018). Reported study results were too heterogeneous (I^2 = 83%) to calculate a pooled effect on inhospital mortality. The certainty of evidence is low due to very serious inconsistencies (meta-analysis not possible due to significant heterogeneity and lack of overlap between confidence intervals). Instead, we provided the reported confidence intervals and the effect estimate that were reported in both primary studies (Analysis 2.1; Summary of findings 2). It thus remains uncertain if multifaceted interventions (including a CPW) reduce inhospital mortality.

Philbin 2000 (n = 10 hospitals, 2906 participants, n = 1504 participants post-intervention) reported no difference in inhospital mortality for patients with heart failure in the CPW group (5.2% mortality) compared with usual care (3.8% mortality; OR 1.41 [95% CI 0.86 to 2.32]). Wang 2018 (n = 40 hospitals, 3980 participants) reported a decrease in inhospital mortality for patients with acute ischemic stroke in the CPW group as opposed to usual care (0.5% mortality with CPW and 1% with usual care, OR 0.48 [95% CI 0.23 to 0.99]).

2.2 Mortality (up to 6 months)

Three randomized trials reported on mortality (up to 6 months) (n = 6531 participants; Cole 2002; Philbin 2000; Wang 2018). It is uncertain whether multifaceted CPWs make any difference to mortality (up to 6 months) compared to usual care as the certainty of the evidence is low (OR 1.05, 95% CI 0.88 to 1.25; P = 0.61; I^2 = 0%; three studies; 6531 participants; low level of certainty; Analysis 2.2).

The certainty of evidence was low due to serious risk of bias (Wang 2018) and serious imprecision (CI for overall effect cannot exclude appreciable benefit or harm). Additionally, there were differences in follow-up time windows (Summary of findings 2).

Sensitivity analysis based on excluding one study at high risk of bias (Wang 2018) did not substantially alter the result (OR 1.07, 95% CI 0.85 to 1.35; P = 0.58; I^2 = 0%; 2 studies, 1731 participants (Analysis 2.6).

2.3 Inhospital complications

One randomized trial (n = 140 participants) in the multifaceted intervention group reported inhospital complications (Ju 2019). Ju 2019 tested a CPW for the management of cirrhosis patients and defined inhospital complications as 'irregular bleeding in the digestive tract, infection, hepatic encephalopathy, and the hepatorenal syndrome'. They reported six complications in 70 patients (8.6%) in the CPW group as opposed to 16 complications in 70 patients (22.9%) in the usual care group (P = 0.02), indicating lower odds in the CPW group (OR 0.32; 95% CI 0.12 to 0.87; P = 0.02; 1 study; 140 participants; low-certainty evidence; Summary of findings 2). It is uncertain whether multifaceted CPWs reduce inhospital complications. The certainty of the evidence was downgraded to low due to very serious imprecision as results were only available for one study with a small sample size.

2.4 Hospital readmission (up to 6 months)

Two randomized trials (n = 1569) in the multifaceted intervention group reported on hospital readmissions up to six months (Kampan 2006; Philbin 2000) but, due to the high level of statistical heterogeneity (I^2 = 84%), we did not report on the pooled estimate (Analysis 2.3). The certainty of evidence is low due to very serious inconsistencies (meta-analysis not possible due to significant heterogeneity and lack of overlap between confidence intervals) (Summary of findings 2). It is thus uncertain whether multifaceted CPWs reduce hospital readmission (up to 6 months).

Philbin 2000 reported 169 readmission events for heart failure up to six months for 840 CPW patients (20.1%) versus 141 readmissions for 664 patients (21.3%) in the control group (-1.2%; 95% CI -16.4% to 15.9%; OR 0.93 [95% CI 0.72 to 1.20]) during the management of heart failure patients with a CPW. Kampan 2006 reported two readmission events for hypoglycemia at three months for 33 patients (6%) with diabetes in the CPW group as opposed to 11 readmissions for 32 patients (34%) in the usual care group (OR 0.12 [95% CI 0.02 to 0.60]).

Philbin 2000 also reported on readmissions for all-cause reasons (up to 6 months) and found no difference between the CPW and the usual care group (P = 0.93).

2.5 Length of hospital stay (days)

Five studies (1789 participants) in the multifaceted intervention group reported on length of hospital stay (Brattebø 2002; Cole 2002; Ju 2019; Kampan 2006; Philbin 2000). Four (n = 1504)were randomized trials (Cole 2002; Ju 2019; Kampan 2006; Philbin 2000) and one (285 participants) was an ITS study (Brattebø 2002).

Four randomized trials (n = 1936) reported on length of hospital stay (Cole 2002; Ju 2019; Kampan 2006; Philbin 2000) and were assessed for statistical pooling but demonstrated significant heterogeneity (I^2 = 89%; Analysis 2.4; See Summary of findings 2), precluding

meta-analysis on length of stay. The certainty of evidence is low due to very serious inconsistencies (meta-analysis not possible due to significant heterogeneity and lack of overlap between confidence intervals). It thus remains uncertain if multifaceted interventions, including a CPW, reduce the length of hospital stay.

Two RCTs reported reductions in length of hospital stay between the multifaceted intervention group and usual care (Kampan 2006; Ju 2019), and two randomized trials reported no difference in length of hospital stay between the multifaceted intervention group and usual care (Cole 2002; Philbin 2000). None of the included randomized studies had a high risk of bias.

Kampan 2006 reported a length of hospital stay of 3.94 days (SD 1.03) for 33 participants in the multifaceted intervention group, including a CPW as opposed to 6.38 days (SD 4.04) for 32 participants in the usual care group (no P value reported). Ju 2019 reported a length of stay of 5.15 days (SD 1.9) for 70 participants in the multifaceted intervention group, including a CPW as opposed to 9.13 days (SD 1.25) for 70 participants in the usual care group (P < 0.001).

One included study (N = 285) used an ITS approach (Brattebø 2002; additional Table 7) and found no difference in duration of mechanical ventilation in ICU between the multifaceted intervention group, including a CPW and the usual care group (Brattebø 2002).

2.6 Hospital costs and charges

Four randomized studies (n = 2015 participants) in the multifaceted intervention group reported on hospital costs and/or charges (Bauer 2006; Ju 2019; Kampan 2006; Philbin 2000) but, due to the high level of statistical heterogeneity (I^2 = 98%), we did not report on the pooled estimate (Analysis 2.5; Summary of findings 2). The certainty of evidence is very low due to very serious imprecision (meta-analysis not possible due to significant heterogeneity and lack of overlap between confidence intervals) and serious indirectness in outcome measures. It thus remains very uncertain if multifaceted interventions (including a CPW) reduce hospital costs and charges.

One RCT (n = 140) reported on cost reductions for the CPW group (Ju 2019). The investigators reported USD 2832.66 for the CPW group, as opposed to hospitalization costs of USD 4826.29 for the usual care group (P = 0.001). The remaining three RCTS found no difference in hospital costs and/or charges reported between CPW and usual care groups (Bauer 2006; Kampan 2006; Philbin 2000).

Additional Table 3 provides cost data as reported in the primary studies, whereas additional Table 2 provides price data adjusted to US dollars and translated into the year 2016.

2.7 Adherence to recommended practice

Two randomized studies (n = 6304) in the multifaceted intervention group reported on adherence to recommended practice between CPW and usual care groups (Philbin 2000; Wang 2018). Both randomized trials found no difference in outcomes related to adherence to recommended practice (Philbin 2000; Wang 2018; additional Table 8). We could not combine the reported adherence measures due to the risk of duplicate counting of participants from Philbin 2000. The certainty of evidence is low due to very serious inconsistencies (meta-analysis not possible due to risks of duplicate counting). It thus remains uncertain if multifaceted interventions (including a CPW) improve adherence to recommended practice (Summary of findings 2).

Philbin 2000 reported on three different measures of adherence to recommended practice (i.e., evaluation, documentation and diet counseling) and found no difference between CPW and usual care groups. Wang 2018 reported on the proportion of patients who received all the recommended practices for which the patient was eligible, and found no differences between both groups (53.8% in the CPW group versus 47.8% in the usual care group, P = 0.06).

One CBA study (n = 101) (Bookbinder 2005; additional Table 9) measured adherence to recommended practice for symptom assessment during the last two days of life (possible scores from 0 to 12) and reported an increase in symptom assessment in the CPW group versus usual care (10.3 versus 9.4; P = 0.001).

DISCUSSION

Clinical pathways are implemented in hospitals world-wide for the management of a variety of clinical conditions and interventions. In this updated review we set out to identify if CPWs are associated with changes in practice and improved outcomes for patient and health services. We screened and analyzed a further 20,474 search hits and added 31 more studies for a total of 58 included studies, of which 41 were randomized trials (12 were cluster-randomized trials), nine were ITS studies, four were CBA studies and four were non-randomized studies. This review included a broad range of clinical conditions and procedures across numerous ward settings and countries. As per our original review, we divided the analysis and results into stand-alone CPWs and CPWs implemented as part of a multifaceted intervention. Two new studies (Ju 2019; Wang 2018) were assessed in terms of the impact of CPW as a multifaceted intervention, providing new data on inhospital mortality, mortality follow-up, inhospital complications, length of hospital stay, hospital costs, and adherence to recommended practice.

Summary of main results

Stand-alone clinical pathway interventions

Forty-nine studies compared stand-alone CPWs with usual care. Due to the high level of statistical and contextual heterogeneity between studies, it is uncertain if stand-alone CPWs have an effect on inhospital mortality and mortality (up to 6 months) compared to usual care (low certainty). Stand-alone CPWs likely reduce inhospital complications (moderate certainty) and may make no difference to hospital readmissions (very low certainty), compared to usual care. Stand-alone CPWs likely decrease length of hospital stay compared to usual care (moderate certainty). While there is uncertainty regarding the cost-effectiveness of CPWs due to heterogeneity, most studies indicate a reduction in costs (very low certainty). Stand-alone CPWs may slightly increase adherence to recommended practice, compared to usual care (low certainty).

Multifaceted clinical pathway interventions

Nine studies compared multifaceted CPWs with usual care. It is uncertain whether multifaceted CPWs reduce inhospital mortality (low certainty) and they may make no difference to mortality (up to 6 months) compared to usual care (low certainty). It is uncertain whether multifaceted CPWs reduce inhospital complications (low

certainty) or hospital readmission (up to 6 months) (low certainty) compared to usual care. It is also uncertain whether multifaceted CPWs make any difference to length of hospital stay (low certainty), hospital cost and charges (very low certainty), and adherence to recommended practice, compared to usual care (low certainty).

The remainder of the discussion combines both types of CPW.

Overall completeness and applicability of evidence

This comprehensive review includes 58 studies from 19 countries investigating the impact of CPW on 13 separate conditions or interventions, mostly in urban hospital settings. The impact of CPWs was reported broadly across patient outcomes (14 studies), professional practice (15 studies), length of hospital stay (37 studies) and hospital costs (19 studies).

We believe the comprehensive, broad-ranging nature of the search and included studies make the findings broadly relevant to hospital settings, but findings are compromised by the resulting heterogeneity. One of the recommendations from the previous version of this review (Rotter 2010) was the exploration of disease-specific pathways with a subgroup analysis if there were a sufficient number of studies (at least ten) available for each subgroup comparison. We had also planned to compare included studies in a subgroup analysis by country because there may be certain healthcare delivery designs that benefit more or less from the use of CPWs. However, the low number of studies available for each comparison did not support a subgroup analysis for this review update, and this necessitates further investigation with a sufficient number of studies in the future.

Furthermore, we could not determine the relative effectiveness of different implementation strategies by conducting a subgroup analysis based on implementation scores. That is, we could not investigate which implementation strategies were associated with enhanced adherence to recommended practice and, subsequently, improved patient and health service outcomes.

The lack of a detailed description of the specific strategies carried out by the hospitals to implement the CPWs, as well as any other quality improvement initiatives that might have been implemented concurrently, has direct implications for our comparison between stand-alone and multifaceted interventions. The rationale for grouping and analyzing stand-alone and multifaceted interventions separately was to confirm that any potential observed effects were not driven by intervention components peripheral to the CPW, and to uncover any potential synergies between CPW and other multifaceted components. Grouping and comparing multifaceted interventions including a CPW versus stand-alone CPW interventions, however, comes at the cost of lower statistical power and only provides valuable information if a substantial number of studies are included in each group and if the range of implementation strategies and initiatives are well described by researchers. Considering these limitations, we believe the evidence in future updates of this review would be strengthened by merging stand-alone and multifaceted interventions in the meta-analysis and using subgroup analysis to explore potential differences between the two types of interventions.

Last but not least, it is important to understand that we refer to 'stand-alone CPW interventions' in this review as complex clinical pathway interventions. The comparison with multifaceted interventions including a CPW does not mean that single CPWs are not complex interventions. We describe (Kinsman 2010, Lawal 2016) CPWs as complex clinical interventions, regardless of whether they have been implemented in combination with other interventions or as a 'single' CPW intervention.

Certainty of the evidence

We evaluated the certainty of the seven reported outcomes using GRADE. For stand-alone CPWs, we found moderate-certainty evidence (two outcomes), low-certainty evidence (three outcomes) and very low-certainty evidence (two outcomes). Serious risk of bias, stemming mostly from knowledge of the allocation of the intervention and lack of protection against contamination, was identified in all outcomes comparing stand-alone CPWs except inhospital mortality, length of hospital stay and hospital costs and charges. Serious or very serious inconsistencies were apparent for all outcomes in stand-alone CPWs, as indicated by considerable heterogeneity between studies except for mortality (up to 6 months), inhospital complications and hospital readmission. Serious imprecision due to wide confidence intervals was also apparent for inhospital mortality and mortality (up to 6 months) and very serious imprecision for hospital readmission. Serious indirectness in outcome measures was identified for hospital costs and charges for stand-alone CPWs.

For multifaceted CPWs we found low-certainty evidence (6 outcomes) and very low-certainty evidence (1 outcome). Imprecision was serious or very serious, indicating that the research does not provide a reliable indication of the likely effect on mortality (up to 6 months), inhospital complications and hospital costs and charges. Inconsistency was serious or very serious for inhospital mortality, hospital readmissions, length of hospital stay and adherence to recommended practice. Serious risk of bias was identified for mortality (up to 6 months), and serious indirectness was identified for costs and charges.

Potential biases in the review process

To avoid publication bias, we employed an extensive and highly sensitive search strategy for study identification owing to the complex nature of CPW and the broad review questions investigated. The search strategy remained unchanged for the most recent search in July 2024.

We developed and used our refined working definition of CPW due to the high variation in the terminologies in which CPWs are described. The validated checklist on what constitutes a CPW helped to include clinical pathway interventions irrespective of the terminology used in the study. Two people independently screened all search results in the screening and full-text stage. We used imputation techniques to approximate missing data for a few studies where primary authors did respond to requests for assistance.

Agreements and disagreements with other studies or reviews

This review remains the most comprehensive systematic review investigating the effects of CPWs on length of hospital stay, professional practice outcomes, patient outcomes, and costs in hospital. This updated review adds new data to the previous Cochrane Review on this topic (Rotter 2010). One finding from this

update is consistent with that found in the original review; stand-alone CPWs are likely to reduce inhospital complications. Similar to the original review, there is very low certainty that stand-alone CPWs may reduce hospital readmission (up to 6 months). In line with the previous review, we found considerable heterogeneity in reports on hospital costs and charges and adherence to recommended practice. Mortality (up to 6 months) was reported by three studies and was pooled for meta-analysis. However, the certainty of evidence for this outcome was low, and thus it remains uncertain if CPW reduces mortality within six months. Results for adherence to recommended practice were highly heterogenous and could not be pooled for meta-analysis.

Similarly, due to considerable heterogeneity across studies, we cannot provide strong conclusions regarding improvements in hospital costs and charges for the CPW intervention versus usual care. In a non-Cochrane systematic review, Renholm 2002 reported that CPWs were associated with reduced costs. Renholm's review is differentiated from our review by two main characteristics: it is more than twenty years old, and it included studies not meeting Cochrane quality criteria. Previously, we reported *(*Rotter 2012*)* that simple pre-post designs reported greater effects than studies meeting Cochrane inclusion criteria and this may explain Renholm's more positive findings.

Other systematic reviews on this topic are disease-specific and reported mixed results for length of stay and costs (Kwan 2003; Van Herck 2010). These studies appear to support our findings about the complexity and heterogeneity associated with combining CPW evaluation results across a range of settings.

AUTHORS' CONCLUSIONS

Implications for practice

This review provides evidence based on 58 primary studies conducted in 19 countries. The quality of the evidence was most commonly graded as low, although moderate-quality evidence existed for inhospital complications and length of stay in stand-alone CPWs. For these outcomes, CPWs are likely to result in reductions in inhospital complications and shorter length of stay. While the studies could not be pooled together due to the manner in which the outcomes are reported, the studies generally show that stand-alone CPWs may slightly increase adherence to recommended practice, including documentation practices and guidelines use. The evidence for multifaceted CPWs is uncertain for all included outcomes.

The low and very low-certainty evidence associated with most of the outcomes included in this review does not permit robust evidence-based conclusions. Although some variation exists in the direction of effects reported by primary studies, this may be due to differences in health systems, clinical conditions, and other context-specific factors. By definition, CPWs are embedded in the local context and culture, which may make comparisons across countries and health systems more challenging.

The evidence around stand-alone CPWs is generally uncertain about inhospital mortality, mortality (up to 6 months), hospital readmissions (up to 6 months), and hospital costs and charges. These findings are replicated from our previous Cochrane Systematic Review completed in 2010 (Rotter 2010). Conversely, in this update, the length of hospital stay was about one day less in stand-alone CPWs than for usual care. Although there is twice the amount of data since the last review, the quality of evidence generated makes drawing more definitive conclusions across stand-alone and multi-faceted CPWs impossible.

For decision-makers in hospitals, the current state of evidence, as shown by this review, creates a difficult situation. Given that the implementation and sustainable use of CPWs requires a substantial amount of resources, while at the same time their effect on relevant outcomes remains unclear, the decision whether to pursue employing CPWs for certain diseases or treatments is not easy. Therefore, it seems reasonable that clinicians and multidisciplinary teams prioritize pathways that are a high concern for inhospital complications and/or length of stay, and/or require standardization of provider practices in documentation or other clinical activities. Clinicians and multidisciplinary teams could monitor mortality, hospital readmissions, costs and charges, and adherence to recommended practice data to see if pathways in their specific practice context show benefit. Finally, our attempts to elicit and compare the effectiveness of CPW implementation strategies were compromised by limited reporting. More innovative research and better implementation studies are necessary to better understand what specific interventions drive the successful implementation of evidence-based CPWs at the bedside.

Implications for research

The review highlights the limited understanding generated by conducting more of the same types of studies (randomized trials, CBA studies, non-randomized trials and ITS) included in this update. The number of published studies reporting the impact of CPW in hospitals has increased substantially, but the overall quality of the studies has not improved, partly due to the heterogeneity identified in the results of studies included in this review. Our search strategy identified 20,474 hits from the last 14 years, compared to approximately 3000 from the previous 20 years. In addition, only 31 studies from those 20,474 hits merited inclusion, compared to a similar number of included studies (27) from 3000 hits in 2009. The proportion of studies meeting Cochrane criteria has decreased from 0.9% in 2009 to 0.15% in 2024.

This update has more than doubled the number of included studies to 58 but has revealed minimal new insights regarding if, how, and why CPWs affect patient outcomes, hospital readmissions, hospital costs and charges, and adherence to recommended practice. Future studies using the same designs predicated on linearity and predictability will remain subject to high levels of statistical and contextual heterogeneity if included in a Cochrane review. Higher trial quality achieved by blinding of participants, a clear definition of usual care in comparator arms of randomized trials, and the prevention of contamination bias, could overcome these problems. Yet, these measures are difficult to implement when conducting studies. Future research should be augmented by methods that recognize the complexity of the systems and people implementing complex CPW interventions. Further, it should seek to understand how a CPW may influence practice, not simply measure whether it has an impact. Therefore, studies exploring the nature of CPW development and CPW knowledge-practice translation are needed to gain greater insight into the impact of CPW in clinical settings. Such studies would need to include clear descriptions of implementation strategies and approaches that facilitate the exploration of the uptake of CPWs by health professionals. Comparing those findings to measures

of adherence to key components of CPWs' use would provide a deeper understanding of how CPWs influence practice changes and outcomes. Other possible quantitative parameters to be explored in the same context comprise job satisfaction measured on validated scales, staff turnover, successful training of providers, and knowledge of staff regarding key components of the treatments targeted by the CPWs in place.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Aizawa 2002

Study characteristics		
Methods	Individual randomized trial	
Participants	Urological (adult) male patients (n = 69) recruited from a Japanese urban area were allocated to the intervention (n = 32; mean age 70 years) or control group (n = 37; mean age 72 years).	
Interventions	Clinical pathway intervention (paper format) for invasive transurethral resection of the prostate Intervention during 1999 and 2000 Control: "usual care" or non-pathway care and representing the standard of care prior to the pathway implementation "Moderate" implementation score	
Outcomes	Mean length of stay, duration of catheterization and hospital charges, reported as Japanese insurance points. 6-month follow-up period	
Notes	No funding reported and no Declaration of Interest	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Incomplete outcome data (attrition bias) (All)	Low risk	No missing outcome data

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* Indicates the major publication for the study

Aizawa 2002 *(Continued)*

Blinding of participants and personnel (All)	Low risk	Objective outcomes used: We compared the 2 groups in regard to the average of total hospital charges (insurance points), average length of hospital stay and complications after the operations. The total hospital charges were calculated from the medical fee receipts.
Protection against contamination (RCT, NRCT, CBA)	High risk	Same hospital, therefore, likely to have contamination. The patients were admitted into our hospital for transurethral resection of prostate (TURP). Any patients who came from different departments, rehospitalized within 3 months after their previous hospitalization and had complication of urology, e.g. urethral stone and malignancy, were not included.
Selective reporting (reporting bias) (All)	Low risk	All the prespecified outcomes have been reported in the prespecified way.
Other bias (all)	Unclear risk	It is unclear whether differences in patient groups had any influence on outcomes.

Almalki 2017

Study characteristics	
Methods	Pragmatic, parallel, single-blind randomized controlled trial
Participants	Patients with community-acquired kidney injury (AKI) (n = 38) were allocated to the intervention (n = 18; age 69 years [SD 10.9]) or usual care (n = 20; age 69 years [SD 11.0]).
Interventions	Non-invasive multidisciplary pathway in electronic format for patients presenting to the ER with AKI during 2012 and 2013 "Low" implementation score
Outcomes	Length of stay Inhospital mortality and 30-day readmission rates Other AKI pathway-specific targeted outcomes assessed were: medication reconciliation performed by the physician and pharmacist within 24-h of ED admission, the patient's oxygen saturation was maintained at greater than 90% on day 1, renal ultrasound was performed within 24-hours of ED admission, and nephrology consultation on day 1.
Notes	Funded by the The Clinical Research Fund of the King Abdullah International Medical Research Centre, Saudi Arabia (RC 10/134/J). No declaration of interest.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Patients were randomized by permuted blocks of unequal sizes through a computer-generated sequence in a 1:1 ratio.
Allocation concealment (selection bias)	Low risk	Allocation concealment was done through opaque sealed envelopes provided to the on-call resident by the ED pharmacy.
Incomplete outcome data (attrition bias) (All)	Low risk	A post hoc per-protocol analysis was conducted excluding nine patients due to misclassifications (n = 2), lost to follow-up (n = 5), and discontinued care (n = 2).

Almalki 2017 *(Continued)*

Blinding of participants and personnel (All)	Low risk	The primary outcome measure was objective (i.e. LOS)
Protection against contamination (RCT, NRCT, CBA)	High risk	During weekends and holidays, some of the clinical pathway physicians provided care to usual care patients and vice versa. Additionally, over weekends due to limited workforce, not all services were provided to the patients.
Selective reporting (reporting bias) (All)	Low risk	All prespecified outcomes reported
Other bias (all)	Unclear risk	Limitations reported by authors: small effect size, not checked for adherence, restrictive patient eligibility criteria

Bartlett 2017

Study characteristics	
Methods	Interrupted time series
Participants	297 pediatric patients admitted with asthma (n = 297; age range 2-28 years): 160 pre-intervention, and 137 children post-intervention
Interventions	Asthma clinical pathway based on best evidence from guidelines during 2013 and 2014 "High" implementation score
Outcomes	Length of stay Clinical pathway adherence (asthma order set usage). Thirteen measures from 160 patients were taken before the introduction of the CPW and 21 measures from 137 patients after.
Notes	No funding reported and no Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Intervention independent of other changes (ITS)	High risk	It is possible that other factors contributed to the change. In the post-intervention period, pulmonary pediatric became a consult only service which may have affected ALOS; in addition, there were fewer pediatric asthma admissions in the post-intervention group despite spanning the same period as the pre-intervention group. Also challenges included continued provision of education about the pathway for residents, RTs, nurses and faculty to keep up with staffing turnover. Also - there were other critical incidents during the study period - August 2014, enterovirus D68 outbreak; Dec. 2014 peak in influenza infections. Also May 2015 audit
Shape of intervention effect prespecified (ITS)	Low risk	Point of analysis was the point of intervention.
Intervention unlikely to affect data collection (ITS)	Unclear risk	ALOS, reduced variability in practice, and cost of inpatient pediatric asthma care
Incomplete outcome data (attrition bias) (All)	Unclear risk	Not stated

Bartlett 2017 *(Continued)*

Blinding of participants and personnel (All)	Low risk	Extracted from the EMR
Selective reporting (reporting bias) (All)	Low risk	All prespecified measured reported
Other bias (all)	Low risk	The study appears to be free of other sources of bias.

Bauer 2006

Study characteristics	
Methods	Individual randomized multi-center controlled trial
Participants	Psychiatric adult patients with bipolar disorder (n = 306) recruited in urban and regional US settings treated in mental health outpatient clinics countrywide
Interventions	Participants were allocated to a clinical pathway intervention (n = 157; age 47 years [10.1]) combined with case management for bipolar disorder as opposed to usual care (n = 149; age 47 years [10.1]) between 1997 and 2000. Pathway intervention contains detailed collaborative care plan, scheduled care and patient self management enhancement. "High" implementation score
Outcomes	Intervention costs, direct outpatient costs, hospital inpatient costs, psychiatric inpatient costs and medical/surgical inpatient costs
Notes	The Department of Veterans Affairs Cooperative studies program 430. No declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Allocation sequence adequately generated
Allocation concealment (selection bias)	Low risk	Telephonic randomization used
Incomplete outcome data (attrition bias) (All)	Low risk	No missing outcome data
Blinding of participants and personnel (All)	Low risk	The study chair and sites remained blind to outcome until follow-up was complete.
Protection against contamination (RCT, NRCT, CBA)	High risk	Intervention was implemented with excellent fidelity. However, no mention of protection from contamination
Selective reporting (reporting bias) (All)	Low risk	Detailed study protocol available; all of the study's prespecified outcomes have been reported in the pre-specified way.
Other bias (all)	Low risk	The study appears to be free of other sources of bias.

Bernard 2011

Study characteristics	
Methods	Individual randomized controlled trial
Participants	Adult patients with hyperglycemia (n = 176) presenting to the ED of an urban university medical center
Interventions	Participants were allocated to the clinical pathway intervention (electronic format) (n = 87; age 55 years [13]) versus usual care (n = 89; age 55 years [13]) from May 2008 to June 2009. "Moderate" implementation score
Outcomes	Blood glucose levels (mg/dL) ED LOS (hr) % of patients treated with insulin in ED % of patients admitted
Notes	No funding reported and no Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	From May 2008 through June 2009, patients presenting to the Rush University Medical Center ED with a history of type 2 diabetes […] were randomized to an intervention group (INT) or to a usual care group (UC) after giving informed consent.
Allocation concealment (selection bias)	Unclear risk	After informed consent was obtained by the study staff, implementation of the protocol was carried out by the ED staff. ED nurses were trained in the study protocol.
Incomplete outcome data (attrition bias) (All)	Unclear risk	No mention of patients lost to follow-up
Blinding of participants and personnel (All)	Low risk	Objective measured used. We compared differences between groups in the mean admission BG level, mean daily BG level, mean BG level before each meal, hospital LOS, and frequency of hypoglycemic events.
Protection against contamination (RCT, NRCT, CBA)	High risk	After informed consent was obtained by the study staff, implementation of the protocol was carried out by the ED staff. ED nurses were trained in the study protocol. House staff members have been educated on the Rush inpatient insulin protocol on which the INT protocol was based. The Rush inpatient diabetes protocol is implemented via a single computerized order set in which all patients should receive mealtime insulin using aspart and a basal insulin.
Selective reporting (reporting bias) (All)	Low risk	All measured outcomes reported for both groups, We compared differences between groups in the mean admission BG level, mean daily BG level, mean BG level before each meal, hospital LOS, and frequency of hypoglycemic events.
Other bias (all)	Low risk	No other sources noted

Bittinger 1995

Study characteristics	
Methods	Individual randomized controlled trial
Participants	Adult patients with congestive heart failure (n = 60) admitted to the intensive care unit of the hospital
Interventions	Participants were randomized to clinical pathway group (n = 15; age 73.0 years [10.6]) versus usual care group (n = 15; age 75.0 years [11.0]) in 1993. "Moderate" implementation score
Outcomes	Satisfaction scores and interpersonal scores (staff and participants)
Notes	No funding reported and no Declaration of Interest

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Subjects meeting the selection criteria were assigned to the control or experimental group on a random basis".
Allocation concealment (selection bias)	Unclear risk	Thirty slips of paper with case management and 30 slips of paper with usual care were placed in separate envelopes and sealed.
Incomplete outcome data (attrition bias) (All)	High risk	"Four subjects originally included in the study were unable to complete the study due to clinical deterioration".
Blinding of participants and personnel (All)	Unclear risk	No evidence of blinding of healthcare professionals
Protection against contamination (RCT, NRCT, CBA)	Unclear risk	No evidence of protection against contamination as the study was conducted in the ICU unit of one hospital
Selective reporting (reporting bias) (All)	Low risk	Results for all primary and secondary outcomes were presented.
Other bias (all)	High risk	"The care provided by any individual may have positively or negatively influenced the overall patient satisfaction scores with nursing".

Bookbinder 2005

Study characteristics	
Methods	Controlled before-and-after study. 2 general medical units (clusters) served as control sites and 3 cluster units including one palliative care ward served as experimental sites.
Participants	Palliative end of life care patients (n = 267) recruited from a urban setting in the US. The age range reported was 69 to 78 years for both the experimental patients (n = 111) and control patients (n = 156).
Interventions	Participants were allocated to a clinical pathway intervention (paper format) (n = 111; age range 69 to 78 years) versus usual care (n = 156; age range 69 to 78 years) for nine months in 2003. "High" implementation score
Outcomes	Number of symptoms assessed and problematic symptoms identified

Bookbinder 2005 *(Continued)*

	Number of interventions and inpatient consultations (patient outcomes) High implementation score
Notes	No funding reported and no Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	CBA design
Allocation concealment (selection bias)	High risk	CBA design
Incomplete outcome data (attrition bias) (All)	Unclear risk	Insufficient information
Blinding of participants and personnel (All)	High risk	Subjective measures used (CAT, PAT, PCQN); no mention of blinding: Using the CAT, baseline data were collected retrospectively from the charts of patients who died on the three study units and two comparison units during the year prior to the study. The PAT was completed by study personnel to track the extent to which the care given to patients placed on the PCAD pathway was consistent with the pathway. Nurses from study units completed the PCQN prior to implementation of the PCAD intervention, and again four months after the intervention.
Protection against contamination (RCT, NRCT, CBA)	High risk	The pilot was quasi-experimental and involved the acquisition of relevant pre-post data from patient records and nursing staff on the three study units and on two general medical units (the “comparison units”).
Selective reporting (reporting bias) (All)	Unclear risk	Insufficient information
Other bias (all)	High risk	Many factors may have limited our ability to quantify a positive effect related to the PCAD pathway and PCAD intervention. We could not exercise control over multiple extraneous variables within the system (e.g. referral to the consultation team of the DPMPC), cultural and leadership styles within each unit, exposure of staff to other educational offerings in pain or symptom management, and varied patient diagnoses.

Brattebø 2002

Study characteristics

Methods	Interrupted time series
Participants	Ventilated adult patients in an ICU (n = 285) within a urban setting in Norway. The mean age reported ranged from 52 to 55 and the baseline period included 147 patients, whereas the post-intervention period covered 138 participants.
Interventions	Complex clinical pathway intervention combined with continuous feedback, posters, emails and flyers (n = 138) versus usual care (n = 147) in 2000. Mean age reported to entire sample was 52 to 55 years.

Brattebø 2002 *(Continued)*

	"High" implementation score
Outcomes	Ventilation patient-days per month
Notes	Funded by the Norwegian Medical Association and Haukeland University Hospital

Risk of bias

Bias	Authors' judgement	Support for judgement
Intervention independent of other changes (ITS)	Unclear risk	No mention of other changes
Shape of intervention effect prespecified (ITS)	Unclear risk	ITS design although not specified (based on figures only)
Intervention unlikely to affect data collection (ITS)	Low risk	Baseline data were taken from the intensive care unit's clinical database (Regina), which has been in use for several years. Severity of illness was measured by the SAPS II scoring system. Ventilator time (measured in 24 hour-days, for example, 6 hours = 0.25 days), length of stay in the intensive care unit (in days), and mortality were also recorded. Our department has also operated a confidential reporting system for adverse effects that may be related to sedation practices.
Incomplete outcome data (attrition bias) (All)	Low risk	No missing outcome data
Blinding of participants and personnel (All)	Low risk	No mention of who performed data collection; ventilator time, length of stay and mortality all objective measures
Selective reporting (reporting bias) (All)	Low risk	All the study prespecified outcomes have been reported.
Other bias (all)	Unclear risk	The data compared to the baseline proceed from the intervention period making it difficult to interpret the observed results and to know whether they are due to the intervention effect or other factors.

Brennan 2018

Study characteristics

Methods	Interrupted time series analysis
Participants	246 pediatric patients with status asthmaticus (aged 2-18)
Interventions	Participants were treated according to a status asthmaticus clinical pathway (n = 105) versus usual care (n = 141) between August 2015 and August 2016. "Moderate" implementation score
Outcomes	Length of stay in ICU Hospital length of stay Duration of continuous nebulised albuterol

Brennan 2018 *(Continued)*

Notes	No funding reported and no Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Intervention independent of other changes (ITS)	High risk	Investigators employed an ITS analysis without a comparison group. Other confounding factors could have caused the effects reported.
Shape of intervention effect prespecified (ITS)	High risk	Process control chart as specific form of an ITS analysis has been employed. Control limits were defined using three sigma above and below the centre line. Sample size estimation has been described in the paper narratively, but no formula or reference provided.
Intervention unlikely to affect data collection (ITS)	Low risk	The methods of data collection (although more frequent in the experimental group) were the same before and after the intervention.
Incomplete outcome data (attrition bias) (All)	High risk	Five units withdrew after the project commenced, following a decision from their management (three units withdrew after the project pretest and two units withdrew after the project began).
Blinding of participants and personnel (All)	Low risk	The primary outcome was variablity in PICU LOS and albuterol duration (objective measures).
Selective reporting (reporting bias) (All)	Low risk	All factors included in the model
Other bias (all)	Low risk	Potential poor adherence to the pathway, but significant effects still observed

Brook 1999

Study characteristics

Methods	Individually randomized controlled trial
Participants	Adult patients requiring mechanical ventilation (n = 321) recruited from an urban American teaching hospital within a medical ICU
Interventions	Participants were allocated to clinical pathway intervention (paper format) (n = 162; mean age 57.8 years) versus usual care (n = 159; mean age 57.8 years) in 1997. "Moderate" implementation score
Outcomes	ICU length of stay Mean hospital length of stay Number of acquired organ system derangements Inhospital mortality
Notes	No funding reported and no Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement

Brook 1999 *(Continued)*

Random sequence generation (selection bias)	Low risk	Patients were randomly assigned, at the time of initiation of mechanical ventilation, to have their sedation managed by a nursing-implemented sedation protocol or by a traditional non-protocol approach. Blocked randomization was accomplished using opaque, sealed envelopes, which were opened at the time each patient was enrolled in the study.
Allocation concealment (selection bias)	Low risk	Blocked randomization was accomplished using opaque, sealed envelopes, which were opened at the time each patient was enrolled in the study.
Incomplete outcome data (attrition bias) (All)	Low risk	A total of 106 patients who died during the study period were classified as censored because these patients did not undergo successful weaning from mechanical ventilation. These 106 patients were included in all univariate analyses but were censored from the Kaplan-Meier analysis.
Blinding of participants and personnel (All)	Low risk	Objective outcomes used: The primary outcome measure was the duration of mechanical ventilation. Secondary outcome measures included intensive care unit and hospital lengths of stay, hospital mortality, the development of organ system derangements, reintubation, and tracheostomy.
Protection against contamination (RCT, NRCT, CBA)	High risk	Same hospital therefore likely to have contamination: Patients were randomly assigned, at the time of initiation of mechanical ventilation, to have their sedation managed by a nursing-implemented sedation protocol or by a traditional non-protocol approach.
Selective reporting (reporting bias) (All)	Low risk	The study prespecified outcomes have been reported in the prespecified way.
Other bias (all)	Low risk	The study appears to be free of other sources of bias.

Chadha 2000

Study characteristics	
Methods	2 x 2 balanced incomplete block controlled before-and-after study
Participants	946 adult female patients treated in hospital gynecology units in Scotland with menorrhagia (n = 497) or urinary incontinence (n = 449)
Interventions	National guidelines for menorrhagia and urinary incontinence were adapted into local protocols at participating hospitals - two hospitals implemented protocols for menorrhagia (n = 497; age 40.1 years [6.8]) and two hospitals implemented protocols for urinary incontinence (n = 449; age 40.4 years [7.3]) in 1998 "High" implementation score
Outcomes	Compliance with recommendations Appropriate surgical treatment rates
Notes	Healthcare providers in the control group were protected against contamination. No funding reported and no Declaration of Interest
Risk of bias	

Chadha 2000 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	CBA design
Allocation concealment (selection bias)	High risk	CBA design
Incomplete outcome data (attrition bias) (All)	Low risk	Reason for missing outcome data unlikely to be related to the true outcome
Blinding of participants and personnel (All)	High risk	The local research assistant at each hospital abstracted process of care data. The analyses were based on compliance with the national guidelines (or local protocols where these differed from the national guidelines). Since in the substantive analyses both conditions were analyzed simultaneously, it was necessary to identify key areas of process of care which were comparable across the two conditions. Six such areas of clinical practice identified were: initial hospital assessment of women; appropriate use of hospital investigations; inappropriate use of hospital investigations; appropriate first-line treatment; appropriate pre-surgery assessment; and use of surgical treatments.
Protection against contamination (RCT, NRCT, CBA)	Low risk	The study used a 2 x 2 balanced incomplete block controlled before-and-after design. Doctors in the two hospitals in the West of Scotland were to adhere to their locally developed protocol for menorrhagia and act as a controls for urinary incontinence, whereas doctors in the two hospitals in the East of Scotland were to adhere to their locally developed protocol for urinary incontinence and act as controls for menorrhagia. Data were collected on a sample of women with either condition managed before, and an analogous sample of women with either condition managed after the introduction of the respective protocol at each hospital. This design has a number of advantages: doctors at any one hospital manage women for both the study (protocol) and control (no protocol) conditions, and thus act as their own controls; the Hawthorne effect is minimized since all doctors receive a similar level of intervention; and the analysis can consider the effects of the intervention on both conditions simultaneously, thus increasing the power of the study.
Selective reporting (reporting bias) (All)	Low risk	All the prespecified outcomes have been reported in the prespecified way.
Other bias (all)	Unclear risk	Only 57% and 45% of the women returned the questionnaire at six and twelve months follow-up for the analysis of outcome of care. Use of endometrial biopsy was already a widely discussed subject for policy recommendations at the time and may have influenced the clinicians at the control hospitals for menorrhagia. There were wide and unexpected variations and differences in some aspects of process of care during the baseline period in the study and control hospitals for both conditions with potential ceiling effects. There were some problems associated with poor recording in the hospital casenotes of what was done. While these problems do not alter the guidelines ability to change practice, they do undermine the ability of this study to detect that change since this study was dependent upon information recorded in the hospital casenotes.

Chen 2004

Study characteristics

Chen 2004 *(Continued)*

Methods	Individual randomized single-center controlled trial
Participants	Asthmatic children (n = 42) recruited from a Taiwan medical childrens hospital
Interventions	Participants were allocated to a clinical pathway (paper format) (n = 20; age 5.5 years [3.0[) versus usual care (n = 22; age 5.5 years [3.0]) in 2002. Multifaceted intervention combined a CPW with counselling and educational sessions targeting parents. "High" implementation score
Outcomes	Emergency room presentations Hospital readmissions. Follow-up period was 3 months.
Notes	No funding reported and no declaration of interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Concealment not explained
Incomplete outcome data (attrition bias) (All)	Low risk	No missing outcome data
Blinding of participants and personnel (All)	Unclear risk	Data on the health status were collected by using a diary and a chart record for follow-up data. Data on other outcome variables were collected in the questionnaire.
Protection against contamination (RCT, NRCT, CBA)	Unclear risk	Subjects who satisfied the inclusion criteria were randomized into the control group of 22 parents or the experimental group of 20 parents. The control group received usual care for asthma management. . . The experimental group received a copy of a CACM in addition to the usual care.
Selective reporting (reporting bias) (All)	Unclear risk	The study outcomes are not clearly defined in the article, making it difficult to judge whether the results are free of selective reporting.
Other bias (all)	Unclear risk	Insufficient information to assess whether other important risk of bias exists

Chen 2019

Study characteristics

Methods	Patient randomized controlled trial. According to the abstract of this publication, 186 patients were randomized to either group A (clinical pathway) or group B (control, usual care) with 93 patients in each group.
Participants	In this investigation, there was a mismatch of information between the abstract and the main body of the paper. The abstract provided information on 186 patients, randomized to group A (N = 93) and group B (N = 93). However, in the main paper, the following number of participants was published and included for data analysis: 102 stroke patients were randomized to either group A (stroke pathway, N = 51) or group B (control, N = 51). We used the information provided in the body of the paper, and not

Chen 2019 *(Continued)*

	the information from the abstract. The difference in terms of the number of participants might refer to study dropouts, but this information has not been provided in this publication. Patients with ischemic stroke for 7-15 days were included in this trial. Exclusion criteria were: patients with severe liver and kidney dysfunction, a history of cerebral infarction and cerebral embolism, decompensated cardiac insufficiency, motor dysfunction, cognitive impairment, communication impairment, and those patients who did not cooperate with the treatment.
Interventions	Chen and colleagues compared 'the routine rehabilitation nursing model' (control group: including routine rehabilitation training and psychological counselling) with 'an early rehabilitation clinical pathway (observation group).' The multidisciplinary pathway intervention included shared decission-making, care planning, and a health manual. This intervention has been combined with a 'psychological nursing intervention,' aiming to improve communication with the patient and their families, assessing the psychological status of the patient, and to increase health literacy. The so called 'psychological intervention also includes elements of language training and the assessment of swolling functions. Last but not least, the experimental group used elements of care planning (including a time frame and daily updates).' Context: The First People's Hospital of Jingzhou Rehab Department, Jingzhou, Hubei, China
Outcomes	Chen and colleagues employed the Modified Barthel Index (MBI), the Fugl-Meyer Motor Function Rating Scale (FMA), and stroke-specific quality of life scale (SS-QOL) in order to compare group A (pathway) and group B (control).
Notes	Implementation of the clinical pathway not reported. Discrepancy between abstract and paper in terms of the number of participants

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Page 11429, Materials and methods: Authors stated that 140 patients were randomly divided into the observation and control groups. No additional information reported on allocation process
Allocation concealment (selection bias)	Unclear risk	Page 11429, Materials and methods: Authors stated that 140 patients were randomly divided into the observation and control groups. No additional information reported on allocation process
Incomplete outcome data (attrition bias) (All)	Unclear risk	Page 11429. No information provoded about dropouts. It reads like there were no dropouts.
Blinding of participants and personnel (All)	Unclear risk	No information reported on blinding study personnel or patients
Protection against contamination (RCT, NRCT, CBA)	Unclear risk	No information about potential contamination of healthcare professionals in both groups
Selective reporting (reporting bias) (All)	Unclear risk	No study protocol cited and or identified in the literature. So, we could not compare proposed vs. reported outcomes in this RCT.
Other bias (all)	Unclear risk	Insufficient information reported to assess whether an important risk of bias exists

Choong 2000

Study characteristics

Methods	Pseudo-randomized single-center controlled clinical trial

Choong 2000 *(Continued)*

Participants	Hospitalized orthopedic adult patients (n = 111) with femoral neck fracture. Patients were recruited from an orthopedic urban hospital setting in Melbourne, Australia.
Interventions	Participants were allocated to a clinical pathway intervention (n = 55; mean age 84 years) versus usual care (n = 56; mean age 84 years) from October 1997 to November 1998. "Low" implementation score
Outcomes	Length of stay Days to mobilization Confusional status Inhospital complications, post-discharge complications Readmission rates
Notes	Funded by the Victorian Center for Ambulatory Care Innovation. No Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Non-random sequence generation process used. Patients were allocated on the basis of their unit record number, even numbers to the control group, and odd numbers to the clinical pathway group.
Allocation concealment (selection bias)	Unclear risk	The method used by the administrative clerk in charge of the allocation sequence was not described.
Incomplete outcome data (attrition bias) (All)	Low risk	No data missing
Blinding of participants and personnel (All)	Low risk	Outcomes generally objective: duration of stay, inpatient complications, post-discharge complications and readmissions
Protection against contamination (RCT, NRCT, CBA)	Unclear risk	The study was conducted at St Vincent's Hospital, Melbourne, Victoria (a tertiary referral hospital affiliated with the University of Melbourne) […] One hundred and eleven patients were allocated to one of two groups (control or clinical pathway) by an administrative clerk, who was independent of the study and unaware of the study hypothesis.
Selective reporting (reporting bias) (All)	Low risk	All the study prespecified outcome have been reported in the prespecified way.
Other bias (all)	Low risk	The study appears to be free of other bias.

Cole 2002

Study characteristics	
Methods	Individual randomized single-center controlled trial

Cole 2002 *(Continued)*

Participants	Geriatric medical patients presenting to the ED (n = 227) with suspected delirium were recruited from an urban Canadian setting and admitted to the general medical units within the study hospital in Montreal.
Interventions	Participants were allocated to a clinical pathway intervention (paper format) (n = 113; age 82.7 years [7.5]) versus usual care (n = 114; age 82.0 years [7.1]) between March 1996, and January 1999. The multidisciplinary intervention combined a CPW with consultation and follow-up by a geriatric internist or psychiatrist, and follow-up in hospital by the study nurse. ."High" implementation score
Outcomes	Length of stay Mortality at 8 weeks Discharge destination Dependency
Notes	Funded by GlaxoSmithKline, United Kingdom. The contract granted Ingenix Inc. complete oversight of the study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Stratified randomization was used; that is, independent randomization was done within group of prevalent and incident cases respectively. Furthermore, they performed blocking using blocks of different sizes to guarantee a similar number of patients in the control and the intervention groups at any point and to ensure that the intervention team was not overloaded by a large number of patients during any period. Unequal block size also helped to maintain blinding as to treatment allocation.
Allocation concealment (selection bias)	Low risk	Patients were randomly allocated by means of computer-generated random numbers to receive the intervention or usual care on the five medical units.
Incomplete outcome data (attrition bias) (All)	Low risk	On 113 patients randomized to the intervention group, 110 received the intervention. No reason is given for the 3 missing patients; however this is unlikely to influence the outcome.
Blinding of participants and personnel (All)	Low risk	To check the extent of blinding of the research assistant during the study, the assistant was asked to guess which study group a convenience sample of 18 patients (whom the research assistant had recently assessed) belonged to. The research assistant responses were correct for 2 of 4 patients in the intervention group and 3 of 5 patients in the usual care group.
Protection against contamination (RCT, NRCT, CBA)	Low risk	It was not feasible to randomly assign patients to intervention or control units in the hospital; however in the previous trial there was no evidence of contamination when patients in the two groups were managed in the same unit.
Selective reporting (reporting bias) (All)	Low risk	All of the prespecified (primary and secondary) outcomes that are of interest in the review have been reported in the prespecified way.
Other bias (all)	Low risk	The study appears to be free of other biases.

Costantini 2014

Study characteristics	
Methods	Multi-center cluster-randomized trial .
Participants	8 intervention block-clusters and 8 control block-clusters including 308 adult cancer patients requiring palliative care in Italy
Interventions	Participants were allocated to a clinical pathway intervention (paper format) (n = 147; age 75.6 years [10.8]) versus usual care (n = 161; age 75.2 years [11.9]) during 2011 to 2013. "High" implementation score
Outcomes	Quality of care Scores for: advance care planning, respect, dignity and kindness, informing and making decisions, family emotional support, co-ordination of care, family self-efficacy, overall control of pain, overall control of breathlessness, overall control of nausea or vomiting
Notes	Funded by the Italian Ministry of Health and Marruzza Lefebvre D'Ovidio Foundation-Onlus. No Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization was centralized at the trial center of the National Cancer Research Institute of Genoa, which verified the eligibility and recorded details of each pair of wards and matched PCTs, assigned a numerical code for identification, and recorded the allocation.
Allocation concealment (selection bias)	Low risk	In this cluster-randomized trial, pairs of general medicine hospital wards were stratified by region, matched for assessment period, and randomly assigned to the LCP-I program or to follow standard healthcare practice.
Incomplete outcome data (attrition bias) (All)	Low risk	Effects likely underestimated by lower response in control group. A smaller proportion of family members responded in the control wards than in the intervention wards (70% vs 81%), and a higher proportion refused to be interviewed in the control wards than in the intervention wards (25% vs 16%; P = 0.090; table 2). Similarly, a lower proportion of face-to-face interviews were done in the control wards than in the intervention wards (69% vs 78%; P = 0.115; table 2).
Blinding of participants and personnel (All)	High risk	Our research interviewers were professionals with experience in supporting bereaved family members, and were trained to listen to their concerns and views in a supportive manner. All masking and randomization was described in study so it is unlikely interviewers were blinded.
Protection against contamination (RCT, NRCT, CBA)	Low risk	To prevent contamination, only one ward per hospital was identified for inclusion in the study. During the LCP-I implementation, no training course for care of the dying patients was undertaken in the control wards as per usual practice.
Selective reporting (reporting bias) (All)	Low risk	Used same questions for both groups. All outcomes reported. The toolkit was developed and validated to measure the quality of care at the end-of-life from the perspective of family members.

Costantini 2014 *(Continued)*

Other bias (all)	Low risk	No other sources noted

Cunningham 2008

Study characteristics	
Methods	Cluster-randomized trial
Participants	13 intervention block-clusters and 13 control block-clusters (298 patients)
Interventions	Participants were allocated to a clinical pathway intervention for the management of acute asthma in children (n = 163; age 5.7 years [2.9]) versus usual care (n = 135; age 5.8 years [3.2]) between August 2004 and February 2005. "High" implementation score
Outcomes	Length of stay Prednisolone usage Hospital admission rate Rate of recovery Education provided Prescribing errors
Notes	Funded by the Sick Kids Friends Foundation (Edinburgh) and Roche Award Grant. No Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Patients received care according to permuted block cluster randomization (7-day periods in blocks of 8 weeks) generated before the start of the study.
Allocation concealment (selection bias)	High risk	Allocation of clusters was not concealed. Seven-day clusters began on Monday morning at 9:00 A.M., and finished on Monday morning at 8:59 A.M. ED triage nurses dispensed the appropriate documentation to staff during each cluster period.
Incomplete outcome data (attrition bias) (All)	Unclear risk	No mention of patients lost to follow-up
Blinding of participants and personnel (All)	High risk	Data collection was cross-checked for consistency in the first 50 patients. Two study members (C.L., M.D.) independently assessed prescribing records with discrepancies resolved by agreement (C.L., M.D., S.C.).
Protection against contamination (RCT, NRCT, CBA)	High risk	The study was conducted in the emergency department (ED) and the medical wards of a pediatric university hospital in Edinburgh, Scotland, UK. Patients received care according to permuted block cluster randomization (7-day periods in blocks of 8 weeks) generated before the start of the study.
Selective reporting (reporting bias) (All)	Low risk	All outcomes reported (LOS and prescribing errors)

Cunningham 2008 *(Continued)*

Other bias (all)	Low risk	No other sources noted

Delaney 2003

Study characteristics	
Methods	Individual randomized single-center controlled trial
Participants	Adult surgical patients requiring laparotomy and intestinal resection(n = 64) were recruited from an urban US setting.
Interventions	Participants were allocated to a clinical pathway intervention (paper format) (n = 31; mean age 50.6 years) or usual care (n = 33; mean age 41.9 years) in 2001. "Moderate" implementation score
Outcomes	Length of stay Pain scores Quality of life Hospital satisfaction Readmission Complications
Notes	No funding reported and no Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization was performed with sealed envelopes prepared by the biostatistics department.
Allocation concealment (selection bias)	Low risk	Sealed envelopes used
Incomplete outcome data (attrition bias) (All)	Low risk	No missing outcome data
Blinding of participants and personnel (All)	High risk	A baseline visual analog pain score (VAS), McGill pain score questionnaire (MGPQ), Short Form-36 (SF-36) and a previously validated quality-of-life questionnaire (Cleveland Clinic Global Quality of Life (CGQL)) were completed at randomization, discharge or POD 10, and POD 30. Complications were determined prospectively and were reassessed by telephone follow-up or outpatient visit 30 days after surgery.
Protection against contamination (RCT, NRCT, CBA)	Low risk	Protocol Violations: These were noted, but analysis was performed by intention-to-treat principles. Four TRAD patients did not have nasogastric tubes inserted. Two TRAD patients were ambulated around the nursing floor on the first postoperative day.
Selective reporting (reporting bias) (All)	Low risk	All prespecified outcomes have been reported in the prespecified way.

Delaney 2003 *(Continued)*

Other bias (all)	Unclear risk	Insufficient information to assess the risk of bias due to contamination between intervention and control groups

Deng 2014 (ICH)

Study characteristics

Methods	Randomized controlled trial
Participants	Stroke patients in China (n = 332)
Interventions	Participants admitted to hospital following a hemorrhagic stroke were allocated to a clinical pathway intervention (n = 166; age 66.3 years [8.9[) versus usual care (n = 166; age 66.7 years [8.6[) between March and October 2010. "Moderate" implementation score
Outcomes	Length of hospital stay Costs (hospitalization and drugs) Rates of infection and mortality National Institute of Health Stroke Scale and Barthel Index
Notes	Funded by the National Health and Family Planning Commission of China No Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient data provided: "This population was randomized into 2 groups: a conventional group (control; n = 166) and a CP group (n = 166)".
Allocation concealment (selection bias)	Low risk	Both the control and CP groups demonstrated comparable National Institute of Health Stroke Scale levels both at the time of admission and 14 days after treatment without significant difference of mortality or infection between the 2 groups. A $\chi 2$ analysis of Barthel Index of patients showed no significant difference between the 2 groups at either the time of admission or after 90 days of treatment (Table 5).
Incomplete outcome data (attrition bias) (All)	High risk	Study did not explain missing data (Methods Section suggests control n = 166 and CP n = 166, table 5 suggests control n = 213/208 and CP n = 166/162)
Blinding of participants and personnel (All)	Unclear risk	No mention of allocation prevention. Some outcomes are objective (e.g. LOS), others subjective (e.g. cost).
Protection against contamination (RCT, NRCT, CBA)	Unclear risk	Not described in the study
Selective reporting (reporting bias) (All)	Low risk	All outcomes addressed
Other bias (all)	Low risk	No other obvious sources of bias

Deng 2014 (TIA)

Study characteristics	
Methods	Randomized controlled trial
Participants	426 participants with transient ischemic attack (TIA) in China.
Interventions	Participants were allocated to a clinical pathway intervention (n = 213; age 58.8 years [13.3]) versus usual care (n = 213; age 60.2 years [10.8]) between March and October 2010. "Moderate" implementation score
Outcomes	Length of hospital stay Costs (hospitalization and drugs) Incidence of stroke within 90 days
Notes	National Health and Family Planning Commission of China. No Declaration of Interest

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Insufficient data provided on method of randomization
Allocation concealment (selection bias)	Unclear risk	Insufficient data provided on allocation concealment
Incomplete outcome data (attrition bias) (All)	Low risk	No evidence of missing data (see table 3)
Blinding of participants and personnel (All)	Unclear risk	No mention of allocation prevention. Some outcomes are objective (e.g. LOS), while other subjective (e.g. cost)
Protection against contamination (RCT, NRCT, CBA)	Unclear risk	No measures against contamination described in the study
Selective reporting (reporting bias) (All)	Low risk	All prespecified outcomes reported
Other bias (all)	Low risk	No other obvious sources of bias

Doherty 2006a

Study characteristics	
Methods	Multi-center controlled before-and-after study (CBA). Authors used a cluster design; 8 hospitals were matched pairwise and one randomly allocated to the experimental group.
Participants	Adult asthmatic patients (n = 187) recruited from 8 rural settings in Australia and presented to the ED
Interventions	Participants were allocated to a clinical pathway intervention (paper format) (n = 98; mean age 33 years) versus usual care (n = 89; mean age 37 years) between January 2004 and April 2005.

Doherty 2006a *(Continued)*

	"High" implementation score
Outcomes	Severity of asthma Use of spirometry, ipratropium, systemic steroids, antibiotics and STAMP
Notes	Funded by the National Institute of Clinical Studies. No Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	CBA design
Allocation concealment (selection bias)	High risk	CBA design
Incomplete outcome data (attrition bias) (All)	Unclear risk	Number of patients differed between pre- and post-intervention. No reasons for missing data provided
Blinding of participants and personnel (All)	Unclear risk	Based on estimates of attendances with asthma for these hospitals, 7 months of pre-intervention data were collected from 1 January to 31 July 2004 and 7 months of post-intervention data were collected from 1 October 2004 to 30 April 2005.
Protection against contamination (RCT, NRCT, CBA)	Low risk	The study hospitals were subjected to an EBI outlined below. The control hospitals had no additional intervention to help implement established guidelines for asthma. The National Asthma Council and Respiratory Therapeutic Guidelines have been available for years and form the basis of the NSW Health guidelines, which have been disseminated to hospitals throughout NSW. Dissemination of guidelines without a dedicated implementation plan is a common method used by health departments to transfer knowledge to clinicians.
Selective reporting (reporting bias) (All)	Unclear risk	Main outcome of the study not clearly defined in the methods section; outcomes appear only in the results section. The author uses an audit to determine the outcomes of the study; however, the results and the protocol of this audit are not presented. It is then difficult to determine whether the article is free of selective reporting or not.
Other bias (all)	Unclear risk	Insufficient information to assess whether an important risk of bias exists. Characteristics of intervention and control group at baseline not shown

Doig 2008

Study characteristics

Methods	Cluster-randomized controlled trial with 27 clusters
Participants	1118 critically ill and malnourished ICU patients requiring intravenous feeding
Interventions	Participants were allocated to a clinical pathway intervention to improve feeding practices (n = 561; age 58.8 years [9.6]) versus usual care (n = 557; age 59.5 years [9.3]) between November 2003 and May 2004. "High" implementation score

Doig 2008 *(Continued)*

Outcomes	Length of stay Systemic antibiotics Inhospital mortality Invasive mechanical ventilation Organ system dysfunction Witnessed aspiration Serum albumin
Notes	DOI: Lead Researcher Dr. Doig received academic research grants from Fresenius-Kabi Deutschland GmbH and Baxter Healthcare Pty Ltd. and speakers honoraria from Pharmatel-Fesenius-Kabi Pty Ltd. Ms Simpson received academic research grants from Fresenius-Kabi Deutschland GmbH and Baxter Healthcare Pty Ltd. and speakers honoraria from Pharmatel-Fesenius-Kabi Pty Ltd. Funded by the Australian and New Zealand Intensive Care Foundation. Foundation had no role in study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Midway through the run-in period, hospitals were randomized to intervention or control groups. At the time of randomization one author (S.F.) provided a random number used to seed an SAS (SAS Institute Inc, Cary, North Carolina) algorithm (developed by G.S.D.) that generated the specific allocation sequence used in the trial.
Allocation concealment (selection bias)	Low risk	Midway through the run-in period, hospitals were randomized to intervention or control groups.
Incomplete outcome data (attrition bias) (All)	Low risk	Nonparticipating ICUs did not differ from participating ICUs with regard to major ICU-level characteristics. Sixty-six percent (6/9) of nonparticipating sites were metropolitan referral centers compared with 70% (19/27) of participating sites.
Blinding of participants and personnel (All)	Unclear risk	The primary outcome were, all-cause hospital discharge mortality […] secondary outcomes were on count data (e.g. length of stay, number of days of clinically significant organ dysfunction).
Protection against contamination (RCT, NRCT, CBA)	Low risk	Control ICUs collected data but were not invited to participate in the guideline development conference and remained unaware of the contents of the guideline and the supporting practice change strategy.
Selective reporting (reporting bias) (All)	Low risk	All outcomes reported (hospital discharge mortality, length of stay, clinically significant organ dysfunction).
Other bias (all)	Low risk	No other sources noted

Dowsey 1999

Study characteristics

Dowsey 1999 *(Continued)*

Methods	Individual randomized single-center controlled trial
Participants	Elective (adult) orthopedic patients (n = 163) for hip and knee arthroplasty within an urban Australian setting
Interventions	Participants were allocated to a clinical pathway intervention (paper format) (n = 92: mean age 66 years) versus usual care (n = 71; mean age 66 years) in 1997. "Moderate" implementation score
Outcomes	Length of stay Number of days required for sitting out of bed and for ambulation Complications Hospital readmission
Notes	No funding reported and no Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Patients were randomly allocated to either the control or clinical pathway group by a clerical assistant who was blinded to their demographic and clinical profiles.
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgment yes or no
Incomplete outcome data (attrition bias) (All)	Low risk	Twelve patients were excluded by the criteria listed in the methods: having revision arthroplasty, simultaneous bilateral joint arthroplasty, arthroplasty for acute trauma or complex tumor surgery. Reason for missing data unlikely to be related to the true outcome
Blinding of participants and personnel (All)	Low risk	Outcomes generally objective: length of stay (calculated from the time of the patient's admission to the time of discharge and expressed in days); time to sitting out of bed and ambulation (time between surgery and the patient's first day of sitting out of bed or walking with assistance); complications (wound infections, including all wound erythema lasting more than 24 hours, chest infections, deep vein thrombosis [DVT] as diagnosed by clinical features and confirmed by ultrasonography, joint dislocation, decubitus pressure areas, failure to cope at home and a decreased range of motion after discharge); readmission (for complications during a follow-up period of three months from discharge); and discharge matching (between the presumptive discharge destination given at the preadmission clinic and the patient's postdischarge destination)
Protection against contamination (RCT, NRCT, CBA)	Low risk	Patients randomly allocated to the clinical pathway received proactive treatment whereby specific goals were set each day for the patient and treating team. Their hospital records included a special written protocol which listed milestones to be achieved, identified tests that should be ordered, set daily tasks for patients and members of the treating team, and provided space for documenting any variation in treatment or patient response. Each intervention was signed by the treating health professional and the discharge plan was re-evaluated daily to ensure it remained realistic and appropriate to the patient's needs. The clinical pathway formalized in writing the participation of the various members of the treating team.

Dowsey 1999 *(Continued)*

		Patients not allocated to the pathway received reactive treatment whereby the treating team responded to the will and condition of the patient in providing postoperative care.
Selective reporting (reporting bias) (All)	Low risk	All of the study's prespecified outcomes have been reported in the prespecified way.
Other bias (all)	Low risk	The study appears to be free of other sources of bias.

Fakhr-Movahedi 2015

Study characteristics	
Methods	Quasi-experimental controlled clinical trial
Participants	138 participants with coronary artery disease
Interventions	Participants were allocated to a clinical pathway intervention (n = 69; 41% aged < 60 years) versus usual care (n = 69; 33% aged < 60 years) in 2013. "Low" implementation score
Outcomes	Anxiety and depression score Patient satisfaction
Notes	No funding reported and no Declaration of Interest

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	Quasi-experimental controlled clinical trial (non-randomized)
Allocation concealment (selection bias)	Unclear risk	Insufficient information provided
Incomplete outcome data (attrition bias) (All)	Unclear risk	No mention of missing data
Blinding of participants and personnel (All)	Low risk	The levels of patient's anxiety, depression and satisfaction were measured as the study outcomes. To prevent measurement bias, a non-participant in this study collected data. Anxiety and depression in patients were measured in two stages: after admission to the CCU (pretest) and at the time of discharge from CCU (post-test). Patient's satisfaction was measured only after discharge from CCU (post-test).
Protection against contamination (RCT, NRCT, CBA)	High risk	In order to prevent contamination of the participants, according to environment of the CCU, the total numbers of beds in the CCU (10 beds) were randomly divided into two halves and apart from each other as: 5 beds were considered for the CP group and 5 beds for the RUT group.
Selective reporting (reporting bias) (All)	Unclear risk	Methods: The levels of patient's anxiety, depression and satisfaction were measured as the study outcomes.

Fakhr-Movahedi 2015 *(Continued)*

		All outcomes addressed in results. Some concern as no protocol published and study not registered
Other bias (all)	Low risk	No other obvious sources of bias

Falconer 1993

Study characteristics		
Methods	Individual randomized single-center controlled trial	
Participants	Adult stroke patients for rehabilitation (n = 121) recruited from an urban university teaching hospital in USA	
Interventions	Participants were allocated to a clinical pathway intervention (electronic format) (n = 53; mean age 68.6 years) versus usual care (n = 68; mean age 67.6 years) in 1991. "Moderate" implementation score	
Outcomes	Length of stay Hospital charges Patient satisfaction and functional status	
Notes	Funded by the Robert Wood Johnston Foundation. No Declaration of Interest	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Insufficient information about the sequence generation process to permit judgment yes or no
Allocation concealment (selection bias)	Unclear risk	Method of concealment not described
Incomplete outcome data (attrition bias) (All)	Low risk	Seven randomly assigned patients did not complete the rehabilitation program because of sickness (CPM group n = 3, control group n = 4) and were dropped from the study. Reason for missing data unlikely to be related to true outcome
Blinding of participants and personnel (All)	Unclear risk	The main outcome measures were length of stay, hospital charges, and functional status. […] Functional status was measured by the Functional Independence Measure […] the FIM is a standardized, performance based, observer-rated assessment of self-care. [...] The professional most relevant to the item scored the item.
Protection against contamination (RCT, NRCT, CBA)	Unclear risk	No description of potential contamination
Selective reporting (reporting bias) (All)	Low risk	All of the prespecified outcomes have been reported in the prespecified way.
Other bias (all)	Unclear risk	The study appears to be free of other sources of contamination.

Gomez 1996

Study characteristics	
Methods	Individual randomized single-center controlled trial
Participants	Adult medical patients with suspected myocardial infarction (n = 100) recruited from an urban university hospital in the USA
Interventions	Participants were allocated to a clinical pathway intervention (n = 50; mean age 50 years) versus usual care (n = 50; mean age 53 years) in 1993 and 1994. "Moderate" implementation score
Outcomes	Length of stay (hours) Hospital charges Rehospitalization within 30 days
Notes	Funded by the Deseret Foundation, Intermountain Health Care, Salt Lake City and an unrestricted grant from Genetech, Inc. South San Francisco, California. No Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization to either routine care or to the ROMIO strategy (rapid rule-out protocol) was performed by opening sequentially numbered envelope containing the treatment assignment.
Allocation concealment (selection bias)	Low risk	Sequential envelopes have been used.
Incomplete outcome data (attrition bias) (All)	Low risk	No missing outcome data
Blinding of participants and personnel (All)	Low risk	Primary end points for comparison were 1) length of hospital stay; and 2) hospital charges after randomization […] Secondary end points included 1) missed diagnoses; 2) post-randomization hospital charges by category […] and 3) frequency of making a final diagnosis of acute myocardial infarction.
Protection against contamination (RCT, NRCT, CBA)	High risk	Because this study was not performed in a blinded manner and the intent was to increase efficiency, attending physicians for patients in the routine care group may have been biased towards ordering briefer, more economic evaluations.
Selective reporting (reporting bias) (All)	Low risk	All of the prespecified outcomes have been reported in the prespecified way.
Other bias (all)	High risk	The relatively small sample size, low event rate and short follow-up period of this study (30 days) did not allow us to exclude with confidence a small-to-moderate difference in the rate of diagnosing acute ischemic event rates between this emergency department-based protocol and routine care.

Gooch 2012

Study characteristics	
Methods	A large-scale pragmatic randomized.controlled trial
Participants	1570 patients underwent total hip replacement or total knee replacement in Canada.
Interventions	Participants were allocated to a clinical pathway intervention (n = 1066; age 69.0 years [11.1]) versus usual care (n = 504; age 69.0 years [10.4]) between April 2005 and May 2006. High implementation score
Outcomes	HRQoL WOMAC score SF-36
Notes	DOI: Katherine Gooch was employed by ABJHL and became an employee of Abbott Laboratories after the study was completed. Deborah A. Marshall, Peter D. Faris, Cyril Frank and Hoa Kong were employed by ABJHL. Funded by the McCraig Institute for Bone and Joint Health; Alberta Health and Wellness; Norlien Foundation Unrestricted grants – agencies had no role in study design or conduct.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomization tables in permuted blocks of four were used to randomly allocate patients into the intervention (NCP) or control (SOC).
Allocation concealment (selection bias)	Low risk	Upon receipt of completed consent forms and baseline patient questionnaires, a research coordinator randomized patients and assigned them a unique study identification number.
Incomplete outcome data (attrition bias) (All)	Low risk	The observed patterns of missing data were not amenable to a last-observation-carried forward method because there were patients with observations at 12 months that did not have observations at 3 months. Instead, the authors used linear mixed models, which use all available data and provide a flexible approach for modelling outcomes in the presence of missing data as described above.
Blinding of participants and personnel (All)	Unclear risk	No mention of blinding. Would be a concern as a quality of life measure was used as primary outcome. However, the fact that measures were valid and distributed via the mail to patients adds to objectivity.
Protection against contamination (RCT, NRCT, CBA)	Low risk	Orthopedic surgeons and anesthetists provided care to patients in both study groups to ensure that physician characteristics were comparable while all other clinical and hospital staff only provided care within either the NCP or SOC group.
Selective reporting (reporting bias) (All)	Low risk	All outcomes matched protocol (NCT00277186).
Other bias (all)	Low risk	No other obvious sources of bias

Homagk 2016

Study characteristics	
Methods	Randomized controlled trial
Participants	Patients admitted with spondylodiscitis (n = 32)
Interventions	Participants were allocated to a clinical pathway intervention (n = 17; mean age 65.7 years) versus usual care (n = 15; mean age 65.9 years) in 2014. "Low" implementation score
Outcomes	Length of stay (it remained unclear if length of stay data were reported as mean or median values). Number of blood samples taken Documentation Physical and neurological outcomes Level of pain Inflammatory marker Costs of treatment (it remained unclear if costs were reported as mean or median values).
Notes	No funding reported and no Declaration of Interest (Homagk 2016) is a poorly reported pilot study and we have not been successful in obtaining clarification and more data from the authors. For example, no data have been provided for most of the outcomes and no standard deviation (SD) or P values have been reported in the figures or text. Only some data values provided (e.g. it remains unclear if the reported study outcomes were mean or median values, which statistical test had been used to determine P values, and most of the P values have not been reported (only reported as "significant" and "not significant"). Moreover, total cost data for the CPW vs. usual care group have been reported only in the abstract (reported as statistically significant but no P value provided). We made efforts to obtain data from the authors, but the study did not have usable published data for lengths of hospital stay and hospital cost, and we have narratively described the reported study outcomes because we could not synthesize data from this randomized study in our meta-analysis.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	All information provided regarding randomization: "The implementation of the randomization was done during the admission process".
Allocation concealment (selection bias)	Unclear risk	Not reported
Incomplete outcome data (attrition bias) (All)	Unclear risk	No reports of missing data or how missing data were addressed
Blinding of participants and personnel (All)	High risk	Clinical staff could not be blinded to the different interventions provided in the intervention. Some outcomes not objective
Protection against contamination (RCT, NRCT, CBA)	Unclear risk	Therapy with or without pathway was carried out in different departments. Unclear if the same staff treated both patient groups.

Homagk 2016 *(Continued)*

Selective reporting (reporting bias) (All)	High risk	Primary outcomes not well defined in the introduction and results sections
Other bias (all)	Unclear risk	Small sample size

Jalil 2017

Study characteristics	
Methods	Randomized controlled clinical trial
Participants	Hospitalized children requiring noninvasive ventilation for respiratory failure (n = 47)
Interventions	Participants were allocated to a clinical pathway intervention (n = 24; age 9.3 years [4.3]) versus usual care (n = 23; age 9.7 years [5.7]) between May and October 2013. "Moderate" implementation score
Outcomes	Hours of NIV Length of stay Supplemental oxygen use after discontinuation of NIV Severity changes after NIV initiation and respiratory symptoms Proportion of intubations
Notes	No funding reported and no Declaration of Interest

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Simple randomization was performed with the statistical program Epidat 4.0.
Allocation concealment (selection bias)	Low risk	Sequence distribution was delivered through a list with 60 numbers already randomized to the control or intervention group. The subjects were assigned a number determining their group.
Incomplete outcome data (attrition bias) (All)	Low risk	incomplete records - control group n = 1 - incomplete records intervention group n = 2
Blinding of participants and personnel (All)	Low risk	The intervention was blinded to nursing staff; primary outcomes were NIV duration measured in hours/duration of hospital stay measured in hours and supplementary O_2 after discontinuing NIV measured in hours.
Protection against contamination (RCT, NRCT, CBA)	High risk	Patient-randomized study; healthcare professionals could have cared for patients randomized to both groups - potential for contamination
Selective reporting (reporting bias) (All)	Low risk	Objective outcomes: NIV durations; duration of hospital stay; supplemental O_2 duration
Other bias (all)	Low risk	No other obvious sources of bias

Johnson 2000

Study characteristics	
Methods	Individual randomized controlled trial
Participants	Pediatric inpatients admitted for asthma aged 2 to 18 years
Interventions	110 participants were allocated to a clinical pathway intervention (n = 55; mean age 6.6 years) versus usual care (n = 55; mean age 8.2 years) between 1995 and 1997. "Moderate" implementation score
Outcomes	Length of stay (hours) Number of nebulizations during hospitalization Unplanned interventions Hospital charges
Notes	Funded by the Johns Hopkins Miracle Telethon Funds. No Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	No evidence of concealment
Incomplete outcome data (attrition bias) (All)	Low risk	Number of patients excluded and reason of exclusion from analysis have been reported.
Blinding of participants and personnel (All)	Low risk	Study was designed to evaluate 4 main variables. The first of these [was] the duration of hospitalization [...] the number of nebulization therapies [...] and the number of unplanned healthcare interventions. Discharge medications were written on a follow-up form, which was given to a research assistant. This person was blinded to the patient's group assignment.
Protection against contamination (RCT, NRCT, CBA)	Low risk	The control and intervention units were located on different floors within the hospital. Although house staff coverage was the same on both units, there was no exchange of nursing staff between the control and intervention units.
Selective reporting (reporting bias) (All)	Low risk	All of the study prespecified outcomes have been reported in the prespecified way.
Other bias (all)	High risk	The study was limited primarily by an inability to enrol some eligible patients because of bed shortages. Clinical and demographic characteristics of intervention and control groups not comparable at baseline. Our intervention group had a higher number of patients who received steroids before their arrival to the ED. Difference in the mean age of our 2 groups

Ju 2019

Study characteristics	
Methods	Randomized controlled trial, but unclear method of randomization. Power calculation not reported, and it remains unclear how the 140 patients with cirrhosis and gastrointestinal hemorrhage were assigned to one of the two groups.
Participants	140 patients with cirrhosis and gastrointestinal bleeding were assigned to either usual care (N = 70; group A) or with the support of a clinical pathway combined with a psychological intervention (N = 70; group B).
Interventions	The investigators compared routine nursing (Group A), with patients treated on a clinical pathway 'combined' with a psychological intervention. The psychological interventions aimed to improve the health literacy of the patient and his family. The clinical pathway document contains a medical staff and patient form and is updated on a daily basis. So, the content of the pathway intervention combined standard nursing methods with health knowledge education. Context: The clinical pathway has been implemented in the Fifth People's Hospital of Jiangsu Wuxi, Jiangsu, China.
Outcomes	Primary and secondary outcomes not described in this paper. The team of investigators employed the following patient outcomes in their study: LOS, hospital cost, and inhospital complications (including bleeding, infection, hepatic encephalopathy, and the hepatorenal syndrome). Also, the self-rating depression scale (SDS), the self-rating anxiety scale (SAS), the GQOLI-74 (quality of life), and care satisfaction were employed to compare both groups.
Notes	Ju and colleagues 2019 – have incorrectly used a Chi-square test for “care satisfaction”. This outcome has been removed. Also, implementation efforts not reported in this primary publication

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Page 12951, Materials and methods: Authors stated that 140 patients were randomly divided into two groups.
Allocation concealment (selection bias)	Unclear risk	Method of concealment not reported in the paper
Incomplete outcome data (attrition bias) (All)	Unclear risk	Incomplete outcome data have not been addressed in this paper.
Blinding of participants and personnel (All)	Unclear risk	Not reported if this study was conducted in a blinded approach
Protection against contamination (RCT, NRCT, CBA)	Unclear risk	No information about potential contamination of healthcare professionals in both groups reported
Selective reporting (reporting bias) (All)	Unclear risk	No study protocol cited or identified by our highly sensitive search filter. So, we could not compare the proposed outcomes between protocol and publication.
Other bias (all)	Unclear risk	Insufficient information to assess whether an important risk of bias existed

Kaiser 2020

Study characteristics	
Methods	Interrupted time series design adjusted for patient characteristics. 12 months before and 15 months after the intervention
Participants	Children aged 6 years (range 3-9) admitted with the primary diagnosis of asthma. 68 US hospitals completed the study (n = 12013 admissions or participants) . A random sample of 20 charts per months were used for data collection and analysis.
Interventions	CPW for pediatric inhospital asthma management. Implementation included local champions, external facilitators, mentors, education, QI methods, and audit and feedback.
Outcomes	LOS, early administration of bronchodilator (1. ordered at admission, 2. odered at 1-hour frequency, 3. ordered at 3-hour frequency), documented screening for secondhand tobacco smoke exposure, documented referral of caregivers to smoking cessation resources, 7-day readmission, 7-day ED re-presentation
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Intervention independent of other changes (ITS)	High risk	…our observational study may be affected by the Hawthorne effect, secular trends, or other potential confounders.
Shape of intervention effect prespecified (ITS)	Low risk	ITS design with target outcomes
Blinding of participants and personnel (All)	High risk	The intervention included training of staff.
Selective reporting (reporting bias) (All)	Low risk	Prespecified outcomes were reported.

Kampan 2006

Study characteristics	
Methods	Individual randomized single-center controlled trial
Participants	Patients admitted to Taksin Hospital, Bangkok, with type 2 diabetes and hypoglycaemia (n = 65)
Interventions	Participants were allocated to a clinical pathway intervention combined with counseling (n = 33; age 64.4 years [11.1]) versus usual care (n = 32; age 64.4 years [11.1]) between July and December 2005. "Moderate" implementation score
Outcomes	Length of stay Cost Number of capillary blood tests Readmissions with recurrent hypoglycemia

Kampan 2006 *(Continued)*

Notes	No funding reported and no Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No evidence of randomization
Allocation concealment (selection bias)	Unclear risk	No evidence of concealment
Incomplete outcome data (attrition bias) (All)	Low risk	No missing outcome data
Blinding of participants and personnel (All)	Low risk	Used objective measures: Length of stay, cost, number of capillary blood glucose tests, readmission rate
Protection against contamination (RCT, NRCT, CBA)	Unclear risk	No description of potential contamination
Selective reporting (reporting bias) (All)	Low risk	All the prespecified outcomes have been reported in the pre-specified way.
Other bias (all)	Unclear risk	Insufficient information to assess whether other important risk of bias existed

Kim 2002

Study characteristics	
Methods	Individual randomized controlled trial
Participants	Adult patients presenting to the emergency department with newly diagnosed or new-onset atrial fibrillation (n = 18)
Interventions	Participants were allocated to an accelerated clinical pathway intervention (n = 9; age not reported) versus usual care (n = 9; age not reported) during 1999 and 2000. "Low" implementation score
Outcomes	Length of stay Hospital costs
Notes	Funded by Pharmacia – Upjohn Pharmaceuticals, Kalamazoo MI (Dr Kim & Dr Eagle). No Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization process not clearly described. Patients were randomized after enrollment on the basis of the assigned code to either the traditional strategy of hospital admission or to an accelerated ED-based clinical pathway.

Kim 2002 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	No evidence of concealment
Incomplete outcome data (attrition bias) (All)	Low risk	No missing outcome data
Blinding of participants and personnel (All)	Low risk	Used objective measures: length of stay, actual direct costs
Protection against contamination (RCT, NRCT, CBA)	Unclear risk	The study was approved by the institutional review board and conducted at a university medical center.
Selective reporting (reporting bias) (All)	Low risk	All of the study prespecified outcomes have been reported in the prespecified way.
Other bias (all)	Low risk	The study appears to be free of other sources of bias.

Kinsman 2012

Study characteristics	
Methods	Clustered-randomized controlled trial including six clusters
Participants	Adult patients with acute myocardial infarction (n = 108) treated at rural EDs of three intervention hospitals and three control hospitals in Australia
Interventions	Participants were allocated to a clinical pathway intervention (n = 57; age 64.7 years [15.9]) versus usual care (n = 51; age 57.6 years [13.2]) between November 2008 and March 2009. "High" implementation score
Outcomes	Arrival time to thrombolysis Arrival time to ECG
Notes	Funded by the Monash University Faculty Strategic Grants Scheme and Group of 8DAAD German Research Exchange Program. No Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization within pairs to either the intervention (n = 3) or control (n = 3) groups occurred by a simple coin toss.
Allocation concealment (selection bias)	Low risk	A cluster-RCT was conducted involving six rural hospitals with emergency departments that treated AMI patients on-site.
Incomplete outcome data (attrition bias) (All)	Low risk	No mention of patients lost to follow-up
Blinding of participants and personnel (All)	High risk	Data collectors were not blinded to allocation of the service to intervention or control.
Protection against contamination (RCT, NRCT, CBA)	Low risk	Pairs of hospitals were matched according to the anticipated number of eligible patients and on the basis of geographical separation, in order to minimize

Kinsman 2012 *(Continued)*

		the risk of a control hospital being influenced by procedures at an intervention hospital and vice versa.
Selective reporting (reporting bias) (All)	Low risk	All outcomes reported (time to thrombolytic administration)
Other bias (all)	Low risk	No other sources noted

Kiyama 2003a

Study characteristics	
Methods	Individual randomized controlled trial in a single hospital
Participants	Adult patients admitted for gastrectomy for cancer to Nippon Medical School Hospital, Japan (n = 85)
Interventions	Participants were allocated to a clinical pathway intervention (n = 47; age 63.0 years [12.9]) versus usual care (n = 38; age 66.8 years [12.1]) from January to December 2001. "Low" implementation score
Outcomes	Length of preoperative stay in hospital (days) Length of postoperative stay in hospital (days) Inhospital morbidity and complications
Notes	No funding reported and no Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Patients allocation by availability of beds. The patients were randomly assigned to either the main building or the east building of the participating hospital, depending on the availability of beds.
Allocation concealment (selection bias)	Unclear risk	No evidence of concealment
Incomplete outcome data (attrition bias) (All)	Unclear risk	No reason for missing data provided
Blinding of participants and personnel (All)	Low risk	Objective measured used: Cost, the lengths of pre- and postoperative hospital stay; the morbidity rate and postoperative complications; and, the rate of target achievement at 24 hours and at days 4, 7 and 14
Protection against contamination (RCT, NRCT, CBA)	Unclear risk	No mention of contamination (however we did not have access to the original study)
Selective reporting (reporting bias) (All)	Unclear risk	Insufficient information to permit judgment yes or no
Other bias (all)	Unclear risk	Insufficient information to assess whether an important risk of bias existed

Kollef 1997

Study characteristics	
Methods	Individual randomized controlled trial
Participants	Adult patients requiring mechanical ventilation in the medical and surgical intensive care units of Barnes Hospital and Jewish Hospital (USA) (n = 357)
Interventions	Participants were allocated to a clinical pathway intervention (n = 179; age 62.3 years [17.3]) versus usual care (n = 178; age 62.3 years [16.8]) between July and October 1995. "Moderate" implementation score
Outcomes	Duration of mechanical ventilation Number requiring reintubation Inhospital mortality Length of stay
Notes	No funding reported and no Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Patients were randomly assigned, at the time of ICU admission, to receive protocol-directed weaning implemented by nurses and respiratory therapists or physician-directed weaning from mechanical ventilation. Stratification according to ICU site was done to ensure the same distribution of patients from the four participating ICUs in the two study groups. A stratified, randomization strategy was employed to reduce variation in the outcome measure due to differences in patient characteristics and medical practices among the four ICUs.
Allocation concealment (selection bias)	Low risk	This stratification was accomplished with separate, blocked, randomization schedules for each ICU, using opaque, sealed envelopes, which were opened at the time each patient was enrolled in the study.
Incomplete outcome data (attrition bias) (All)	Low risk	Reason for missing outcome data unlikely to be related to the true outcome. A total of 377 patients were enrolled in the study. Twelve patients were not randomized due to trauma or burns to the head and face. Eight other eligible patients were not randomized due to either oversight or mortality early after ICU admission. Thus, 357 patients were randomized and analyzed, of whom 179 (50.1%) received protocol-directed weaning and 178 (49.9%) received physician-directed weaning.
Blinding of participants and personnel (All)	Low risk	The primary outcome measure was the duration of mechanical ventilation from tracheal intubation until discontinuation of mechanical ventilation. Other outcome measures included need for reintubation, length of hospital stay, hospital mortality rate, and hospital costs.
Protection against contamination (RCT, NRCT, CBA)	Unclear risk	Patients randomized within ICUs, probably high risk but not explicitly stated. Limitations mentioned potential competition as ICU staff couldn't be blinded but no risk of contamination.
Selective reporting (reporting bias) (All)	Low risk	All of the study's prespecified (primary and secondary) outcomes that are of interest in the review have been reported in the prespecified way.

Kollef 1997 *(Continued)*

Other bias (all)	Low risk	The study appears to be free of other sources of bias.

Li 2018

Study characteristics		
Methods	A prospective individual randomized controlled trial	
Participants	A total of 118 patients with diagnosed acute myocardial infarction that were undergoing transradial PCI	
Interventions	Participants were allocated to a clinical pathway intervention (n = 62; age 56.1 years [5.8]) versus usual care (n = 56; age 55.8 years [6.3]) between February 2013 and April 2014. "High" implementation score	
Outcomes	Door-to-balloon time Length of stay Total hospitalization cost and daily hospitalization cost Patient satisfaction Postoperative complications	
Notes	No funding reported and no Declaration of Interest	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	The patients were arbitrarily divided into two groups using the random number table method.
Allocation concealment (selection bias)	Unclear risk	Insufficient information reported
Incomplete outcome data (attrition bias) (All)	Low risk	The authors did not report any missing data.
Blinding of participants and personnel (All)	Unclear risk	Door-to-balloon time (min) and hospital stay (d) are objective measures and rated as low risk. Cost has the potential for subjectivity and rated as high risk. No protocol referenced (protocol could objectively outline how cost would be calculated). Quality of life has the potential for subjectivity and rated as high risk.
Protection against contamination (RCT, NRCT, CBA)	High risk	The patients were arbitrarily divided into two groups.
Selective reporting (reporting bias) (All)	Low risk	All outcomes are pointed in the method section are addressed in the results. The article did not reference a study protocol.
Other bias (all)	Low risk	No other obvious sources of bias

Marelich 2000

Study characteristics	
Methods	Single-center individual randomized controlled trial
Participants	A total of 335 adult patients from medical and surgical (trauma) ICUs were enrolled at the University of California, Davis, Medical Center.
Interventions	Participants were allocated to a ventilation management clinical pathway (n = 82; age 56.6 years [16.0[) versus usual care (n = 82; age 54.5 years [17.1]) between June 1997 and May 1998. "Moderate" implementation score
Outcomes	Duration of mechanical ventilation Ventilation-associated pneumonia
Notes	Funded by the Hibbard E. Williams MD Research Fund. No Declaration of Interest

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomization was by opaque, sealed, numbered envelopes stratified for MICU and trauma services and for ICU.
Allocation concealment (selection bias)	Low risk	Sealed envelopes used
Incomplete outcome data (attrition bias) (All)	Low risk	Reasons for patients' exclusion presented. Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups. There were no differences in the proportions of patients censored within the combined treatment and control groups and MICU and trauma subgroups.
Blinding of participants and personnel (All)	Low risk	Objective outcomes used: The total duration of mechanical ventilation and the incidence of VAP were defined as primary outcomes a priori. Secondary outcomes were the duration of mechanical ventilation from study entry to discontinuation of ventilator support, the duration of mechanical ventilation from initiation of mechanical support to meeting ventilator discontinuation criteria, the ventilator discontinuation failure rate and death.
Protection against contamination (RCT, NRCT, CBA)	Low risk	Patients randomized to the control group were managed as per standard ICU practice. Physicians' orders were required for all ventilator changes and weaning assessment. Algorithmic orders were allowed. No specific information on the VMP was provided any participating physician. Physicians caring for patients randomized to the experimental (VMP) group were instructed not to interfere with the ventilator management by the RCP unless the patient was in respiratory distress or was unstable.
Selective reporting (reporting bias) (All)	Low risk	The study protocol is available and all study prespecified (primary and secondary) outcomes have been reported in the prespecified way.
Other bias (all)	Low risk	The study appears to be free of other sources of bias.

Marrie 2000

Study characteristics	
Methods	Multi-center cluster-randomized controlled trial of 19 hospitals
Participants	A total of 1743 adult patients presenting with community-acquired pneumonia to emergency departments of participating Canadian hospitals
Interventions	Participants arriving via the emergency department were allocated to a clinical pathway intervention (n = 716; age 64.1 years [3.5]) versus usual care (n = 1027; age 64.2 years [5.1]) between January and August 1998. "Low" implementation score
Outcomes	Quality of life (measured by SF-36) Length of stay
Notes	DOI: Drs. Marrie and Feagan have received speaking honoraria from Janssen-Ortho Inc. Dr. Lau and Ms. Wheeler are employees of Janssen-Ortho Inc and own company stock. No funding reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	The randomization procedure was stratified by type of institution (teaching or community hospital) and matched by the historical LOS (obtained from a feasibility study).
Allocation concealment (selection bias)	Low risk	Random assignment was generated by computer.
Incomplete outcome data (attrition bias) (All)	Unclear risk	Uncertain risk of bias as there are insufficient details in the article to permit judgement of yes or no.
Blinding of participants and personnel (All)	Low risk	The Short-Form 36 Physical Component Summary (SF-36 PCS) scale, a generic quality-of-life measure, was selected as the primary measure of efficacy. This 36-question instrument has been previously validated in patients with CAP. Scores range from 0 to 100; higher scores indicate better quality of life. Secondary outcome measures were pneumonia-related complications (respiratory failure, systemic sepsis, emphysema, new onset of congestive heart failure, or atrial fibrillation), ICU admission, readmission to hospital, and death. All clinical outcomes were independently validated by 2 investigators (T.J.M. and B.G.F.) who were unaware of the treatment assignment and who also evaluated antibiotic regimens and determined whether 1, 2, or more than 2 classes of antibiotics had been administered. Disagreement was resolved by consensus.
Protection against contamination (RCT, NRCT, CBA)	Low risk	Since critical pathways are implemented at the institutional level, hospitals, rather than individual patients, were randomly assigned to either introduce the pathway or continue conventional management. The centers were Canadian teaching or community hospitals whose administrations (1) were willing to allow the institution to be allocated to either of the 2 strategies for a 6-month period and (2) agreed not to implement any of the components of the critical pathway if assigned to conventional management.
Selective reporting (reporting bias) (All)	Unclear risk	First outcome: The difference between the intervention hospitals and the controls is not clearly reported. The results are presented in a graph so we don't have the exact numbers (to be used in a meta-analysis, for example). Second

Marrie 2000 *(Continued)*

		outcome: baseline measurement not presented and P values not shown for the control group
Other bias (all)	High risk	Unit of analysis error as the randomization unit (hospitals) is different from the unit of analysis (patients)

Muehling 2008

Study characteristics	
Methods	Single-center, prospective, randomized controlled trial
Participants	58 patients undergoing lung resections in Germany
Interventions	Participants were allocated to a clinical pathway intervention (n = 30; mean age 67 years) versus conservative treatment (n = 28; mean age 64 years) in 2006. "Low" implementation score
Outcomes	Postoperative ventilation Length of stay in intensive care unit (ICU) and hospital Pulmonary complications Morbidity and mortality
Notes	No funding reported and no Declaration of Interest

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random assignment to intervention (fast-track CPW) or control (usual care)
Allocation concealment (selection bias)	Unclear risk	Difficult to decipher allocation process
Incomplete outcome data (attrition bias) (All)	Low risk	Data were reported completely.
Blinding of participants and personnel (All)	High risk	Clinical staff could not be blinded to the different interventions provided in the intervention.
Protection against contamination (RCT, NRCT, CBA)	High risk	No protection against contamination
Selective reporting (reporting bias) (All)	Low risk	All predefined outcomes were reported.

Panella 2009

Study characteristics

Panella 2009 *(Continued)*

Methods	Two-arm cluster-randomized controlled trial
Participants	Adult heart failure patients (n = 429) from 14 hospitals
Interventions	Participants were allocated to a clinical pathway intervention (n = 214; age 81.7 years [8.5]) versus usual care (n = 215; age 79.5 years [8.5]) between March 2003 and October 2004. "High" implementation score
Outcomes	Inhospital mortality Appropriateness of stay Unscheduled readmissions Length of stay Cost of admission LVT assessment at discharge Number transferred to another hospital Advice for smoking cessation Written instructions at discharge
Notes	Funded by the Italian Ministry of Health (Special Programs art. 12 bis D.lgs 229/99 and Marche Region). No Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A simple randomization procedure was carried out in each stratification sample before the intervention, and patient randomization was carried out using computer-generated sequence with allocation concealment.
Allocation concealment (selection bias)	Low risk	A cluster design was used because of the ethical and logistical issues associated with the implementation of CPs, which involves a series of complex actions at the institutional level.
Incomplete outcome data (attrition bias) (All)	Low risk	Five units withdrew after the project commenced, following a decision from their management (three units withdrew after the project pretest and two units withdrew after the project began).
Blinding of participants and personnel (All)	High risk	High risk for secondary measures only; primary measure (mortality) objective and therefore low risk. Staff members were trained in data collection at two educational events. Data were collected using a standardized data extraction tool that used web technology, and were anonymously entered into a secure database housed at the University of Eastern Piedmont.
Protection against contamination (RCT, NRCT, CBA)	Low risk	To participate in the study, the administrators of the units had to allow the institution to be allocated to either of the two research groups (CP or current practice) for a period of 1 year, and had to agree not to implement a CP for the acute care and/or rehabilitation of stroke if their institution was assigned to the UC group.

Panella 2009 *(Continued)*

Selective reporting (reporting bias) (All)	Low risk	All factors included in the model
Other bias (all)	Low risk	No other sources noted

Panella 2012

Study characteristics	
Methods	Multi-centre cluster-randomized trial
Participants	476 stroke patients admitted to one of the 14 included acute ischemic stroke units. Patients were allocated to seven experimental clusters (experimental group) and seven control clusters (control group).
Interventions	Participants were allocated to a clinical pathway intervention (n = 238; age 74.5 [10.8]) versus usual care (n = 238; age 74.0 years [11.7]) between July 2005 and May 2007. "High" implementation score
Outcomes	Mortality Use of diagnostic and therapeutic procedures Implementation of organized care Length of stay Re-admission Dependency levels Complications
Notes	Funded by the Italian Ministry of Health (Special Programs art. 12 bis D.lgs 229/99) and Marche Region. No Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A simple randomization procedure was carried out in each stratification sample before the intervention, and patient randomization was carried out using a computer-generated sequence with allocation concealment.
Allocation concealment (selection bias)	Low risk	A cluster design was used because of the ethical and logistical issues associated with the implementation of CPs, which involves a series of complex actions at the institutional level.
Incomplete outcome data (attrition bias) (All)	High risk	Five units withdrew after the project commenced, following a decision from their management (three units withdrew after the project pretest and two units withdrew after the project began).
Blinding of participants and personnel (All)	High risk	High risk for secondary measures only; primary measure (mortality) objective and therefore low risk Staff members were trained in data collection at two educational events. Data were collected using a standardized data extraction tool that used web tech-

Panella 2012 *(Continued)*

		nology, and were anonymously entered into a secure database housed at the University of Eastern Piedmont.
Protection against contamination (RCT, NRCT, CBA)	Low risk	To participate in the study, the administrators of the units had to allow the institution to be allocated to either of the two research groups (CP or current practice) for a period of 1 year, and had to agree not to implement a CP for the acute care and/or rehabilitation of stroke if their institution was assigned to the UC group.
Selective reporting (reporting bias) (All)	Low risk	All factors included in the model
Other bias (all)	Low risk	No other potential sources noted

Panella 2018

Study characteristics	
Methods	Cluster-randomized controlled trial in 26 hospitals in Belgium, Italy and Portugal
Participants	15 hospitals treating patients admitted with proximal femur fracture were randomized to the intervention group and 11 to the control group (total n = 514 patients). The study authors also reported on the number (n = 113 healthcare professionals) of disciplines who were members of the team to describe baseline characteristics on a hospital level (table 1). 66 professionals were reported in the intervention group vs 47 professionals in the control group. This information has been used to compare the baseline characteristics of intervention and control hospitals, but it was not included in the data analysis.
Interventions	Participants were allocated to a clinical pathway intervention (n = 301; age 81.4 years [7.5]) versus usual care (n = 213; age 81.2 years [7.0]) between October 2010 and May 2014. "High" implementation score
Outcomes	Six-month mortality Thirty-day mortality Readmission Functional status Length of stay
Notes	Funded by the European Pathway Association (E-P-A) and an Unrestricted Education Grant from Pfizer SA. Funders had no role in the study.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Source of information (Appendix 1 - online availiable -homepage injury). Hospitals were stratified by country, teaching versus non-teaching hospitals, < 600 and ≥ 600 hospital beds, and < 300 patients and ≥ 300 patients annually admitted and then randomly assigned to the intervention or control group.
Allocation concealment (selection bias)	Low risk	The allocation sequence was computer-generated using a random number list and statistical software (http://www.randomizer.org). To minimize the risk of testing bias, the measurement protocol was sent to each hospital just before the start of the data collection. Furthermore, a logbook for included patients

Panella 2018 *(Continued)*

		was kept to connect the patient identity to the study number. A logbook for excluded patients was kept to check for selection bias.
Incomplete outcome data (attrition bias) (All)	Low risk	'Intention-to-treat' approach with some incomplete data. Constitutes a low risk of bias for 'incomplete outcome data' as these relatively small numbers of missing data were unlikely to influence the overall results.
Blinding of participants and personnel (All)	Low risk	Primary and secondary measures (mortality, readmission, and SF-36) are objective; therefore risk scored as low. A pathway facilitator delivered the training and extracted study data. Control hospitals did not receive training and only one measurement was performed in the control group to mitigate the Hawthorn effect.
Protection against contamination (RCT, NRCT, CBA)	Low risk	No information about potential contamination of healthcare professionals in control hospitals have been provided. Cluster design constitutes low risk.
Selective reporting (reporting bias) (All)	Low risk	Comparison with study protocol shows that a protocol-driven research approach has been used.
Other bias (all)	Low risk	A few reasonable mitigation strategies have been applied. No other potential biases noted

Philbin 2000

Study characteristics	
Methods	Cluster-randomized multi-center controlled trial
Participants	2906 medical adult patients with heart failure recruited from 10 cluster hospitals
Interventions	Participants were allocated to a multi-faceted quality improvement intervention incorporating a clinical pathway (post-intervention n = 840; mean age 77 years) versus usual care (post-intervention n = 664; mean age 74 years) between November 1996 and July 1997. "Moderate" implementation score
Outcomes	Length of stay Hospital charges Inhospital mortality Quality of life Mortality Readmission Process of care indicators ACE inhibitor use at discharges
Notes	Funded by the VHA Empire State Incorporated and Grants from the New York State Department of Health (grant numbers C011191; C011696 and C013333). No Declaration of Interest

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Philbin 2000 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Randomization procedure not described
Allocation concealment (selection bias)	Unclear risk	There was no evidence of concealment.
Incomplete outcome data (attrition bias) (All)	Low risk	No missing outcome data
Blinding of participants and personnel (All)	High risk	Study nurses, who were employees of the participating hospitals, attended a standardized 6-hour training session before performing chart abstraction. Each nurse and institution was also provided with a comprehensive manual of operations that contained explicit instructions about chart abstraction. During the baseline period, study nurses were unaware of treatment assignment; this blinding was not maintained during the post-intervention phase. Survivors were observed for 6 months after hospital discharge; they were contacted by a study nurse three times during this period to ascertain hospital readmission and vital status. Quality of life, measured with the Ladder of Life and New York Heart Association (NYHA) functional class, were assessed during each telephone follow-up.
Protection against contamination (RCT, NRCT, CBA)	Low risk	Hospitals were randomly assigned based on heart failure case load and average length of stay for heart failure during the baseline period. All components of the quality improvement intervention were introduced to intervention hospitals after the baseline period and before the post intervention period (November 1, 1996, to July 31, 1997). Control hospitals were not restricted from initiating their own local quality management programs, but were barred access to study-related data, documents, and resources.
Selective reporting (reporting bias) (All)	Low risk	All of the study's prespecified outcomes have been reported in the prespecified way.
Other bias (all)	Low risk	Difference between randomization unit (hospitals) and analysis unit (patients) were overcome using appropriate statistical methods. The effects of the intervention were estimated using a linear regression model, with intervention (versus control) as the independent variable, and the differences (baseline minus post-intervention) as the dependent variable; 95% confidence intervals (CI) and P values were estimated. This technique was used because hospitals, not patients, were the units of randomization.

Phillips 2017

Study characteristics	
Methods	A pre-post design with one outcome reported as ITS
Participants	130 pediatric patients (aged 2-7 years) admitted to ICU with status asthmaticus
Interventions	Participants were allocated to a clinical pathway intervention (124 post-intervention; age 7.3 years [4.6]) following a pre-intervention baseline period (n = 130; age 7.4 years [4.4]). The post-intervention period was from September 2015 to October 2016. "High" implementation score
Outcomes	Transition time from continuous to intermittent bronchodilator use Length of stay

Phillips 2017 *(Continued)*

	Readmissions Use of rescue BiPAP
Notes	No funding reported and no Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Intervention independent of other changes (ITS)	Unclear risk	The increase in methylxanthene use in the post-intervention group may have been the result of ease of ordering the medication and associated laboratory evaluations as part of the initial order set. However, it is also possible that the increase in aminophylline use reflected a change in clinical practice given the publication of newer data suggesting benefits of methylxanthene use in certain high-risk pediatric patients with refractory asthma.
Shape of intervention effect prespecified (ITS)	Low risk	Intervention shape used the intervention date as the point of analysis.
Intervention unlikely to affect data collection (ITS)	High risk	The order set, combined with the severity scoring and stepwise therapy pathway, likely resulted in clinicians having higher vigilance to the need for assessment of a patient's readiness to transition.
Incomplete outcome data (attrition bias) (All)	Unclear risk	Not reported
Blinding of participants and personnel (All)	Low risk	Objective measures: mean transition time from continuous to intermittent bronchodilator use, hospital length of stay (LOS), readmissions, use of rescue BiPAP
Selective reporting (reporting bias) (All)	Low risk	All prespecified measures reported
Other bias (all)	Low risk	The study appears to be free of other sources of bias.

Roberts 1997

Study characteristics

Methods	Individual randomized single-center controlled trial
Participants	Medical adult patients with suspected myocardial infarction (n = 165) recruited from a public urban USA teaching hospital
Interventions	Participants were allocated to a clinical pathway intervention (paper format) (n = 82; mean age 47.3 years) versus usual care (n = 83; mean age 48.0 years) in 1995. "Moderate" implementation score
Outcomes	Length of stay (hours) Hospital costs Readmission rate
Notes	No funding reported and no Declaration of Interest

Roberts 1997 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No evidence of randomization
Allocation concealment (selection bias)	Unclear risk	No evidence of concealment
Incomplete outcome data (attrition bias) (All)	Unclear risk	Insufficient information
Blinding of participants and personnel (All)	Low risk	Used objective outcome measures: cost and LOS
Protection against contamination (RCT, NRCT, CBA)	Unclear risk	No description of potential contamination
Selective reporting (reporting bias) (All)	Unclear risk	Insufficient information
Other bias (all)	Unclear risk	Insufficient information to assess whether an important risk of bias exists

Rotter 2014

Study characteristics	
Methods	Interrupted time-series design with six time points before and after the implementation of the intervention
Participants	Adult urological male patients undergoing radical laparoscopic prostatectomy (n = 254) in an urban German University hospital
Interventions	Invasive clinical pathway for treatment of prostate patients undergoing radical laparoscopic prostatectomy in 2011 and 2012. Clinical pathway was in paper format. Mean age pre-intervention was 61.6 years [5.8] versus 62.2 years [4.9] post-intervention. "Moderate" implementation score
Outcomes	Length of stay (ITS analysis) Duration of operation and anesthesia (ITS analysis)
Notes	No funding reported and no Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Intervention independent of other changes (ITS)	Low risk	Although there was no mention of other on-going changes at hospital, six data points before and after the intervention were employed for the ITS study.
Shape of intervention effect prespecified (ITS)	Low risk	Intervention shape used the intervention date as the point of analysis.

Rotter 2014 *(Continued)*

		The regression model determines the linear trend in the series prior to the introduction of the CP, and includes intervention variables to detect any abrupt change in the dependent variable at the time of the intervention and also any difference between the trends before and after the intervention.
Intervention unlikely to affect data collection (ITS)	Low risk	All data were obtained from the databanks of the hospital information system. The documentation of a decent number of patient's data is mandatory for each hospital in Germany. This includes death during hospital stay, number and kind of operations, total hospital stay in days, total stay on the intensive care unit (ICU) and number of transfused blood products. Anesthesia and operation times were obtained from the operation documentation system.
Incomplete outcome data (attrition bias) (All)	Low risk	All variables collected for assessment were examined and reported on in the results section.
Blinding of participants and personnel (All)	Low risk	Objective measures used: Length of stay, duration of operation and anesthesia, patients requiring re-operation, patients requiring blood transfusions
Selective reporting (reporting bias) (All)	Low risk	All prespecified measured reported at follow-up
Other bias (all)	Low risk	The study appears to be free of other sources of bias.

Rutman 2017

Study characteristics	
Methods	Interrupted time series
Participants	632 pediatric patients (age 2 months-18 years) with community-acquired pneumonia were included in the ITS study.
Interventions	Participants were allocated to a clinical pathway intervention between August 2011 and August 2013. Pre-intervention there were 345 participants versus 287 post-intervention and no reported difference in age groups between samples. "High" implementation score
Outcomes	Percentage of patients receiving ampicillin as first-line therapy Percentage of patients with blood cultures and viral testing Costs
Notes	No funding reported and no Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Intervention independent of other changes (ITS)	High risk	The results may have been confounded by other ongoing hospital-wide initiatives to improve antimicrobial stewardship.
Shape of intervention effect prespecified (ITS)	Low risk	Statistical process control was used - used to evaluate variation in processes over time; control charts were used to distinguish variation in a process due to common causes; for balancing measures, segmented linear regression was

Rutman 2017 *(Continued)*

		used - fitted a separate regression line with different intercepts and slopes to each time period (before and after pathway implementation).
Intervention unlikely to affect data collection (ITS)	Low risk	Antibiotic use, radiology, lab testing - routine measures
Incomplete outcome data (attrition bias) (All)	Unclear risk	Not stated
Blinding of participants and personnel (All)	Unclear risk	Not stated
Selective reporting (reporting bias) (All)	Low risk	All prespecified measured reported
Other bias (all)	Low risk	The study appears to be free of other sources of bias.

Seys 2019

Study characteristics	
Methods	Stratified post-test-only cluster-randomized controlled trial
Participants	567 participants were healthcare professionals allocated to a clinical pathway intervention (31 teams) versus 417 healthcare professionals allocated to the usual care groups (25 teams). A total of 56 teams (n = 984 team members) were included in the cluster-randomized study.
Interventions	Study tested the impact of a COPD care pathway implementation on interprofessional team-work. "High" implementation score
Outcomes	Teamwork
Notes	Funded by the European Pathway Association (E-P-A); Unrestricted Education Grant from Pfizer SA. No Declaration of Interest

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	The allocation sequence was computer-generated using a random number list and statistical software (www.randomizer.org).
Allocation concealment (selection bias)	Low risk	Allocation concealment at team level was not possible as hospitals were stratified.
Incomplete outcome data (attrition bias) (All)	High risk	76 teams withdrew from the study (all 23 Irish teams dropped out due to a health policy decision outside the project). The overall response rate was 73.4%.
Blinding of participants and personnel (All)	High risk	To minimize the risk for testing bias, the measurement protocol was sent to each hospital just before the start of the data collection. Results were primarily based on self-reported measures (using questionnaires), causing some limitations such as possible social desirability bias.

Seys 2019 *(Continued)*

Protection against contamination (RCT, NRCT, CBA)	Low risk	No information about potential contamination of healthcare professionals in control hospitals have been provided. Cluster design consitutes low risk.
Selective reporting (reporting bias) (All)	Low risk	All pre-defined outcomes were reported.

Smith 2004

Study characteristics	
Methods	Non-randomized multi-center controlled before-and-after study (CBA)
Participants	Adult patients with chronic obstructive pulmonary disease (COPD) (n = 1230) recruited from 4 urban settings in South Australia
Interventions	Participants were allocated to a clinical pathway intervention (n = 839) versus usual care (n = 391) in 2001. Mean age was reported; no significant difference between groups. "High" implementation score
Outcomes	Length of stay (no values reported; only level of significance reported) Readmission rate per 100 participant-days Mortality per 100 patient-days
Notes	Funded by the South Australian Department of Human Services and the NHMRC. No Declaration of Interest

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	CBA design
Allocation concealment (selection bias)	High risk	CBA design
Incomplete outcome data (attrition bias) (All)	Low risk	Because of potential clustering effects within hospitals and the overlap of some patients between the pre-intervention and intervention phases, a minimum sample size of 500 patients was set for each phase. Adjustment for potential confounding was undertaken by Poisson regression analysis with allowance made for clustering by hospital, patient identifier and time on trial. Participants who were in both the pre-intervention and intervention phases were omitted.
Blinding of participants and personnel (All)	Low risk	Used objective outcomes: The two outcome measures were 1) readmission rate, and 2) death rate.
Protection against contamination (RCT, NRCT, CBA)	Low risk	No mention of contamination (however unlikely due to clustering by hospital)

Smith 2004 *(Continued)*

Selective reporting (reporting bias) (All)	Low risk	Results clearly presented. Study protocol available and all of the study's prespecified (primary and secondary) outcomes that are of interest for the review have been reported in the prespecified way.
Other bias (all)	Unclear risk	There was insufficient information to assess the presence of other sources of bias.

Smith 2019

Study characteristics	
Methods	Interrupted time series
Participants	Pediatric asthma patients admitted to a community hospital without an intensive care unit
Interventions	Participants were allocated to a clinical pathway intervention (n = 60; mean age 7.4 years) versus usual care (n = 69; mean age 7.1 years) between September 2014 and August 2016. "Moderate" implementation score
Outcomes	Length of stay Time to albuterol administration
Notes	No funding reported and no Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Intervention independent of other changes (ITS)	High risk	The authors believe that, outside of the ICU setting, the pathway was used to give people "permission" to use albuterol more agressively, which ultimately improved patient outcomes.
Shape of intervention effect prespecified (ITS)	Low risk	ITS analyses were conducted by using segmented regression models to estimate the impact of the clinical pathway intervention.
Intervention unlikely to affect data collection (ITS)	Low risk	Data extracted from the electronic health record by the same staff. Some additional measures for patients in the intervention group were recorded by the respiratory therapist providing patient care manually on the printed critical asthma pathway form.
Incomplete outcome data (attrition bias) (All)	Unclear risk	Not stated
Blinding of participants and personnel (All)	Low risk	Primary outcomes were time to albuterol administered q4h and hospital LOS (objective).
Selective reporting (reporting bias) (All)	Low risk	All prespecified measures reported
Other bias (all)	High risk	They report deviations from the pathways in 24 patients.

Sulch 2002

Study characteristics	
Methods	Individual randomized single-center controlled trial
Participants	Adult stroke patients for rehabilitation (n = 152) recruited from a teaching hospital in London
Interventions	Participants were allocated to a clinical pathway intervention (n = 76; age 75 years [11]) versus usual care (n = 76; age 74 years [10]) in 1998. "High" implementation score
Outcomes	Length of stay Duration of therapy input Barthel index at 26 weeks Mortality at 26 weeks Discharge destination
Notes	Funded by the NHS R&D Executive North Thames Research Implementation Committee (Project no B6.58). No Declaration of Interest

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Patients allocation made on the basis of a computer-generated list of random numbers
Allocation concealment (selection bias)	Unclear risk	No evidence of concealment
Incomplete outcome data (attrition bias) (All)	Low risk	No missing outcome data
Blinding of participants and personnel (All)	High risk	Research assessments were undertaken by 2 observers who were not directly involved in patient care. Both observers undertook independent assessments on each patient, and scores on which there was agreement were used. The k value for interobserver agreement, 0.78 for Barthel and 0.86 for Rankin scores, differed; the observers reviewed the patient together to arrive at a consensus.
Protection against contamination (RCT, NRCT, CBA)	Low risk	The study was carried out on a stroke rehabilitation unit, which consisted of 2 separate bed areas managed by separate teams of nurses. Although both areas had a well-developed multidisciplinary approach to patient care, the 2 teams worked independently of each other, with separate team meetings. The ICP was introduced in one area where all patients using this methodology were treated and the other was used as the control setting with conventional multidisciplinary care.
Selective reporting (reporting bias) (All)	Low risk	All of the study's prespecified outcomes have been reported in the prespecified way.
Other bias (all)	Low risk	The study appears to be free of other sources of bias.

Tilden 1987

Study characteristics	
Methods	Interrupted time series
Participants	Patients identified by nurses as "potentially battered" in an urban emergency department in USA (n = 892)
Interventions	Participants were allocated to a clinical pathway intervention (n = 447; age not reported) versus usual care (n = 445; age not reported) in 1985. "Moderate" implementation score
Outcomes	Rate for documentation of "battered" women. Follow-up from index admission until discharge
Notes	No funding reported and no Declaration of Interest

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Intervention independent of other changes (ITS)	High risk	Some mention of other factors (media regarding topic, hospital push for improved charting)
Shape of intervention effect prespecified (ITS)	Unclear risk	ITS design although not specified (based on figures only)
Intervention unlikely to affect data collection (ITS)	Low risk	Data were collected from patient records […] records of all female trauma patients (n = 447) were reviewed for documentation of battery within the nursing notes. Records were reviewed by research assistants trained in coding of the data.
Incomplete outcome data (attrition bias) (All)	Low risk	No missing outcome data
Blinding of participants and personnel (All)	Unclear risk	Data were collected from patient records […] records of all female trauma patients (n = 447) were reviewed for documentation of battery within the nursing notes. Records were reviewed by research assistants trained in coding of the data.
Selective reporting (reporting bias) (All)	Unclear risk	Insufficient information
Other bias (all)	High risk	The study has several potential sources of bias related to the specific study design used. It is possible that other factors occurred during this time that increased the nurses' motivation to improve identification. For example, new media coverage about the problem of domestic violence has been increasing. Also nursing administration at the hospital has been encouraging staff of all departments in the hospital to improve their charting by being more specific and detailed. These or other unidentified events, might have intensified the effect of the intervention.

Trombetti 2013

Study characteristics	
Methods	Non-randomized controlled trial

Trombetti 2013 *(Continued)*

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Participants	Malnourished elderly patients admitted into the general ward of an urban hospital (n = 694)
Interventions	Participants were allocated to a clinical pathway intervention (n = 465; age 84 years [8[) versus usual care (n = 229; age 85 years [7]) between April and July 2008. "Low" implementation score
Outcomes	Proportion of nutritional counseling requests Number of nutritional supplements prescribed Length of stay Proportion of patients receiving an enriched meal Inhospital mortality Functional dependence
Notes	Funded by the Geneva University Hospital. No Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	The MNA was administered and the related intervention was applied to all patients admitted to the university geriatric hospital during the 3-month study period in three (including the orthogeriatric unit) of the five floors of the hospital. On the two other floors, usual standard nutritional care was administered.
Allocation concealment (selection bias)	Low risk	Allocation was at the ward level. As the intervention was delivered at a ward level and not at an individual level, the ethics committee did not request individual written informed consent.
Incomplete outcome data (attrition bias) (All)	Unclear risk	No mention of patients lost to follow-up
Blinding of participants and personnel (All)	Low risk	Objective measures used; majority of data was determined through lab work (conducted at central clinical laboratory)
Protection against contamination (RCT, NRCT, CBA)	Unclear risk	The MNA was administered and the related intervention was applied to all patients admitted to our university geriatric hospital during the 3-month study period in three (including the orthogeriatric unit) of the five floors of the hospital. On the two other floors, usual standard nutritional care was administered.
Selective reporting (reporting bias) (All)	Low risk	The primary outcome was the 3-week evolution of serum IGF-I with the evolution of albumin, C-reactive protein and weight as secondary outcomes. All outcomes reported pre and post-implementation
Other bias (all)	Low risk	No other obvious sources of bias

Usui 2004

Study characteristics

Usui 2004 *(Continued)*

Methods	Pseudo-randomized single-center controlled trial
Participants	Hospitalized patients with community acquired pneumonia (n = 61) in an urban Japanese setting
Interventions	Participants were allocated to a clinical pathway intervention (electronic format) (n = 30; mean age 44.0 years) versus usual care (n = 31; mean age 51.4 years) in 2012 "Low" implementation score
Outcomes	Length of stay Duration of antibiotic infusion Treatment success rate Costs
Notes	No funding reported and no Declaration of Interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	This was a non-randomized controlled trial that was carried out in a single center.
Allocation concealment (selection bias)	High risk	This was a non-randomized controlled trial that was carried out in a single center.
Incomplete outcome data (attrition bias) (All)	Unclear risk	Insufficient reporting of attrition/exclusion to permit judgment of yes or no
Blinding of participants and personnel (All)	Low risk	Authors explicitly stated that primary outcome measures were assessed blindly OR outcome variables were objective e.g. LOS, drug level assessed by a standardized test.
Protection against contamination (RCT, NRCT, CBA)	Unclear risk	Insufficient information
Selective reporting (reporting bias) (All)	Unclear risk	Insufficient information
Other bias (all)	Unclear risk	Insufficient information to determine other sources of bias

Vanhaecht 2016

Study characteristics

Methods	Cluster-randomized controlled trial
Participants	Hospitalized patients with COPD (n = 342) in hospitals in Italy, Belgium and Portugal
Interventions	Participants were allocated to a clinical pathway intervention (n = 174; age 69.4 years [10.8]) versus usual care (n = 168; age 70.4 years [9.7[) between October 2010 and May 2014. "High" implementation score

Vanhaecht 2016 *(Continued)*

Outcomes	Hospital readmission rate Length of stay Mortality Adherence to guidelines
Notes	DOI: MD has been a part of the advisory board for AstraZeneca, Boehringer-Pfizer, GSK, Nycomed, Novartis, Altana and Dompe. MD has performed consulting work for Boehringer-Pfizer, GSK and Novartis and receives lecture fees from these companies (totalling < 10,000 Euro per annum). MD received a grant of 45,000 Euro/year from AstraZeneca and 25,000 Euro/year from GSK. KV, WS, and MP are board members of the European Pathway Association. Funded by the European Pathway Association (E-P-A); Unrestricted Education Grant from Pfizer SA; Clinical Research Fund of University Hospitals Leuven, Belgium. Funders had no role in the study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The allocation sequence was computer-generated by a principal investigator at the co-ordination center at Leuven University, using a random number list and statistical software (http://www.randomizer.org).
Allocation concealment (selection bias)	High risk	Allocation concealment at team level was not possible and therefore general hospitals were stratified by country level, hospital type (teaching versus non-teaching), hospital size (> 600 and ≤ 600 beds) and annual patient volume for COPD exacerbation (> 300 patients and ≤ 300 patients) and then randomly assigned to the intervention group or to the control group.
Incomplete outcome data (attrition bias) (All)	High risk	43 hospitals withdrew after randomization, which resulted in a smaller sample size than initially targeted. The authors stated that it was reasonable to assume that the lower power of the study may have led to a failure in detecting statistically significant differences.
Blinding of participants and personnel (All)	Low risk	All data, except for the measurements at discharge, were collected by an external researcher outside the clinical team. At discharge, a structured interview of the patient by a team member was performed to collect information on previous home situation and therapy before admission, which did not imply any risk for bias of the measurements. The detailed data collection protocol was sent to the study co-ordinator of each hospital just before the start of the data collection.
Protection against contamination (RCT, NRCT, CBA)	Low risk	No information about potential contamination of healthcare professionals in control hospitals have been provided. Cluster design consitutes low risk.
Selective reporting (reporting bias) (All)	Low risk	All pre-defined outcomes were reported.
Other bias (all)	Low risk	A few reasonable mitigation strategies have been applied. No other potential biases noted

Wang 2018

Study characteristics

Wang 2018 *(Continued)*

Methods	Multi-center, open-label, cluster-randomized clinical trial
Participants	40 hospitals in China admitting stroke patients (n = 3980)
Interventions	Participants were allocated to a clinical pathway intervention (n = 2003; median age 65 years [IQR 57-73]) versus usual care (n = 1977; median age 65 years [IQR 56-74]) between August 2014 and July 2016. The multi-faceted intervention combined a CPW with care protocols, quality co-ordinator oversight, and performance measure monitoring and feedback. "High" implementation score
Outcomes	Adherence to performance measures Inhospital mortality
Notes	DOI: DR Bettger reported consulting for the Ohio Department of Health and serving on committees for the Centers for Disease Control and Prevention (CDC) Paul Coverdell National Acute Stroke Registry. Dr Peterson reported being a principal investigator of the data co-ordinating and analysis center for the American Heart Association/American Stroke Association's Get With the Guidelines (GWTG). Dr. Peterson is also a JAMA associate editor but was not involved in the review or decision for article publication. Dr. Fonarow reported being a member of the GWTG steering committee and receiving grant funding from the Patient-Centred Outcomes Research Institute and the National Institutes of Health. Dr. Schwarmm reported being the chair of the GWTG-Stroke Clinical Workgroup of the American Heart Association and principal investigator of a National Institute of Neurological Disorders and Stroke (NINDS)-funded clinical trial; grant funding and nonfinancial support from Genetech and consulting for the Joint Commission, CDC and Massachusetts Department of Public Health Funded by the Ministry of Science and Technology, and the Ministry of Health of the People's Republic of China (National S & T Major Project of China: 2011BAIO8BO2, 2012ZXO9303, 2013BAIO9B14, 2013BAIO9B03, 2015BAI12B02, 2015BAI12BA04, 2016YFC0901000, 2016YFC0901002, 2017YFC1307900, 2017YFC1307905, 2017YFC1310900, 2017YFC1310901 and 2017YFC1310903). Beijing Municipal Committee of Science and Technology (D15110700200000, D1511000002015001, D151100002015002, Z161100000516223, Z141107002514125). Beijing Institute for Brain Disorders (BIBD-PXM2013_014226_07_000084). Beijing Key Laboratory for Cerebrovascular Disease (BZ0101). University of Hong Kong Stanley Ho Alumni Challenge Fund; University of Hong Kong Research Committee Seed Funding Award (104004215) and Sanofi

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Participants were randomized within the strata and assigned (1:1) to intervention or control groups using a random number generating software.
Allocation concealment (selection bias)	Low risk	An independent statistician concealed the generated sequence until the group was assigned.
Incomplete outcome data (attrition bias) (All)	Low risk	No missing data reported
Blinding of participants and personnel (All)	High risk	Clinical staff could not be blinded to the different interventions provided in the intervention. Concealed allocation and blind adjudication of outcomes were used to avoid bias.
Protection against contamination (RCT, NRCT, CBA)	Unclear risk	The cluster-randomized design reduced the likelihood of contamination between intervention and control groups. Not clear if the staff moved between intervention and control sites

Wang 2018 *(Continued)*

Selective reporting (reporting bias) (All)	Low risk	All pre-defined outcomes were reported.
Other bias (all)	Low risk	No other obvious source of bias

ACE: angiotensin-converting enzyme
AKI: acute kidney injury
ALOS: average length of stay
AMI: acute myocardial infarction
BG: blood glucose
BiPAP: bilevel positive airway pressure
CACM: childhood asthma care map
CAP: community acquired pneumonia
CAT: chart audit tool
CBA: controlled before after
CCU: coronary care unit
CGQL: Cleveland Clinic Global Quality of Life
COPD: chronic obstructive pulmonary disease
CP: clinical pathway
CPM: The Critical Path Method
CPW: clinical pathway
DVT: deep vein thrombosis
ED: emergency department
EGI: eosinophilic gastrointestinal disease
EMR: electronic medical record
ER: emergency room
GQOLI-74: Generic Quality of Life Inventory-74
HRQOL: health-related quality of life
ICH: intracranial hemorrhage
ICP: integrated care pathway
ICU: intensive care unit
IGF-1: insulin-like growth factor-1
INT: intervention
IQR: interquartile range
ITS: interrupted time series
LCP-I: Liverpool care pathway-Italian context
LOS: length of stay
LVT: left ventricular thrombus
MGPQ: McGill pain score questionnaire
MICU: medical intensive care unit
MNA: mini-nutritional assessment
NCP: new clinical pathway
NIV: non-invasive ventilation
NSW: New South Wales
NYHA: New York Heart Association
PAT: process audit tool
PCAD: palliative care for advanced disease
PCI: percutaneous coronary intervention
PCQN: palliative care knowledge quiz
PCS: Physical Component Summary
PCT: specialist palliative care team
PICU: pediatric intensive care unit
POD: post-operative day
q4h: every 4 hours
QI: quality improvement
RCP: respiratory care practitioner
ROMIO: ruling out myocardial ischemia
RUT: routine care
SAPS II: Simplified acute physiology score II

SAS: self-rating anxiety scale
SD: standard deviation
SDS: self-rating depression scale
SF-36: Short Form
SOC: standard of care
SS-QOL: stroke-specific quality of life scale
STAMP: short-term asthma management plans
TIA: transient ischemic attack
TRAD: traditional post operative care
TURP: transurethral resection of prostate
UC: usual care
VAP: ventilator-associated pneumonia
VAS: visual analog pain score
VMP: ventilator management protocol
WOMAC: Western Ontario and McMaster University Osteoarthritis Index

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Abbott 2006	Investigators evaluated the adoption of a ventilator-associated pneumonia clinical practice guideline that did not appear to be multidisciplinary and did not meet the minimum criteria for definition of a clinical pathway.
Abe 2001	Did not meet EPOC study design criteria as investigators compared a four-weeks short versus an eight-weeks long rehabilitation program by comparing a historical control with a concurrent experimental group.
Abisheganaden 2001	Did not meet EPOC study design criteria as investigators compared an asthma care path with traditional care and employed a simple pre-post comparison.
Abularrage 2005	Did not meet inclusion criteria as investigators compared two different endovascular abdominal aortic aneurysm repair operation techniques. Pathway only used for better standardization in both study arms.
Adam 2006	Did not meet EPOC study design criteria as investigators evaluated an implementation of a sedation guideline by employing a time-series design at high risk of bias.
Adcock 1998	CPW content criteria not met as it was not a pathway intervention
Aeyels 2018	A multicenter pre-post intervention study. Study did not meet EPOC study design criteria for a controlled before-and-after study design
Aeyels 2018b	A multicenter pre-post intervention study. Study did not meet EPOC study design criteria for a controlled before-and-after study
Afonso 2017	The authors explored an enhanced recovery pathway for patients undergoing micro-surgical breast reconstruction vs a historical control group. The pre-post design did not meet EPOC study design criteria.
Allen 2009	Did not meet inclusion criteria as the intervention was not conducted in the hospital setting
Angelidou 2017	The studies explored the rigorous implementation of a new guideline by a multidisciplinary team to decrease use of acid-suppressing medications. The intervention did not meet criteria for our working definition of the clinical pathway, as it provided a general guideline that could be "feasibly implemented in other similar settings providing inpatient care" (i.e. thus not adapted to local structures).

Study	Reason for exclusion
Annette 2005	Investigators reported outcomes from implementing clinical guidelines for nutrition in a neurosurgical intensive care unit. Study did not meet EPOC study design criteria for a controlled before-and-after study design as data collection was not contemporaneous at intervention and control sites.
Aoshima 2002	Did not meet EPOC study design criteria as investigators evaluated the usefulness of a clinical pathway for community-acquired pneumonia by using a simple pre-post comparison
Arko 2001	Did not meet inclusion criteria as investigators compared two different operation techniques for aneurysm repair, and it was not a pathway study.
Arrick 2019	The study investigated the implementation of an ERAS protocol (Enhanced Recovery After Surgery) in colorectal surgery using an observational cohort design, which did not meet EPOC study design criteria. The ERAS program provides general guidelines for different conditions that are not necessarily adapted to the local structures of each hospital.
Asano 2002	This study of the impact of a clinical pathway for Benign Prostatic Hyperplasia did not meet EPOC design criteria for a controlled before-and-after study as only a single sample pre- and post-intervention was tested.
Astanehe 2018	The authors prospectively evaluated an ERAS-based clinical care pathway for micro-surgical breast reconstruction and compared their outcomes with a previous cohort of women treated with usual care. The study design did not meet EPOC study design criteria.
Ayieko 2011	CPW content criteria not met as it was not a pathway intervention as the intervention focused on implementing clinical practice guidelines
Bai 2018	The study investigated the effects of clinical pathways on medical care in Chinese hospitals. The study did not meet Cochrane EPOC study design criteria.
Bailit 2013	CPW content criteria not met as it was not a pathway intervention and the study is a modeling study
Ban 2012	Did not meet EPOC study design criteria as investigators evaluated the usefulness of a clinical pathway for chronic obstructive pulmonary disease (COPD) by using a simple pre-post comparison
Bapat 2017	The authors described the development and implementation of an integrated care pathway for chronic subdural hematomas. The design using pre-post interventions did not meet the EPOC design criteria.
Bardiau 2003	Did not meet ITS quality criteria as investigators evaluated the effectiveness of a pathway intervention for pain management by employing 3 series measures
Barlow 2007	Did not meet CBA quality criteria as the study was investigating the effectiveness of an intervention designed to reduce "door-to-antibiotic time" in community-acquired pneumonia by using only one control group
Bauer 2009a	Did not meet inclusion criteria as the intervention was not focused on hospitalized patients
Benenson 1999	Did not meet ITS quality criteria as investigators used a time- series design at high risk of bias. ITS quality criteria not met because only three data points pre- and post-implementation tested
Berenholtz 2004a	Did not meet intervention minimum criteria (content criteria) as only three out of five pathway criteria met
Bermejo 2009	Did not meet inclusion criteria as the intervention was not focused on hospitalized patients but outpatients suffering from depression

Study	Reason for exclusion
Bertram 2023	Did not meet inclusion criteria, because of wrong setting (primary care)
Bhat 2024	Single site before-and-after study did not meet study design criteria.
Blackburn 1997	Did not meet EPOC study design criteria as a simple pre-post comparison was employed to investigate a cohort of patients managed by a pathway for carotid endarterectomy (CEA) versus traditional management
Blegen 1995	This study of managed care did not meet inclusion criteria for a controlled before-and-after study as data collection was not contemporaneous at intervention and control sites.
Board 2000b	Randomized controlled study comparing inhospital care guided by a pathway versus hospital at home following a standardized pathway for home-care and early discharge. Did not meet inclusion criteria as home-care group was not in a hospital setting
Boodaie 2018	Two cohorts (2013 and 2015) pre-post-intervention used to explore the effects of a perioperative care map for patients with morbid obesity undergoing major surgery. Study design did not meet the EPOC design criteria.
Bradywood 2017	Pre-post-intervention design aimed at exploring evidence-based quality improvement measures for lumbar spine fusion patients. The design did not meet EPOC criteria.
Brunenberg 2005	Investigators compared a clinical pathway for joint replacement versus traditional care. Did not meet EPOC design criteria as a simple pre-post comparison used
Burns 2005	Did not meet minimum criteria for definition of a clinical pathway as it was not multidisciplinary
Bush 1979	Investigators compared a drug therapy protocol in an HMO versus non-protocol care. Did not meet content criteria as intervention was not multidisciplinary
Cabezas 2009	Did not meet inclusion criteria as intervention was designed for primary care centers
Card 1998	Did not meet EPOC study design criteria as investigators evaluated the impact of clinical pathways for total hip replacement versus usual care by employing a simple pre-post comparison
Carpintero 2009	Did not meet EPOC study design criteria as investigators employed a simple pre-post comparison between four time points to evaluate a protocol for patients with osteoporotic fracture
Carr 2019	The study did not meet the EPOC design criteria.
Carratala 2012	Not multidisciplinary. Did not meet the definition of a pathway
Carter-Brooks 2018	Observational cohort study of the implementation of a urogynecology ERAS pathway. Design did not meet EPOC design criteria and protocol not specifically adapted to local structures
Casalta 2009	Did not meet EPOC study design criteria as investigators employed a traditional before-and-after study without employing two intervention and two control sites
Casas 2006	Did not meet study inclusion criteria as study was conducted in a primary care setting
Chamouard 2023	Study was a comparative, non-randomized design that did not meet study design inclusion criteria.
Chen 2022	CPW content criteria not met as it was not a pathway intervention
Cheney 2005	Did not meet EPOC study design criteria as pathway investigation based on a simple pre-post comparison with a historical cohort

Study	Reason for exclusion
Chu 2001a	Did not meet inclusion criteria as not comparative and subjective experience with a computerized pathway tool reported
Conway 2009	Did not meet EPOC study design criteria as pathway investigation based on a simple pre-post comparison
Coons 2007	Did not meet ITS design criteria as authors evaluated the effectiveness of a standardized strategy for patients with acute myocardial infarction or heart failure by testing fewer than three time periods pre- and post-intervention
Counsell 2007	Did not meet study inclusion criteria as study was conducted in a primary care setting
Covinsky 1998	Did not meet minimum criteria for definition of a clinical pathway as it was not multidisciplinary
D'Souza 2019	The authors studied the impact of an ERAS protocol as part of quality improvement initiatives for patients undergoing colorectal surgery in a community hospital using pre-post-intervention cohorts; thus, an experimental design that did not meet EPOC design criteria
DeLuca 2009	Randomized controlled trial that explored the effects of emergency clinical stroke patients carried out in a pre-hospital setting (i.e. emergency medical settings); thus, not meeting our setting of inclusion criteria
Denbo 2018	The authors compared consecutive patients treated after implementation of pancreatectomy clinical pathways with patients treated before implementation, a design that did not meet the EPOC design criteria for inclusion.
Deneckere 2013	The study met EPOC study design criteria and the definition of pathway. A posterior publication (i.e. Seys and colleagues 2017) included the data reported in Deneckere and colleagues 2013 so the study has been excluded to avoid duplication of data.
Dragun 2024	ERAS protocol did not meet CPW criteria for translating evidence into local structures.
Du 2014	The study described a quality improvement program for patients with acute coronary syndromes that included a clinical pathway intervention. The pathway was adapted to the Chinese context by 22 cardiologists; thus, the intervention did not meet the working definition for a pathway (i.e. multidisciplinary and adapted to local structures).
Duncan 2013	Did not meet requirements for an EPOC study design as the investigators utilized a before-after study without two control and two intervention sites.
Dunn 2022	CPW content criteria not met as it was not a pathway intervention
Eagle 1990	Did not meet minimum criteria for definition of a clinical pathway as it was not multidisciplinary
Edworthy 2007	Authors evaluated a medical prevention program. Did not meet minimum criteria 3 and 4 for the definition of a clinical pathway
Featherall 2018	Patients with total hip arthroplasty were compared before and after the implementation of a care pathway. Cohort design did not meet EPOC criteria.
Ferri 2006	This report on patient perceptions of a clinical pathway for laparoscopic surgery did not meet the design criteria for a controlled before-and-after study as only a single-sample pre- and post-intervention was tested.
Finotto 2006	Authors evaluated a nursing intervention for delirium patients. Study did not meet minimum criteria for definition of a clinical pathway as it was not multidisciplinary.

Study	Reason for exclusion
Fletcher 2017	The authors explored a novel pathway for early discharge of adolescent idiopathic scoliosis as compared to a similar volume scoliosis center at another children's hospital where a more traditional postoperative protocol was used. The design did not meet EPOC criteria for inclusion.
Garcia-Aymerich 2007	Authors evaluated an integrated care intervention for COPD. Did not meet inclusion criteria as the setting was primary care and the randomization of participants was after hospital discharge. RCT design
Garin 2011	Did not meet EPOC study design criteria as investigators used a simple pre-post comparison to evaluate the clinical pathway
Gas 2019	This study evaluated the implementation of a clinical pathway for acute urinary retention. The experimental design did not meet the EPOC criteria for inclusion.
Gellert 2019	This study evaluated the impact of a multi-component quality improvement intervention for pediatric asthma care. Outcomes were assessed over three intervention periods, but ITS data could not be extracted.
Gerard 2018	Authors used a pre-post design to evaluate the postoperative management of perforated appendicitis. The design did not meet EPOC criteria for inclusion.
Gibbon 2002	This study of the impact of an intervention to improve staff attitudes in stroke care did not meet design criteria for a controlled before-and-after study as only a single sample pre- and post-intervention was tested.
Givens 2007	Study evaluated the effects of a pain management protocol and did not meet ITS design criteria as investigators tested fewer than three time periods pre- and post-intervention.
Glotzbecker 2019	They explored the implementation of a multidisciplinary clinical pathway to reduce surgical site infection rate after posterior spinal fusion by comparing a pre- and post-period, a design that did not meet EPOC criteria for inclusion.
Gounder 2003	This multicenter study of an intervention to improve the management of pneumonia did not meet EPOC study design criteria as control and intervention sites were not comparable within the 12 participating hospitals.
Hanekom 2013	Did not meet EPOC study design criteria as investigators used a exploratory, controlled, pragmatic sequential time block clinical trial
Hashine 2021	Single sample descriptive survey study did not meet inclusion criteria for study design.
Horn 2007	Did not meet study inclusion criteria as investigators focused on the use of a collaborative care model for patients in the outpatient setting
Hussain 2017	The study compared a standard care pathway with a new pathway for patients with fecal incontinence. The pathway was introduced in a clinic that took place every 8 weeks; thus, it was not assessed in our setting of interest.
Kaiser 2018	Retrospective cohort study that explored the implementation of pathway in multiple centers and did not meet the EPOC criteria for inclusion.
Kajikawa 2004	This evaluation of a clinical pathway for the management of tonsillectomy in adults used a simple, single-sample pre-post comparison that did not meet EPOC criteria for controlled before-and-after studies.

Study	Reason for exclusion
Kazui 2004	This evaluation of the effectiveness of a clinical pathway for the diagnosis and treatment of dementia and for the education of families did not meet EPOC study design criteria as investigators employed a single-sample pre-post comparison.
Ke 2022	CPW content criteria not met as it was not a pathway intervention
Keetch 1998	This study explored LOS impact of a pathway for decreasing hospital stay after radical prostatectomy. It utilized a single sample before-and-after study in one ward. Did not meet design criteria for a controlled before-and-after study as only a single sample pre- and post-intervention was tested
Kelly 2000b	Investigators evaluated an asthma clinical pathway. Did not meet EPOC study design criteria as a pre-post comparison was used.
Kight 1999	Investigators evaluated a clinical pathway for open donor nephrectomy. Did not meet EPOC study design criteria for a controlled before-and-after study as only a single sample pre- and post-intervention was tested
Kinsman 2004a	Investigators evaluated a clinical pathway for AMI. Did not meet EPOC study design criteria as only a single-sample pre-post comparison employed
Lange 2018	The study design (before-after implementation) did not meet the EPOC inclusion criteria.
Lee 2002	Effects of a pathway for pulmonary lobectomy on several outcomes were evaluated by employing a simple pre-post design. Did not meet EPOC study design criteria
Lee 2023	Did not meet CPW inclusion criteria because of wrong intervention
Lei 2012	The study explored the influence of integrative medicine clinical pathways on prognosis for acute myocardial infarction. It did not meet the criteria for our working definition of CPW.
Letton 2013	Did not meet EPOC study design criteria as investigators used a before-and-after design without two intervention and two control sites
Li 2016	Pathway created and implemented by nurses. The study did not meet the multidisciplinary criteria for the definition of a clinical pathway.
Li 2018b	The study explored an enhanced recovery after surgery (ERAS) pathway. The ERAS protocol was not implemented to local structures, thus not meeting the definition of pathway.
Lindberg 2016	The study explored the processes associated with the implementation of a clinical pathway for patients with colorectal cancer. The outcomes reflected the process of implementing (e.g. number of pathways implemented) rather than the outcomes of the pathways themselves.
Loeb 2006	Not hospital setting
Lu 2019	The study explored a clinical nursing pathway for bedsores in senile bedridden patients. The pathway was described as implemented by nurses only, thus not meeting the multidisciplinary criteria for a pathway.
Luo 2021	This discussion paper proposed a CPW implementation framework. Discussion papers were not included in this review.
Ma 2017	Intervention reported as a clinical nursing pathway, thus not meeting multidisciplinary criteria for a pathway

Study	Reason for exclusion
Mattart 2017	The study explored a left colon clinical pathway using a pre-post-implementation design. The study did not meet EPOC design criteria.
Mo 2010	Did not meet EPOC study design criteria as investigators used a quasi-experimental design without the use of two intervention and two control sites
Mohamed 2018	Participants were consecutively assigned to usual care or clinical pathway-directed care between October–December 2014, and January–April 2015, respectively. Pre-post design did not meet EPOC criteria.
Moller 2011	Did not meet EPOC study design criteria for NRCT as investigators did not utilize at least two intervention and two control sites
Mooney 2022	Did not meet inclusion criteria because of virtual community or primary care setting
Morse 2018	One group collected pre-intervention and two post-interventions of a clinical pathway to reduce ICU usage. The design did not meet inclusion criteria.
Mou 2013	Not multidisciplinary, as the pathway was used by surgeons only. The intervention did not meet the definition of a pathway.
Nucifora 2009	Study did not meet inclusion criteria for a clinical pathway as the intervention used was not multidisciplinary.
Okon 2004	Intervention did not meet the pathway definition as it was not multidisciplinary.
Owen 2006	Investigators evaluated the implementation of a pre-dialysis clinical pathway for patients with chronic kidney disease by using a time series. Did not meet ITS design criteria as data were not analyzed appropriately
Paskowski 2011	Did not meet EPOC study design criteria as the investigators used NRCT without two intervention and two control sites
Pinzon 2009	Did not meet EPOC study design criteria as investigators used a simple before-after study
Porter 1998	Did not meet EPOC design criteria as authors evaluated the effectiveness of a clinical pathway for patients undergoing pancreaticoduodenectomy by employing a simple pre-post comparison
Process 2014	General guidelines not adapted to local structures. Did not meet the definition of a pathway
Qin 2019	The study did not meet EPOC study design criteria.
Ritchie 2024	The setting of aged care did not meet inclusion criteria for hospital CPWs.
Rolnick 1998	Did not meet EPOC design criteria as authors evaluated a strategy of an active management of labor by using a simple pre-post comparison
Ross 2004	Did not meet EPOC design criteria as investigators evaluated the effects of a clinical pathway for atrial fibrillation by employing a case-control design
Schroeder 2024	Wrong study setting. The CPW was not trialed in a hospital.
Schwarzbach 2010	Cohorts from pre- and post-intervention were compared. Study did not meet EPOC study design criteria for inclusion.
Shabunin 2021	Simple before-and-after study design did not meet review inclusion criteria.

Study	Reason for exclusion
Shahid 2024	This study was a review of strategies to implement evidence into practice. Reviews are not an included study design.
Short 1997	Did not meet EPOC design criteria as authors evaluated a charting by exception pathway versus usual management by using a simple pre-post comparison
Smulowitz 2018	The authors explored the impact of the implementation of a clinical pathway (heart pathway) using a pre-post design. The study did not meet EPOC design criteria for inclusion.
Soria-Aledo 2008	This study evaluating a clinical pathway for thyroidectomy did not meet EPOC design criteria as a combined controlled before-and-after and time-series design did not meet methodological criteria for the number of control groups and number of time points tested.
Srinivasan 2009	Did not meet EPOC study design criteria as investigators used a NRCT without two intervention and two control sites
Summers 1998	Did not meet EPOC design criteria as the authors evaluated a stroke clinical pathway by using a time series without three points before and after the intervention
Ten 2014	Did not meet EPOC design criteria as investigators evaluated a simple pre-post evaluation design
Thilly 2003	Intervention did not meet multidisciplinary content criterion as it is a practice guideline for ACE inhibitor use. Inclusion criteria not met
Tosun 2006	Did not meet EPOC design criteria as the authors evaluated a complex intervention including a pathway by employing a simple pre-post comparison
Turley 1994	Did not meet EPOC design criteria as investigators compared a strategy for congenital heart failure versus usual care by employing a case-control design with matched pairs
Unemura 2002	Did not meet EPOC design and quality criteria as authors evaluated the introduction of a clinical pathway for colorectal polypectomy by using a post-implementation questionnaire survey
Van der Kolk 2017	Patients with pancreaticoduodenectomy treated with a clinical pathway were compared with a historical control group that followed usual care. The pre-post design did not meet EPOC criteria for inclusion.
Van der Kolk 2018	The study did not meet EPOC design criteria.
Verdu 2009	The study design did not meet EPOC criteria for inclusion.
Walsh 2001	Did not meet EPOC design criteria as investigators evaluated a critical pathway strategy for infra-inguinal bypass surgery by using a simple pre-post comparison
Wang 2002	Did not meet CBA design criteria as authors investigated a management intervention to reduce unnecessary testing in the coronary care unit by employing a controlled before-and-after design with only one control group
Wang 2011	Clinical pathway was used to direct participants to Chinese medicine or usual care. Wrong intervention
Wang 2018b	The intervention consisted of a decision-making tool. The study did not meet the criteria for the definition of a pathway.

Study	Reason for exclusion
Waters 1999	Authors evaluated clinical pathways for the management of four trauma diagnoses by using time series with 2 measures tested before and 2 measures after. The study did not meet ITS design criteria.
Wu 2010	Study did not meet the criteria for a clinical pathway as the intervention was not multidisciplinary.
Yamana 2009	Did not meet any of the EPOC study design criteria as investigators used a simple pre-post comparison for evaluating a clinical pathway for diabetic patients
Yamauchi 2003	Did not meet ITS quality criteria as authors evaluated a clinical pathway for inpatients with gastric ulcers by using a time-series design with 3 measures in total tested
Yang 2015	The course of treatment was reported as being 3 months long. Wrong setting
Zeler 1992	Authors evaluated a nurse-led intervention after cardiac surgery. Did not meet minimum criteria for the definition of a clinical pathway as it was not multidisciplinary
Zhang 2019	Pre-post design did not meet EPOC criteria.
Zhou 2018	Retrospective observational study. Wrong design
Zorn 1999	PhD thesis did not meet EPOC design criteria as the author evaluated the impact on length of stay of a CPW in the treatment of patients receiving total joint replacements by employing a simple pre-post comparison.

AMI: acute myocardial infarction
CBA: controlled before-after
CEA: carotid endarterectomy
COPD: chronic obstructive pulmonary disease
CPW: clinical pathway
EPOC: Effective Practice and Organization of Care
ERAS: Enhanced Recovery After Surgery
HMO: health maintenance organization
ITS: interrupted time-series
NRCT: non-randomized controlled trial

Characteristics of studies awaiting classification *[ordered by study ID]*

Cadilhac 2022

Methods	Stepped-wedge cluster-randomized trial
Participants	Nine hospitals (clusters) participated, and 144 clinicians attended 18 intervention workshops.
Interventions	STELAR intervention, comprising four components
Outcomes	Primary Outcome: Single composite measure that summarized the proportion of all required care provided to patients based on the clinical indicators included in each hospital's action plan
Notes	

Chong 2013

Methods	Pseudo-randomized study but allocation to CPW and control groups was at cluster level. Data analysis was conducted at patient level.
Participants	162 patients after a new hip fracture were included. 92 were randomized to the experimental CPW group, and 70 patients to the control group.
Interventions	Hip fracture integrated care pathway compared to usual care
Outcomes	Modified Barthel Index, ambulatory status, SF-12, LOS, discharge destination, hospital readmission and mortality
Notes	Orginal study data requested on Nov 14, 2023

Courtney 2022

Methods	Investigators conducted a 20-week pilot controlled clinical trial.
Participants	Participants were adolescents (age 14–18) with a primary diagnosis of major depressive disorder recruited from one of two outpatient psychiatric clinics at academic hospitals. Thirty-five youth were allocated to the pathway and 31 were allocated to treatment-as-usual.
Interventions	Care pathway for the treatment of depression in adolescents
Outcomes	Trial feasibility outcomes were of primary interest, including clinician fidelity to the care pathway.
Notes	

De Luca 2007

Methods	C-RCT
Participants	20 emergency departments
Interventions	Emergency clinical pathway for stroke patients
Outcomes	Primary outcome: proportion of eligible acute stroke patients referred to the stroke unit (SU)
Notes	A copy of the CPW intervention has been requested. Awaiting author response

Hsu 2020

Methods	Pilot RCT
Participants	Participants (n = 51) were randomized to standard care (“control”, n = 29) or sleep clinical pathway (“intervention”, n = 22).
Interventions	Sleep clinical pathway

Hsu 2020 *(Continued)*

Outcomes	Sleep quality measured by Pittsburgh Sleep Quality Index (PSQI), Hopkins Rehabilitation Engagement Rating Scale (HRERS), Fatigue Severity Scale (FSS), Patient Satisfaction with Sleep Scale, and actigraphy
Notes	

Karimi 2023

Methods	Multi-center RCT, conducted in intensive care
Participants	200 intubated patients
Interventions	Oral healthcare protocol on ventilator-associated pneumonia patients in intensive care unit
Outcomes	Percentage of VAP diagnoses as main outcome assessed using clinical pulmonary infection score (CPIS)
Notes	

Kumar 2024

Methods	RCT
Participants	30 patients admitted for colorectal surgery, with 14 patients in the CPW group and 16 in the control group
Interventions	Intervention (peri-operative protocol) has not been well described in the paper. Thus, we requested a copy of the intervention to decide on inclusion/exclusion.
Outcomes	Hospital stay, complications, 30-day readmission rates, and mortality
Notes	Awaiting author response

Li 2015

Methods	We are still awaiting translation of the methods section.
Participants	200 patients who underwent laparoscopic cholecystectomy. 100 allocated to CPW and 100 allocated to the control group 李金英, 黄丽美, 方珍. 临床护理路径应用于腹腔镜胆囊切除术患者的疗效. ######## 2015; 23(7): 1170-1173 [DOI: 10.11569/wcjd.v23.i7.1170]
Interventions	Clinical nursing pathway in patients undergoing laparoscopic cholecystectomy
Outcomes	
Notes	This study has been published in Chinese. We are working on a translation of the methods section to decide on in- or exclusion.

Mahant 2023

Methods	Interrupted time-series analysis (ITS) of children undergoing elective tonsillectomy at community and children's hospitals in Ontario
Participants	111,411 children that underwent tonsillectomy: 51,967 in the QBP period and 59,444 in the pre-QBP period
Interventions	Best practice, evidence-informed tonsillectomy perioperative care pathway
Outcomes	Age-standardized and sex-standardized rates for all-cause tonsillectomy-related revisits within 30 days, opioid prescription fills within 30 days and index tonsillectomy inpatient admission
Notes	

McKee 2024

Methods	Prospective stepped-wedge type III hybrid effectiveness-implementation study
Participants	21 general EDs within Intermountain. 298 patients in the pre-intervention cohort, and 317 in the post-intervention cohort.
Interventions	Standardized stroke protocol in emergency departments
Outcomes	Implementation outcome measures focused on adoption, penetration, and fidelity as defined by Proctor and colleagues
Notes	

Park 2022

Methods	ITS
Participants	61 eligible CPWs and a total of 44,062 patients who underwent elective surgeries
Interventions	Clinical pathway on antibiotic prophylaxis
Outcomes	Adherence to systematic and appropriate duration of antibiotic prophylaxis
Notes	

Puchalski 2022

Methods	ITS
Participants	A total of 113 and 300 patients were enrolled in the pre-implementation and post-implementation phases.
Interventions	Tailored sepsis treatment protocol

Puchalski 2022 *(Continued)*

Outcomes	Primary outcome was the proportion of patients receiving appropriate sepsis care.
Notes	

Vogel 2024

Methods	Stepped-wedge, cluster-randomized pilot trial
Participants	Eligible clusters were four hospitals with > 4000 births annually and cesarean rates ≥ 30%. Eligible women were those giving birth at ≥ 20 weeks' gestation.
Interventions	Implementation of the World Health Organization Labor Care Guideline (LCG)
Outcomes	Primary outcome was the cesarean rate among women.
Notes	

Yeates 2023

Methods	Stepped-wedge, C-RCT
Participants	5 emergency departments (ED) in Alberta, with 2878 patients (1164 female, 1713 male) aged 5–17 years
Interventions	Clinical pathway for acute care of pediatric concussion
Outcomes	Risk of persistent symptoms, provision of consistent information to patients and families, and referral for outpatient follow-up
Notes	

CPIS: clinical pulmonary infection score
CPW: clinical pathway
C-RCT: cluster-randomized control trial
ED: emergency department
FSS: Fatigue Severity Scale
HRERS: Hopkins Rehabilitation Engagement Rating Scale
ITS: interrupted time-series
LCG: Labour Care Guide
LOS: length of stay
PSQI: Pittsburgh Sleep Quality Index
RCT: randomized controlled trial
QBP: Quality-Based Procedures
SF-12: 12-Item Short Form Survey
STELAR: Shared Team Efforts Leading to Adherence Results
SU: stroke unit
VAP: ventilator-associated pneumonia

DATA AND ANALYSES

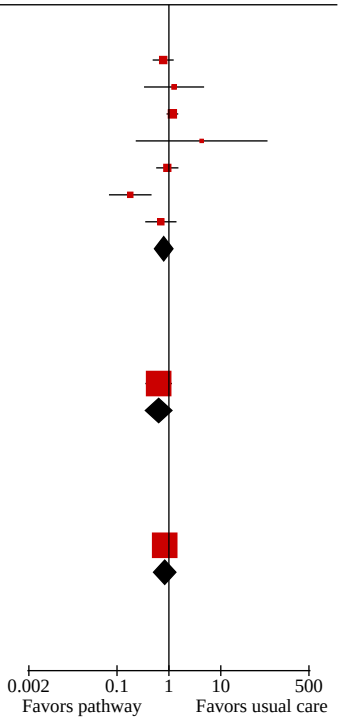
Comparison 1. Stand-alone clinical pathway versus usual care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Inhospital mortality	9		Odds Ratio (IV, Random, 95% CI)	Subtotals only
1.1.1 RCT	7	4603	Odds Ratio (IV, Random, 95% CI)	0.79 [0.53, 1.20]
1.1.2 NRCT	1	694	Odds Ratio (IV, Random, 95% CI)	0.63 [0.35, 1.14]
1.1.3 CBA	1	509	Odds Ratio (IV, Random, 95% CI)	0.83 [0.51, 1.36]
1.2 Mortality (up to 6 months)	3	805	Odds Ratio (IV, Random, 95% CI)	1.37 [0.72, 2.60]
1.3 Inhospital complications	12		Odds Ratio (IV, Random, 95% CI)	Subtotals only
1.3.1 RCT	11	3668	Odds Ratio (IV, Random, 95% CI)	0.57 [0.41, 0.80]
1.3.2 NRCT	1	111	Odds Ratio (IV, Random, 95% CI)	0.67 [0.27, 1.66]
1.4 Hospital readmission (up to 6 months)	11		Odds Ratio (IV, Random, 95% CI)	Subtotals only
1.4.1 RCTs	9	1578	Odds Ratio (IV, Random, 95% CI)	0.67 [0.44, 1.03]
1.4.2 NRCT	1	111	Odds Ratio (IV, Random, 95% CI)	0.31 [0.06, 1.63]
1.4.3 CBA	1	509	Odds Ratio (IV, Random, 95% CI)	2.14 [1.39, 3.30]
1.5 Length of hospital stay (days)	23		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.5.1 RCT studies	21	5201	Mean Difference (IV, Random, 95% CI)	-1.12 [-1.60, -0.65]
1.5.2 NRCT studies	2	755	Mean Difference (IV, Random, 95% CI)	-1.65 [-4.98, 1.69]
1.6 Hospital cost and charges	10		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.6.1 RCT studies hospital cost and charges	10		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.7 Adherence to recommended practice	4		Odds Ratio (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.7.1 RCT	3		Odds Ratio (IV, Random, 95% CI)	Totals not selected
1.7.2 NRCT	1		Odds Ratio (IV, Random, 95% CI)	Totals not selected
1.8 Sensitivity analysis: Risk of bias inhospital mortality (studies at high RoB excluded)	5	3795	Odds Ratio (IV, Random, 95% CI)	0.77 [0.45, 1.29]
1.9 Sensitivity analysis: Risk of bias 6 months mortality (studies at high RoB excluded)	2	514	Odds Ratio (IV, Random, 95% CI)	1.80 [0.95, 3.43]
1.10 Sensitivity analysis: Risk of bias inhospital complications (studies at high RoB excluded)	5	2222	Odds Ratio (IV, Random, 95% CI)	0.58 [0.39, 0.88]
1.11 Sensitivity analysis: Risk of bias hospital readmission (up to 6 months; studies at high RoB excluded)	5	1122	Odds Ratio (IV, Random, 95% CI)	0.77 [0.33, 1.82]
1.12 Sensitivity analysis: Risk of bias length of hospital stay in days (studies at high RoB excluded)	12	3275	Mean Difference (IV, Random, 95% CI)	-1.05 [-1.66, -0.44]

Analysis 1.1. Comparison 1: Stand-alone clinical pathway versus usual care, Outcome 1: Inhospital mortality

Study or Subgroup	log[OR]	SE	CPW Total	Usual care Total	Weight	Odds Ratio IV, Random, 95% CI
1.1.1 RCT						
Brook 1999	-0.2536	0.2379	162	159	20.2%	0.78 [0.49 , 1.24]
Deng 2014 (ICH)	0.2293	0.68	166	166	7.1%	1.26 [0.33 , 4.77]
Doig 2008	0.1549	0.1319	561	557	24.7%	1.17 [0.90 , 1.51]
Gooch 2012	1.4524	1.4917	1066	504	1.8%	4.27 [0.23 , 79.53]
Kollef 1997	-0.0706	0.2517	179	178	19.6%	0.93 [0.57 , 1.53]
Panella 2009	-1.7148	0.4819	214	215	11.2%	0.18 [0.07 , 0.46]
Panella 2012	-0.3567	0.3537	238	238	15.4%	0.70 [0.35 , 1.40]
Subtotal (Wald[a])			**2586**	**2017**	**100.0%**	**0.79 [0.53 , 1.20]**
Test for overall effect: Z = 1.10 (P = 0.27)						
Heterogeneity: Tau² (DL[b]) = 0.16; Chi² = 17.02, df = 6 (P = 0.009); I² = 65%						
1.1.2 NRCT						
Trombetti 2013	-0.4547	0.3007	465	229	100.0%	0.63 [0.35 , 1.14]
Subtotal			**465**	**229**	**100.0%**	**0.63 [0.35 , 1.14]**
Test for overall effect: Z = 1.51 (P = 0.13)						
Heterogeneity: Not applicable						
1.1.3 CBA						
Smith 2004	-0.186329578	0.253272226	334	175	100.0%	0.83 [0.51 , 1.36]
Subtotal			**334**	**175**	**100.0%**	**0.83 [0.51 , 1.36]**
Test for overall effect: Z = 0.74 (P = 0.46)						
Heterogeneity: Not applicable						
Test for subgroup differences: Chi² = 0.52, df = 2 (P = 0.77), I² = 0%						



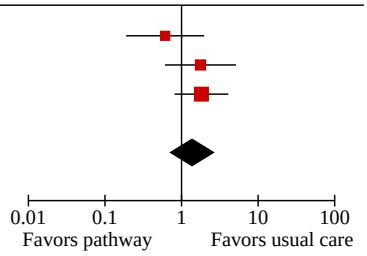
Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Analysis 1.2. Comparison 1: Stand-alone clinical pathway versus usual care, Outcome 2: Mortality (up to 6 months)

Study or Subgroup	log[OR]	SE	CPW Total	Usual care Total	Weight	Odds Ratio IV, Random, 95% CI
Vanhaecht 2016	-0.4927	0.5987	157	134	25.2%	0.61 [0.19 , 1.98]
Sulch 2002	0.5697	0.5442	76	76	29.5%	1.77 [0.61 , 5.14]
Panella 2018	0.5983	0.4121	229	133	45.3%	1.82 [0.81 , 4.08]
Total (Wald[a])			**462**	**343**	**100.0%**	**1.37 [0.72 , 2.60]**
Test for overall effect: Z = 0.96 (P = 0.34)						
Test for subgroup differences: Not applicable						
Heterogeneity: Tau² (DL[b]) = 0.07; Chi² = 2.51, df = 2 (P = 0.29); I² = 20%						



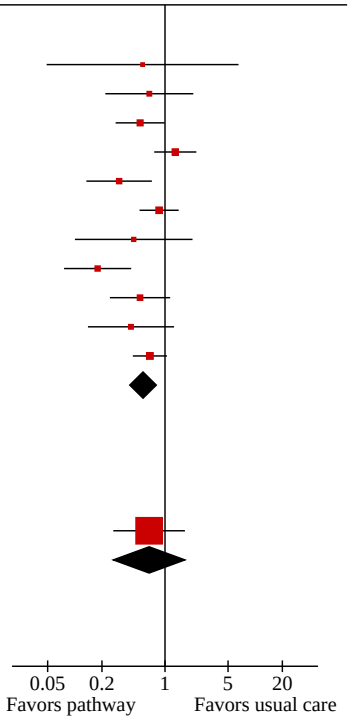
Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Analysis 1.3. Comparison 1: Stand-alone clinical pathway versus usual care, Outcome 3: Inhospital complications

Study or Subgroup	log[OR]	SE	CPW Total	Usual care Total	Weight	Odds Ratio IV, Random, 95% CI
1.3.1 RCT						
Aizawa 2002	-0.5718	1.2493	32	37	1.7%	0.56 [0.05 , 6.53]
Delaney 2003	-0.4005	0.5728	31	33	6.2%	0.67 [0.22 , 2.06]
Deng 2014 (ICH)	-0.6349	0.3193	166	166	11.8%	0.53 [0.28 , 0.99]
Deng 2014 (TIA)	0.2624	0.2744	213	213	13.2%	1.30 [0.76 , 2.23]
Dowsey 1999	-1.1712	0.4265	92	71	9.0%	0.31 [0.13 , 0.72]
Gooch 2012	-0.1508	0.2546	1066	504	13.9%	0.86 [0.52 , 1.42]
Kiyama 2003a	-0.7985	0.7657	47	38	4.1%	0.45 [0.10 , 2.02]
Li 2018	-1.7201	0.4368	62	56	8.8%	0.18 [0.08 , 0.42]
Marelich 2000	-0.6373	0.3925	166	169	9.8%	0.53 [0.24 , 1.14]
Muehling 2008	-0.8685	0.5604	30	28	6.4%	0.42 [0.14 , 1.26]
Panella 2012	-0.3857	0.2221	229	219	15.0%	0.68 [0.44 , 1.05]
Subtotal (Wald[a])			**2134**	**1534**	**100.0%**	**0.57 [0.41 , 0.80]**
Test for overall effect: Z = 3.25 (P = 0.001)						
Heterogeneity: Tau² (DL[b]) = 0.15; Chi² = 20.86, df = 10 (P = 0.02); I² = 52%						
1.3.2 NRCT						
Choong 2000	-0.4055	0.4663	55	56	100.0%	0.67 [0.27 , 1.66]
Subtotal			**55**	**56**	**100.0%**	**0.67 [0.27 , 1.66]**
Test for overall effect: Z = 0.87 (P = 0.38)						
Heterogeneity: Not applicable						
Test for subgroup differences: Chi² = 0.10, df = 1 (P = 0.75), I² = 0%						



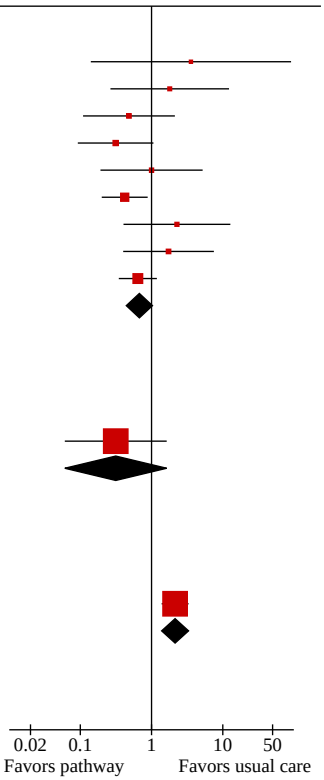
Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Analysis 1.4. Comparison 1: Stand-alone clinical pathway versus usual care, Outcome 4: Hospital readmission (up to 6 months)

Study or Subgroup	log[OR]	SE	CPW Total	Usual care Total	Weight	Odds Ratio IV, Random, 95% CI
1.4.1 RCTs						
Aizawa 2002	1.273	1.6508	32	37	1.7%	3.57 [0.14 , 90.79]
Almalki 2017	0.5878	0.9775	18	20	4.6%	1.80 [0.26 , 12.23]
Delaney 2003	-0.7295	0.7568	31	33	7.5%	0.48 [0.11 , 2.13]
Dowsey 1999	-1.1611	0.6234	92	71	10.6%	0.31 [0.09 , 1.06]
Gomez 1996	0	0.8422	50	50	6.1%	1.00 [0.19 , 5.21]
Panella 2009	-0.8675	0.3785	214	215	24.3%	0.42 [0.20 , 0.88]
Panella 2018	0.8202	0.8809	178	118	5.6%	2.27 [0.40 , 12.77]
Roberts 1997	0.549	0.7475	82	83	7.7%	1.73 [0.40 , 7.49]
Vanhaecht 2016	-0.4432	0.3139	139	115	31.8%	0.64 [0.35 , 1.19]
Subtotal (Wald[a])			**836**	**742**	**100.0%**	**0.67 [0.44 , 1.03]**
Test for overall effect: Z = 1.82 (P = 0.07)						
Heterogeneity: Tau² (DL[b]) = 0.05; Chi² = 9.01, df = 8 (P = 0.34); I² = 11%						
1.4.2 NRCT						
Choong 2000	-1.1569	0.84	55	56	100.0%	0.31 [0.06 , 1.63]
Subtotal			**55**	**56**	**100.0%**	**0.31 [0.06 , 1.63]**
Test for overall effect: Z = 1.38 (P = 0.17)						
Heterogeneity: Not applicable						
1.4.3 CBA						
Smith 2004	0.760805829	0.221645884	334	175	100.0%	2.14 [1.39 , 3.30]
Subtotal			**334**	**175**	**100.0%**	**2.14 [1.39 , 3.30]**
Test for overall effect: Z = 3.43 (P = 0.0006)						
Heterogeneity: Not applicable						
Test for subgroup differences: Chi² = 16.34, df = 2 (P = 0.0003), I² = 87.8%						



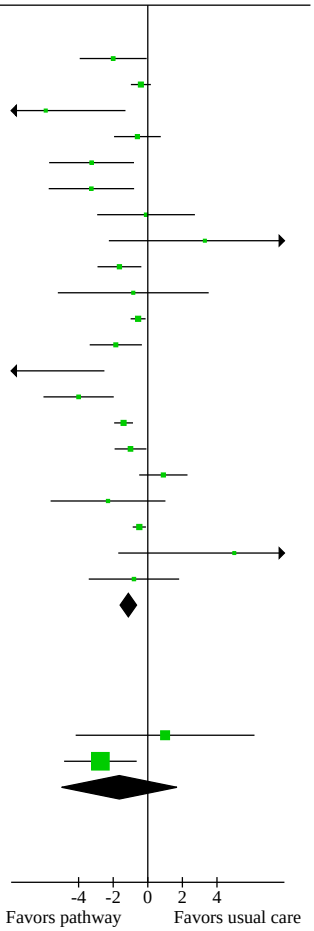
Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Analysis 1.5. Comparison 1: Stand-alone clinical pathway versus usual care, Outcome 5: Length of hospital stay (days)

Study or Subgroup	CPW Mean	CPW SD	CPW Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Random, 95% CI
1.5.1 RCT studies								
Aizawa 2002	12.7	2.8	32	14.7	5.2	37	4.0%	-2.00 [-3.94 , -0.06]
Bernard 2011	2.7	2	87	3.1	1.9	89	10.4%	-0.40 [-0.98 , 0.18]
Brook 1999	14	17.3	162	19.9	24.2	159	1.0%	-5.90 [-10.51 , -1.29]
Delaney 2003	5.2	2.5	31	5.8	3	33	6.2%	-0.60 [-1.95 , 0.75]
Deng 2014 (ICH)	17.93	11.4	166	21.18	11.4	166	2.9%	-3.25 [-5.70 , -0.80]
Deng 2014 (TIA)	9.93	13	213	13.19	13	213	2.8%	-3.26 [-5.73 , -0.79]
Doig 2008	24.2	23.7	540	24.3	23.6	537	2.3%	-0.10 [-2.92 , 2.72]
Falconer 1993	35.6	15.5	53	32.3	15.4	68	0.7%	3.30 [-2.25 , 8.85]
Gomez 1996	0.64	0.5	53	2.28	5.3	68	6.6%	-1.64 [-2.91 , -0.37]
Jalil 2017	7.8	3.2	24	8.64	10.2	23	1.1%	-0.84 [-5.20 , 3.52]
Johnson 2000	1.68	1.1	50	2.24	1.1	50	11.2%	-0.56 [-0.99 , -0.13]
Kim 2002	0.25	0.2	9	2.1	2.3	9	5.5%	-1.85 [-3.36 , -0.34]
Kiyama 2003a	18.1	9.5	47	28.2	22.3	38	0.4%	-10.10 [-17.69 , -2.51]
Li 2018	10.52	5.3	62	14.52	5.9	56	3.8%	-4.00 [-6.03 , -1.97]
Marrie 2000	8.2	1.9	87	9.6	2.1	124	10.6%	-1.40 [-1.94 , -0.86]
Panella 2009	10.4	4.7	201	11.4	4.7	201	8.4%	-1.00 [-1.92 , -0.08]
Panella 2012	11.78	6.6	215	10.88	7.9	205	6.0%	0.90 [-0.50 , 2.30]
Panella 2018	12.35	18.2	283	14.65	18.2	195	1.8%	-2.30 [-5.62 , 1.02]
Roberts 1997	1.38	1.2	82	1.87	1.3	83	11.4%	-0.49 [-0.87 , -0.11]
Sulch 2002	50	19	76	45	23	76	0.5%	5.00 [-1.71 , 11.71]
Vanhaecht 2016	12	10.5	152	12.8	12.4	146	2.6%	-0.80 [-3.41 , 1.81]
Subtotal (Wald[a])			**2625**			**2576**	**100.0%**	**-1.12 [-1.60 , -0.65]**
Test for overall effect: Z = 4.64 (P < 0.00001)								
Heterogeneity: Tau² (DL[b]) = 0.48; Chi² = 54.86, df = 20 (P < 0.0001); I² = 64%								
1.5.2 NRCT studies								
Trombetti 2013	38	34	465	37	32	229	29.2%	1.00 [-4.17 , 6.17]
Usui 2004	8.03	4.18	30	10.77	4.18	31	70.8%	-2.74 [-4.84 , -0.64]
Subtotal (Wald[a])			**495**			**260**	**100.0%**	**-1.65 [-4.98 , 1.69]**
Test for overall effect: Z = 0.97 (P = 0.33)								
Heterogeneity: Tau² (DL[b]) = 2.94; Chi² = 1.73, df = 1 (P = 0.19); I² = 42%								
Test for subgroup differences: Chi² = 0.09, df = 1 (P = 0.76), I² = 0%								



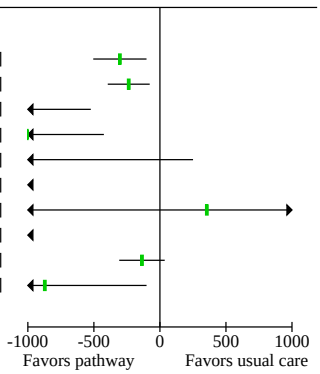
Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

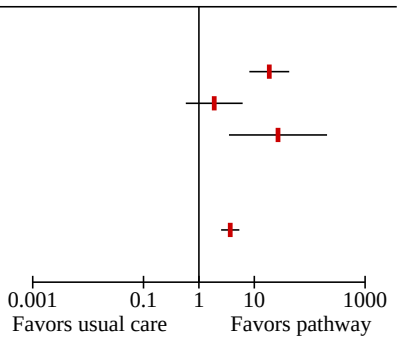
Analysis 1.6. Comparison 1: Stand-alone clinical pathway versus usual care, Outcome 6: Hospital cost and charges

Study or Subgroup	CPW Mean	CPW SD	CPW Total	Usual care Mean	Usual care SD	Usual care Total	Mean Difference IV, Random, 95% CI
1.6.1 RCT studies hospital cost and charges							
Deng 2014 (ICH)	2002.56	1110.63	166	2305.68	723.12	166	-303.12 [-504.73 , -101.51]
Deng 2014 (TIA)	1569.64	788.97	213	1805.82	880.53	213	-236.18 [-394.95 , -77.41]
Gomez 1996	1924.79	2523.74	50	8606.61	22074.1	50	-6681.82 [-12840.19 , -523.45]
Johnson 2000	3425.12	1563.86	55	4434.02	1563.86	55	-1008.90 [-1593.39 , -424.41]
Kim 2002	1180.39	534.57	9	2314.65	2051.44	9	-1134.26 [-2519.27 , 250.75]
Kiyama 2003a	13380.86	2515.63	47	17206.63	7001.15	38	-3825.77 [-6165.07 , -1486.47]
Kollef 1997	40800.54	39537.31	179	40445.3	38137.01	178	355.24 [-7703.03 , 8413.51]
Li 2018	5730.05	287.34	62	8039.14	303.99	56	-2309.09 [-2416.12 , -2202.06]
Panella 2009	3356.72	843.52	201	3492.57	916.19	201	-135.85 [-308.02 , 36.32]
Roberts 1997	2348.62	1555.5	82	3220.14	3220.14	83	-871.52 [-1641.76 , -101.28]



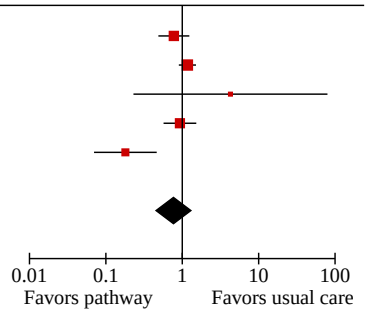
Analysis 1.7. Comparison 1: Stand-alone clinical pathway versus usual care, Outcome 7: Adherence to recommended practice

Study or Subgroup	log[OR]	SE	Usual care Total	CPW Total	Odds Ratio IV, Random, 95% CI
1.7.1 RCT					
Panella 2012	2.9253	0.4227	139	229	18.64 [8.14 , 42.68]
Seys 2019	0.6366	0.6027	24	29	1.89 [0.58 , 6.16]
Sulch 2002	3.288	1.0399	76	76	26.79 [3.49 , 205.65]
1.7.2 NRCT					
Doherty 2006a	1.302	0.1932	42	47	3.68 [2.52 , 5.37]



Analysis 1.8. Comparison 1: Stand-alone clinical pathway versus usual care, Outcome 8: Sensitivity analysis: Risk of bias inhospital mortality (studies at high RoB excluded)

Study or Subgroup	log[OR]	SE	CPW Total	Usual Care Total	Weight	Odds Ratio IV, Random, 95% CI
Brook 1999	-0.2536	0.2379	162	159	25.9%	0.78 [0.49 , 1.24]
Doig 2008	0.1549	0.1319	561	557	30.2%	1.17 [0.90 , 1.51]
Gooch 2012	1.4524	1.4917	1066	504	2.9%	4.27 [0.23 , 79.53]
Kollef 1997	-0.0706	0.2517	179	178	25.3%	0.93 [0.57 , 1.53]
Panella 2009	-1.7148	0.4819	214	215	15.8%	0.18 [0.07 , 0.46]
Total (Wald[a])			**2182**	**1613**	**100.0%**	**0.77 [0.45 , 1.29]**



Test for overall effect: Z = 0.99 (P = 0.32)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL[b]) = 0.22; Chi² = 16.08, df = 4 (P = 0.003); I² = 75%

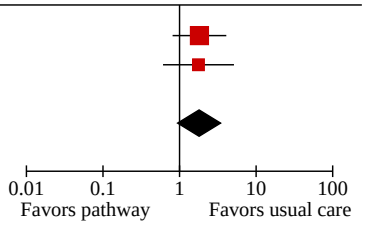
Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Analysis 1.9. Comparison 1: Stand-alone clinical pathway versus usual care, Outcome 9: Sensitivity analysis: Risk of bias 6 months mortality (studies at high RoB excluded)

Study or Subgroup	log[OR]	SE	CPW Total	Usual care Total	Weight	Odds Ratio IV, Random, 95% CI
Panella 2018	0.5983	0.4121	229	133	63.6%	1.82 [0.81 , 4.08]
Sulch 2002	0.5697	0.5442	76	76	36.4%	1.77 [0.61 , 5.14]
Total (Wald[a])			**305**	**209**	**100.0%**	**1.80 [0.95 , 3.43]**

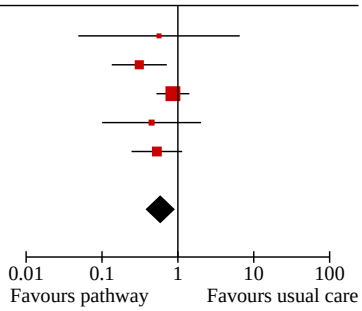


Test for overall effect: Z = 1.79 (P = 0.07)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL[b]) = 0.00; Chi² = 0.00, df = 1 (P = 0.97); I² = 0%

Footnotes
[a]CI calculated by Wald-type method.
[b]Tau² calculated by DerSimonian and Laird method.

Analysis 1.10. Comparison 1: Stand-alone clinical pathway versus usual care, Outcome 10: Sensitivity analysis: Risk of bias inhospital complications (studies at high RoB excluded)

Study or Subgroup	log[OR]	SE	CPW Total	Usual care Total	Weight	Odds Ratio IV, Random, 95% CI
Aizawa 2002	-0.5718	1.2493	32	37	2.8%	0.56 [0.05 , 6.53]
Dowsey 1999	-1.1712	0.4265	92	71	20.7%	0.31 [0.13 , 0.72]
Gooch 2012	-0.1508	0.2546	1066	504	45.5%	0.86 [0.52 , 1.42]
Kiyama 2003a	-0.7985	0.7657	47	38	7.2%	0.45 [0.10 , 2.02]
Marelich 2000	-0.6373	0.3925	166	169	23.8%	0.53 [0.24 , 1.14]
Total (Wald[a])			**1403**	**819**	**100.0%**	**0.58 [0.39 , 0.88]**

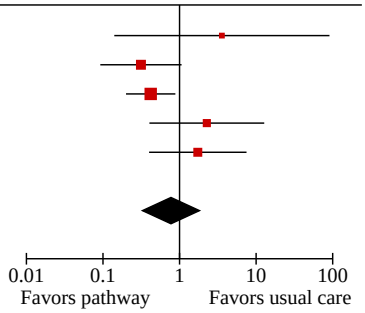


Test for overall effect: Z = 2.54 (P = 0.01)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL[b]) = 0.03; Chi² = 4.63, df = 4 (P = 0.33); I² = 14%

Footnotes
[a]CI calculated by Wald-type method.
[b]Tau² calculated by DerSimonian and Laird method.

Analysis 1.11. Comparison 1: Stand-alone clinical pathway versus usual care, Outcome 11: Sensitivity analysis: Risk of bias hospital readmission (up to 6 months; studies at high RoB excluded)

Study or Subgroup	log[OR]	SE	CPW Total	Usual care Total	Weight	Odds Ratio IV, Random, 95% CI
Aizawa 2002	1.273	1.6508	32	37	6.1%	3.57 [0.14 , 90.79]
Dowsey 1999	-1.1611	0.6234	92	71	23.8%	0.31 [0.09 , 1.06]
Panella 2009	-0.8675	0.3785	214	215	34.4%	0.42 [0.20 , 0.88]
Panella 2018	0.8202	0.8809	178	118	16.1%	2.27 [0.40 , 12.77]
Roberts 1997	0.549	0.7475	82	83	19.7%	1.73 [0.40 , 7.49]
Total (Wald[a])			**598**	**524**	**100.0%**	**0.77 [0.33 , 1.82]**

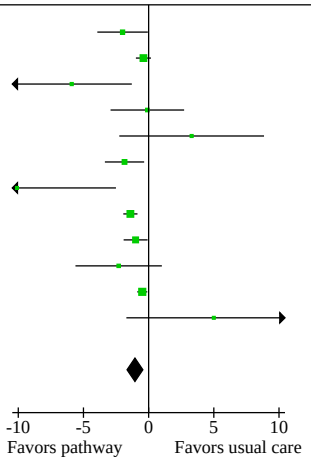


Test for overall effect: Z = 0.59 (P = 0.55)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL[b]) = 0.41; Chi² = 7.44, df = 4 (P = 0.11); I² = 46%

Footnotes
[a]CI calculated by Wald-type method.
[b]Tau² calculated by DerSimonian and Laird method.

Analysis 1.12. Comparison 1: Stand-alone clinical pathway versus usual care, Outcome 12: Sensitivity analysis: Risk of bias length of hospital stay in days (studies at high RoB excluded)

Study or Subgroup	CPW Mean	CPW SD	CPW Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Random, 95% CI
Aizawa 2002	12.7	2.8	32	14.7	5.2	37	6.8%	-2.00 [-3.94 , -0.06]
Bernard 2011	2.7	2	87	3.1	1.9	89	18.6%	-0.40 [-0.98 , 0.18]
Brook 1999	14	17.3	162	19.9	24.2	159	1.6%	-5.90 [-10.51 , -1.29]
Doig 2008	24.2	23.6593	540	24.3	23.5932	537	3.8%	-0.10 [-2.92 , 2.72]
Falconer 1993	35.6	15.5	53	32.3	15.4	68	1.1%	3.30 [-2.25 , 8.85]
Kim 2002	0.25	0.15	9	2.1	2.3	9	9.4%	-1.85 [-3.36 , -0.34]
Kiyama 2003a	18.1	9.5	47	28.2	22.3	38	0.6%	-10.10 [-17.69 , -2.51]
Marrie 2000	8.2	1.9	87	9.6	2.1	124	19.0%	-1.40 [-1.94 , -0.86]
Panella 2009	10.4	4.697	201	11.4	4.697	201	14.8%	-1.00 [-1.92 , -0.08]
Panella 2018	12.35	18.167	283	14.65	18.167	195	2.9%	-2.30 [-5.61 , 1.01]
Roberts 1997	1.38	1.18	82	1.87	1.33	83	20.5%	-0.49 [-0.87 , -0.11]
Sulch 2002	50	19	76	45	23	76	0.8%	5.00 [-1.71 , 11.71]
Total (Wald[a])			**1659**			**1616**	**100.0%**	**-1.05 [-1.66 , -0.44]**



Test for overall effect: Z = 3.40 (P = 0.0007)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL[b]) = 0.43; Chi² = 29.01, df = 11 (P = 0.002); I² = 62%

Footnotes
[a]CI calculated by Wald-type method.
[b]Tau² calculated by DerSimonian and Laird method.

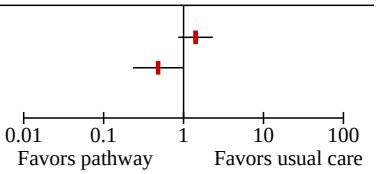
Comparison 2. Multifaceted intervention (including clinical pathway) versus usual care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Inhospital mortality	2		Odds Ratio (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.2 Mortality (up to 6 months)	3	6531	Odds Ratio (IV, Random, 95% CI)	1.05 [0.88, 1.25]
2.3 Hospital readmission (up to 6 months)	2		Odds Ratio (IV, Random, 95% CI)	Totals not selected
2.4 Length of hospital stay (days)	4		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.5 Hospital cost and charges	4		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.5.1 Hospital cost and charges	4		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.5.2 Hospital charges	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.5.3 Hospital costs	3		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.6 Sensitivity analysis: Risk of bias 6-month mortality (studies at high risk of bias excluded)	2	1731	Odds Ratio (IV, Random, 95% CI)	1.07 [0.85, 1.35]

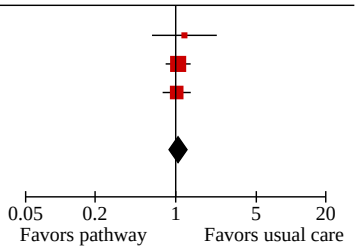
Analysis 2.1. Comparison 2: Multifaceted intervention (including clinical pathway) versus usual care, Outcome 1: Inhospital mortality

Study or Subgroup	log[OR]	SE	CPW Total	Usual care Total	Odds Ratio IV, Random, 95% CI
Philbin 2000	0.34359	0.254263	840	664	1.41 [0.86 , 2.32]
Wang 2018	-0.733969	0.36977	2400	2400	0.48 [0.23 , 0.99]



Analysis 2.2. Comparison 2: Multifaceted intervention (including clinical pathway) versus usual care, Outcome 2: Mortality (up to 6 months)

Study or Subgroup	log[OR]	SE	CPW Total	Usual care Total	Weight	Odds Ratio IV, Random, 95% CI
Cole 2002	0.173953	0.329955	113	114	7.7%	1.19 [0.62 , 2.27]
Philbin 2000	0.04879	0.127185	840	664	51.6%	1.05 [0.82 , 1.35]
Wang 2018	0.019803	0.143235	2400	2400	40.7%	1.02 [0.77 , 1.35]
Total (Wald[a])			**3353**	**3178**	**100.0%**	**1.05 [0.88 , 1.25]**

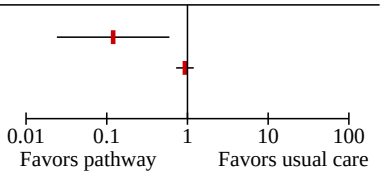


Test for overall effect: Z = 0.51 (P = 0.61)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL[b]) = 0.00; Chi² = 0.18, df = 2 (P = 0.91); I² = 0%

Footnotes
[a]CI calculated by Wald-type method.
[b]Tau² calculated by DerSimonian and Laird method.

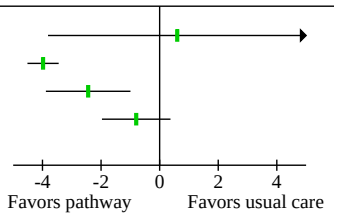
Analysis 2.3. Comparison 2: Multifaceted intervention (including clinical pathway) versus usual care, Outcome 3: Hospital readmission (up to 6 months)

Study or Subgroup	log[OR]	SE	CPW Total	Usual care Total	Odds Ratio IV, Random, 95% CI
Kampan 2006	-2.12026	0.819015	33	32	0.12 [0.02 , 0.60]
Philbin 2000	-0.07257	0.128108	840	664	0.93 [0.72 , 1.20]



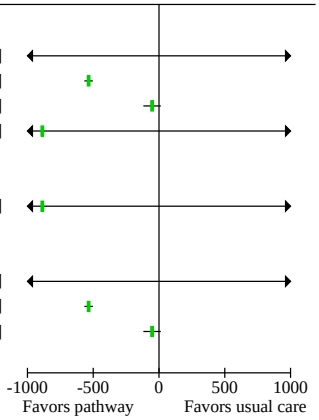
Analysis 2.4. Comparison 2: Multifaceted intervention (including clinical pathway) versus usual care, Outcome 4: Length of hospital stay (days)

Study or Subgroup	CPW Mean	CPW SD	CPW Total	Usual care Mean	Usual care SD	Usual care Total	Mean Difference IV, Random, 95% CI
Cole 2002	19.7	17.1	113	19.1	16.8	114	0.60 [-3.81 , 5.01]
Ju 2019	5.15	1.9	70	9.13	1.25	70	-3.98 [-4.51 , -3.45]
Kampan 2006	3.94	1.03	33	6.38	4.04	32	-2.44 [-3.88 , -1.00]
Philbin 2000	6.2	11.49	840	7	11.49	664	-0.80 [-1.97 , 0.37]



Analysis 2.5. Comparison 2: Multifaceted intervention (including clinical pathway) versus usual care, Outcome 5: Hospital cost and charges

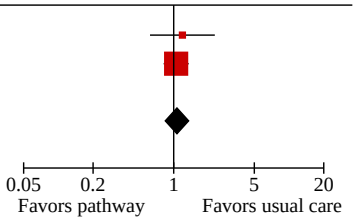
Study or Subgroup	CPW Mean	CPW SD	CPW Total	Usual care Mean	Usual care SD	Usual care Total	Mean Difference IV, Random, 95% CI
2.5.1 Hospital cost and charges							
Bauer 2006	37143.14	49956.98	157	40459.33	49956.98	149	-3316.19 [-14514.75 , 7882.37]
Ju 2019	760.31	84.77	70	1295.41	107.43	70	-535.10 [-567.16 , -503.04]
Kampan 2006	153.07	82.18	33	205.7	173.56	32	-52.63 [-118.98 , 13.72]
Philbin 2000	-509.2	18593.15	840	377.83	18593.15	664	-887.03 [-2779.38 , 1005.32]
2.5.2 Hospital charges							
Philbin 2000	-509.2	18593.15	840	377.83	18593.15	664	-887.03 [-2779.38 , 1005.32]
2.5.3 Hospital costs							
Bauer 2006	37143.14	49956.98	157	40459.33	49956.98	149	-3316.19 [-14514.75 , 7882.37]
Ju 2019	760.31	84.77	70	1295.41	107.43	70	-535.10 [-567.16 , -503.04]
Kampan 2006	153.07	82.18	33	205.7	173.56	32	-52.63 [-118.98 , 13.72]



Analysis 2.6. Comparison 2: Multifaceted intervention (including clinical pathway) versus usual care, Outcome 6: Sensitivity analysis: Risk of bias 6-month mortality (studies at high risk of bias excluded)

Study or Subgroup	log[OR]	SE	CPW Total	Usual care Total	Weight	Odds Ratio IV, Random, 95% CI
Cole 2002	0.173953	0.329955	113	114	12.9%	1.19 [0.62 , 2.27]
Philbin 2000	0.04879	0.127185	840	664	87.1%	1.05 [0.82 , 1.35]
Total (Wald[a])			**953**	**778**	**100.0%**	**1.07 [0.85 , 1.35]**

Test for overall effect: Z = 0.55 (P = 0.58)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL[b]) = 0.00; Chi² = 0.13, df = 1 (P = 0.72); I² = 0%



Footnotes

[a]CI calculated by Wald-type method.
[b]Tau² calculated by DerSimonian and Laird method.

ADDITIONAL TABLES

Table 1. Costing method and cost/charges for included studies

Study ID	Costs measure	Country	Costing method	Costs/charges included	Costs/charges excluded
Comparison 1: single CPW intervention versus usual care					
Aizawa 2002	Insurance data (points)	Japan	Hospital charges: including direct & indirect costs	Dosage, injection, treatment, operation and anesthesia, examination, diagnostic, room, medical care	Not reported

Table 1. Costing method and cost/charges for included studies *(Continued)*

Deng 2014 (TIA)	Hospital costs in US$	China	Remains unclear due to poor reporting. The authors only referred to hospitalization costs and drug costs. No information provided on the use of direct and indirect costs for calculating cost estimates. Also, it remains unclear what price-year the authors have used, and they did not provide information on how they have translated their cost data into US dollars (e.g. deflator used).	Drug costs for hospital stay are direct cost. How the hospitalization cost has been estimated (e.g. including direct and indirect cost) remains unclear.	Not reported
Deng 2014 (ICH)	Hospital costs in US$	China	Remains unclear due to poor reporting. The authors only referred to hospitalization costs and drug costs. No information provided on the use of direct and indirect costs for calculating cost estimates. Also, it remains unclear what price year the authors have used, and they did not provide information on how they have translated their cost data into US dollars (e.g. deflator used).	Drug costs for hospital stay are direct cost. How the hospitalization cost has been estimated (e.g. including direct and indirect cost) remains unclear.	Not reported
Falconer 1993	Hospital charges to proxy costs of rehabilitation	USA	Hospital charges	Charges for hospital bed-days, medical and rehabilitation services (including professional fees), equipment, drugs and procedures (radiographs, laboratory tests, injections)	Not reported
Gomez 1996	Hospital charges	USA	Hospital charges	Room, nursing care, laboratory, therapeutics and tests	Physician fees
Homagk 2016	Hospital costs	Germany	Direct & indirect costs	Medical staff, employees, material costs for drugs, implants, medical infrastructure, and overhead costs	Not reported
Ju 2019	Hospital costs (Yuan)	China	Not reported	Not reported	Not reported
Johnson 2000	Hospital charges	USA	Hospital charges	Room, medication, laboratory tests and respiratory therapy	Physician fees
Kim 2002	Hospital costs	USA	Direct costs	Remains unclear; only "total direct costs" reported	Professional fees

Table 1. Costing method and cost/charges for included studies *(Continued)*

Kiyama 2003a	Hospital costs	Japan	Direct costs	Total medical costs including medication and examination (physician fees)	Fixed costs
Kollef 1997	Hospital costs	USA	Not reported	Not reported	Physician fees
Li 2018	Hospitalization costs	China	Not reported. Costing method reported as 'total and average daily hospitalization costs'	Not reported	Not reported
Roberts 1997	Hospital costs	USA	Direct & indirect costs	Professional fees	Not reported
Rutman 2017	Hospital costs	USA	Cost of care for ED discharges and hospital admissions. Remains unclear if direct and indirect costs have been used in the cost estimates	Remains unclear if direct and indirect costs have been used in the cost estimates	The investigators excluded cost outliers (left skewed cost outcomes) by assigning the 99th percentile value (from the cost data distribution) for the outlier value.
Usui 2004	Insurance data (points)	Japan	Hospital charges: including direct costs	Treatment (antibiotic infusion), laboratory and radiography tests	Fixed costs
Panella 2009	Hospital charges	Italy	Activity-based costing	Cost of hospital care (admission)	Not reported
Comparison 2: Multifaceted intervention including a CPW versus usual care					
Bauer 2006	Hospital costs	USA	Direct costs	Not reported	Not reported
Kampan 2006	Hospital costs	Thailand	Remains unclear; only "mean costs" reported	Not reported	Not reported
Philbin 2000	Hospital charges	USA	Hospital charges	Not reported	Professional fees

Abbreviations:
CPW: clinical pathway
ED: Emergency Department
USA: United States of America

Table 2. Cost/charges data, standardized to the year 2016 (CCEMG EPPI tool used)

Study ID	Cost/charges measure	Price year used	Deflator used	Exchange rates	Target currency	Experimental	E-N (SD)	Control	C-N (SD)
Comparison 1: single CPW intervention versus usual care									
Aizawa 2002	Hospital charges (insurance points)	2000	None	Insurance points	None	48,424	32 (4438)	55366	37 (168)
Deng 2014 (TIA)	Hospitalization costs for TIA	2013	GDPD values (IMF)*	PPP values*	US $ year 2016	1569.64	213 (788.97)	1805.82	213 (880.53)
Deng 2014 (TIA)	Drug costs for TIA	2013	GDPD values (IMF)*	PPP values*	US $ year 2016	655.68	213 (389.06)	764.16	213 (377.13)
Deng 2014 (ICH)	Hospitalization costs for ICH	2013	GDPD values (IMF)*	PPP values*	US $ year 2016	2002.56	166 (1110.63)	2305.68	166 (723.12)
Deng 2014 (ICH)	Drug costs for ICH	2013	GDPD values (IMF)*	PPP values*	US $ year 2016	1110.63	166 (348.83)	1346.62	166 (402.09)
Falconer 1993	(median) Hospital charges bed-days	median (87-91)	GDPD values (IMF)*	PPP values*	US $ year 2016	24,924.02	53 (SD not reported)	24,889.50	68 (SD not reported)
Falconer 1993	(median) Hospital charges services	median (87-91)	GDPD values (IMF)*	PPP values*	US $ year 2016	19,416.23	53 (SD not reported)	16,533.74	68 (SD not reported)
Falconer 1993	(median) Hospital charges drugs	median (87-91)	GDPD values (IMF)*	PPP values*	US $ year 2016	1950.43	53 (SD not reported)	1751.93	68 (SD not reported)
Falconer 1993	(median) Hospital charges; other charges	median (87-91)	GDPD values (IMF)*	PPP values*	US $ year 2016	4137.32	53 (SD not reported)	3229.42	68 (SD not reported)
Gomez 1996	Hospital charges initial stay	1994	GDPD values (IMF)*	PPP values*	US $ year 2016	1924.79	50 (2523.74)	8606.61	50 (22,074.10)
Gomez 1996	Hospital charges at 30 days	1994	GDPD values (IMF)*	PPP values*	US $ year 2016	2143.00	50 (2611.03)	8818.80	50 (22,028.95)
Homagk 2016	Total hospitalization costs	2013	GDPD values (IMF)*	PPP values*	US $ year 2016	16215.21	17 (SD not reported)	28655.91	15 (SD not reported)
Johnson 2000	Hospital room charges	1997	GDPD values (IMF)*	PPP values*	US $ year 2016	3425.12	55 (1563.86)	4434.02	55 (1563.86)

Table 2. Cost/charges data, standardized to the year 2016 (CCEMG EPPI tool used) *(Continued)*

Johnson 2000	Hospital medication charges	1997	GDPD values (IMF)*	PPP values*	US $ year 2016	183.56	55 (152.26)	217.72	55 (152.26)
Johnson 2000	Hospital lab tests charges	1997	GDPD values (IMF)*	PPP values*	US $ year 2016	29.88	55 (93.92)	59.77	55 (93.92)
Johnson 2000	Hospital charges respiratory therapy	1997	GDPD values (IMF)*	PPP values*	US $ year 2016	59.77	55 (458.20)	355.75	55 (458.20)
Kim 2002	Direct hospital costs (excluding professional fees)	2000	GDPD values (IMF)*	PPP values*	US $ year 2016	1180.39	9 (534.57)	2314.65	9 (2051.44)
Kiyama 2003a	Direct variable mean hospital costs (including medication and professional fees)	2001	GDPD values (IMF)*	PPP values*	US $ year 2016	13380.86	47 (2515.63)	17,206.63	38 (7001.15)
Kiyama 2003a	Direct costs medication	2001	GDPD values (IMF)*	PPP values*	US $ year 2016	1695.01	47 (1004.15)	2410.03	38 (1573.04)
Kiyama 2003a	Direct daily costs	2001	GDPD values (IMF)*	PPP values*	US $ year 2016	519.91	47 (76.36)	495.58	38 (138.68)
Kollef 1997	Hospital costs (poor reporting: seems to be direct costs)	1995	GDPD values (IMF)*	PPP values*	US $ year 2016	40,800.54	179 (39,537.31)	40,445.30	178 (38,137.01)
Li 2018	Total hospitalization costs	2013	GDPD values (IMF)*	PPP values*	US $ year 2016	5730.05	62 (287.34)	8039.14	56 (303.99)
Li 2018	Average daily hospitalization costs	2013	GDPD values (IMF)*	PPP values*	US $ year 2016	517.41	62 (29.15)	625.68	56 (31.23)
Panella 2009	Hospital charges	2004	GDPD values (IMF)*	PPP values*	US $ year 2016	3356.72	214 (843.52)	3492.57	215 (916.19)
Roberts 1997	Direct and indirect hospital costs (doctors & nurses fees included)	1993	GDPD values (IMF)*	PPP values*	US $ year 2016	2348.62	82 (1555.50)	3220.14	83 (3220.14)
Usui 2004	Hospital charges (insurance points)	2002/2003	None	Insurance points	None	2338	30 (12,291)	34048	31 (12,291)
Usui 2004	Hospital charges antibiotic infusion	2002/2003	None	Insurance points	None	3285	30 (2027)	3928	31 (2027)

Table 2. Cost/charges data, standardized to the year 2016 (CCEMG EPPI tool used) *(Continued)*

Usui 2004	Hospital charges laboratory costs	2002/2003	None	Insurance points	None	3220	30 (3097)	5785	31 (3097)
Usui 2004	Hospital charges radiology costs	2002/2003	None	Insurance points	None	1438	30 (1194)	2471	31 (1194)
Comparison 2: Multifaceted intervention including a CPW versus usual care									
Bauer 2006	3-year mean intervention costs (direct costs)	2004	GDPD values (IMF)*	PPP values*	US $ year 2016	76,717.81	157 (78,880.72)	80442.62	149 (72,619.39)
Bauer 2006	Direct costs (direct variable costs)	2004	GDPD values (IMF)*	PPP values*	US $ year 2016	25,914.97	157 (19,773.60)	25,104.03	149 (19,773.60)
Bauer 2006	Hospital inpatient costs (direct costs)	2004	GDPD values (IMF)*	PPP values*	US $ year 2016	50,802.84	157 (68,328.55)	55,338.58	149 (68,328.55)
Bauer 2006	Psychiatric inpatient costs (direct costs)	2004	GDPD values (IMF)*	PPP values*	US $ year 2016	34,271.74	157 (51,779.96)	38,316.42	149 (51,779.96)
Bauer 2006	Medical surgical inpatient costs (direct costs)	2004	GDPD values (IMF)*	PPP values*	US $ year 2016	16,531.10	157 (28,798)	13523	149 (28,798)
Ju 2019	Hospitalization costs. Remains unclear which costs are included	2019 (Estimate:. Neither study period nor price year reported	GDP values (IMF)*	PPP values	US $ year 2016	760.31	70 (84.77)	1295.41	70 (107.43)
Kampan 2006	Hospital costs (poor reporting: seems to be direct and indirect hospital costs	2005	GDPD values (IMF)*	PPP values*	US $ year 2016	293.37	33 (157.48)	394.19	32 (332.61)
Philbin 2000	Hospital charges	1995	GDPD values (IMF)*	PPP values*	US $ year 2016	-691.31	840 (25,242.39)	512.95	664 (25,242.39)

Abbreviations:
CCEMG: Campbell and Cochrane Economics Methods Group
CPW: Clinical Pathway
C -N: number of participants in control group
E-N: number of participants in experimental group

EPPI: Evidence for Policy and Practice Information and Coordinating Centre
GDPD: gross domestic product deflator index
ICH: intracerebral hemorrhage
IMF: International Monetary Fund
PPP: purchasing power parity
SD: standard deviation
TIA: transient ischemic attack

Table 3. Original reported costs/charges data

Study ID	Country	Price year/ study period	Cost/charges measure	Original currency	Pathway	E-N (SD)	Usual care	C-N (SD)
(Comparison 1: single CPW intervention versus usual care								
Aizawa 2002	Japan	2000	Hospital charges (insurance points)	insurance points	48,424	32 (4438)	55,366	37 (16805)
Deng 2014 (TIA)	China	2013	Hospitalization costs for TIA	US $	1507.72	213 (757.85)	1734.58	213 (845.79)
Deng 2014 (TIA)	China	2013	Drug costs for TIA	US $	629.81	213 (373.71)	734.01	213 (362.25)
Deng 2014 (ICH)	China	2013	Hospitalization costs for ICH	US $	1923.56	166 (1066.82)	2214.72	166 (694.59)
Deng 2014 (ICH)	China	2013	Drug costs for ICH	US $	1066.82	166 (335.07)	1293.50	166 (386.23)
Falconer 1993	USA	89	(median) Hospital charges bed-days	US $	14,440	53 (SD not reported)	14,420	68 (SD not reported)
Falconer 1993	USA	89	(median) Hospital charges services	US $	11,249	53 (SD not reported)	9579	68 (SD not reported)
Falconer 1993	USA	89	(median) Hospital charges drugs	US $	1130	53 (SD not reported)	1015	68 (SD not reported)
Falconer 1993	USA	89	(median) Hospital charges; other charges	US $	2397	53 (SD not reported)	1871	68 (SD not reported))
Gomez 1996	USA	1994	Hospital charges initial stay	US $	1297	50 (1677)	5719	50 (14668)

Table 3. Original reported costs/charges data *(Continued)*

Gomez 1996	USA	1994	Hospital charges at 30 days	US $	1424	50 (1735)	5860	50 (14638)
Homagk 2016	Germany	2013	Total hospitalization costs (unclear if mean or median values have been reported)	EUR €	12076	17 (SD not reported)	21341	15 (SD not reported)
Johnson 2000	USA	97	Hospital room charges	US $	2407	55 (1099)	3116	55 (1099)
Johnson 2000	USA	97	Hospital medication charges	US $	129	55 (107)	153	55 (107)
Johnson 2000	USA	97	Hospital lab tests charges	US $	21	55 (66)	42	55 (66)
Johnson 2000	USA	97	Hospital charges respiratory therapy	US $	42	55 (322)	250	55 (322)
Kim 2002	USA	2000	Direct mean hospital costs (excluding professional fees)	US $	870	9 (394)	1706	9 (1512)
Kiyama 2003a	Japan	2001	Direct mean hospital costs (including medication and professional fees)	Jen	1,502,587	47 (282,489)	1,932,197	38 (786185)
Kiyama 2003a	Japan	2001	direct mean costs medication	Jen	190,339	47 (112,760)	270,631	38 (176643)
Kiyama 2003a	Japan	2001	Direct mean daily costs	Jen	58,383	47 (8575)	55651	38 (15573)
Kollef 1997	USA	1995	Hospital costs (poor reporting: seems to be direct costs	US $	27680	179 (26,823)	27,439	178 (25873)
Li 2018	China	2013	Total hospitalization costs	US $	5504	62 (276)	77,220	56 (292)
Li 2018	China	2013	Average daily hospitalization costs	US $	517.41	62 (28)	601	56 (30)
Panella 2009	Italy	2004	Cost of hospital care (admission)	EUR €	2125	214 (534)	2211	215 (580)
Roberts 1997	USA	1993	direct and indirect hospital costs (doctors & nurses fees included)	US $	1528	82 (1012)	2095	83 (2095)
Usui 2004	Japan	2002/2003	Hospital charges (insurance points)	insurance points	24,338	30 (12,291)	34,048	31 (12291)
Usui 2004	Japan	2002/ 2003	hospital charges antibiotic infusion	insurance points	3285	30 (2027)	3928	31 (2027)

Table 3. Original reported costs/charges data *(Continued)*

Usui 2004	Japan	2002/2003	Hospital charges laboratory costs	insurance points	3220	30 (3097)	5785	31 (3097)
Usui 2004	Japan	2002/2003	Hospital charges radiology costs	insurance points	1438	30 (1194)	2471	31 (1194)
Comparison 2: Multifaceted intervention including a CPW versus usual care								
Bauer 2006	USA	2004	3 years mean intervention costs (direct costs)	US $	61,398	157 (63,129)	64,379	149 (58118)
Bauer 2006	USA	2004	direct outpatient costs (direct costs)	US $	20,740	157 (15,825)	20,091	149 (15825)
Bauer 2006	USA	2004	hospital inpatient costs (direct variable costs)	US $	40,658	157 (54,684)	44,288	149 (54684)
Bauer 2006	USA	2004	psychiatric inpatient costs (direct costs)	US $	27,428	157 (41,440)	30,665	149 (41440)
Bauer 2006	USA	2004	medical surgical inpatient costs (direct costs)	US $	13,230	157 (28,798)	13,523	149 (28798)
Ju 2019	China	2019	hospitalization cost	Yuan	2832.66	70 (315.83)	4826.29	70 (400.25)
Kampan 2006	Thailand	2005	hospital costs (poor reporting: seems to be direct and indirect hospital costs	BAHT	2744	33 (1473)	3687	32 (3111)
Philbin 2000	USA	1995	hospital charges	US $	-469	840 (17,125)	348	664 (17125)

Abbreviations:
C-N: number of participants in control group
E-N: number of participants in experimental group
EUR: Euro
ICH: intracerebral hemorrhage
ID: identification
SD: standard deviation
TIA: transient ischemic attack
USA: United States of America

Table 4. Primary study characteristics for included studies

Study ID	CPW condition/Procedure	Type of ward	Sample size	Study type	Country	Overall risk of bias
Comparison 1: single CPW intervention versus usual care						
Aizawa 2002	TURP	Surgical/urology unit	69	P-RCT	Japan	Unclear risk
Almalki 2017	Acute kidney injury	Medical unit/ nephrology	38	P-RCT	Saudi Arabia	High risk
Bartlett 2017	Pediatric asthma care	Pediatric ward	297	ITS	USA	High risk
Bernard 2011	Type 2 diabetes mellitus	Emergency Department	176	P-RCT	USA	Unclear risk
Bittinger 1995	Heart failure	ICCU and Medical unit	30	P-CRT	USA	High risk
Brennan 2018	Pediatric asthma care	PICU	246	ITS	USA	High risk
Brook 1999	Mechanical ventilation	Medical ICU	321	P-RCT	USA	Low risk
Chadha 2000	Menorrhagia and urinary incontinence	Gynecological unit	946	CBA	UK	High risk
Choong 2000	Femoral neck fracture	Orthopedic unit	111	NRCT	AUS	Unclear risk
Costantini 2014	End-of-life care	End-of-life ward	308	C-RCT	Italy	High risk
Cunningham 2008	Asthma	Emergency Department	251	C-RCT	UK	High risk
Delaney 2003	Laparotomy and intestinal resection	Rehabilitation	64	P-RCT	USA	High risk
Deng 2014 (TIA)	Transient ischemic attack	Stroke care unit	426	P-RCT	China	High risk
Deng 2014 (ICH)	Intracerebral hemorrhage	Stroke care unit	332	P-RCT	China	High risk
Doherty 2006a	Asthma care	Medical units of the hospitals	187	CBA	AUS	High risk
Dowsey 1999	Hip and knee arthroplasty	Orthopedic unit	163	P-RCT	AUS	Unclear risk
Doig 2008	Malnutrition	ICU	1118	C-RCT	AUS/NZ	Low risk
Fakhr-Movahedi 2015	Anxiety & depression in coronary artery disease	Coronary care unit	138	CCT	Iran	High risk
Falconer 1993	Stroke rehabilitation	Stroke rehabilitation	121	P-RCT	USA	Unclear risk

Table 4. Primary study characteristics for included studies *(Continued)*

Gomez 1996	Suspected MI	Coronary Care unit/ chest pain evaluation unit	100	P-RCT	USA	High risk
Gooch 2012	Primary hip and knee replacement	Surgical unit	1570	P-RCT	Canada	Low risk
Homagk 2016	Spondylodiscitis	Not reported	32	RCT	Germany	High risk
Jalil 2017	Acute lower respiratory infection	Medical unit/respiratory medicine	60	P-RCT	Chile	High risk
Johnson 2000	Asthmatic children	Emergency and pediatric wards	110	P-RCT	USA	High risk
Kaiser 2020	Asthmatic children (2-17 years)	Pediatrics	12,013	ITS	USA	Unclear Risk
Kim 2002	Atrial fibrillation	Emergency Department	18	P-RCT	USA	Unclear risk
Kinsman 2012	MI	Emergency Department	115	C-RCT	AUS	Low risk
Kiyama 2003a	Gastrectomy	Surgical ward	85	P-RCT	Japan	Unclear risk
Kollef 1997	Mechanical ventilation	Medical & Surgical ICU	357	P-RCT	USA	Low risk
Li 2018	Acute MI	Acute MI unit	118	P-RCT	China	High risk
Marelich 2000	Mechanical ventilation	Medical ICU	253	P-RCT	USA	Low risk
Marrie 2000	Pneumonia	Emergency Department	1743	C-RCT	Canada	Unclear risk
Muehling 2008						High risk
Panella 2009	Heart failure	Medical unit	429	C-RCT	Italy	Unclear risk
Panella 2012	Acute ischemic stroke	Stroke units	476	C-RCT	Italy	High risk
Panella 2018	Proximal femoral fracture	General hospital	514	C-RCT	Belgium, Italy, Portugal	Low risk
Phillips 2017	Children with status asthmaticus	PICU	254	ITS	USA	High risk
Roberts 1997	CPW chest pain/possible MI	Emergency/telemetry observational units	165	P-RCT	USA	Unclear risk
Rotter 2014	Radical laparoscopic prostatectomy	Surgical ward	254	ITS	Germany	Low risk

Table 4. Primary study characteristics for included studies *(Continued)*

Rutman 2017	Community-acquired pneumonia	ED and inpatient	632	ITS	USA	High risk
Seys 2019	COPD exacerbation or PFF	General hospitals	984	C-RCT	Belgium, Italy, Portugal	High risk
Smith 2004	CPW COPD	Medical Unit	1230	CBA	AUS	High risk
Smith 2019	Pediatric asthma care	Pediatric inpatient unit	129	ITS	USA	High risk
Sulch 2002	Stroke rehabilitation	Stroke rehabilitation	152	P-RCT	UK	Unclear risk
Tilden 1987	Identification of battered woman	Emergency Department	892	ITS	USA	High risk
Trombetti 2013	Malnutrition	Medical Unit	694	P-RCT	Switzerland	Unclear risk
Usui 2004	Pneumonia	Medical Unit/respiratory medicine	61	NRCT	Japan	High risk
Vanhaecht 2016	COPD exacerbation	General hospitals	342	C-RCT	Belgium, Italy and Portugal	High risk
Comparison 2: Multifaceted intervention including a CPW versus usual care						
Bauer 2006	Bipolar disorder	Mental health clinic	306	P-RCT	USA	Low risk
Bookbinder 2005	Palliative care	Palliative care	267	CBA	USA	High risk
Brattebø 2002	Mechanical ventilation	Surgical ICU	285	ITS	Norway	Low risk
Chen 2004	Asthmatic children	Pediatric unit	42	P-RCT	Taiwan	Unclear risk
Cole 2002	Care of delirium in older medical patients	Medical Unit	227	P-RCT	Canada	Low risk
Ju 2019	Cirrhosis and gastrointestinal hemorrhage	Not reported	140	P-RCT	China	Unclear risk
Kampan 2006	Diabetic patients admitted with hypoglycemia	Medical Unit	65	P-RCT	Thailand	Unclear risk
Philbin 2000	Patients with heart failure	Medical Unit	2906	C-RCT	USA	Unclear risk
Wang 2018	Acute ischemic stroke	Emergency departments, neurological wards	4800	C-RCT	China	High risk

Abbreviations and definitions:

Acute: General acute hospital
AUS: Australia
CBA: controlled before-after study
CCT: controlled clinical trial
COPD: chronic obstructive pulmonary disease
CPW: clinical pathway
C-RCT: cluster-randomized clinical trial
DVT: deep vein thrombosis
ED: Emergency department
Extended care: rehabilitation or palliative facilities
ICU: Intensive care unit
ICCU: intensive coronary care unit
ITS: interrupted time series
MI: myocardial infarction
Other: psychiatric or mental health clinic/hospital
NRCT: non-randomized controlled trial
NZ: New Zealand
PFF: peak flow flow rate
PICU: pediatric intensive care unit
P-RCT: patient-randomized clinical trial
TURP: transurethral resection of the prostate
UK: United Kingdom
USA: United States of America

Table 5. Dichotomous primary study results post-intervention measures

Study ID	Dichotomous outcome post-intervention	E-events	E-N	%	C-events	C-N	%
Comparison 1: single CPW intervention versus usual care							
Aizawa 2002	Inhospital complications	1	32	3%	2	37	5%
Aizawa 2002	Rehospitalization within 6 months	1	32	3%	0	37	0%
Almalki 2017	Inhospital mortality	0	18	0.0%	0	20	0.0%
Almalki 2017	30-day readmission rates	3	18	16.7%	2	20	10.0%
Almalki 2017	Hospital complications	0	18	0.0%	0	20	0.0%
Brook 1999	Inhospital mortality	49	162	30%	57	159	36%
Choong 2000	Inhospital complications	10	55	18%	14	56	25%
Choong 2000	Readmission rates (28 days)	2	55	4%	6	56	11%
Delaney 2003	Hospital readmissions within 30 days	3	31	10%	6	33	18%
Delaney 2003	Inhospital complications	7	31	23%	10	33	30%
Deng 2014 (TIA)	Incidence of a stroke within 90 days	35	213	16.4%	28	213	13.1%
Dowsey 1999	Hospital readmission at 3-month follow-up	4	92	4%	9	71	13%
Dowsey 1999	Complications for up to 3 months	10	92	11%	20	71	28%
Gomez 1996	Rehospitalization within 30 days	3	50	6%	3	50	6%
Gooch 2012	Inpatient mortality within 30 days post-surgery	4	1066	0.4%	0	504	0.0%
Gooch 2012	Hip dislocation within 30 days post-surgery	5	451	1.1%	0	226	0.0%
Gooch 2012	Aggregate measures of inhospital complications within 30 days post-surgery	46	1066	4%	25	504	5%
Kiyama 2003a	Morbidity rate in hospital	3	47	6%	5	38	13%

Table 5. Dichotomous primary study results post-intervention measures *(Continued)*

Kiyama 2003a	Inhospital complications until discharge	3	47	6%	5	38	13%
Kollef 1997	Hospital mortality	40	179	22%	42	178	24%
Li 2018	Postoperative complications; changes in psychological status	4	62	6.5%	9	56	16.1%
Li 2018	Postoperative complications; abdominal pain and bleeding	3	62	4.8%	11	56	19.6%
Li 2018	Postoperative complications; subcutaneous HMRG	3	62	4.8%	9	56	16.1%
Marelich 2000	Rate of ventilator-assisted pneumonia (medical ICU)	6	82	7%	8	88	9%
Marelich 2000	Rate of ventilator-assisted pneumonia (surgical ICU)	5	84	6%	12	81	15%
Marelich 2000	Rate of ventilator-assisted pneumonia (combined ICUs)	11	166	7%	20	169	12%
Panella 2012	Inhospital mortality 30 days from admission to hospital	18	238	7.6%	25	238	10.5%
Panella 2012	Inhospital mortality 7 days from admission to hospital	7	238	2.9%	16	238	6.7%
Panella 2012	Inhospital mortality 30 days from stroke attack	18	238	7.6%	25	238	10.5%
Panella 2012	Pressure sore incidence rate	4	229	1.7%	12	219	5.5%
Panella 2012	Inhospital complication rate	53	229	23.1%	67	219	30.6%
Panella 2012	Post-discharge complication rate	12	103	11.7%	0	27	0.0%
Panella 2012	Inhospital readmission rates (30 days)	0	211	0.0%	0	194	0.0%
Panella 2018	6-month mortality	27	229	11.8%	9	133	6.8%
Panella 2018	30-day mortality	16	234	6.8%	3	145	2.1%

Table 5. Dichotomous primary study results post-intervention measures *(Continued)*

Panella 2018	30-day readmission	13	206	6.3%	4	139	2.9%
Panella 2018	6-month readmission	21	178	11.8%	5	118	4.2%
Roberts 1997	Hospital admission rate	37	82	45%	83	83	100%
Roberts 1997	Rehospitalization after 8 weeks	5	82	6%	4	83	5%
Smith 2004	Hospital mortality	49	334	15%	30	175	17%
Sulch 2002	Mortality at 26 weeks	10	76	13%	6	76	8%
Vanhaecht 2016	6-month readmission	38	139	27.34%	38	115	33.04%
Vanhaecht 2016	30-day readmission	15	155	9.68%	22	144	15.28%
Vanhaecht 2016	6-month mortality	18	157	11.46%	18	134	13.43%
Vanhaecht 2016	30-day mortality	3	168	1.79%	2	153	1.31%
Comparison 2: Multifaceted intervention including a CPW versus usual care							
Cole 2002	Mortality at 8 weeks	25	113	22%	22	114	19%
Ju 2019	Inhospital complications	6	70	8.57%	16	70	22.86%
Kampan 2006	Readmissions with hypoglycemia within 3 months	2	33	6%	11	32	34%
Philbin 2000	Inhospital mortality	44	840	5%	25	664	4%
Philbin 2000	Heart failure mortality (6 months)	105	840	13%	84	664	13%
Philbin 2000	All-cause mortality (6 months)	183	840	22%	139	664	21%
Philbin 2000	Readmission for heart failure (6 months)	169	840	20%	141	664	21%
Philbin 2000	Readmission - all causes (6 months)	363	840	43%	293	664	44%
Trombetti 2013	Inhospital mortality	28	465	6%	20.6	229	9%
Wang 2018	New vascular events at 3 months	93	2400	3.9%	127	2400	5.3%

Table 5. Dichotomous primary study results post-intervention measures *(Continued)*

Wang 2018	Disability at 3 months	418	2180	19.2%	443	2105	21.0%
Wang 2018	Death in hospital	11	2400	0.5%	23	2400	1.0%
Wang 2018	Death at 3 months	66	2400	2.8%	76	2400	3.2%
Wang 2018	Death at 6 months	103	2400	4.3%	101	2400	4.2%

Abbreviations:
ACE: angiotensin-converting enzyme
C: control
C -N: number of participants in control group
CPW: clinical pathway
E: experimental
E-N: number of participants in experimental group
GP: general practitioner
HMRG: hemorrhage
ICU: intensive care unit
QOL: quality of life

Table 6. Continuous primary study results post-intervention measures

Study ID	Outcome	E-mean	E-SD	E-N	C-mean	C-SD	C-N	P value as far as reported	95% CI as far as reported
Comparison 1: single CPW intervention versus usual care									
Aizawa 2002	LOS (days)	12.70	2.80	32.00	14.70	5.20	37.00		
Almalki 2017	Median LOS days	4.96	IQR 6.57	18	4.80	IQR 6.57	20	0.77	
Bernard 2011	ED Length of stay (days)	0.23	0.1	87.00	0.2	0.1	89.0	0.06	
Bernard 2011	Hospital length of stay (days)	2.7	2.0	87.0	3.1	1.9	89.0	0.58	
Bernard 2011	Number of ED patients admitted	60 (69%)		87	61 (69%)		89.0		
Brook 1999	Duration of mechanical ventilation (in hours)	89.10	133.60	162.00	124.00	153.60	159.00		

Table 6. Continuous primary study results post-intervention measures *(Continued)*

Brook 1999	LOS ICU stay (days)	5.70	5.90	162.00	7.50	6.50	159.00		
Brook 1999	LOS hospital stay (days)	14.00	17.30	162.00	19.90	24.20	159.00		
Brook 1999	Number of acquired organ system derangements (surrogate measure for in-hospital complications)	2.84	1.40	162.00	2.90	1.50	159.00		
Choong 2000	LOS (days)	6.60	3.35	55.00	8.00	3.35	56.00	0.0300	
Choong 2000	Days to mobilization (days)	1.60	1.44	55.00	2.20	1.44	56.00	0.0300	
Cunningham 2008	Length of stay (days)	37.6		136	40.7		115	0.07	
Doig 2008	LOS in hospital (days)	24.2		561	24.3		557	0.97	
Doig 2008	LOS in ICU (days)	9.1		561	9.9		557	0.42	
Doig 2008	Invasive mechanical ventilation/10-patient days	7.69		561	7.21		557	0.70	
Doig 2008	Deaths at hospital discharge N(%)	172		561	153		557	0.75	
Delaney 2003	LOS days (primary LOS until discharge)	5.20	2.50	31.00	5.80	3.00	33.00		
Delaney 2003	Total LOS days including time spent in readmission	5.40	2.50	31.00	7.10	4.80	33.00		
Deng 2014 (TIA)	Length of stay in days	9.93	62.90	213	13.19	69.03	213	0.010	
Deng 2014 (ICH)	Length of stay in days	17.93	81.81	166	21.18	83.75	166	0.010	
Dowsey 1999	LOS (days)	7.10	3.67	92.00	8.60	3.67	71.00		(1.03-1.30)
Dowsey 1999	Days until sitting out of bed	1.94	2.80	92.00	3.42	2.80	71.00	0.0010	(1.05-1.95)
Dowsey 1999	Days until ambulation	2.19	3.83	92.00	3.61	3.83	71.00	0.0200	(0.94-1.98)
Falconer 1993	LOS (days)	35.60	15.50	53.00	32.30	15.40	68.00		
Gomez 1996	LOS (days)	0.64	0.51	53.00	2.28	5.25	68.00		

Table 6. Continuous primary study results post-intervention measures *(Continued)*

Gomez 1996	LOS (hours)	15.40	12.20	50.00	54.6	126.00	50.00	
Homagk 2016	Duration of hospital stay	17.2		17	26.0		15	
Jalil 2017	Duration of hospital stay	187.4	77.9	24	207.5	244.1	23	0.700
Jalil 2017	Duration of non-invasive ventilation (NIV) in hours	90.7	43.8	24	96.1	50.4	23	0.690
Johnson 2000	LOS (days)	1.68	1.12	50.00	2.24	1.12	50.00	
Johnson 2000	LOS (hours)	40.30	26.80	55.00	53.7	26.80	55.00	0.0100
Kim 2002	LOS (days)	0.25	0.15	9.00	2.1	2.30	9.00	
Kiyama 2003a	LOS (days) preoperative hospital stay	9.00	3.20	47.00	12.6	6.00	38.00	0.0010
Kiyama 2003a	LOS (days) postoperative hospital stay	18.10	9.50	47.00	28.2	22.30	38.00	0.0100
Kollef 1997	Duration of mechanical ventilation (in hours) following commencement of weaning	69.40	123.70	179.00	102	169.10	178.00	0.2900
Li 2018	Length of hospital stay (days)	10.52	5.3	62	14.52	5.85	56	0.001
Marrie 2000	LOS (unadjusted days) for cluster effects	8.20	1.90	716.00	9.60	2.10	1027.00	
Marelich 2000	Duration of mechanical ventilation (medical ICU), median values reported	3.25	11.32	82.00	9.67	11.32	88.00	0.0003
Marelich 2000	Duration of mechanical ventilation (combined ICUs), median values reported	2.83	5.42	166.00	5.17	5.42	169.00	0.0001
Panella 2009	Death (inhospital mortality)	5.6		214	15.4		215	0.001
Panella 2009	Rate of unscheduled readmissions	7.9		214	13.9		215	0.053
Panella 2009	LOS (days)	10.4		214	11.4		215	0.028
Panella 2009	Cost of admission (Euros)	2125		214	2211		215	0.11

Table 6. Continuous primary study results post-intervention measures *(Continued)*

Panella 2012	Hospital LOS (days)	11.78	6.6	229	10.88	7.9	219	0.190	
Panella 2018	Hospital LOS (days)	12.35	7.82	301	14.65	6.94	213	0.158	
Roberts 1997	LOS (days)	1.38	1.18	82.00	1.87	1.33	83.00		
Roberts 1997	LOS (hours)	33.10	28.40	82.00	44.8	31.80	83.00		
Rotter 2014	LOS (days)	9.16	0.9	123	9.11	1	131	0.91	
Rotter 2014	Duration of operation (min)	241.99	14.5	123	272.86	28.2	131	0.038	
Rotter 2014	Duration of anesthesia (min)	323.51	17.89	123	354.06	30.58	131	0.061	
Sulch 2002	LOS (days)	50.00	19.00	76.00	45	23.00	76.00		
Trombetti 2013	LOS (days)	38	34	465	37	32	229	0.613	
Usui 2004	LOS (days)	8.03	4.18	30.00	10.77	4.18	31.00	0.0130	
Vanhaecht 2016	LOS	12		174	12.8		168	0.960	
Comparison 2: Multifaceted intervention including a CPW versus usual care									
Cole 2002	LOS days	19.70	17.10	113.00	19.10	16.80	114.00		
Ju 2019	LOS days	5.15	1.9	70	9.13	1.25	70	< 0.001	
Kampan 2006	LOS (days)	3.94	1.03	33.00	6.38	4.04	32.00		
Philbin 2000	LOS (days) all hospitals pooled	-1.80	17.69	840.00	-0.70	17.69	664.00		(-2.9 - 0.7)

Abbreviations:
ADR: adverse drug reaction
C: control
C-mean: mean of outcome in the control group
C -N: number of participants in control group
C-SD: standard deviation in the control group
E: experimental
ED: emergency department
E-mean: mean of outcome in the experimental group
E-N: number of participants in experimental group

E-SD: standard deviation in the experimental group
ICU: intensive care unit
IQR: interquartile range
LOS: length of stay
N (%): total sample size (percentage)
NIV: non-invasive ventilation
QOL: Quality of life
SF-36: 36-item Short Form Survey

Table 7. ITS studies data

Study ID	Outcome measures reported	Baseline		Post-intervention		Time-interval between measures	Outcome results
		N	Number of time points	N	Number of time points		
Bartlett 2017	LOS (days) in means	160	13	137	21	One month	Decrease in LOS from 2.9 days baseline to 2.3 days after implementation of the CPW (P < 0.01)
Brattebø 2002	Ventilation patient days per month	147	11	138	11	One month	No change in number of ventilation days (P = 0.834)
Brennan 2018	Variability in PICU LOS (high, standard –st- or low LOS)	141	22	105	22	Two weeks	No trend in a decrease in variability (P value not available)..
Brennan 2018	Mean PICU LOS (hours)	141	22	105	22	Two weeks	Reduction in mean PICU LOS in hours (16 versus 13 hr; P = 0.0009)
Brennan 2018	Mean hospital LOS (hours)	141	22	105	22	Two weeks	Reduction in median hospital LOS in hours (37 versus 31hr; p = 0.02).
Brennan 2018	Mean duration of continuous nebulized albuterol (hours)	141	22	105	22	Two weeks	Decrease in median duration of continuous nebulized albuterol in hours (10.8 versus 7.3 hr; P = 0.0008)
Kaiser 2020	Length of stay (LOS) in hours	300	15	240	10	One month	No statistically significant reduction of LOS for CPW hospitals (36 hours v 33 hours; 95% CI: 0.94 to 1.06)
Kaiser 2020	% early administration of bronchodilator (1. ordered at admission, 2. ordered at 1-hour	300	15	240	10	One month	Pathway implementation was associated with statistically significant increases in the odds of early administration of

Table 7. ITS studies data *(Continued)*

	frequency, 3. ordered at 3-hour frequency)						bronchodilator via MDI (OR 3.94; 95% CI: 2.85 to 5.44)
Kaiser 2020	% documented screening for second-hand tobacco smoke exposure	300	15	240	10	One month	Screening for secondhand tobacco smoke exposure was not associated with pathway implementation (OR 1.28; 95% CI: 0.95 to 1.73)
Kaiser 2020	% documented referral of caregivers to smoking cessation resources	300	15	240	10	One month	Pathway implementation was associated with statistically significant increases in the odds of caretaker referral to smoking cessation resources (OR: 2.22; 95% CI: 1.38 to 3.57)
Kaiser 2020	% 7-day readmission	300	15	240	10	One month	Percentage (%) 7-day readmission was not significantly associated with pathway implementation (OR 1.08; 95% CI: 0.95 to 1.22)
Kaiser 2020	% 7-day ED re-presentation	300	15	240	10	One month	Percentage (%) 7-day ED representation was not significantly associated with pathway implementation (OR 1.06; 95% CI: 0.38 to 1.95)
Phillips 2017	Inhaled bronchodilator therapy transition time (hours)	130	12	124	13	One month	There was a 4.9-h decrease in the mean transition time from continuous to intermittent bronchodilator use (31.9 versus 27.0, P = 0.033) following the intervention.
Rotter 2014	LOS (days)	123	6	131	6	4-week	No significant difference in LOS (9 days before and after; P = 0.910)
Rotter 2014	Duration of operation (min)	123	6	131	6	4-week	Reduction in mean operation time of 30.6 min (P = 0.038) following CPW
Rotter 2014	Duration of anesthesia (min)	123	6	131	6	4-week	Non-significant reduction in mean anesthesia time of 30.5 (P = 0.061)
Rutman 2017	% of admitted patients receiving ampicillin as first-line therapy for CAP	113	12	113	12	One month	Increased use of ampicillin from 8% baseline to 54% (P < 0.05)

Table 7. ITS studies data *(Continued)*

Rutman 2017	% of admitted patients with blood cultures or viral testing	113	12	113	12	One month	Increased adherence to guideline recommended blood cultures from 35% baseline to 63% (P < 0.05), and increased respiratory viral testing from 52% baseline to 84% (P < 0.05)
Rutman 2017	Cost - admitted patients	113	12	113	12	One month	No significant change in cost (P[int] = 0.42; 95% CI: -3347 to 1462)
Rutman 2017	Cost - discharged from ED patients	232	12	232	12	One month	No significant change in cost –discharged from ED patients (P[int] = 0.22; 95% CI: -67 to 277)
Smith 2019	Mean hours hospital LOS	69	11	60	7	Two months	Non-significant decrease in hospital LOS of 12.4 hours from baseline to post-intervention (P = 0.239)
Smith 2019	Mean hours to 4-hourly albuterol administration	69	11	60	7	Two months	Significant decrease in the time (10.2 hours) to administer the correct dose of albuterol (P < 0.0001)
Tilden 1987	Patients identified by nurses as battered (in %)	447	4	445	4	4 weeks	Increased documentation of female victims of domestic violence (P = 0.03)

Abbreviations:
CAP: community-acquired pneumonia
CI: confidence interval
CPW: clinical pathway
ED: emergency department
P (int): P-value for difference between pre- and post-pathway intercepts
LOS: length of stay
MDI: metered dose inhaler
OR: odds ratio
PICU: pediatric intensive care unit

Table 8. Dichotomous adherence to recommended practice post-intervention measures

Study ID	Dichotomous adherence measures post-intervention	Experimental events	E-N	%	Control events	C-N	%

Table 8. Dichotomous adherence to recommended practice post-intervention measures *(Continued)*

Comparison 1: single CPW intervention versus usual care

Almalki 2017	Physician medication reconciliation	18	18	100.0%	20	20	100.0%
Almalki 2017	Pharmacist medication reconciliation	7	18	38.9%	5	20	25.0%
Chadha 2000	Appropriate use of hospital investigations (menorrhagia)	217	472	46%	233	416	56%
Chadha 2000	Appropriate use of hospital investigations (urinary incontinence)	179	416	43%	179	472	38%
Chadha 2000	Inappropriate use of hospital investigations (menorrhagia)	99	472	21%	75	416	18%
Doherty 2006a	Aggregate measures	155	250	62%	71	231	31%
Doherty 2006a	Assessment of severity of asthma	29	47	62%	6	42	14%
Doherty 2006a	Use of spirometry	29	47	62%	3	42	7%
Kinsman 2012	Number of eligible participants receiving thrombolytic drugs	25	32	78%	21	25	84%
Kinsman 2012	Number of eligible participants receiving thrombolytic drug within 30 mins	12	32	37%	15	25	62%
Kinsman 2012	Number of eligible participants having ECG within 10 minutes	23	32	72%	20	25	83%
Kiyama 2003a	Target achievements day 1	41	47	87%	21	38	54%
Kiyama 2003a	Target achievements day 4	46	47	98%	30	38	78%
Kiyama 2003a	Target achievements day 7	43	47	91%	26	38	68%
Panella 2012	Information, advice, and support from the multidisciplinary team given to the patients (and with their consent, to the caregivers)	204	204	100.0%	115	133	86.5%
Panella 2012	Use of clinical protocols	221	229	96.5%	83	139	59.7%

Table 8. Dichotomous adherence to recommended practice post-intervention measures *(Continued)*

Panella 2012	Use of CT/MRI brain scan within 48 hours of admission	223	229	97.4%	209	219	95.4%
Panella 2018	Performance of adequate analgesia preoperatively	263	301	87.4%	185	213	86.9%
Panella 2018	Assessment of pre-fracture mobility status	267	301	88.7%	71	213	33.3%
Panella 2018	Performance of X-ray of affected hip	230	301	76.4%	136	213	63.8%
Seys 2019	Use of guidelines	22	29	75.86%	15	24	62.50%
Sulch 2002	Process of care (nutritional assessment)	49	66	74%	14	64	22%
Sulch 2002	Process of care (documentation of goals)	75	76	99%	56	76	74%
Sulch 2002	Process of care (documented death/follow-up)	68	76	89%	53	76	70%
Vanhaecht 2016	Performance of ABG measurement during first 24 hours of admission	136	174	78.16%	126	168	75.00%
Vanhaecht 2016	Performance of chest X-ray during first 24 hours of admission	160	174	91.95%	143	168	85.12%
Vanhaecht 2016	Performance of electrocardiogram during first 24 hours of admission	134	174	77.01%	121	168	72.02%
Comparison 2: Multifaceted intervention including a CPW versus usual care							
Philbin 2000	Process of care - evaluation	638	840	76%	485	664	73%
Philbin 2000	Process of care - documentation	529	840	63%	511	664	77%
Philbin 2000	ACE inhibitor use at discharge	529	840	63%	438	664	66%
Wang 2018	All-or-nothing performance measure (proportion of patients who received all the performance measures for which the patient was eligible)	1290	2400	53.8%	1147	2400	47.8%
Wang 2018	Dysphagia screening (beginning of hospitalization)	2255	2328	96.9%	2040	2139	95.4%

Table 8. Dichotomous adherence to recommended practice post-intervention measures *(Continued)*

Wang 2018	Antithrombotics (at discharge)	2272	2324	97.8%	2141	2305	92.9%

Abbreviations:
ABG: arterial blood gas
ACE: angiotensin-converting enzyme
C: control
C-N: number of participants in control group
CPW: clinical pathway
CT: computed tomography
E: experimental
ECG: electrocardiogram
E-N: number of participants in experimental group
MRI: magnetic resonance imaging

Table 9. Continuous adherence to recommended practice post-intervention measures

STUDY ID	Outcome measure	E-Mean	E-SD	E-N	C-Mean	C-SD	C-N	P value as far as reported	95% CI as far as reported
Comparison 1: single CPW intervention versus usual care									
Bernard 2011	Number of patients treated with insulin	100		87.00	54		89.0		
Chadha 2000	Compliance with five recommendations for initial hospital assessment (urinary incontinence)	3.80	1.52	416.00	3.10	1.52	472.00		(0.5 to 0.9)
Costantini 2014	Coordination of care	81.4		115	76.8		110	0.04	
Fakhr-Movahedi 2015	PSI patient education (7 items)	3.7	0.56	69	3.45	0.64	69	0.019	
Jalil 2017	Supplemental oxygen duration post NIV in hour	34.6	40.4	24	39.6	44.4	23	0.680	
Li 2018	Door to balloon time (minutes)	75.354	5.606	62	88.30	6.157	56	0.001	
Panella 2018	Preoperative management	70.54	22.85	301	56.42	22.67	213	0.036	

Table 9. Continuous adherence to recommended practice post-intervention measures *(Continued)*

Panella 2018	Perioperative management	60.24	26.58	301	52.9	21.19	213	0.216
Panella 2018	Postoperative management	36.69	14.72	301	34.28	12.65	213	0.762
Trombetti 2013	Proportion of nutrition counseling requests (%)	43		465	32		229	< 0.05
Trombetti 2013	Number of nutritional supplements prescribed (%)	38		465	30		229	< 0.05
Trombetti 2013	Proportion of patients receiving an enriched meal (%)	20		465	8		229	0.0001
Comparison 2: Multifaceted intervention including a CPW versus usual care								
Bookbinder 2005	Symptoms assessed during the last two days of life (possible scores from 0 to 12). Adjusted mean values	10.3		51	9.4		50	0.001
Bookbinder 2005	Symptoms assessed during the last two days of life (possible scores from 0 to 12). Unadjusted mean values	10.5		51	9.5		50	
Wang 2018	Composite performance measure (total number of eligible performance measures performed divided by the total number of performance measures for which a given patient was eligible)	88.2	15.1	2400	84.8	18.2	2400	0.020

Abbreviations:
C: control
CI: confidence interval
C-N baseline: number of participants in control group at baseline
E: experimental
E-N baseline: number of participants in experimental group at baseline
NIV: non-invasive ventilation
PSI: patient satisfaction instrument
SD: standard deviation

Table 10. Implementation strategies reported in included studies

Study ID	Clinician involvement in CPW development	Implementation team	Evidence-practice gap identification prior to implementation	Identification of potential barriers to change	Reminder systems	Audit and feedback	Education sessions	Local opinions leaders	Overall rating
Aizawa 2002	Y	Y	-	-	-	Y	-	N	Moderate
Almalki 2017	Y	-	-	-	-	-	-	-	Low
Bartlett 2017	Y	Y	Y	Y	Y	Y	Y	Y	High
Bauer 2006	Y	Y	Y	Y	Y	Y	Y	Y	High
Bernard 2011	Y	Y	Y	N	N	N	Y	N	Moderate
Bittinger 1995	Y	Y	-	N	N	N	Y	Y	Moderate
Bookbinder 2005	Y	Y	Y	Y	Y	Y	Y	-	High
Brattebø 2002	Y	Y	Y	Y	Y	Y	Y	-	High
Brennan 2018	Y	-	Y	-	-	-	-	-	Moderate
Brook 1999	Y	-	Y	-	-	-	-	-	Moderate
Chadha 2000	Y	Y	-	-	Y	N	Y	Y	High
Chen 2004	Y	Y	Y	Y	-	Y	Y	Y	High
Choong 2000	Y	-	-	-	-	-	-	-	Low
Cole 2002	Y	Y	Y	-	-	Y	Y	-	High
Costantini 2014	Y	Y	Y	N	N	N	Y	Y	High
Cunningham 2008	Y	-	Y	N	-	Y	Y	Y	High

Table 10. Implementation strategies reported in included studies *(Continued)*

Chen 2019	Y	Y	-	-	-	-	Y	-	Low
Delaney 2003	Y	Y	-	Y	-	Y	-	-	Moderate
Deng 2014 (TIA)	Y	-	-	-	-	Y	-	-	Moderate
Deng 2014 (ICH)	Y	-	-	-	-	Y	-	-	Moderate
Doherty 2006a	Y	Y	Y	Y	Y	N	-	-	High
Doig 2008	Y	Y	Y	N	Y	Y	Y	Y	High
Dowsey 1999	Y	-	-	-	Y	Y	-	Y	Moderate
Fakhr-Movahedi 2015	Y	-	-	-	-	-	-	-	Low
Falconer 1993	Y	Y	N	-	-	Y	Y	-	Moderate
Gomez 1996	Y	-	Y	-	-	-	-	-	Moderate
Gooch 2012	Y	Y	Y	-	Y	Y	-	Y	High
Homagk 2016	Y	-	-	-	-	-	-	-	Low
Jalil 2017	Y	-	-	-	-	-	-	Y	Moderate
Johnson 2000	Y	Y	-	-	N	N	Y	Y	Moderate
Ju 2019	Y	Y	-	-	-	-		-	Low
Kaiser 2020	Y	Y	Y	Y	Y	Y	Y	Y	High
Kampan 2006	-	Y	-	-	-	Y	-	-	Moderate
Kim 2002	-	-	Y	-	-	-	-	-	Low
Kinsman 2012	Y	Y	Y	N	Y	Y	Y	Y	High
Kiyama 2003a	-	-	Y	-	-	-	-	-	Low
Kollef 1997	N	-	-	-	Y	N	Y	Y	Moderate

Table 10. Implementation strategies reported in included studies *(Continued)*

Li 2018	Y	Y	-	-	-	Y	Y	Y	High
Marelich 2000	Y	Y	-	-	Y	-	-	-	Moderate
Marrie 2000	-	-	-	-	Y	-	-	-	Low
Muehling 2008	Y	-	-	-	-	-	-	-	Low
Panella 2009	Y	Y	Y	-	-	-	Y	Y	High
Panella 2012	Y	Y	-	-	-	Y	Y	Y	High
Panella 2018	Y	Y	Y	-	-	Y	Y	Y	High
Philbin 2000	Y	Y	-	-	-	Y	Y	-	Moderate
Phillips 2017	Y	Y	Y	-	Y	Y	Y	Y	High
Roberts 1997	Y	-	Y	-	-	-	-	-	Moderate
Rotter 2014	Y	N	Y	N	N	N	Y	Y	Moderate
Rutman 2017	Y	Y	-	-	Y	Y	Y	Y	High
Seys 2019	Y	Y	Y	-	-	Y	Y	Y	High
Smith 2004	Y	Y	Y	-	-	Y	Y	-	High
Smith 2019	Y	Y	-	-	Y	-	Y	-	Moderate
Sulch 2002	Y	-	Y	Y	-	-	Y	Y	High
Tilden 1987	-	Y	Y	-	Y	-	Y	-	Moderate
Trombetti 2013	-	-	-	N	N	N	N	N	Low
Usui 2004	Y	-	-	-	-	-	-	-	Low
Vanhaecht 2016	Y	Y	Y	-	-	Y	Y	Y	High
Wang 2018	Y	Y	Y	Y	-	Y	Y	Y	High

Abbreviations:
-: unclear
CPW: clinical pathway
N: no
Y: yes

APPENDICES

Appendix 1. Working definition for a clinical pathway

MINIMUM CRITERIA FOR A CLINICAL PATHWAY	
1. Is it a structured multidisciplinary care plan?	**YES** **NO** **Can't tell**
2. Is it used to channel the translation of guidelines or evidence into local structures?	**YES** **NO** **Can't tell**
3. Does it detail the 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)?	**YES** **NO** **Can't tell**
4. Does it aim to standardize care for a specific clinical problem, procedure or episode of care in a specific population?	**YES** **NO** **Can't tell**
Source of information for minimum criteria for a clinical pathway (CPW) (page numbers):	
Eligibility: **All 4 Criteria – must be "yes"** **Eligibility: EXCLUDE/CONTINUE**	

Appendix 2. Appendix: Search strategies

We searched MEDLINE using the following search strategy:

Medline (OVID)

2024 Update: 25/07/2024

Ovid MEDLINE(R) ALL <1946 to July 24, 2024>		
1	(clinical adj2 pathway?).ti.	2130
2	critical pathways/	8069

(Continued)

3	((clinical or critical) adj1 (pathway? or path?)).ti,ab.	9277
4	((care adj2 algorithm?) or clinical algorithm?).ti,ab.	2259
5	(care adj1 pathway?).ti,ab.	8232
6	(treatment adj3 algorithm?).ti,ab.	12396
7	(management protocol? or treatment protocol?).ti,ab.	30767
8	(care adj1 (plan? or map?)).ti,ab.	11445
9	(protocol? adj1 (nursing or directed or guided)).ti,ab.	971
10	((local or locally) adj2 adapt* adj5 guideline?).ti,ab.	136
11	(treatment model? adj10 standardi*).ti,ab.	23
12	(standardi* adj3 protocol?).ti,ab.	19267
13	systematic detection.ti,ab.	369
14	or/2-13	96687
15	clinical protocols/	30141
16	(treat* or therap*).ti,ab.	8729224
17	15 and 16	15078
18	practice guidelines as topic/	129094
19	(implement* or pathway or protocol?).ti,ab.	2265561
20	18 and 19	18803
21	(guideline? adj1 (implement* or pathway or protocol?)).ti,ab.	4009
22	or/20-21	21571
23	14 or 17 or 22	128984
24	(hospital or hospitals or hospitalis* or hospitaliz*).ti,ab.	1724631
25	exp hospital units/	140912
26	exp hospitals/	328428
27	exp hospital departments/	211984
28	hospitalization/	141577
29	or/24-28	2061057
30	1 or (23 and 29)	30785

(Continued)

31	randomized controlled trial.pt.	617446
32	controlled clinical trial.pt.	95575
33	multicenter study.pt.	350633
34	pragmatic clinical trial.pt.	2382
35	(randomis* or randomiz* or randomly).ti,ab.	1206388
36	groups.ab.	2709892
37	(trial or multicenter or multi center or multicentre or multi centre).ti.	382475
38	(intervention? or effect? or impact? or controlled or control group? or (before adj5 after) or (pre adj5 post) or ((pretest or pre test) and (posttest or post test)) or quasiexperiment* or quasi experiment* or pseudo experiment* or pseudoexperiment* or evaluat* or time series or time point? or repeated measur*).ti,ab.	12612119
39	non-randomized controlled trials as topic/	1108
40	interrupted time series analysis/	2137
41	controlled before-after studies/	758
42	or/31-41	13982120
43	exp animals/	27348618
44	humans/	22106965
45	43 not (43 and 44)	5241653
46	review.pt.	3355564
47	meta analysis.pt.	204907
48	news.pt.	225991
49	comment.pt.	1038854
50	editorial.pt.	699640
51	cochrane database of systematic reviews.jn.	16666
52	comment on.cm.	1038271
53	(systematic review or literature review).ti.	319477
54	or/45-53	10287981
55	42 not 54	10081568
56	30 and 55	18011

(Continued)

57	limit 56 to dt=20220430-20240725	2245

2. Embase (OVID)

2024 update 25/07/2024

Embase Classic+Embase <1947 to 2024 July 24>

1	(clinical adj2 pathway?).ti.	3263
2	*critical pathway/	3865
3	((clinical or critical) adj1 (pathway? or path?)).ti,ab.	14447
4	((care adj2 algorithm?) or clinical algorithm?).ti,ab.	3371
5	(care adj1 pathway?).ti,ab.	14080
6	(treatment adj3 algorithm?).ti,ab.	18819
7	(management protocol? or treatment protocol?).ti,ab.	45837
8	(care adj1 (plan? or map?)).ti,ab.	17746
9	(protocol? adj1 (nursing or directed or guided)).ti,ab.	1585
10	((local or locally) adj2 adapt* adj5 guideline?).ti,ab.	187
11	(treatment model? adj10 standardi*).ti,ab.	28
12	(standardi* adj3 protocol?).ti,ab.	29791
13	systematic detection.ti,ab.	496
14	or/2-13	143452
15	*clinical protocol/	12121
16	(treat* or therap*).ti,ab.	12527112
17	15 and 16	5169
18	*practice guideline/	102953
19	(implement* or pathway or protocol?).ti,ab.	3017680
20	18 and 19	17309

(Continued)

21	(guideline? adj1 (implement* or pathway or protocol?)).ti,ab.	5915
22	or/20-21	21692
23	14 or 17 or 22	167742
24	(hospital or hospitals or hospitalis* or hospitaliz*).ti,ab.	2792704
25	exp *"hospital subdivisions and components"/	201324
26	exp *hospital/	380021
27	*hospitalization/	51827
28	exp *hospital patient/	45170
29	or/24-28	2977424
30	1 or (23 and 29)	40603
31	randomized controlled trial/	838697
32	controlled clinical trial/	474005
33	quasi experimental study/	12816
34	pretest posttest control group design/	698
35	time series analysis/	42030
36	experimental design/	27828
37	multicenter study/	400383
38	(randomis* or randomiz* or randomly).ti,ab.	1710867
39	groups.ab.	3901366
40	(trial or multicentre or multicenter or multi centre or multi center).ti.	547220
41	(intervention? or effect? or impact? or controlled or control group? or (before adj5 after) or (pre adj5 post) or ((pretest or pre test) and (posttest or post test)) or quasiexperiment* or quasi experiment* or pseudo experiment* or pseudoexperiment* or evaluat* or time series or time point? or repeated measur*).ti,ab.	16876770
42	or/31-41	18761741
43	(systematic review or literature review).ti.	374613
44	cochrane database of systematic reviews.jn.	17742
45	exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/	36568690
46	human/ or normal human/ or human cell/	28359632

(Continued)

47	45 not (45 and 46)	8281823
48	43 or 44 or 47	8669624
49	42 not 48	14696595
50	30 and 49	27367
51	limit 50 to yr="2017 -Current"	14920
52	limit 51 to embase	6732
53	limit 52 to dc=20220405-20240725	2822

3. The Cochrane Library

2024 UPDATE: 25 Jul 2024	
Database	Issue/year (e.g. 3/2013)

Search Name:	
Date Run:	25/07/2024 18:28:37
Comment:	

ID	Search	Hits
#1	(clinical near/2 pathway?):ti	288
#2	[mh "critical pathways"]	326
#3	((clinical or critical) near/1 (pathway? or path?)):ti,ab	774
#4	((care near/2 algorithm?) or (clinical next algorithm?)):ti,ab	309
#5	(care near/1 pathway*):ti,ab	1076
#6	(treatment near/3 algorithm*):ti,ab	1338
#7	((management next protocol?) or (treatment next protocol?)):ti,ab	6722
#8	(care near/1 (plan? or map?)):ti,ab	1589
#9	(protocol? near/1 (nursing or directed or guided)):ti,ab	396
#10	((local or locally) near/2 adapt* near/5 guideline?):ti,ab	21

(Continued)

#11	((treatment next model?) near/10 standardi*):ti,ab	5
#12	(standardi* near/3 protocol?):ti,ab	2871
#13	(systematic next detection):ti,ab	19
#14	{or #2-#13}	14810
#15	[mh "clinical protocols"]	27849
#16	(treat* or therap*):ti,ab	1E+06
#17	#15 and #16	23604
#18	[mh "practice guidelines as topic"]	3186
#19	(implement* or pathway or protocol?):ti,ab	214945
#20	#18 and #19	849
#21	(guideline? near/1 (implement* or pathway or protocol?)):ti,ab	533
#22	#20 or #21	1275
#23	#14 or #17 or #22	39101
#24	[mh hospitals]	5895
#25	[mh "hospital departments"]	5437
#26	[mh "hospital units"]	6805
#27	[mh hospitalization]	20485
#28	(hospital or hospitals or hospitalis* or hospitaliz*):ti,ab	229878
#29	{or #24-#28}	241292
#30	#1 or (#23 and #29) with Publication Year from 2021, with Cochrane Library publication date Between Apr 2022 and Aug 2024, in Trials	288

4. Trials Registers

ClinicalTrials.gov								
	Date searched							
			30/8/2016	8/2/2017	3-4-2019	15-3-2021	4/1/2022	25/7/2024
No.	**Search terms**	**Results**	**Results**	**Results**	**Results**	**Results**	**Results**	**Results**
	"clinical pathway" OR "clinical algorithm" OR "treatment pathway"	104	122	134	67	162	329	265
WHO International Clinical Trials Registry Platform (ICTRP)								
	Date searched (if different to summary sheet):							
			30/8/2016	8/2/2017	3-4-2019	4/1/2022	25/7/2024	
No.	**Search terms**	**Results**	**Results**	**Results**	**Results**	**Results**	**Results**	
	clinical pathway	43	50	55	88	148	163	
	clinical algorithm	8	9	13	19	28	31	
	treatment pathway	10	11	14	24	37	43	
	TOTAL =	61	70	82	131	213	237	

Appendix 3. Grey Literature Searches

Keywords used for Advanced Google search, Web of Science (Science Citation Index), and Open Grey (Most recent date: Sept 29 2020)

1) hospital

2) “clinical path*” OR “guideline*” OR “care map*” OR “critical path*”

-first 45 hits

Title of article or source	Relevant (R) or Irrelevant (IR)
1. The association of in-hospital guideline adherence and longitudinal post-discharge mortality in older patients with non-ST-segment elevation myocardial infarction (Shah 2015)	
2. Potential benefits, limitations, and harms of clinical guidelines (Woolfe 1999)	
3. Hospital Stay Guideline for Hospitals and Disability Service Organisations Disability Health Network (Gov., Western Australia) https://ww2.health.wa.gov.au/-/media/Files/Corporate/general-documents/Health-Networks/Disability/PDF/160106-POL-Hospital-Stay-Guideline-FINAL-formatted.pdf	
4. Guideline for the Admission and Hospital Management of Pregnant Women/Individuals Who Are a Confirmed or Suspect Case of COVID-19 BC Centre for Disease Control http://www.bccdc.ca/Health-Professionals-Site/Documents/Pregnancy-COVID19-Hospital-Admission-Treatment.pdf	IR
5. COVID-19 rapid guideline: arranging planned care in hospitals and diagnostic services National Institute for Health and Care Excellence https://www.nice.org.uk/guidance/ng179	IR
6. Can Practice Guidelines Safely Reduce Hospital Length of Stay? Results from a Multicenter Interventional Study Weingarten 1998 https://www.amjmed.com/article/S0002-9343(98)00129-6/pdf	
7. Clinical Practice Guidelines The Hospital for Sick Children (Sick Kids), 2020 https://www.sickkids.ca/clinical-practice-guidelines/clinical-practice-guidelines/index.aspx	IR
8. Home to the Hospital to Home Transitions Guideline Alberta Health Services, 2020 https://together4health.albertahealthservices.ca/home-to-hospital-to-home?tool=brainstormer (Engagement Summary on right side)	IR

(Continued)

9. Home to Hospital to Home Transitions (webpage) Alberta Health Services, 2020 https://www.albertahealthservices.ca/info/Page17125.aspx	IR
10. Clinical pathway Wikipedia https://en.wikipedia.org/wiki/Clinical_pathway	IR
11. Critical Path Network: Hospital discharge process can be more efficient Relias Media, 2009 https://www.reliasmedia.com/articles/113414-critical-path-network-hospital-discharge-process-can-be-more-efficient	IR
12. The nursing work of hospital-based clinical practice guideline implementation: An explanatory systematic review using Normalisation Process Theory May, Sibley & Hunt, 2013 https://www.sciencedirect.com/science/article/pii/S0020748913002010	IR
13. Our Clinical Guidelines present statements of best practice based on thorough evaluation of evidence The Royal Women's Hospital, 2020 https://www.thewomens.org.au/health-professionals/clinical-resources/clinical-guidelines-gps	IR
14. CLINICIAN RESOURCES (webpage) Child Health BC, 2020 https://www.childhealthbc.ca/clinician-resources/resource-search	IR
15. 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings Siegel 2007 https://www.cdc.gov/infectioncontrol/pdf/guidelines/isolation-guidelines-H.pdf	IR
16. Addendum B: Hospital in the Home (HITH) Guideline Queensland Health, 2020 https://www.health.qld.gov.au/__data/assets/pdf_file/0026/960803/hith-addendum-guideline.pdf	IR
17. Policy Guideline -----Hospital in the Home Policy Guideline Department for Health and Ageing, Government of South Australia, 2017 https://www.sahealth.sa.gov.au/wps/wcm/connect /58f0a00041d3ff9ea33ef3fc48414beb/Guideline_ Hospital+in+the+Home_11072017.pdf?MOD= AJPERES&CACHEID=ROOTWORKSPACE-58f0a00041d3ff9ea33ef3fc48414beb-niQ9ahK	IR

(Continued)

18. Access to tools such as clinical practice guidelines, protocols, procedures, care paths, care plans, pre-printed orders and forms Fraser Health, 2018 https://www.fraserhealth.ca/employees/student-practice-education/student-placement-orientation/clinical-decision-support-tools#.X21vgy-96fU	IR
19. Home to hospital to home transitions guideline being developed Alberta College of Pharmacy, 2020 https://abpharmacy.ca/articles/home-hospital-home-transitions-guideline-being-developed	IR
20. Telepractice College of Nurses of Ontario (CNO), 2020 https://www.cno.org/globalassets/docs/prac/41041_telephone.pdf	IR
21. About Clinical Guidelines (nursing) The Royal Children's Hospital Melbourne, 2020 https://www.rch.org.au/rchcpg/	IR
22. Clinical Practice Guidelines The Royal Children's Hospital Melbourne, 2020 https://www.rch.org.au/clinicalguide/about_rch_cpgs/ Welcome_to_the_Clinical_Practice_Guidelines/	IR
23. Guideline for the management of COVID-19 patients during hospital admission in a non-intensive care setting Jeschke 2020 https://www.tandfonline.com/doi/full/10.1080/20018525.2020.1761677	IR
24. Home to hospital to home transitions guideline being developed Alberta College of Pharmacy, 2020 https://abpharmacy.ca/articles/home-hospital-home-transitions-guideline-being-developed	IR
25. Clinical Guideline Highlights (webpage) Journal of Hospital Medicine, 2020 https://www.journalofhospitalmedicine.com/jhospmed/clinical-guideline-highlights	IR
Sept 28 2020	
26. INTER-HOSPITAL TRANSFER GUIDELINE Trauma Victoria, 2014	IR
27. Choice of Birthplace Association of Ontario Midwives, 2020	IR

(Continued)

https://www.ontariomidwives.ca/cob	
28. BC Children's Hospital Emergency Department Guidelines Royal Columbian https://www.rchemerg.com/Clinical/Guidelines-Order-Sets/Pediatrics/BC-Children-s-Hospital-Emergency-Department-Guidelines	IR
29. Organizing Care and Relationships for Families: Care Map Boston Children's Hospital, 2020 http://www.childrenshospital.org/integrated-care-program/care-mapping	IR
Sept 29 2020	
30. CLINICAL GUIDELINE Recommendations for Major Trauma Management During the COVID-19 Pandemic Trauma Services, BC, 2020	IR
31. Clinical Standards Texas Children's Hospital, 2020 https://www.texaschildrens.org/departments/safety-outcomes/clinical-standards	IR
32. Guidelines and Measures Agency for Healthcare Research and Quality https://www.ahrq.gov/gam/index.html	IR
33. Medication Error Guideline Fadic 2020 https://fadic.net/medication-error-guideline/	IR
34. Overview of clinical practice guidelines Paul Shekelle 2020 https://www.uptodate.com/contents/overview-of-clinical-practice-guidelines	IR
35. Evidence Booster: Best Practice Guideline Implementation to Reduce Hospital-Acquired Pressure Injuries Registered Nurses Association, 2020 https://rnao.ca/bpg/resources/evidence-booster-best-practice-guideline-implementation-reduce-hospital-acquired-press	IR
36. New evidence-based clinical practice guideline timely supports hospital infection control of coronavirus disease 2019 Li 2020 https://academic.oup.com/pcm/article/3/1/1/5748339	
37. BC Guidelines	IR

(Continued)

Government of British Columbia https://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines	
38. Clinical guideline for homeless and vulnerably housed people, and people with lived homelessness experience Pottie 2020 https://www.cmaj.ca/content/192/10/E240	
39. Clinical Practice Guidelines: A Primer on Development and Dissemination Murad 2017 https://www.mayoclinicproceedings.org/article/S0025-6196(17)30025-3/pdf	IR
40. 2019 Provincial Guideline BC emergency health services, 2019 https://umbraco.bcas.ca/media/1829/2019-pre-hospitaltriage-transport-guidelines_july-26-2019.pdf	IR
41. Association between in-hospital guideline adherence and postdischarge major adverse outcomes of patients with acute coronary syndrome in Vietnam: a prospective cohort study Nguyen 2017 https://bmjopen.bmj.com/content/7/10/e017008.citation-tools	
42. BC Children's Hospital Emergency Department Guidelines Royal Columbia Hospital https://www.rchemerg.com/Clinical/Guidelines-Order-Sets/Pediatrics/BC-Children-s-Hospital-Emergency-Department-Guidelines	IR
43. GUIDELINE SUMMARIES Guideline Central https://www.guidelinecentral.com/summaries/	IR
44. Health Facility Briefing & Design International Health Facility Guidelines, 2016 http://healthfacilityguidelines.com/ViewPDF/ViewIndexPDF/iHFG_part_b_outpatients_unit	IR
45. Clinical standards Texas Children’s Hospital, 2020 https://www.texaschildrens.org/departments/safety-outcomes/clinical-standards	IR

Appendix 4. Handsearching

(Most recent date: Oct 28, 2020)

International Journal of Care Coordination. Volume 18 Issue 1 to Volume 23, Issue 1

Professional Case Management. Volume 20 Issue 1 to Volume 25 Issue 5

International Journal of Integrated Care. Volume 16 (January-March 2016) to Volume 20 (July-September 2020)

Pediatric Quality and Safety. Volume 1 Issue 1 to Volume 5 Issue 4

Journal of Clinical Pathways. Volume 1 Issue 1 to Volume 6 Issue 8

Guidelines in Practice. Volume 18 Issue 1 to Volume 23 Issue 10

Pediatric Safety and Quality. Volume 1 Issue 1 to Volume 5 Issue 5

Pediatrics. Volume 135 Issue 1 to Volume 146 Issue 5

Appendix 5. Data extraction sheet

Data Collection Form

Study ID number .....

STUDY STATUS

Pending

Included

Excluded

Did both reviewers agree on inclusion/exclusion?	**No**
Notes, including source(s) of disagreement	

Primary Author Email Address for correspondence: Email address

DATA EXTRACTION FORM:
Clinical Pathways: Effects on Professional Practice, Patient Outcomes,
Length of Stay and Hospital Costs
Name of Reviewer:

MINIMUM CRITERIA FOR A CLINICAL PATHWAY	
1. Is it a structured multidisciplinary care plan?	**YES** **NO** **Can't tell**
2. Is it used to channel the translation of guidelines or evidence into local structures?	**YES** **NO** **Can't tell**

(Continued)

3. Does it detail the 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)?	**YES** **NO** **Can't tell**
4. Does it aim to standardize care for a specific clinical problem, procedure or episode of care in a specific population?	**YES** **NO** **Can't tell**
Source of information for minimum criteria for a clinical pathway (CPW) (page numbers):	
Eligibility: **All 4 Criteria – must be "yes"** **Eligibility: EXCLUDE/CONTINUE**	

STUDY DESIGN	
Type of study (using EPOC criteria):	**RCTs**
RCT: participants randomly allocated; has a control group	**NRCTs**
NRCTs: participants quasi-randomly allocated; has a control group	**CBA**
CBA: participants non-randomly allocated; has a control group	**ITS**
ITS: no control group. Must have 3 data points before and after intervention	
Record specific method here (e.g. Multicenter, cross-over design)**:**	
For RCTs, NRCTs or CBA:	
Level of randomization/allocation?	**Individual level**
Was randomization at the level of individual participants (e.g. patients) or were groups randomly assigned (e.g. ward, hospital)?	**Cluster**
Level of analysis	**Individual level**
Were results analyzed as events per hospital?	**Cluster**
If CBA:	
Contemporaneous data collection?	**Done**
The timing of data collection pre- and post-intervention must be the same for both study and control sites. DONE = dates mentioned NOT CLEAR = dates not mentioned - STOP DATA EXTRACTION UNTIL CONFIRMED NOT DONE = STOP DATA EXTRACTION	**Not clear** **Not done**

(Continued)

Appropriate choice of control sites AND at least two control sites? Control and study sites need to be comparable on issues such as reimbursement system, level of care, setting, academic status. NOT CLEAR = can't tell if sites are comparable - STOP DATA EXTRACTION UNTIL CONFIRMED NOT DONE = STOP DATA EXTRACTION	**Done** **Not clear** **Not done**
If ITS:	
Clearly defined point in time when the intervention occurred? Intervention must have occurred at a clearly defined point in time. NOT CLEAR = not reported in paper STOP DATA EXTRACTION UNTIL CONFIRMED NOT DONE = STOP DATA EXTRACTION	**Done** **Not clear** **Not done**
At least three data points before and after the intervention? NOT CLEAR = e.g. number of discrete data points not mentioned in table or text - STOP DATA EXTRACTION UNTIL CONFIRMED NOT DONE = STOP DATA EXTRACTION	**Done** **Not clear** **Not done**
Source of information for study design (page numbers):	
Eligibility: If not the above design, or have selected NOT DONE, then EXCLUDE **Reason for exclusion: _____ or CONTINUE**	

SETTING & PARTICIPANTS	
Geographic location of the hospital Where was the hospital/s situated?	**Remote** **Rural** **Regional** **Urban** **Not clear**
Country Where was the study conducted? Not clear if information is not available	**Not clear** **Specify** _____
Description of health professionals targeted Which health professionals were expected to utilize the CPW? **Provide description here:** (page no.)	**Specialists/Surgeons** **Nurses** **Allied health** **Multidisciplinary** **Others (specify)**

(Continued)

	_____
	Not clear
Number of health professionals targeted How many health professionals were involved (include both intervention and control sites)	**n = not stated**
Demographic characteristics of health professionals Was a description of the healthcare professionals who were the target of the CPW provided?	**Gender (% male):** **Gender (% female):** **Age range:** **Not stated**
Section of hospital where intervention took place What specific ward or unit was the CPW introduced into?	**Medical** **Surgical** **Emergency** **Rehab** **Aged care** **Hospital-wide** **Other (specify)** _____ **Not clear**
Description of patients What were the characteristics of the patients?	**Outpatients** **Presenting to ED** **Hospitalized** **Other (specify)** _____
Inclusion criteria for patients Were the inclusion criteria for patients clearly stated and appropriate? **Inclusion criteria for cluster?** For cluster trials, were the inclusion criteria for clusters (e.g. hospitals, wards) clearly stated and appropriate?	**Done** **Not clear** **Not done** **Done** **Not clear** **Not done** **Not applicable**
Number of patients included How many patients were included in the study? How many in intervention and control groups?	**Number of groups** **Intervention** **Control**

(Continued)

	Number of participants	
	Intervention	**n =**
	Control	**n =**
	Total number of participants	**n =**
Characteristics of patients included. What were the demographic characteristics of thepatients who were recruited?	**Gender (% male):** **Gender (% female):** **Age range:** **Ethnicity:** **Not stated**	
Power calculation: Was a power calculation explicitly stated? **Record specific power calculation here:** (page no.) **For cluster trials, did power calculation allow for the effects of clustering?** e.g. do they mention intra-class correlation co-efficient?	**Done** **Not clear** **Not done** **Yes** **No** **Not applicable**	
ELIGIBILITY: If the setting is not a hospital or patients are not hospitalized, then EXCLUDE **Reason for exclusion:_____ or CONTINUE**		

CLINICAL PATHWAY CHARACTERISTICS	
Type of intervention: Was the CPW combined with any other type of intervention (e.g. electronic medical records, academic detailing) or was it a stand-alone intervention?	**CPW versus usual care** **Intervention including CPW versus intervention without CPW** **Intervention including CPW versus usual care** **Other (specify)** _____
Description of intervention: (page no.)	
Invasive or non-invasive intervention targeted? INVASIVE examples = CPW for gastrectomy; PTCA; laparoscopic cholecystectomy; hip and knee arthroplasty	**Invasive** **Non-invasive**

(Continued)

NON-INVASIVE examples = CPW for stroke; pneumonia; asthma

Specify intervention or diagnosis targeted:	
What was the purpose of the CPW? What did the authors state as the main reason the CPW was developed/introduced?	**Appropriate mgmt.** **Cost containment** **Other (specify)** _____ **Not clear**
Was there a multi-faceted implementation process? Was the process of development of the CPW described? **Short description of the collaborative process:** (page no.)	**Done** **Not clear** **Not done**
Was the content of the CPW evidence based? DONE = content of CPW based on a systematic review or ≥ one RCT or best practice guidelines NOT CLEAR = not stated NOT DONE = content clearly not evidence-based	**Done** **Not clear** **Not done**
What was the format of the CPW? Was the CPW paper-based and part of a hard copy medical record or was it electronic?	**Paper** **Electronic** **Other (specify)** _____ **Not clear**
Was the CPW adapted for local use? DONE = format of CPW adapted in collaboration with users/clinicians NOT CLEAR = not stated NOT DONE = no collaboration with users/clinicians on the format of CPW	**Done** **Not clear** **Not done**
Was there clinician involvement in the development of CPW? DONE = clearly stated that clinicians were involved in the content of CPW	**Done** **Not clear** **Not done**
Was there an implementation team?	**Done** **Not clear** **Not done**
Were evidence-practice gaps identified prior to the implementation of the CPW? DONE = gaps identified by local audit	**Done** **Not clear**

(Continued)

NOT CLEAR = anecdotal or evidence not local	**Not done**
NOT DONE = no audit or identifying of evidence-practice gaps	
Were barriers to change identified?	**Done**
DONE = barriers clearly stated	**Not clear**
NOT CLEAR = barriers may have been identified	**Not done**
NOT DONE = barriers to change not stated	
Were reminder systems incorporated into implementation?	**Done**
DONE = formal reminder system described e.g. posters, computer reminders	**Not clear**
NOT CLEAR = reminder system may have been used	**Not done**
NOT DONE = reminder system not described	
Was audit and feedback incorporated into implementation?	**Done**
DONE = audit and feedback process clearly stated	**Not clear**
NOT CLEAR = audit and feedback may have been used	**Not done**
NOT DONE = no description of audit and feedback provided	
Were education sessions used to implement CPW?	**Done**
DONE = education sessions attended by the majority of users/clinicians	**Not clear**
NOT CLEAR = education sessions may have been provided and may have been attended by users/clinicians	**Not done**
NOT DONE = no education sessions provided or attended by users/clinicians	
Were local opinion leaders used to implement CPW?	**Done**
DONE = clear identification and utilization of local opinion leaders	**Not clear**
NOT CLEAR = local opinion leaders may have been involved	**Not done**
NOT DONE = no evidence of utilization of local opinion leaders	
Evidence-based implementation strategy:	**A (high)**
A = 7-10 criteria checked as “Done”	**B (moderate)**
B = 2-6 criteria checked as “Done”	**C (low)**
C = 0-1 criteria checked as “Done”	
What was the source of funding for the study?	**Nil**
Who funded the study?	**Govt**
	Commercial
	Health service
	Voluntary body
	Charity

(Continued)

	Research **Other (specify)** **_____** **Not clear**

Eligibility: If intervention does not clearly include a CPW, then EXCLUDE

Reason for exclusion:_____ or CONTINUE

OUTCOME MEASURE(S):

NB: Primary outcomes are those that correspond to the primary hypothesis or question as defined by the authors. Other outcomes may be incorporated if they are relevant to patient outcomes and professional practice, and meet the EPOC quality criteria.

Main outcome measures (list):

1.

2.

3.

4.

5.

Other

Was compliance or adherence to CPW measured and reported?	**Yes (specify)** **_____** **No**
What was the length of post–intervention follow-up?	
Was there a possible ceiling effect? (i.e. little room for improved outcomes)	
Ceiling effect identified by the investigator:	**Yes (specify)** **_____** **No** **Not relevant**
Ceiling effect identified by the reviewer:	**Yes (specify)** **_____** **No** **Not relevant**
Were outcomes measured in a clinical (i.e. not test) situation?	**Done**

(Continued)

	Not clear
	Not done
Are the results relevant and interpretable?	**Done**
	Not clear
	Not done

Eligibility: If outcomes are not relevant to our stated review aims, then EXCLUDE

Reason for exclusion: _____ or CONTINUE

Did both reviewers agree on inclusion/exclusion and study quality?	**Yes / No**
If no, what was the source(s) of the disagreement?	

Appendix 6. GRADE evidence profiles

Stand-alone clinical pathway compared to usual care for secondary care and the effects on professional practice, patient outcomes, length of hospital stay and hospital costs

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With usual care	With stand-alone clinical pathway		Risk with usual care	Risk difference with stand-alone clinical pathway
Inhospital mortality											
4603 (7 RCTs)	not serious	serious[a]	not serious	serious[b]	none	⨁⨁◯◯ Low	314/2017 (15.6%)	290/2586 (11.2%)	**OR 0.79** (0.53 to 1.20)	156 per 1000	**29 fewer per 1000** (from 67 fewer to 25 more)
Mortality (up to 6 months)											
852 (3 RCTs)	serious[c]	not serious	not serious	serious[d]	none	⨁⨁◯◯ Low	12/374 (3.2%)	138/478 (28.9%)	**OR 1.37** (0.72 to 2.60)	32 per 1000	**11 more per 1000** (from 9 fewer to 47 more)
Inhospital complications (e.g. rate of infections, pressure injuries, pain, uncontrolled bleeding)											
3668 (11 RCTs)	serious[c]	not serious	not serious	not serious	none	⨁⨁⨁◯ Moderate	259/1534 (16.9%)	200/2134 (9.4%)	**OR 0.57** (0.41 to 0.80)	169 per 1000	**65 fewer per 1000** (from 92 fewer to 29 fewer)
Hospital readmission (up to 6 months)											
1578 (9 RCTs)	serious[c]	not serious	not serious	very serious[e]	none	⨁◯◯◯ Very low	97/742 (13.1%)	95/836 (11.4%)	**OR 0.67** (0.44 to 1.03)	131 per 1000	**39 fewer per 1000** (from 69 fewer to 3 more)
Length of hospital stay (days) from admission until discharge											
5201 (21 RCTs)	not serious	serious[a]	not serious	not serious	none	⨁⨁⨁◯	2576	2625	-		MD **1.12 days lower** (1.6 lower to 0.65 lower)

(Continued)

						Moderate					
Hospital cost and charges											
2113 (10 RCTs)	not serious	very serious[f]	serious[f]	not serious	none	⊕◯◯◯ Very low	1049	1064	-	The mean hospital cost and charges were zero.	**0** (0 to 0)
Adherence to recommended practice											
573 (3 RCTs)	serious[c]	serious[a]	not serious	not serious	none	⊕⊕◯◯ Low	-/239	-/334	not estimable	0 per 1000	

CI: confidence interval; **MD:** mean difference; **OR:** odds ratio

Explanations

a. Downgraded one level due to serious inconsistency (substantial unexplained heterogeneity)

b. Downgraded one level due to serious imprecision despite optimal information size (n~4000) being met; CIs could not exclude appreciable benefit or harm

c. Downgraded one level due to serious risk of bias in included studies

d. Downgraded one level due to serious imprecision

e. Downgraded two levels due to very serious imprecision (CIs could not exclude appreciable benefit or harm)

f. Downgraded two levels due to very serious inconsistency and one level due to serious indirectness in outcome measures

Multifaceted intervention (including clinical pathway) compared to usual care for secondary care and the effects on professional practice, patient outcomes, length of hospital stay and hospital costs

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With usual care	With multifaceted intervention (including clinical pathway)		Risk with usual care	Risk difference with multifaceted intervention (including clinical pathway)
Inhospital mortality											
6304 (2 RCTs)	not serious	very serious[a]	not serious	not serious	none	⨁⨁◯◯ Low		55/3240 (1.7%)	not estimable	0 per 1000	
Mortality (up to 6 months)											
6531 (3 RCTs)	serious[b]	not serious	not serious	serious[b]	none	⨁⨁◯◯ Low	262/3178 (8.2%)	331/3353 (9.9%)	**OR 1.05** (0.88 to 1.25)	82 per 1,000	**4 more per 1000** (from 9 fewer to 19 more)
Inhospital complications (rate of irregular bleeding or infection)											
140 (1 RCT)	not serious	not serious	not serious	very serious[c]	none	⨁⨁◯◯ Low	16/70 (22.9%)	6/70 (8.6%)	**OR 0.32** (0.12 to 0.87)	229 per 1000	**142 fewer per 1000** (from 194 fewer to 24 fewer)
Hospital readmission (up to 6 months)											
1569 (2 RCTs)	not serious	very serious[a]	not serious	not serious	none	⨁⨁◯◯ Low	-/696	6/873 (0.7%)	not estimable	0 per 1000	
Length of stay (days) from admission until discharge											
1936 (4 RCTs)	not serious	very serious[a]		not serious	none	⨁⨁◯◯ Low	880	1056	-	The mean length of stay (days) from admission until discharge was zero.	MD **0** (0 to 0)

(Continued)

Hospital cost and charges											
2015 (4 RCTs)	not serious	not serious	serious[d]	very serious[d]	none	⊕◯◯◯ Very low	915	1100	-	The mean hospital cost and charges was zero.	MD **0** (0 to 0)
Adherence to recommended practice											
6202 (2 RCTs)	not serious	very serious[e]	not serious	not serious	none	⊕⊕◯◯ Low	-/3040	-/3162	not estimable	0 per 1000	

CI: confidence interval; **MD:** mean difference; **OR:** odds ratio

Explanations

a. Downgraded two levels due to very serious inconsistency (meta-analysis not possible due to significant heterogeneity and lack of overlap between confidence intervals)

b. Downgraded two levels due to serious risk of bias and serious imprecision; despite optimal information size (~4000) being met, CIs could not exclude appreciable harm or benefit

c. Downgraded two levels due to very serious imprecision: only one study with a small sample size

d. Downgraded three levels due to very serious imprecision (meta-analysis not possible due to significant heterogeneity and lack of overlap between CIs) and serious indirectness in outcome measures

e. Downgraded two levels due to very serious inconsistency (meta-analysis not possible due to risks of duplicate counting)

WHAT'S NEW

Date	Event	Description
6 June 2025	Amended	Typo fixed in Abstract

HISTORY

Protocol first published: Issue 3, 2007
Review first published: Issue 3, 2010

Date	Event	Description
14 May 2025	New search has been performed	Search date 25 July 2024
14 May 2025	New citation required and conclusions have changed	We included 31 new studies in this update; the total numer of included studies in the review is now 58. We listed 13 new studies awaiting classification; the total number of studies awaiting classification is now 14.
31 August 2021	New citation required but conclusions have not changed	We included 31 new studies in this update; the total number of included studies in the review is now 58.
3 April 2019	New search has been performed	This is the first update of this Cochrane Review (Rotter 2010). We conducted a new search and updated the Background section. We incorporated the latest MECIR and EPOC standards in the review and used GRADE to assess the certainty of evidence. We added new review authors for the update.

CONTRIBUTIONS OF AUTHORS

This review update was led by TR and LK. ARW conducted the recent update searches. AL, CC, GG, PW, LAB, LK, UR, TR, KS, CP, AA, AM, ARW, SS assessed studies for inclusion. All the authors participated in data extraction, except when studies included one of the authors; in this case, the author did not participate in data extraction. All authors contributed to data analysis. TR, LK, AA undertook the meta-analysis. TS developed the Summary of Findings tables. TR, LK, AL and AA drafted the review, drawing on contributions from several review authors, and all review authors revised the manuscript critically.

DECLARATIONS OF INTEREST

Thomas Rotter (TR): Author of one of the included studies. The evaluation of this study, including data extraction and risk of bias assessment, was conducted by two other authors not involved in the study. No other conflicts known.

Leigh Kinsman (LK): Author of two of the included studies. The evaluation of these studies, including data extraction and risk of bias assessment, was conducted by two other authors not involved in either of the studies. No other conflicts known.

Agnes Alsius (AA): none known.

Shannon D. Scott (SS): none known.

Adegboyega Lawal (AL): none known.

Ulrich Ronellenfitsch (UR): none known.

Christopher Plishka (CP): none known.

Gary Groot (GG): none known.

Phil Woods (PW): none known.

Chloe Coulson (CC): none known.

Leigh Anne Bakel (LAB): none known.

Kimberly Sears (KS): none known.

Amanda Ross-White (ARW): none known.

Andreas Machotta (AM): Author of one of the included studies. The evaluation of this study, including data extraction and risk of bias assessment, was conducted by two other authors not involved in the study. No other conflicts known.

Timothy J Schultz (TS): none known.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We refined the working definition for the definition of a clinical pathway (CPW). The following four criteria for clinical working definition derived include:

- The intervention was a structured multidisciplinary plan of care;
- The intervention was used to translate guidelines or evidence into local structures;
- The intervention detailed the 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; and
- The intervention aimed to standardize care for a specific population.

An intervention meeting all four criteria was considered to be a clinical pathway.

- Since the protocol was published (Rotter 2007), we split the review into two separate reviews; this review focusing on secondary care and the other on primary care. For literature searching purposes, we removed the colon and changed the title from 'Clinical pathways: effects on professional practice, patient outcomes, length of stay, and hospital costs' to 'Clinical pathways for secondary care and the effects on professional practice, patient outcomes, length of hospital stay and costs'.
- 'Adverse event' was listed as a separate secondary outcome in the protocol. However, due to the overlap with another outcome, 'inhospital complications', we recorded 'adverse events' as a type of inhospital complication.
- 'Quality measures' of professional practice were removed as a separate outcome, as it was reported as adherence to recommended practice.
- Staff satisfaction was not objectively measured in any of the studies identified in the 2010 search and was removed as an outcome.
- We initially planned a fixed-effect and random-effects meta-analysis; however, we only conducted random-effects meta-analyses owing to the assumption of the variation in the effect estimates across the included studies.
- The first version of this review did not include a 'Summary of findings' table. For this update, we incorporated a number of changes in order to ensure the review complied with updated MECIR standards by including two 'Summary of findings' tables with seven outcomes that were defined post hoc.
- We planned to add two additional outcomes for this review update: (1) studies that reported length of hospital stay in the form of a geometric mean, and (2) studies that reported on hospital charges. However, this was not possible because of the maximum number of seven outcomes that can be presented in a summary of findings table. The team decided to focus on the most clinically relevant outcomes, length of stay reported as arithmetic mean values, and hospital costs and charges.
- To conform with the EPOC taxonomy for outcomes reported in EPOC reviews, we changed 'adherence to evidence-based practice' to 'adherence to recommended practice'.
- In our review protocol, we stated that we would include mortality at longest follow up. The longest follow-up period in included studies was six months, so we now refer to mortality at longest follow-up as mortality (up to 6 months).

INDEX TERMS

Medical Subject Headings (MeSH)

Bias; Controlled Before-After Studies; *Critical Pathways [economics]; *Hospital Costs [statistics & numerical data]; Humans; Interrupted Time Series Analysis; *Length of Stay [statistics & numerical data]; Non-Randomized Controlled Trials as Topic; *Professional Practice; Randomized Controlled Trials as Topic; *Secondary Health Care [economics]