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Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs (Review)

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[Intervention Review]

Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

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ABSTRACT

Background

Clinical pathways are structured multidisciplinary care plans used by health services to detail essential steps in the care of patients with a specific clinical problem. They aim to link evidence to practice and optimise clinical outcomes whilst maximising clinical efficiency.

Objectives

To assess the effect of clinical pathways on professional practice, patient outcomes, length of stay and hospital costs.

Search methods

We searched the Database of Abstracts of Reviews of Effectiveness (DARE), the Effective Practice and Organisation of Care (EPOC) Register, the Cochrane Central Register of Controlled Trials (CENTRAL) and bibliographic databases including MEDLINE, EMBASE, CINAHL, NHS EED and Global Health. We also searched the reference lists of relevant articles and contacted relevant professional organisations.

Selection criteria

Randomised controlled trials, controlled clinical trials, controlled before and after studies and interrupted time series studies comparing stand alone clinical pathways with usual care as well as clinical pathways as part of a multifaceted intervention with usual care.

Data collection and analysis

Two review authors independently screened all titles to assess eligibility and methodological quality. Studies were grouped into those comparing clinical pathways with usual care and those comparing clinical pathways as part of a multifaceted intervention with usual care.

Main results

Twenty-seven studies involving 11,398 participants met the eligibility and study quality criteria for inclusion. Twenty studies compared stand alone clinical pathways with usual care. These studies indicated a reduction in in-hospital complications (odds ratio (OR) 0.58; 95% confidence interval (CI) 0.36 to 0.94) and improved documentation (OR 11.95: 95%CI 4.72 to 30.30). There was no evidence of differences in readmission to hospital or in-hospital mortality. Length of stay was the most commonly employed outcome measure with most studies reporting significant reductions. A decrease in hospital costs/ charges was also observed, ranging from WMD +261 US$ favouring usual care to WMD -4919 US$ favouring clinical pathways (in US$ dollar standardized to the year 2000). Considerable heterogeneity prevented meta-analysis of length of stay and hospital cost results. An assessment of whether lower hospital costs contributed to cost shifting to another health sector was not undertaken.

Seven studies compared clinical pathways as part of a multifaceted intervention with usual care. No evidence of differences were found between intervention and control groups.

Authors' conclusions

Clinical pathways are associated with reduced in-hospital complications and improved documentation without negatively impacting on length of stay and hospital costs.

PLAIN LANGUAGE SUMMARY

Clinical pathways in hospitals.

Decision-making in hospitals has evolved from being opinion-based to being based on sound scientific evidence. This decision-making is recognised as evidence-based practice. Perpetual publication of new evidence combined with the demands of every-day practice makes it difficult for health professionals to keep up to date. Clinical pathways 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. Clinical pathways have been implemented worldwide but the evidence about their impact from single trials is contradictory. This review aimed to summarise the evidence and assess the effect of clinical pathways on professional practice (e.g. quality of documentation), patient outcomes (e.g. mortality, complications), length of hospital stay and hospital costs.

Twenty-seven studies involving 11,398 participants were included for analysis. The main results were a reduction in in-hospital complications and improved documentation associated with clinical pathways. Complications assessed included wound infections, bleeding and pneumonia. Most studies reported a decreased length of stay and reduction in hospital costs when clinical pathways were implemented. Considerable variation in study design and settings prevented statistical pooling of results for length of stay and hospital costs. Generally poor reporting prevented the identification of characteristics common to successful clinical pathways.

The authors concluded that clinical pathways are associated with reduced in-hospital complications

BACKGROUND

Clinical pathways (CPWs) aim to link evidence to practice for specific health conditions and, therefore, optimise patient outcomes and maximise clinical efficiency. For the purpose of this review CPWs are defined as structured multidisciplinary care plans which detail essential steps in the care of patients with a specific clinical problem. They support the translation of clinical guidelines into local protocols and clinical practice (Campbell 1998). Whilst clinical guidelines provide generic recommendations, clinical pathways detail the local structure, systems and time-frames to address these recommendations. As an example, a clinical guideline that includes the recommendation that a person hospitalised for heart surgery attend an outpatient cardiac rehabilitation program post discharge will be implemented locally in a hospital's heart surgery clinical pathway that provides detail regarding local mechanisms such as what referral form to use, when to submit the referral, to whom it should be submitted, and who is responsible for completing the referral process. Clinical pathways are also variously

referred to as 'integrated care pathways', 'critical pathways', 'care plans', 'care paths' and 'care maps'. In addition to the support of evidence based practice, CPWs have been proposed as a strategy to optimise resource allocation in a climate of increasing healthcare costs (Kimberly 2009).

Along with the global trend of the economisation of (acute) health care, evidenced by the case mix (CM) prevalence worldwide, there is a striking association with the prevalence of clinical pathway interventions to tackle this dramatic change in health care reimbursement (Kimberly 2009)**.** Therefore, substantial resources have been expended on pathway development, implementation, and maintenance. For example, more than 80% of hospitals in the United States use CPWs for at least some of their interventions (Saint 2003). However, individual studies into the impact of CPWs have produced conflicting outcomes. Some studies report that the introduction of CPWs for a broad range of interventions or diagnoses including stroke management (Quaglini 2004), inguinal hernia repair (Joh 2003), laparoscopic surgery (Uchiyama 2002), pancreaticoduodenectomy (Porter 2000), and the management of fractured neck of femur (Choong 2000), can reduce the length of stay (LOS) and total costs of acute hospital admissions while maintaining quality of care, improving patient outcomes, interdisciplinary co-operation and staff satisfaction (Mabrey 1997; Maxey 1997; Fujihara-Isosaki 98; Hanna 1999; Jacavone 1999). Conversely, there are studies reporting no benefit regarding LOS and total costs. These include CPWs implemented for femoral neck fracture in older people (Roberts 2004), acute exacerbations of bronchial asthma (Bailey 1998), carotid endarterectomy (Dardik 1997), and head and neck cancer (Yueh 2003). Rigorous evaluation of the effectiveness of CPWs and improved understanding of the reasons behind their success or failure, are necessary before additional resources are consumed developing and implementing more CPWs.

In summary, the results of studies regarding the impact of CPWs on patient outcomes, professional practice, length of stay and resource utilization vary considerably. The overall quality and scope of studies investigating CPWs has not been adequately analysed (Saint 2003). A systematic review and meta-analysis is required to reconcile CPW studies with differing results.

OBJECTIVES

This review addressed the following question:

What is the effect of clinical pathways (CPWs) on professional practice, patient outcomes, length of stay (LOS) and hospital costs?

The specific objectives of this review were:

(1) To search the literature for studies which evaluate CPW interventions.

(2) To identify relevant studies according to methodological and contextual inclusion criteria.

(3) To summarize included studies narratively and according to methodological quality.

(4) To describe the overall effects of CPWs on health professional practice, patient outcomes, LOS and hospital costs.

(5) To identify factors that may contribute to the effectiveness of CPWs. Factors were categorized as:

- Setting (general acute, Intensive Care Unit (ICU), Emergency Department (ED), extended care, other)
- Intervention development and implementation quality
- Invasive or non-invasive nature of patient management guided by CPW (e.g., CPW for gastrectomy; Percutaneous Transluminal Coronary Angioplasty (PTCA); laparoscopic cholecystectomy; hip and knee arthroplasty etc., versus CPW for clinical conditions such as stroke, pneumonia and asthma)
- Specified conditions or interventions guided by CPW (e.g., CPW for PTCA; hip and knee arthroplasty and pneumonia).

(6) To apply statistical meta-analysis to included studies if supported by adequate quality and homogeneity.

To address these objectives, the following comparisons were undertaken:

(1) Patients managed according to CPW compared to usual care. Impact on patient outcomes, professional practice, length of hospital stay and hospital costs.

(2) Patients managed within a multifaceted intervention including a CPW compared to usual care. Impact on patient outcomes, professional practice, length of hospital stay and hospital costs were examined.

We also explored the effects of the following characteristics of the intervention on the magnitude of effect across studies (subgroup analysis):

(1) Effect of high quality studies versus low quality studies (subgroup analysis regarding the study design).

(2) Country(s) where the study was carried out.

(3) The date of study / year of publication (adjusting for temporal trends).

METHODS

Criteria for considering studies for this review

Types of studies

Randomized controlled trials (RCTs), controlled clinical trials (CCTs), controlled before and after studies (CBAs) and interrupted time series analysis (ITS) were included after meeting Effective Practice and Organisation of Care (EPOC) methodological design and quality criteria. While there are validated criteria for experimental studies, criteria for CBAs and ITS are less developed and validated criteria are only available from the EPOC website (Bero 2010). Therefore, we present briefly the simplified EPOC gold standard of non-experimental CBAs and ITS studies considered for inclusion as readers may not be aware of:

Controlled before and after studies (CBAs):

CBAs are experimental studies with at least two intervention sites and two control sites but allocation was not random. This was a recent editorial decision and included CBA studies within this review will be reassessed for inclusion when the review is updated (Bero 2010). Data is collected on the control and intervention groups before the intervention is introduced and then further data is collected after the intervention has been introduced.

Interrupted time series designs (ITS):

Represent a robust method of measuring the effect of an intervention as a trend over time. Useful design when recruitment of a control cohort is impractical, e.g. change in hospital policy. Three or more data points are collected before and after the intervention as a minimum standard (Bero 2010). The intervention effect is measured against the pre-intervention trend.

Types of participants

There were three types of participants considered relevant for this review:

1) Health professionals, including doctors, nurses, physiotherapists, pharmacists, occupational therapists, social workers, dietitians, psychologists, psychiatrists, speech pathologists and dentists involved in CPW utilisation in the hospital setting.

2) Hospitalized patients (in-patient and out-patient settings) with conditions managed on a CPW, irrespective of diagnosis.

3) Hospitals evaluating the impact of CPWs.

Types of interventions

Clinical pathways (CPWs) are structured multidisciplinary care plans which detail essential steps in the care of patients with a specific clinical problem. They support the translation of clinical guidelines into local protocols and their subsequent application to clinical practice (Campbell 1998). For the purposes of this review, the intervention of interest was the implementation of a CPW aimed at guiding patient management for a specified condition. For this reason we excluded dissemination of clinical practice guidelines alone, unless the guidelines were translated into a CPW. We expected that most studies would compare CPW intervention with usual care in the same setting. Studies of multifaceted interventions were included if the CPW aspect 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, studies in which a multifaceted intervention incorporating a CPW compared to the same intervention without a CPW element were included.

We undertook a three stage process aiming to develop an evidence informed and practical criteria to define a clinical pathway. The four stages included:

1. Identify publications exploring the scope and definition of clinical pathways (or similar terms).
2. Synthesise previously suggested criteria and derive a draft criteria for testing.
3. Pilot test the level of agreement between review authors when applying criteria to identified studies.

A search of electronic databases and communication with the European Pathways Association revealed three sentinel articles that described the characteristics of a clinical pathway (Campbell 1998; De Bleser 2006; Vanhaecht 2006).

The following five criteria were derived from the three sentinel articles mentioned above:

1. The intervention was a structured multidisciplinary plan of care.
2. The intervention was used to channel the translation of 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.
4. The intervention had time-frames of criteria-based progression (i.e. steps were taken if designated criteria were met).
5. The intervention aimed to standardize care for a specific clinical problem, procedure or episode of care in a specific population.

These criteria were tested by three of the team (TR, LK and EJ) to develop consensus. Poor reporting of interventions made assessment of the five criteria problematic. Subsequently, an intervention was defined as a clinical pathway if it was a structured multidisciplinary plan of care and at least three of the remaining four criteria were met (that is, it met the first criteria and any three of the remaining four). These criteria were tested by applying them to five papers. There was 100% agreement between the three review authors regarding whether an intervention was a clinical pathway. These criteria were then adopted by the review group and applied to studies identified.

Intervention development and implementation quality

Previous studies (including EPOC reviews) have demonstrated that implementation of interventions to improve professional

practice benefit from being multifaceted and including 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 opinions leaders as part of the process (Cluzeau 1999; Doherty 2006; Grimshaw 1998; Grimshaw 2001; Kinsman 2004a; Stone 2002). In order to gauge how evidence informed the development and implementation of the CPW, information pertaining to each of these ten possible criteria were extracted from each included study. Initially we planned to extract information on all ten criteria and to score each study according to how many of the ten possible criteria had been completed. However, reporting of design and implementation characteristics was very poor in the included studies in particular for the following three indicators: identification of potential barriers to change, incorporation of reminder systems, and use of local opinions leaders. Even though we believe these to be important we did not include them in the implementation quality assessment as they would not discriminate between studies. Instead, the remaining seven indicators were extracted and scored as 'reported' or 'not reported'. In the case of missing information, we attempted to contact study authors for clarification.

Types of outcome measures

We included all objectively measured patient outcomes, professional practice, length of stay (LOS) and hospital costs.

Patient outcomes included inpatient mortality, mortality at longest follow-up, hospital readmissions, in-hospital complications, adverse events, ICU admissions and discharge destination.

Professional practice outcomes included quality measures appropriate to the specific aim of the CPW, staff satisfaction and adherence to evidence based practice (for example, time to mobilisation post surgery or effects on quantity and quality of documentation).

Length of stay (LOS) was assessed by extracting the duration of hospital stay measured in hours or days that were reported in the included studies.

Hospital costs included cost of hospitalisation and any appropriate resource utilisation data as a surrogate measure for studies that did not report primary hospital-cost-data, for example hospital charges data and country-specific insurance points.

Hospital costs

Hospital costs data were reported as direct hospital costs (only variable direct costs included), as total costing approach (variable direct hospital costs + fixed indirect costs) including administration or other overhead costs and as hospital charges (hospital fees) or country specific insurance points (Japan).

Therefore the differences between these measures and hospital costs are briefly explained and discussed on a country by country basis.

Hospital charges

In contrast to hospital costs, hospital charges are often used to proxy hospital costs but charges are very difficult to interpret in comparison with hospital costs and can be very misleading. A good example for hospital charges are DRGs in a case mix context or per diem charges. Depending on the effectiveness of the hospital care delivery processes, the "real" corresponding costs for the hospital can be either lower or higher than the charges reported. However, charges are often used as a proxy because hospital charges are easy to determine and more readily available even if the hospital is not supported by a costing department or appropriate costing data. Like hospital costs, hospital charges can include various different components. In some countries they may include physician fees while in others they are often excluded and therefore can vary considerably between countries.

Hospital charges in the USA

Except in government hospitals and HMO hospitals, physicians are generally paid and billed separately (Meltzer 2005) and therefore hospital charges data in the US is traditionally calculated and reported without physician fees.

Hospital charges in Thailand

In-patient services are reimbursed using a Thai version of case-mix or DRG system and public hospital charges usually exclude doctor fees (Lumbiganon 2009). Medical doctors working for public hospitals receive the salary directly from the government. However, private hospital providers use reimbursement systems that vary considerably, mostly a combination of case mix and fee for services (FFS).

Hospital charges in Japan

Hospital charges in Japan have usually two components, the case mix component (DPC) and the fee-for-service component (Kimberly 2009) and the health care system is characterised by two major schemes of treatments: the public scheme covered by the national health insurance and the private scheme. Therefore, patients pay the doctor fee indirectly in the national insurance scheme (Hayashi 2009). It is possible that one hospital offers both schemes. In conclusion, doctor's treatment fee's are included directly and indirectly in the charge of both schemes (Hayashi 2009).

Country specific insurance points in Japan

All treatments and medications covered under Japanese public insurance have been assigned points representing the relative fee (Kimberly 2009). Hospitals use this points to calculate the fees they charge and these calculations are varying between public and private hospitals. This has relevance for the Japanese context but the results cannot be generalized or transferred to other health care systems and the nature of the reported insurance data comprise the same disadvantages as it applies for hospital charges.

Search methods for identification of studies

See: EPOC methods used in reviews.

The Database of Abstracts of Reviews of Effectiveness (DARE) was searched for related reviews.

The following electronic databases were searched for primary studies:

(a) The EPOC Register (and the database of studies awaiting assessment) (*see* SPECIALISED REGISTER under GROUP DETAILS).

(b) The Cochrane Central Register of Controlled Trials (CENTRAL).

(c) Bibliographic databases, including MEDLINE, EMBASE, CINAHL, NHS EED, and Global Health.

Other sources:

(d) Handsearching of those high-yield journals and conference proceedings which had not already been handsearched on behalf of the Cochrane Collaboration.

(e) Reference lists of all papers and relevant reviews identified.

(f) We contacted authors of relevant papers regarding any further published or unpublished work.

(g) We contacted authors of other reviews in the field of effective professional practice regarding relevant studies of which they may be aware.

(h) We searched ISI Web of Science for papers which had cited studies included in the review.

(i) We contacted professional associations (e.g., European Pathways Association) regarding further published or unpublished work.

We searched electronic databases using a strategy developed incorporating the methodological component of the EPOC search strategy combined with selected MeSH terms and free text terms relating to clinical or critical pathways. This search strategy was translated into the other databases using the appropriate controlled vocabulary as applicable. We did not apply language restrictions. The MEDLINE search strategy is provided as Appendix 1.

Data collection and analysis

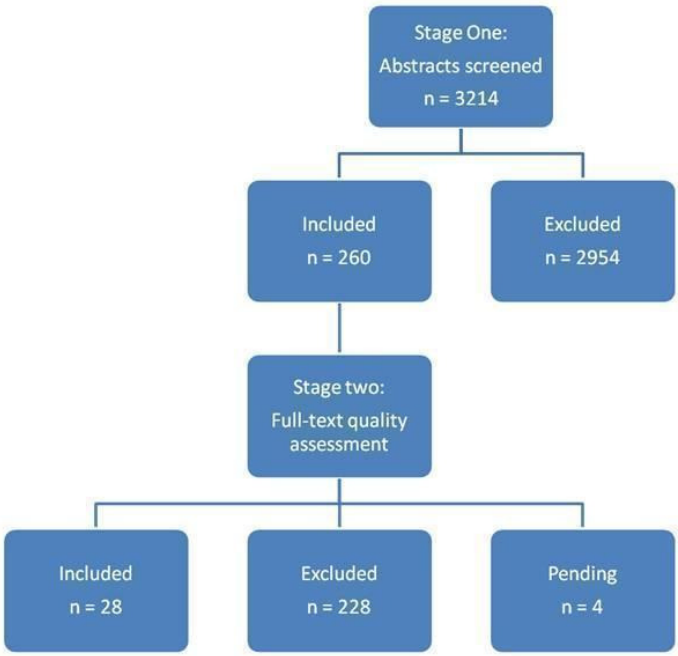
Screening

Two review authors independently screened all titles and abstracts (LK and EJ for professional practice and patient outcomes; TR and AM for relevance regarding LOS and hospital costs) to assess which studies met the inclusion criteria. All titles and abstracts were pooled and duplicates deleted. We retrieved the full text copies of all potentially relevant papers. Unresolved disagreements on inclusion were referred to a third review author. Two full text papers and the methods sections of 6 primary studies that had been published in languages other than English were fully translated into English.

Data management

We recorded details on the number of retrieved references, the number of obtained full text papers and the number of included and excluded articles (Figure 1). We managed this data in Endnote and the reason for excluding retrieved studies was recorded. We then transferred this data into RevMan.

Figure 1. Flow-chart for number of hits. Please note that the total number of included full-text articles (n = 28) stated above equates to twenty-seven included studies as the Sulch (2000 and 2002) study results were reported over two articles.



Data abstraction

We extracted data using a standardized data extraction sheet and extracted directly from trial reports. When necessary, we sought additional information from the authors of the primary studies. We entered the relevant data into the RevMan software (see Appendix 2 study assessment & data collection form).

Quality assessment and analysis

Two review authors (LK and EJ for patient outcomes and professional practice; TR and AM for LOS and hospital costs) assessed the methodological quality of all included studies using the EPOC risk of bias tool and categorized them as low, moderate or high risk. We referred unresolved disagreements on risk of bias classification to a third review author. We excluded studies classified as high risk of bias.

Hospital costs and charges were assessed and calculated in the individual studies. We considered reported hospital cost data as direct costs, as full costing approaches and hospital charges. There was insufficient reported data to synthesise full economic evaluations. We investigated the direct cost / charges-effects of CPWs (cost / charges-analysis) not the cost-effectiveness. Cost / charges data is presented in US$ for the common price year 2000 by using the "CCEMG-EPPI-Centre Cost Converter" (Version 1.0), a web-based tool that can be used to adjust an estimate of cost expressed in one currency and price year to a target currency and / or price year (Shemilt 2008; Shemilt 2010). Costs / charges were adjusted for inflation by applying Gross Domestic Product deflators ('GDPD values') or using government recommended rates and providing a sensitivity analysis with a common discount rate recommended in the literature (Drummond 1996). Additionally, we have provided the un-discounted cost data to allow readers to recalculate the results using any discount rate (additional Table 1-Table 2).

We had planned to concentrate only on reported hospital costs data rather than on hospital fees or charges. Due to the low number of high quality studies evaluating hospital costs; we investigated all objective cost data available including hospital charges as well as hospital cost surrogates such as Japanese insurance points.

We reported data in natural units. In the case of missing standard deviations, the appropriate transformation was undertaken. For continuous outcome measures a summary effect size and the weighted mean difference with 95% confidence levels, was estimated. Additionally, a standardized mean difference (SMD) and summary effect size in meta-analysis were estimated for statistical pooling of a variety of costs or charges measured as a direct result of the different methods of cost calculations used (direct versus full cost approach), different cost outcomes reported (hospital costs versus charges), and hospital cost surrogates used (Deeks 2008).

Combining studies

We have presented the results of studies in tabular form (Table 3; Table 4; Table 5; Table 6; Table 7; Table 8; Table 9) and made an assessment of the effects of studies, based upon the quality, the size and direction of effect observed. Studies were statistically pooled and the results combined and depicted if there were enough comparable primary studies or a subgroup of studies.

We observed both considerable statistical and contextual heterogeneity with a broad range of disparate outcomes measured, many different settings in which care is delivered, and a wide range of diagnoses and types of patients included in the different study designs. This made statistical pooling difficult, but if there appeared a comparable body of studies amenable to meta-analysis, then we calculated a summary estimate and displayed the pooled results graphically. We undertook both fixed and random-effects meta-analysis to assess the robustness of the results. Any study that appeared to be an outlier was assessed by sensitivity analysis (Deeks 2008).

We assessed statistical heterogeneity and potential publication bias in the results of each meta-analysis both by inspection of graphical presentations (funnel plots) and by calculating a test of heterogeneity (I squared test (I^2)).

Ongoing studies

We identified and described ongoing studies, where available, detailing the primary author, research question(s), methods and outcome measures together with an estimate of the reporting date.

Dealing with missing data

SD and P values

If a primary study did not provide information about the standard deviation, we used the approximative 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 (Higgins 2008).

Intracluster correlation coefficient (ICC)

Cluster-RCTs that do not account for clustering were re-calculated with respect to the number of participants per group also called "computing an effective sample size" with an estimate of an intracluster correlation coefficient (ICC) taken from a ICC database of the University of Aberdeen (ICC-database 2008). Where possible, an attempt was made to select a similar intervention with comparable study characteristics reporting an ICC.

ITS data presented graphically

Results arising from both included ITS studies (Brattebo 2002; 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 Microsoft Paint file.
- 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 total number of pixels using this approach. Pixels per unit of measure is then calculated by dividing 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 2004).

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of studies awaiting classification; Characteristics of ongoing studies.

See Table of characteristics of included studies. Twenty-seven studies met the inclusion criteria for the definition of a CPW and methodological quality. Results from the study by Sulch were reported in two separate publications (2000 and 2002).

Nineteen of the included studies were RCTs (Aizawa 2002; Bauer 2006; Brook 1999; Chen 2004; Cole 2002; Delaney 2003; Dowsey 1999; Falconer 1993; Gomez 1996; Johnson 2000; Kampan 2006; Kim 2002; Kiyama 2003; Kollef 1997; Marelich 2000; Marrie 2000; Philbin 2000; Roberts 1997; Sulch 2000; Sulch 2002), four were CBAs (Bookbinder 2005; Chadha 2000; Doherty 2006; Smith 2004), two were CCTs (Choong 2000; Usui 2004) and two were ITS (Brattebo 2002; Tilden 1987). Out of the nineteen RCTs, two were cluster-randomised studies (Philbin 2000; Marrie 2000).

Included studies targeted a large range of conditions. Across the 27 studies there were 19 different conditions targeted. Chest pain, mechanical ventilation, pneumonia and stroke had more than one included study (Gomez 1996; Roberts 1997; Brook 1999; Kollef

1997; Marelich 2000; Marrie 2000; Usui 2004; Falconer 1993; Sulch 2000; Sulch 2002). Please see the Table "Characteristics of Included Studies" for detailed information of all of the included pathway conditions or clinical indications.

Thirteen of the studies were conducted in the United States (Bauer 2006; Bookbinder 2005; Brook 1999; Delaney 2003; Falconer 1993; Gomez 1996; Johnson 2000; Kim 2002; Kollef 1997; Marelich 2000; Philbin 2000; Roberts 1997; Tilden 1987), four in Australia (Choong 2000; Doherty 2006; Dowsey 1999; Smith 2004), three in Japan (Aizawa 2002; Kiyama 2003; Usui 2004), two each in the United Kingdon (Sulch 2000; Sulch 2002; Chadha 2000) and Canada (Cole 2002; Marrie 2000), and one each in Thailand (Kampan 2006), Taiwan (Chen 2004) and Norway (Brattebo 2002).

The settings of the studies were extracted and recorded into one of five categories representing various areas of the hospital. Fifteen studies were conducted in a general acute ward (for example medical, surgical, paediatrics, gynaecology)(Aizawa 2002; Chadha 2000; Chen 2004; Choong 2000; Cole 2002; Doherty 2006; Dowsey 1999; Gomez 1996; Johnson 2000; Kampan 2006; Kiyama 2003; Marrie 2000; Philbin 2000; Smith 2004; Usui 2004), four in an extended stay facility (for example rehabilitation or palliative care) (Bookbinder 2005; Delaney 2003; Falconer 1993; Sulch 2000; Sulch 2002), four in an ICU (Brattebo 2002; Brook 1999; Kollef 1997; Marelich 2000), three studies were conducted in the Emergency Department (ED) (Kim 2002; Roberts 1997; Tilden 1987), and one (Bauer 2006) in another area (mental health outpatient clinic).

In nine studies the CPW was designed for an invasive procedure (Aizawa 2002; Brattebo 2002; Brook 1999; Choong 2000; Delaney 2003; Dowsey 1999; Kiyama 2003; Kollef 1997; Marelich 2000). Sixteen described CPWs for a non-invasive diagnosis (for example diabetes, stroke, asthma) (Bauer 2006; Bookbinder 2005; Chen 2004; Cole 2002; Doherty 2006; Falconer 1993; Johnson 2000; Kampan 2006; Kim 2002; Marrie 2000; Philbin 2000; Roberts 1997; Smith 2004; Sulch 2000; Sulch 2002; Tilden 1987; Usui 2004) and two described CPWs for combined invasive / non-invasive procedures (for example, suspected MI with or without PTCA) (Chadha 2000; Gomez 1996).

We had planned to compare patients managed according to CPW compared to usual care, and patients managed within a multifaceted intervention (including a CPW) compared to the same intervention without a CPW. However, we found no studies in the second group so instead we categorised the studies into two groups:

(1) Those describing patients managed according to CPW compared to usual care.

(2) Those describing patients managed within a multifaceted intervention including a CPW compared to usual care.

Twenty studies compared a stand-alone CPW to usual care (Aizawa 2002; Brook 1999; Chadha 2000; Choong 2000; Delaney 2003; Doherty 2006; Dowsey 1999; Falconer 1993; Gomez 1996; Johnson 2000; Kim 2002; Kiyama 2003; Kollef 1997; Marelich 2000; Marrie 2000; Roberts 1997; Smith 2004; Sulch 2000; Sulch 2002; Tilden 1987; Usui 2004) and seven compared a multifaceted intervention (including a CPW) to usual care (Bauer 2006; Bookbinder 2005; Brattebo 2002; Chen 2004; Cole 2002; Kampan 2006; Philbin 2000).

Multifaceted pathway interventions were combined with case management elements (Bookbinder 2005; Bauer 2006; Chen 2004; Cole 2002; Kampan 2006) or with complex quality improvement programs (Philbin 2000; Bookbinder 2005). Other investigators used single pathway interventions together with counselling methods (Philbin 2000; Kampan 2006; Bauer 2006; Bookbinder 2005) or in conjunction with external providers such as primary care or extended care agencies (Bauer 2006; Philbin 2000). Further multifaceted strategies contained posters (Brattebo 2002), physician order sheets (Bookbinder 2005) and reminders by the study nurse (Cole 2002).

Implementation Process

The process for developing and implementing the CPW was extracted and recorded according to whether evidence informed strategies had been utilised. Ten possible criteria were coded. Post-hoc we removed the poorly reported criteria (identification of potential barriers to change, incorporation of reminder systems and use of local opinions leaders) leaving 7 criteria that were adequately reported and included in the analysis. Of the 27 included studies, 20 (71%) were classified as scoring 'high' on evidence informed development and implementation as they reported carrying out 4 or more of the 7 possible quality indicators. The remaining 8 (29%) studies were classified as 'low' on evidence informed development and implementation. Of the 7 quality indicators the most commonly reported were use of evidence based content, adaption of evidence for local circumstances and clinician involvement in CPW development. The less commonly reported criteria included use of an implementation team, identification of evidence practice gaps, use of audit and feedback and incorporation of education sessions. Reporting of implementation processes was generally poor and did not lend itself to further analysis on the impact of implementation on CPW effectiveness.

Outcomes

Objectively measured patient outcomes included mortality, hospital readmissions, complications and adverse events.

Professional practice outcomes measured were documentation in medical records, patient satisfaction and quality measures as appropriate to the specific aim of the CPW (e.g., time to mobilisation post surgery).

Length of stay (LOS)

LOS was calculated and reported as total length of hospital stay in hours or in days from admission until discharge. However, Kiyama (2003) calculated LOS from the day of surgery to the day of discharge (Kiyama 2003). Most of the included studies predefined LOS as an economic measure and a surrogate for hospital costs. We present the LOS data in days.

Hospital costs

Hospital costs data were reported as direct variable hospital costs, as total costing approaches (direct variable hospital costs + indirect fixed hospital costs) and hospital charges in US$ or country specific insurance points (please see Types of outcome measures for a brief description of the differences between costs, charges and insurance data). Within this highly variable set of cost measures reported, a direct variable costing approach (not total costing) was used by Bauer et al. and Kim et al. excluding professional fees in both US settings (Bauer 2006; Kim 2002). Kiyama 2003 included professional fees.

A "total costing approach" was reported in two studies, although it was unclear which costing method was used and which costs were included (i.e. professional costs) in the Kampan (2006) study (Kampan 2006; Roberts 1997).

Hospital charges in US$ was reported as median hospital charges by Falconer et al. (1993) and as mean hospital charges by Gomez et al. (1996), Johnson et al. (2000) and Philbin et al. (2000). A surrogate for hospital charges in the form of insurance points were reported in two Japanese investigations (Aizawa 2002; Usui 2004).

Because of the different methods used for generating hospital costs and the highly differing cost outcomes included in the present review (hospital costs, charges and insurance data), we present an overview of the costing method used and which costs/ charges were in- and excluded in the calculations in tabular form (as far as reported).

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	Total hospital charges: including variable & fixed costs	Dosage, injection, treatment, operation and anaesthesia, examination, diagnostic, room, medical care	Not reported
Falconer 1993	Hospital charges to proxy direct 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, therapeutic and tests	Physician fees
Johnson 2000	Hospital charges	USA	Hospital charges	Room, medication, laboratory tests and respiratory therapy	Physician fees
Kim 2002	Hospital costs	USA	Direct variable costs	Remains unclear, only "total direct costs" reported	Professional fees
Kiyama 2003	Hospital costs	Japan	Direct variable costs	Total medical costs including medication and examination (physician	Fixed costs

(*Continued*)

				fees)	
Kollef 1997	Hospital costs	USA	Not reported	Not reported	Physician fees
Roberts 1997	Hospital costs	USA	Total direct variable & fixed costs	Professional fees	Not reported
Usui 2004	Insurance data (points)	Japan	Direct charges: including variable costs	Treatment (antibiotic infusion), laboratory and radiography tests	Fixed costs
Comparison 2: Multifaceted intervention including a CPW versus usual care					
Bauer 2006	Hospital costs	USA	Direct variable 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
Legend: USA = United States of America					

An additional post-hoc outcome of hours of mechanical ventilation support was measured in four studies (Brook 1999; Brattebo 2002; Marelich 2000; Kollef 1997).

In summary, the following table of key characteristics of the 27 included primary studies gives an overview:

Study ID	CPW condition	Type of ward	Type of hospital	Sample size	Study type	Country	Study quality
Comparison 1: single CPW intervention versus usual care							
Aizawa 2002	TURP	Surgical / Urology unit	Acute	69	P-RCT	Japan	Moderate risk (B)
Brook 1999	Mechanical ventilation	Medical ICU	ICU	321	P-RCT	USA	Moderate risk (B)
Chadha 2000	Menorrhagia and urinary incontinence	Gynaecological unit	Acute	946	CBA	UK	Moderate risk (B)
Choong 2000	Femural neck fracture	Orthopadic unit	Acute	111	CCT	AUS	Moderate risk (B)

(*Continued*)

Delaney 2003	CPW Laparotomy and Intestinal Resection	Surgical Rehabilitation	Extended care	64	P-RCT	USA	Moderate risk (B)
Doherty 2006	Asthma care	Medical units of the hospitals	Acute	187	CBA	AUS	Moderate risk (B)
Dowsey 1999	Hip and knee arthroplasty	Orthopadic unit	Acute	163	P-RCT	AUS	Moderate risk (B)
Falconer 1993	Stroke Rehabilitation	Stroke Rehabilitation	Extended care	121	P-RCT	USA	Moderate risk (B)
Gomez 1996	Suspected MI	Coronary Care unit/ Chest pain evaluation unit	Acute	100	P-RCT	USA	Moderate risk (B)
Johnson 2000	Asthmatic children	Emergency and Paediatric wards	Acute	110	P-RCT	USA	Moderate risk (B)
Kim 2002	Atrial fibrillation	Emergency Department	ED	18	P-RCT	USA	Moderate risk (B)
Kiyama 2003	Gastrectomy	Surgical ward	Acute	85	P-RCT	Japan	Moderate risk (B)
Kollef 1997	Mechanical ventilation	Medical & Surgical ICU	ICU	357	P-RCT	USA	Low risk (A)
Marelich 2000	Mechanical ventilation	Medical ICU	ICU	253	P-RCT	USA	Low risk (A)
Marrie 2000	Pneumonia	Emergency Department	Acute	1743	C-RCT	Canada	Moderate risk (B)
Roberts 1997	CPW Chest Pain/ possible MI	Emergency/ telemetry observational units	ED	165	P-RCT	USA	Moderate risk (B)
Smith 2004	CPW COPD	Medical Units	Acute	1230	CBA	AUS	Low risk (A)
Sulch 2000	Stroke Rehabilitation	Stroke Rehabilitation	Extended care	152	P-RCT	UK	Moderate risk (B)

(*Continued*)

Sulch 2002	Stroke Rehabilitation	Stroke Rehabilitation	Extended care	152	P-RCT	UK	Moderate risk (B)
Tilden 1987	Identification of battered woman	Emergency Department	ED	892	ITS	USA	Moderate risk (B)
Usui 2004	Pneumonia	Medical Units/ respiratory medicine	Acute	61	CCT	Japan	Moderate risk (B)
Comparison 2: Multifaceted intervention including a CPW versus usual care							
Bauer 2006	Bipolar disorder	Mental health outpatient clinic VAMC	Other	306	P-RCT	USA	Low risk (A)
Bookbinder 2005	Palliative care	Palliative Care	Extended care	267	CBA	USA	Moderate risk (B)
Brattebo 2002	Mechanical ventilation	Surgical ICU	ICU	285	ITS	Norway	Moderate risk (B)
Chen 2004	Asthmatic children	Pediatric unit	Acute	42	P-RCT	Taiwan	Moderate risk (B)
Cole 2002	Care of delirium in older medical patients	Medical units	Acute	227	P-RCT	Canada	Low risk (A)
Kampan 2006	Diabetic patients admitted with hypoglycaemia	Medical unit	Acute	65	P-RCT	Thailand	Moderate risk (B)
Philbin 2000	Patients with heart failure	Medical Units	Acute	2906	C-RCT	USA	Moderate risk (B)

Legend:
P-RCT = patient randomised clinical trial; C-RCT = cluster randomised clinical trial; CCT = controlled clinical trial; CBA = controlled before and after study; ITS = interrupted time series; USA = United States of America; UK = United Kingdom; AUS = Australia; TURP = transurethral resection of the prostate; MI = myocardial infarction; COPD = chronic obstructive pulmonary disease; Acute = General acute hospital; ICU = Intensive care unit; ED = Emergency department; Extended care = Rehabilitation or palliative facilities; Other = Psychiatric or mental health clinic/ hospital

Risk of bias in included studies

Randomized Controlled Trials (RCT)

We included seventeen RCTs in this review. The methodological quality of included studies is presented in the Table 'Characteristics of included studies'. Of the seventeen RCTs, four had a low risk of bias (Bauer 2006; Cole 2002; Kollef 1997; Marelich 2000). The remaining RCTs had a moderate risk of bias (Aizawa 2002; Brook 1999; Chen 2004; Delaney 2003; Dowsey 1999; Falconer 1993; Gomez 1996; Johnson 2000; Kampan 2006; Kim 2002; Kiyama 2003; Roberts 1997; Sulch 2000; Sulch 2002). Sequence generation was clearly adequate in eight studies (Bauer 2006; Brook 1999; Cole 2002; Delaney 2003; Gomez 1996;Kollef 1997; Marelich 2000; Sulch 2000; Sulch 2002) whilst it was unclear in another eight studies (Aizawa 2002; Chen 2004; Dowsey 1999; Falconer 1993; Johnson 2000; Kampan 2006; Kim 2002; Roberts 1997) and inadequate in one study (Kiyama 2003). Concealment of allocation was clearly adequate in seven studies (Bauer 2006; Brook 1999; Cole 2002; Delaney 2003; Gomez 1996; Kollef 1997; Marelich 2000) and remained unclear in ten randomised studies (Aizawa 2002; Chen 2004; Dowsey 1999; Falconer 1993; Johnson 2000; Kampan 2006; Kim 2002; Kiyama 2003; Roberts 1997; Sulch 2000; Sulch 2002). Two studies reported blinded assessment of main outcomes Bauer 2006; Brook 1999;) whilst it was unclear in thirteen other studies (Aizawa 2002; Chen 2004; Cole 2002; Delaney 2003; Dowsey 1999; Falconer 1993; Johnson 2000; Kampan 2006; Kim 2002; Kiyama 2003; Kollef 1997; Roberts 1997; Sulch 2000; Sulch 2002) and inadequate in the two remaining studies (Gomez 1996;Marelich 2000). Incomplete outcome data was adequately addressed in fifteen studies (Aizawa 2002; Bauer 2006; Brook 1999; Chen 2004; Cole 2002; Delaney 2003 Dowsey 1999 Falconer 1993; Gomez 1996;Johnson 2000; Kampan 2006; Kim 2002; Kollef 1997; Marelich 2000; Sulch 2000; Sulch 2002) whilst it was unclear how it was addressed in two studies (Kiyama 2003;Roberts 1997). Fourteen studies were considered free of selective reporting (Aizawa 2002; Bauer 2006; Brook 1999; Cole 2002; Delaney 2003; Dowsey 1999; Falconer 1993; Gomez 1996; Johnson 2000; Kampan 2006; Kim 2002; Kollef 1997; Marelich 2000; Sulch 2000; Sulch 2002) whilst it was unclear in the remaining three (Chen 2004; Kiyama 2003; Roberts 1997). Nine studies were rated as free of other sources of bias (Bauer 2006; Brook 1999; Cole 2002; Dowsey 1999; Falconer 1993; Kim 2002; Kollef 1997; Marelich 2000; Sulch 2000; Sulch 2002) whilst it was unclear in six other studies (Aizawa 2002; Chen 2004; Delaney 2003; Kampan 2006; Kiyama 2003; Roberts 1997) and two studies were rated as high risk of other sources of bias (Gomez 1996; Johnson 2000). However, since protection against contamination of the control professionals is considered to be problematic within an individually randomised trial design, we checked all RCTs if any protection was reported in the primary investigation. To summarise, processes for protection against contamination were not clearly reported in sixteen studies but clearly addressed in two others (Bauer 2006; Kollef 1997;). However, only two investigations reported sufficient protection against contamination of the professionals (Bauer 2006; Kollef 1997). The remaining 16 primary studies remain unclear if any protection against contamination of the control professionals (masking of the intervention effect) was achieved.

Cluster Randomised Controlled Trials

We included two cluster-randomised controlled trials (Marrie 2000; Philbin 2000).

To avoid unit of analysis error in the (cluster randomised) study from Marrie TJ et al. we applied an intracluster correlation coefficient to account for the impact of clustering on the statistical power of the study (Deeks 2008; Higgins 2008).

For Marrie et al. (Marrie 2000) we re-calculated the number of participants per group or calculated a so called "effective sample size" with an estimate of an intracluster correlation coefficient taken from an ICC database of the University of Aberdeen (ICC-database 2008). This estimate was taken from a similar hospital management intervention assuming similar relative variability within and between clusters (EU biomed 1 study: ICC 0.08). As a result we adjusted the sample size reported and reduced the number of participants in the intervention group from 716 to 87 and in the control group from 1027 to 124. This led to the same effect estimate but to a wider confidence interval and a decrease in the relative weight within the statistical meta-analyses (Deeks 2008; Higgins 2008).

Both cluster RCTs were assessed as moderate risk of bias. Marrie (2000) was assessed as having adequate sequence generation and concealment of allocation as well as blinded assessment of outcomes and clearly addressed processes for protection against contamination (Marrie 2000). The issues of managing incomplete outcome data, risk of selective reporting and protection against contamination of the control professionals (masking of the intervention effect) were unclear in how they were addressed by Marrie (2000). Philbin (2000) adequately addressed the issue of incomplete outcome data and processes for protection against contamination and was assessed as free of selective reporting and other sources of bias (Philbin 2000). The processes of sequence generation, concealment of allocation, protection against contamination of the control professionals (masking of the intervention effect) and blinded assessment of outcomes were assessed as unclear for the Philbin (2000) study.

Controlled Clinical Trials

Two controlled clinical trials with quasi-random allocation were included and had a moderate risk of bias (Choong 2000; Usui 2004). Choong (2000) allocated according to odd and even numbers for the subjects' hospital record numbers whereas the allocation protocol was unclear for Usui (2004). Baseline data was clearly provided by Choong (2000) whilst blinded assessment and protection against contamination were ranked as unclear. Usui (2004) clearly provided baseline data and blinded assessment whilst protection against contamination was unclear.

Controlled Before and After Studies

Four controlled before and after studies that met EPOC methodological criteria were included. One study had a low risk of bias (Smith 2004) whilst the remaining three had a moderate risk of bias (Bookbinder 2005; Chadha 2000; Doherty 2006). Blinded assessment of outcomes was achieved by Bookbinder (2005), Chadha (2000) and Smith (2004) whereas the assessment of outcomes process for Doherty (2006) was unclear. All four studies clearly provided baseline data. All studies adequately provided protection against contamination except Chadha (2000) where the process was unclear.

Interrupted Time Series

Two studies utilised interrupted time series design (Brattebo 2002; Tilden 1987). Both met minimum inclusion criteria including number of points pre and post intervention and the utilisation of appropriate models.

Effects of interventions

Comparison 1: CPW alone versus usual care

Length of Stay (LOS)

Length of stay (LOS) was the most commonly employed outcome measure and the majority of studies reporting LOS data showed a positive impact. Out of the 20 studies categorized as single pathway interventions, 15 (75%) primary studies examined the effect of CPWs on LOS (Aizawa 2002; Brook 1999; Choong 2000; Delaney 2003; Dowsey 1999; Falconer 1993; Gomez 1996; Johnson 2000; Kim 2002; Kiyama 2003; Marrie 2000; Roberts 1997; Smith 2004; Sulch 2000; Usui 2004), 11 showed significant reductions in LOS (Aizawa 2002; Brook 1999; Choong 2000; Dowsey 1999; Johnson 2000; Kim 2002; Kiyama 2003; Marrie 2000; Roberts 1997; Usui 2004). Conversely, Falconer (1993) and Sulch (2000) reported reverse effects or increased LOS associated with CPWs in stroke rehabilitation (please see results / subgroup stroke rehabilitation) that did not reach statistical significance (Falconer 1993; Sulch 2000). Due to poor reporting, all of the LOS data was missing in one study (Smith 2004), whilst the investigators only reported the level of significance (n.s. = statistical difference not significant) without any other information. This led us to 14 studies reporting sufficient LOS data for statistical pooling within this subgroup of single pathway interventions. However, heterogeneity between this subgroup of studies reporting on LOS was substantial (I^2 = 62%) and may refer to both the statistical inconsistency as well as to the varying CPW interventions that were included. As a result, the estimation of an overall pooled effect is not appropriate and the differences from the individual studies in LOS are depicted together with the corresponding confidence intervals without totals (Analysis 1.1). However, the order of magnitude of effects indicates that there are considerable implications on LOS associated with CPWs.

It should be worth noting that length of stay is influenced by institutional context and as such reflect hospital practices with respect to hospitalisation and not necessarily reflect a positive outcome (i.e. LOS will fall as mortality increases, see discussion).

Subgroup analyses

High Quality versus Low Quality Studies

We compared in a descriptive analysis the reported effect of CPWs in high quality studies versus low quality studies and we observed stronger LOS effects for the subgroup of non-randomized studies but this difference was not robust in terms of the sensitivity analysis (fixed versus random-effects model). Therefore, non- randomized and randomized studies were grouped and analysed together according to the predetermined categories used for analysis (Analysis 1.1).

Country

Primary studies were ordered in forest plots by country to examine possible different market effects (Analysis 2.4). We observed greater reported LOS effects from Japanese studies with a pooled reduction of approximately three days (WMD 3.01), followed by studies carried out in Australia (WMD 1.6) and the USA (WMD 0.8). Studies carried out in the USA provided the majority of studies included in the present review but reported the smallest decreases in LOS. A slightly similar pattern was observed in hospital cost and charge outcomes reported.

Year of Study

Studies were ordered in forest plots by year of publication but no association with year for the impact of CPWs on LOS or other outcomes was detected (Analysis 2.5).

Condition or Intervention

There were four conditions or interventions for which there was more than one included study. There were two studies evaluating pathway management for stroke rehabilitation (Sulch 2000; Falconer 1993), pneumonia (Marrie 2000; Usui 2004) , suspected myocardial infarction (Gomez 1996; Roberts 1997) and mechanical ventilation (Brook 1999; Kollef 1997). Further conditions within this subgroup of single pathway interventions were transurethral resection of the prostate (Aizawa 2002), menorrhagia and urinary incontinency (Chadha 2000), femoral neck fracture (Choong 2000), laparotomy and intestinal resection (Delaney 2003), asthma care (Doherty 2006), hip and knee arthroplasty (Dowsey 1999), asthma in children (Johnson 2000), artrial fibrillation (Kim 2002), gastrectomy (Kiyama 2003), chronic obstructive pulmonary disease or COPD (Smith 2004) and a pathway instrument designed for the better identification of female victims of domestic violence (Tilden 1987). Significant clinical and statistical heterogeneity prevented the estimation of an overall pooled effect where studies were grouped according to condition. Therefore we concentrated on subgroup analysis per pathway condition without a total estimate.

Stroke Rehabilitation

Falconer 1993 and Sulch 2000 both reported increased LOS associated with CPWs that did not reach statistical significance in stroke rehabilitation units. Falconer (1993) reported a LOS of 35.6 (SD 15.5) days in the CPWs group versus 32.3 (SD 15.4) days in the control group (OR 3.30; 95% CI -2.25 to 8.85). Sulch (2000)

reported a LOS of 50 (SD 19) days in the CPWs group versus 45 (SD 23) days in the control group (OR 5.00; 95% CI -1.71 to 11.71) (Analysis 2.6). The combined odds ratio for these two studies was 3.9 (95% CI -0.29 to 8.27). Sulch (2000) also compared mortality at 26 weeks (13% versus 8%) and found no statistically significant difference. Sulch published further outcomes from the same study in 2002 and reported no differences in patient satisfaction but significant improvements in the documentation of several processes, including nutritional assessment (P < 0.001) multidisciplinary team goals (p < 0.001) and death (p = 0.024), as well as GP notification of death or discharge (p < 0.001).

Pneumonia

Marrie 2000 and Usui 2004 both reported significant reductions in LOS and duration of intravenous antibiotic infusion when CPWs were implemented for the inpatient management of pneumonia. Marrie reported a LOS of 8.2 (SD 1.9) days in the CPWs group versus 9.6 (SD 2.1) days in the control group (WMD -1.40; 95% CI -1.94, -0.86) whilst duration of intravenous antibiotic infusion was also significantly less in the CPWs group, 4.6 days (SD 0.9) versus 6.3 days (SD 1.4); (WMD -1.70; 95% CI -2.01, -1.39) (Analysis 2.6).

Usui reported a LOS of 8.0 (SD 4.2) days in the CPWs group versus 10.8 (SD 4.2) days in the control group (WMD -2.74; 95% CI -4.84, -0.64) whilst duration of intravenous antibiotic infusion was also significantly less in the CPWs group, 6.5 days (SD 3.5) versus 8.2 days (SD 3.5); (WMD -1.75; 95% CI -3.52, 0.02).

When Marrie (2000) and Usui's (2004) results were statistically combined, LOS decreased -1.67 days (95% CI -2.73, -0.62) and for intravenous antibiotic duration it was -1.70 days (95% CI -2.01, -1.40).

Marrie (2000) found no differences in patient satisfaction between CPW and control groups but no grouped score was possible. There was also no difference between CPW and control groups when quality of life six weeks post antibiotics was measured using the SF-36 (Version 2.0) Physical Component Scale (43 (SD 4.0) versus 42 (SD 4.5)) in Marrie's study (2000).

Suspected Myocardial Infarction

Gomez 1996 and Roberts 1997 both reported decreases in LOS for CPWs implemented in emergency departments for suspected myocardial infarction. Gomez (1996) reported a reduced LOS in the CPW group (0.64 (SD 0.51) days versus 2.28 (SD 5.25); P = 0.0001) . Roberts (1997) reported a LOS of 1.38 (SD 1.18) days in the CPWs group versus 1.84 (SD 1.33; P = 0.08) days in the control group (mean difference -0.49 days; -0.87, -0.11) (Analysis 2.6). This difference did not reach statistical significance. The combined LOS for the Gomez (1996) and Roberts' (1997) studies was WMD -0.90 days (95% CI -1.98, 0.18). No evidence of a statistically significant difference in 30 day readmission was found in the Gomez (1996) study (6% versus 6%) or for eight-week readmission in the Roberts (1997) study (6.1% versus 4.8%). Roberts (1997) reported that this difference was not significant and did not provide a P value.

Mechanical Ventilation

Three studies (Brook 1999; Kollef 1997; Marelich 2000) reported similar reductions in the total time patients required mechanical ventilation in ICU when a CPW was implemented. Brook (1999) reported a mean ventilation time of 89.1 hours (SD 133.6) for the intervention group (n = 162) versus 124 hours (SD 153.6) for the control group (n = 159) that was statistically significant (p = 0.03). Kollef (1997) reported a mean ventilation time of 69.4 hours (SD 123.7) for the intervention group (n = 179) versus 102 hours (SD 169.1) for the control group (n = 178) that was not statistically significant (P = 0.29). The combined WMD for the Brook (1999) and Kollef (1997) studies was -33.72 hours (95% CI -55.73 to -11.71)(Analysis 2.9). Marelich (2000) found a statistically significant reduction in ventilation hours for the intervention group (P = 0.0001) but reported medians and interquartile ranges from which the primary data could not be obtained for calculation of means. The median ventilation hours reported for the intervention group (n = 166) was 68 hours (interquartile range 33-164) versus 124 hours (interquartile range 54-334) for the control group (n = 169)(Analysis 2.8). The different reporting of Marelich's data prevented this study being combined in meta-analysis with other mechanical ventilation studies (Marelich 2000). However, the findings of Marelich's study were consistent with the findings from the other studies measuring the impact of CPWs on mechanical ventilation.

Patient Outcomes: Complications

In-hospital complications were measured in five studies and all reported improvements associated with use of a CPW. 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 in the intervention group versus 14 events for 56 patients in the control group (P = 0.40). Delaney 2003 listed postoperative infection and uncontrolled bleeding as complications for patients following intestinal resection and reported 7 events for 31 patients in the intervention group versus 10 events for 33 patients in the control group (P = 0.58). Kiyama 2003 listed surgery-site problems as complications for patients following gastrectomy and reported 3 events for 47 patients in the intervention group versus 5 events for 38 patients in the control group. Marelich (2000) listed ventilator-associated pneumonia as a complication for patients requiring mechanical ventilation and reported 11 events for 166 patients in the intervention group versus 20 events for 169 patients in the control group (P = 0.06). Aizawa 2002 did not describe specific complications for patients following transurethral resection of the prostate and reported 1 event for 32 patients in the intervention group versus 2 events in 37 patients in the control group.

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 three months post surgery and reported 10 events for 92 patients in the

intervention group, versus 20 events for 71 patients in the control group (P = 0.01).

The combined odds ratio for complications was 0.58 (95% CI 0.36 to 0.94) in favour of CPWs and statistically significant (Analysis 2.19).

There was clinical variance in the range of follow-up periods that were used by the investigators measuring complications as well as the investigators used varying definitions of the term (in-hospital) complications. Other patient outcomes measuring complications were hospital readmission (see hospital readmission up to six months) and mortality (see in-hospital mortality and mortality at 26 weeks).

Patient Outcomes: Hospital readmission up to six months

Six measures were comparable in terms of hospital readmission reported for all causes, and characterised with follow up periods up to six months. Aizawa et al. reported one readmission event for 32 intervention patients versus no readmissions for 37 patients in the control group (P = N.S.) within six months (Aizawa 2002). Choong 2000 reported for a follow up period of 28 days two events for 55 patients in the experimental group versus six events for 56 control patients (P = N.S.). In the study from Dowsey (1999) four out of 92 experimental patients were readmitted within a follow up period of three months versus nine out of 71 patients for the control group (P = 0.06). Gomez reported for a period of 30 days three readmissions for both 50 intervention pathway patients as well as for 50 patients in the control group (Dowsey 1999; Gomez 1996). Roberts et al. observed within an eight week period five rehospitalisations for 82 pathway patients versus four readmission events for 83 control individuals. None of these reported readmission rates reached statistical significance as reported in the primary investigations. Statistical heterogeneity was not present (I^2 = 0%) among the studies. The pooled odds ratio for re-admission was 0.6 (95% CI: 0.32 to 1.13) was not statistically significant (Analysis 2.20). Hospital readmissions were included in the estimate of hospital charges for the Gomez study (hospital charges at 30 days) within comparison I (Gomez 1996)

Patient Outcomes: In-hospital mortality and mortality at 26 weeks

Within the subgroup of single pathway interventions, three studies were comparable and reported in-hospital mortality rates. None of these results were reported as statistically significant (Brook 1999; Kollef 1997; Smith 2004). The pooled odds ratio for in-hospital mortality was 0.84 (95% CI: 0.61 to 1.11) in favour of clinical pathways but did not reach a statistically significant level and statistical heterogeneity was not present among the studies (I^2 = 0%) (Analysis 2.18). Sulch et al. reported differences in survival or death for all causes within 26 weeks of enrolment (Sulch 2000). The investigators reported 10 events of death (all causes) for 76 experimental patients versus six events for 76 control patients.

Professional Practice: Documentation

Three studies measured the impact of CPWs on quality and quantity of documentation in medical records and reported positive findings for the use of CPWs. Doherty 2006 reported a 54% improvement in documentation of severity of asthma in the study hospitals compared to a 3% improvement in the control hospitals. Sulch 2002 measured documentation of team goals for stroke patients and reported compliance in 75 of 76 cases in the intervention versus 56 of 76 cases in the control group (OR: 26.79; 95% CI 3.49 to 205.58). Tilden 1987 measured documented identification of female victims of domestic violence in the emergency department and found no change when time series analysis was utilised (Analysis 2.23). The studies by Doherty 2006 and Sulch 2002 were clinically and statistically comparable, resulting in a pooled and significant result (OR 11.95: 95%CI 4.72 to 30.30) favouring improved documentation with CPWs (Analysis 2.21).

Hospital Costs and Charges

Out of 20 primary investigations grouped as single pathway interventions, eight of the included studies reported on a highly varying set of cost / charge measures. Out of the eight studies considering cost outcomes or surrogates, six found significant lower hospitalization costs / charges or insurance points for pathway groups (Aizawa 2002; Usui 2004; Kiyama 2003; Roberts 1997; Gomez 1996; Johnson 2000). Within the subgroup of hospital costs calculated and reported in the primary studies, two investigations out of three reported a statistically significant decrease in hospital costs for the pathway group (Roberts 1997; Kiyama 2003). On the other hand, each of the two combinable studies reporting on hospital charges (Johnson 2000; Gomez 1996) as well as both studies using surrogate cost outcomes in form of the Japanese insurance points (Aizawa 2002; Usui 2004) reported statistically significant reductions in charges and surrogates for the experimental pathway groups. Moreover, the study by Falconer 1993 reported on different median hospital charges whereas no standard deviation was reported along with the median values per study group. Un-adjusted charges per bed days were US$14,440 for the pathway group versus US$14,420 for the control group respectively. When prices were adjusted for the base year 2000, the charges were US$18,320 for the pathway patients versus US$18,295 for the control patients. Other reported charges were drugs and other services, (Table 1; Table 2). None of these differences in reported charges reached statistical significance.

The statistical inconsistency within both subgroups of hospital charges (I^2 = 69%) and hospital costs (I^2 = 66%) was substantial and compromised the estimation of a pooled effect. Even the high level of heterogeneity per subgroup may refer to the varying CPW interventions included in the present analysis as well as to the considerable methodological variation in the sort of hospital costs included for each study in the primary hospital costs evaluation (see results, hospital costs, in-text table). Within the subgroup of hospital costs calculated and reported in the primary studies (n=3), two evaluations included professional fees (Kiyama 2003, Roberts 1997), whilst in the Kim (2002) evaluation, professional fees were excluded. Additionally, there was also inconsistency in the hospital costing approach/ method employed in the primary

investigations. Two out of three studies included only variable, direct hospital costs (Kim 2002; Kiyama 2003), whereas in the Roberts 1997 study variable direct and (fixed) indirect hospital costs were considered.

As a direct result, we statistically pooled only the two comparable Japanese studies reporting on country specific insurance points (please see comparison 5.16)(Analysis 2.12). The analysis indicated no statistical heterogeneity (I^2 = 0%) and the pooled difference in mean insurance points between both intervention and control groups was WMD -8199.00 (-12357.33 to -4040.66).

Hospital costs and charges are provided in full in tables 1 and 2. Table 1 provides data as reported whereas table 2 provides price data adjusted to US$ dollars standardised to the year 2000 (Table 1; Table 2).

We also considered another summary statistic used for meta-analyses, the standardized mean difference (SMD). This is optional for an appropriate comparison of such a homogeneous group of studies assessing a similar outcome but measured it in a variety of ways (costs, charges or insurance points).

Re-expressing or interpreting the SMDs combined was generally possible but problematic. Multiplying a SMD by a pooled standard deviation of both patient groups reported leads to the original units used (Schüneman 2008). However, since we already grouped and statistically pooled both subgroups of hospital costs and charges whilst facing a substantial level of statistical inconsistency, we used a simpler approach of re-expressing SMDs. Our rule of thumb was defined as follows: a statistically pooled standardized mean value of 0.2 represents a small effect, a mean value of 0.5 a moderate effect, and 0.8 means a large effect size (Schüneman 2008).

According to the statistical pooling of eight standardized mean differences in hospital costs, charges and insurance points, we observed a "moderate" decrease in resource use for the experimental pathway patients SMD -0.52 (95% CI -0.78 to -0.26). (See comparison 2.14 standardized hospital costs data).

Finally, despite the high level of statistical and methodical inconsistency, the order of magnitude of the reported effects of CPWs on hospital costs / charges (including cost surrogate - insurance points) indicated that there are considerable benefits to using CPWs.

Additional sensitivity analysis:

Cluster-randomized trials

To test the robustness of the meta-analytic approach, we re-analyzed the data from Marrie 2000, imputing a reasonable range of intracluster correlation coefficients (ICCs) values (from 0.04 to 0.10) instead of the estimate ICC value of 0.08 (Higgins 2008). This did not materially change the results or the pooled effect estimate and strengthens the confidence in the present meta-analytic approach. Only the relative weights were slightly different and the confident intervals (CI 95 %) were wider or narrower as a direct result of the different number of participants.

Effect of market forces on LOS

Sensitivity analyses were performed to test whether the effect size varied by the countries where the study was carried out (adjusting for market forces: please see Effects of Interventions, subgroup-analyses per country). Subsequently, we tested the hypotheses, that different market forces (reported effect sizes per country) are possibly confounding the conclusions of this meta-analysis (Deeks 2008). After exclusion (stepwise / iterative and all of the primary Japanese studies) of the subgroup of Japanese studies, the LOS effect remained robust and statistically significant, but tended to be smaller (WMD 1.0; subgroup "Japanese studies excluded" versus WMD 1.3; subgroup "all group A single pathway intervention studies" included).

Comparison 2: Multifaceted intervention including a CPW versus usual care

Length of stay (LOS)

Out of the seven primary studies categorized as multifaceted interventions including a CPW element, only three investigations reported LOS measures for statistical comparison (Cole 2002; Kampan 2006; Philbin 2000). None of the differences reported in these studies reached statistical significance whilst Kampan (2006) employed only a small sample size available for analysis (Kampan 2006). The pooled effect for all of the three primary studies categorized as multifaceted interventions was WMD -0.86 days (95% CI -2.52 to 0.81) but not statistically significant (Analysis 3.1). The differences in LOS in the individual studies are depicted together with a total estimate (WMD). Statistical heterogeneity was not present among the three studies (I^2 = 0%) and the subsequent 0% heterogeneity score supports the appropriate grouping of highly diverse CPW interventions included in the present review.

Subgroup analyses

High Quality versus Low Quality

We originally intended to compare the effect of CPWs in high quality studies versus low quality studies. However, there were only three randomized studies within this subgroup of multifaceted interventions reporting on LOS. Other patient outcomes are referring to just one study. Therefore the comparison was unable to be conducted.

Country

Three randomized studies were categorized as complex interventions and statistically pooled. No difference was found regarding the effect of CPWs on LOS when compared by country.

Year of Study

Studies were ordered in forest plots by year but there was no association between year and impact of CPWs on LOS or other outcomes was detected.

Condition or Intervention

Seven separate conditions were analyzed in this group and subgroup analysis was not possible. The different pathway indications were bipolar disorder (Bauer 2006), palliative care (Bookbinder 2005), mechanical ventilation (Brattebo 2002), asthma in children (Chen 2004), delirium in older medical patients (Cole 2002), diabetic patients admitted with hypoglycaemia (Kampan 2006) and heart failure (Philbin 2000).

Patient, professional and economic outcomes

Processes of care

Three studies (Bookbinder 2005; Cole 2002; Philbin 2000) measured the impact of CPWs on processes of care. Bookbinder trialed a CPW for end-of-life care and found a comparative reduction in the number of complications identified (4.8 to 3.7; P = 0.014) and the number of interventions performed (5.1 to 4.1; P = 0.021), whilst there was a comparative increase in the number of inpatient consultations (4.0 to 5.1; p = 0.037). There was no evidence of a statistically significant difference in the number of symptoms assessed. Cole (2002) reported no statistically significant differences detected for discharge processes for a CPW implemented in a medical ward to improve detection of delirium. Raw numbers, including P values, were not available (Cole 2002). Philbin 2000 reported no evidence of a statistically significant difference associated with CPWs when measuring the impact on assessment and documentation of heart failure characteristics.

Resources

Two studies reported statistically significant reductions in use of resources (Chen 2004; Kampan 2006). Chen (2004) reported a reduction in the daily beta-agonist usage rate in children with asthma (0.6 ± SD 0.03 versus 1.32 ± SD 0.41; P < 0.05) whilst Kampan (2006) reported a reduction in the number of capillary blood tests required over three days for patients with diabetes admitted with hypoglycaemia (10.03 ± SD 5.04 versus 12.34 ± SD 5.96; P = 0.048). Brattebo 2002 measured the impact of a CPW on mechanical ventilation time as an objective outcome measure. There was no evidence of a statistically significant difference between intervention and control groups when the original before and after data was re-analysed using time series analysis (P = 0.83). Due to poor reporting, it was not possible to identify whether all relevant resource use was measured and properly justified by the authors (Chen 2004; Kampan 2006).

Hospital readmissions

The impact of a CPW on rate of hospital re-admission was investigated in three studies (Chen 2004; Kampan 2006; Philbin 2000). Chen (2004) and Philbin (2000) found no evidence of a statistically significant impact for children with asthma and heart failure respectively. Hospital readmission in the Chen (2004) study was only reported as "non significant" whilst Philbin et al. reported 169 readmission events for heart failure up to six months for 840 experimental patients vs. 141 readmissions for 664 patients in the control group (p = 0.97). Readmissions for all causes up to six months were 363 events for 840 patients in the experimental group vs. 293 events for 664 control patients (p = 0.93). Kampan (2006) reported a significant reduction in six month readmissions for hypoglycaemia in patients with diabetes (6% versus 34%; P = 0.04). However, statistical inconsistency within this subgroup was substantial and compromised the estimation of a pooled effect on hospital readmissions (Analysis 3.5).

None of these studies included hospital readmissions in the estimate of hospital cost/ charges, but the study from Bauer (2006) reported on 3 years mean intervention costs, including the costs for re-hospitalisation. Bauer did not report re-hospitalisation numbers or rates (Bauer 2006).

Mortality

Two studies measured mortality and reported no evidence of a statistically significant impact of the CPW (Cole 2002; Philbin 2000). The time to follow-up was not documented by Cole (2002) who reported no difference in mortality between intervention and control groups (22.1% versus 19.3%). Philbin (2000) reported no difference in heart failure-related or all-cause mortality at six months (Analysis 3.4).

Hospital Costs and Charges

Three out of seven studies grouped as multifaceted interventions including a CPW element reported on hospital costs / charges (Bauer 2006; Kampan 2006; Philbin 2000). The study by Bauer et. al. reported in particular on a set of cost measures stratified on several criteria, i.e. three year mean intervention costs, direct outpatient costs, hospital inpatient costs, psychiatric inpatient costs and medical / surgical inpatient costs (Bauer 2006). None of these three studies reported statistically significant differences in costs / charges outcomes whilst the study by Kampan (2006) employed only a very small sample size available for analysis and was categorized as probably underpowered (Kampan 2006). Both studies compared the same sort of direct (variable) hospital costs included for each study in the pooled analysis, although it remains unclear if the term "mean costs" used in the Kampan (2006) study refers only to direct costs as further information was not able to be elicited from the chief investigator. The price adjusted and statistically pooled cost effect for the Kampan 2006 and Bauer 2006 studies reporting on hospital cost data was WMD -52.74 US$ (95% CI -119.09, 13.60) representing no statistically significant difference (Analysis 3.2). The differences in hospital costs and charges per subgroup are depicted together (WMD) in US$ for the common price year 2000 without a total estimate.

DISCUSSION

We screened and analysed over 3,000 published studies for this review of the impact of CPWs in hospitals and, after applying inclusion criteria, 27 studies were included with a total of 11,398 participants. Included studies arose from eight different countries for CPWs implemented in many different types of hospital wards and for 21 separate conditions or interventions. The number of included studies, total number of participants and breadth of settings suggest that this review provides a solid profile of the impact of CPWs. The results are relevant to a variety of settings worldwide. The breadth of the review also introduces a degree of clinical and statistical heterogeneity that makes meta-analysis inappropriate for many of the outcomes extracted. Despite this limitation some of our findings remain meaningful for clinicians, managers

and researchers, and eliminate some of the contradictory findings from individual studies.

Findings favouring CPWs

A major finding was the significant reduction in in-hospital complications associated with the introduction of CPWs. All seven studies (Choong 2000; Delaney 2003; Kiyama 2003; Marelich 2000; Aizawa 2002; Dowsey 1999 Bookbinder 2005) that measured complications reported results that favoured CPWs. Six of the seven studies examined invasive conditions or interventions (e.g. surgery, procedures or mechanical ventilation). This reflects the fact that studies of CPWs for invasive conditions were more likely to use complication measures such as infection and bleeding as an objective outcome measure rather than suggesting that CPWs only reduce complication rates for invasive procedures. The pooled result of an absolute risk reduction of 5.6% [n=5 trials] for patients recovering from surgery who were managed on a clinical pathway corresponds to prevention of one complication for every 17 patients treated. This strongly suggests that CPWs have a substantial role to play in patient safety.

Documentation appears to improve with the implementation of a clinical pathway. Clinical and statistical homogeneity supported the pooling of the studies by Doherty 2006 and Sulch 2002 resulting in a substantial and significant result (OR 11.95: 95%CI 4.72 to 30.30) favouring improved documentation with CPWs (Analysis 2.21). Whilst improved documentation may not appear to be an outcome that directly influences patient outcomes, any intervention that enhances communication must have a favourable influence on patient care (Jorm 2009).

LOS in hospital (reported in 11 studies) was significantly reduced when a CPW was introduced. Seven other studies measured LOS and found no statistically significant differences. Whilst statistical heterogeneity prevented pooled analysis the extent of the reduction reported indicates that it is highly likely that CPWs are associated with reduced LOS. This is important when combined with the magnitude of the reduced costs associated with CPWs (for which meta-analysis was also inappropriate). This means that the improved patient outcomes (e.g. fewer complications) and process of care measurements (e.g. improved documentation) do not occur in a setting of increased use of hospital resources.

Multiple studies measured the impact of CPWs on pneumonia (Marrie 2000; Usui 2004), myocardial infarction (Gomez 1996; Roberts 1997) and mechanical ventilation (Brook 1999; Kollef 1997; Marelich 2000; Brattebo 2002). All found that hospital resources were reduced whilst patient outcomes were not adversely affected. This reinforces the notion that CPWs are associated with efficient use of resources and efficiency of care.

There were insufficient numbers of homogenous studies to draw other conclusions at this stage.

Defining a CPW

Despite being utilised in healthcare since the 1980s, no clear definition for CPWs has been widely accepted. Confusion exists about what constitutes a CPW and they are referred to variously as CPWs, critical pathways, care maps, local guidelines and protocols amongst many other less common terms (Vanhaecht 2006). Subsequently, the search criteria were broadly inclusive before assessment of the relevance of the intervention being studied. Minimum criteria were developed for this review based on previous attempts to empirically describe CPWs (Campbell 1998; De Bleser 2006; Vanhaecht 2006) and pilot tested for reliability between authors for this review.

The following five criteria for a CPW were assessed:

1. The intervention was a structured multidisciplinary plan of care.

2. The intervention was used to channel the translation of 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".

4. The intervention had time-frames or criteria-based progression (ie. steps were taken if designated criteria were met).

5. The intervention aimed to standardize care for a specific clinical problem, procedure or episode of care.

An intervention was defined as a CPW if point one (the intervention was a structured multidisciplinary plan of care) was met and in addition, three out of the remaining four criteria were also met.

This approach maximised the identification and assessment of studies where the intervention of interest could be considered a CPW despite the wide variety of terms used in the literature. However, the time and effort taken to identify relevant studies for this review highlights the difficulty facing clinicians and healthcare managers when trying to ascertain and appraise the evidence regarding CPWs. It is imperative that an internationally accepted definition of a clinical pathway is adopted in order for current literature to be easily and widely accessed.

CPW Implementation Processes

In general, the reporting of CPW development and implementation processes was poor. Three of the identified 10 possible quality indicators were so poorly reported that they were dropped from the analysis. Interestingly, these included: identification of potential barriers to change, incorporation of reminder systems and use of local opinions leaders to promote the CPW. Implementation areas that were most likely to be reported included: use of evidence-based content, adaption of evidence for local circumstances and clinician involvement in CPW development. The less commonly reported criteria included use of an implementation team, identification of evidence-practice gaps, use of audit and feedback

and incorporation of education sessions. Given the likelihood of increased uptake with the use of evidence-informed implementation processes, this is an area of concern. Future evaluations of CPWs should specify the development and implementation process undertaken.

Quality of the evidence

The proportion of studies screened that were sufficiently well designed, conducted, and reported to enable inclusion was very small. Of the 3214 search-hits, only 27 studies met inclusion criteria, once the inclusion and EPOC design & quality criteria were applied. The majority of studies excluded from the review after meeting CPW content criteria were simple before and after studies, mostly comparing two or more yearly patient cohorts. This simple study design can be useful for internal monitoring but it is very difficult and misleading to draw meaningful conclusions due to the lack of control and inherent high level of bias.

Also, if a randomised controlled trial-design is considered, baseline measurements should always be undertaken to adjust for baseline differences. Poor reporting was however, a large obstacle in this review and better reporting of study methods could have facilitated the inclusion of more studies for analysis.

Whilst experimental methods such as randomised trials are recommended they may be considered beyond the capacity of many clinicians and researchers. Another well designed evaluation like time series analysis that meets the EPOC gold standard methodological criteria can produce meaningful, rigorous results with the use of very few resources.

Invasive versus non-invasive conditions

According to health economic theories, invasive procedures should be standardized more easily than treatment strategies in conservative sectors due to the lower treatment variance (Schlüchtermann 2005). We observed only slightly clearer LOS effects for invasive pathway conditions versus non-invasive conditions (WMD invasive -1.4 days versus -1.1 days). These results remained robust after excluding all of the Japanese primary studies via sensitivity analysis (WMD invasive -1.2 versus -0.9). However the complication rate was lower for those recovering from surgery and managed on a CPW. Previous suggestions that clearly favour surgical interventions may not be supported by these findings.

Stroke rehabilitation

The findings regarding LOS for the Falconer (1993) and Sulch (2000; 2002) studies were not statistically significant but did not support the decreased LOS from CPWs reported in other studies (Falconer 1993; Sulch 2000; Sulch 2002). This may be explained by the rehabilitation settings in which these studies were conducted already delivering optimal care without use of a clinical pathway. The Stroke Unit Trialists' Collaboration (2007) landmark Cochrane systematic review reported that improved outcomes were associated with admission to a specialized stroke unit and organised multidisciplinary care (Stroke Unit Trialists' Collaboration 2007). The rehabilitation settings described in the Falconer (1993) and Sulch (2000; 2002) studies contained these elements already and it is highly likely their type of care was optimising stroke management without the introduction of a CPW.

Adjusting for different market forces

Studies were ordered in forest plots by country and significant differences were observed. This refers to the country specific market forces and the problematic generalization of the conclusions drawn from this systematic review. Replicating the results of this review in other settings could be problematic (e.g., confounding effects such as market forces). As an example, it could be highly problematic to replicate conclusions drawn from Japanese settings into a US American hospital setting where LOS is historically lower. The market forces in form of the average LOS in acute care by country (OECD-Health-Data 2008) indicate also a country-specific estimate for the potential LOS impact of clinical pathway strategies and are evidenced by the observed LOS patterns from the present review if grouped or sorted by country.

Is LOS a Quality Indicator?

The majority of included studies used LOS as a performance indicator. Most of the included primary studies pre-defined LOS as an "economic" outcome and a surrogate for hospital costs or hospital charges. However, this raises the question, if LOS is an "economic" study endpoint or is it also a quality indicator? In other words, is a decreased LOS outcome always positive or clinically relevant, or are there instances where an increased LOS could indicate better care?

It should be clear, that LOS is always influenced by institutional context and as such reflect hospital practices with respect to hospitalisation and not necessarily reflect a positive outcome. LOS will fall as mortality increases, so it can be difficult to interpret.

We categorized LOS measures as a performance indicator and pre-defined LOS as an objective outcome measure. A reported decrease in LOS is not necessarily positive and can only be considered when patient outcomes are taken into account. However, LOS should always be assessed in context with the research question and in comparison with pre-defined patient measures (i.e. mortality) to avoid misleading conclusions. Results from this review indicate that CPWs are associated with favourable findings (i.e. reduced in-hospital complications) without increasing LOS and hospital costs.

Hospital perspective and costs of hospitalisation

In order to provide a replicable framework for local hospital providers considering the effectiveness of clinical pathways as a patient management strategy we limited the scope of the present review to a hospital perspective. Subsequently, the readers need

to be aware of the biases that may be caused by looking just at hospital costs in an institutional context. There is the potential for pathway interventions to result in capacity and/or cost shifting to other sectors of health care, to patients and their families or to other areas of the economy. Moreover, like LOS outcomes, hospital cost data can be misleading and difficult to interpret. The magnitude of cost savings should always be assessed in context with clinical relevant patient outcomes (i.e. mortality).

AUTHORS' CONCLUSIONS

Implications for practice

This review has established that CPWs may be associated with reduced complications and improved documentation when implemented in hospitals without negatively impacting on LOS or costs. Reduced complications were associated with invasive interventions or surgical conditions such as fractured neck of femur (Choong 2000), intestinal resection (Delaney 2003), gastrectomy (Kiyama 2003), mechanical ventilation (Marelich 2000), transurethral resection of the prostate (Aizawa 2002) and hip or knee arthroplasty (Dowsey 1999).

Implications for research

Quality of CPW studies

Studies measuring the impact of CPWs should incorporate EPOC standards into design to maximise the quality of evidence underpinning this model that is being utilised in a vast array of healthcare settings.

CPW reporting

Future evaluations of CPWs should specify the development and implementation process undertaken. Authors should consider the ten quality criteria described in this review when planning CPW development and implementation.

Grouping and comparing primary studies within pathway conditions for future systematic reviews

The comparison of LOS in days revealed the largest decrease in statistical heterogeneity when grouped per pathway condition. This has implications for future systematic reviews. Assuming a high number of primary pathway investigations meeting the EPOC quality gold standard, future review methods should focus on grouping and comparing within pathway conditions, for example, CPWs for pneumonia. However, this strategy requires a considerable number of primary studies per pathway condition. This strategy is highly supported by the low level of heterogeneity observed by grouping per condition.

Sub-grouping of pathway interventions (stand-alone CPW versus mulifaceted interventions)

The pooling and grouping per pathway characteristics revealed a subsequent 0% level of statistical heterogeneity within the group of complex interventions including a CPW versus usual care. The large decrease in statistical heterogeneity supports the appropriate grouping of similar primary pathway studies and is supported as well by the grouping and pooling of primary pathway studies per condition.

Due to poor reporting we were not able to compare complex interventions including a CPW element versus a single pathway intervention in order to meaningfully to detect factors associated with effective pathway standardization. Poor reporting of the particular pathway intervention, resulted in analyses that were not sensitive enough to reveal critical factors associated with positive pathway effects.

Considering the currently available available evidence, we have insufficient knowledge about the mechanisms through which pathways work. Future research should focus on a better understanding of the key elements of CPWs that have impact on economic and patient outcomes. We recommend further research comparing multifaceted interventions including a pathway element versus single pathway interventions.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Aizawa 2002

Methods	Individual randomized-controlled trial. Randomization method remains unclear (patient allocated "at random") Single blinding unclear. Objective outcomes used. Power calculation remains unclear due to poor reporting.
Participants	Urological male patients (n = 69) recruited from a Japanese urban area. Mean Age was 70 years for the experimental patients (n = 32) and 72 years (n = 37) for the control male patients
Interventions	CPW-Intervention (paper format): Invasive single TURP Intervention, detailing the daily steps in the course of treatment, clinical assessment and patient education. The pathway contains also instructions for the clinical monitoring including vital signs and variance documentation. All CPW criteria met and multiple professions involved. Moderate (B) evidence-based implementation strategy. The reported purpose of the intervention was appropriate management and cost containment Control: control conditions poorly described as "usual care" or non-pathway care and represent the standard of care prior to the pathway implementation
Outcomes	Mean LOS, duration of catheterization and hospital charges, reported as Japanese insurance points. 6 month follow-up period
Notes	Protection against contamination remains unclear.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Comment: insufficient information about the sequence generation to permit judgment "yes" or "no"
Allocation concealment?	Unclear	Comment: insufficient information to permit judgment "yes" or "no"
Blinding? All outcomes	Unclear	Comment: insufficient information to permit judgment "yes" or "no"
Incomplete outcome data addressed? All outcomes	Yes	Comment: no missing outcome data.
Free of selective reporting?	Yes	Comment: all the pre-specified outcomes have been reported in the pre-specified way

Free of other bias?	Unclear	Comment: insufficient information to permit judgement of "yes" or "no"

Bauer 2006

Methods	Individual randomized multi-center controlled trial. Participants were randomized after index hospitalization Concealed computerized telephonic system for randomization in blocks of two to four patients Single blinded outcome assessment. Appropriate power calculation used.
Participants	Psychiatric patients (n = 306) recruited in urban and regional US settings and presented to mental health outpatient clinics countrywide. Mean age was 46,6 years (SD 10,1) for both, the experimental patients (n = 157) and control patients (n = 149)
Interventions	CPW Intervention (paper format): Complex psychiatric collaborative care CPW combined with case management for bipolar disorder. Pathway intervention contains detailed collaborative care plan, scheduled care and patient self management enhancement. Four out of five CPW criteria met and highly (A) evidence-based implementation strategy. Palliative appropriate management and cost containment Control: control conditions or "usual care" for bipolar disorder justified by a clear protocol and helpful for the assessment of generalizations
Outcomes	3 years mean intervention costs, direct outpatient costs, hospital inpatient costs, psychiatric inpatient costs and medical / surgical inpatient costs. 3 years follow-up with repeated measures every 8 weeks
Notes	Protection against contamination of the control professionals reported

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	
Allocation concealment?	Yes	Comment: telephonic randomization used.
Blinding? All outcomes	Yes	Comment: participants were not blinded but outcome measurement unlikely to be influenced by lack of blinding Quote: *"The study chair and sites remained blind to outcome until follow-up was complete."*

Bauer 2006 (*Continued*)

Incomplete outcome data addressed? All outcomes	Yes	Comment: no missing outcome data.
Free of selective reporting?	Yes	Comment: detailed study protocol available, all of the study's pre-specified outcomes have been reported in the pre-specified way
Free of other bias?	Yes	Comment: the study appears to be free of other sources of bias

Bookbinder 2005

Methods	Controlled before and after study (CBA). 2 general medical units (clusters) served as control sites and 3 cluster units including one palliative care ward served as experimental sites. Timing of data collection was contemporaneous and choice of control sites described but not justified by the authors (comparability study and control sites). Reliable outcome measures used Baseline measures clearly reported and no substantial differences detected. Power calculation unclear Single blinded outcome assessment.
Participants	Palliative end of live 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	CPW Intervention (paper format): Complex best practice intervention combined with other interventions, like order sheets, reminders and feedback. All CPW criteria met. CPW condition or target is Palliative Care and multiple professions (palliative care specialists, social workers, ethicists and dieticians) involved. The reported purpose of the intervention was appropriate management. The CPW implementation strategy was highly evidence-based (A) Control conditions: poorly described as "usual care" for palliative patients at 2 general medical units. Control conditions described as "usual care" before quality management initiative was implemented
Outcomes	Number of symptoms assessed, problematic symptoms identified, number of interventions and inpatient consultations (patient outcomes). Follow-up from index admission until end of life
Notes	Protection against contamination of the control professionals reported

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	No	CBA design.

Bookbinder 2005 (*Continued*)

Allocation concealment?	No	CBA design.
Blinding? All outcomes	No	CBA design.
Incomplete outcome data addressed? All outcomes	Unclear	Comment: insufficient information to permit judgment "yes" or "no"
Free of selective reporting?	Unclear	Comment: insufficient information to permit judgment "yes" or "no"
Free of other bias?	No	Quote: *"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."*

Brattebo 2002

Methods	The authors used a statistically controlled time series design (ITS). Baseline and post-intervention measures were depicted graphically and only the mean ventilator time as one out of 3 reported outcomes met EPOC inclusion criteria The number of measures (points in time) were justified by the authors and reliable outcome measures used. Statistical adjustment for serial correlation and power calculation remained unclear. Hospital Information System used for protection against detection bias
Participants	Invasive and non-invasive adult patients (n = 285) recruited from a mixed surgical intensive care unit within a urban setting in Norway. The mean age reported ranged from 52,3 till 55,8 and the baseline period included 147 patients, whereas the post-intervention period covered 138 participants
Interventions	Complex CPW Intervention combined with continuous feedback, posters, E-mails and flyers. Four out of five CPW criteria met. Complex pathway for ventilator support contains a scoring system and was designed for appropriate patient management. Four out of five CPW criteria met and highly (A) evidence-based implementation strategy used Baseline: baseline conditions or "usual care" was reported and justified "at the direction of the physician in charge"
Outcomes	Only the outcome measure "ventilation patient days per month" met EPOC inclusion criteria. LOS and mortality does not meet EPOC inclusion criteria. Follow-up from index admission until discharge

Brattebo 2002 (*Continued*)

Notes	Only the primary outcome "ventilation patient days per month" met EPOC inclusion criteria. Ventilation outcome only graphically depicted and analyzed and extracted with MS paint

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	No	ITS design.
Allocation concealment?	No	ITS design.
Blinding? All outcomes	No	Comment: the objectives of the study were to reduce patient mean time on a ventilator and LOS in intensive care by introducing sedation guidelines. There is an important risk of bias as the staff were not blinded and the interventions were primarily aimed at doctors and nurses
Incomplete outcome data addressed? All outcomes	Yes	Comment: no missing outcome data.
Free of selective reporting?	Yes	Comment: all the study pre-specified outcomes have been reported.
Free of other bias?	Unclear	Comment: 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.

Brook 1999

Methods	*Individually randomized controlled trial. Participants were randomized to the experimental and control group* at the time of initiation of mechanical ventilation. Blocked randomization was accomplished using opaque, sealed envelopes, which were opened at the time each patient was enrolled in the study Objective outcome measures used. Blinding remains unclear. Appropriate power calculation used.
Participants	Non-invasive adult patients (n = 321) recruited from an urban American teaching hospital within a medical ICU. The mean age reported for both groups was 57,8 for the 162 experimental patients versus 58,1 for the 159 patients in the control group and characterized by 90 to 95% white Americans

Brook 1999 (*Continued*)

Interventions	CPW Intervention (paper format): Stand-alone intervention for sedation management including nursing staff empowerment. Pathway intervention was protocol based and designed for appropriate patient management. Four out of five CPW criteria met and low (C) evidence-based implementation strategy used Control conditions: traditional non-protocol approach or "usual care" for mechanical ventilation and sedation management justified by the authors. Physician's driven management or verbal order without empowerment of the nursing profession
Outcomes	Objective outcome measures used, ICU LOS (days) , mean LOS (days), number of acquired organ system derangements and in-hospital mortality. Follow-up period was until discharge
Notes	Protection against contamination of the control professionals remains unclear

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Quote: *"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?	Yes	Quote: *"Blocked randomization was accomplished using opaque, sealed envelopes, which were opened at the time each patient was enrolled in the study."*
Blinding? All outcomes	No	Comment: participants and staff were not blinded.
Incomplete outcome data addressed? All outcomes	Yes	Comment: reasons for excluding patients from the analysis have been reported Quote: *"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."*

Brook 1999 (*Continued*)

Free of selective reporting?	Yes	Comment: the study pre-specified outcomes have been reported in the pre-specified way
Free of other bias?	Yes	Comment: the study appears to be free of other sources of bias

Chadha 2000

Methods	2 x 2 balanced incomplete block controlled before and after study. Two hospitals were allocated to local application of menorrhagia guidelines whilst two hospitals were allocated to local application of urinary incontinence guidelines. Hospitals allocated to the menorrhagia guidelines acted as controls for urinary incontinence whilst hospitals allocated to the urinary incontinence guidelines acted as controls for the menorrhagia guidelines
Participants	Women treated in hospital gynaecology units in Scotland with menorrhagia (n = 497) or urinary incontinence (n = 449). The mean age for those presenting with menorrhagia was 40.1 (SD 6.8) years pre intervention and 40.4 (SD 7.3) years post intervention. The mean age for those presenting with urinary incontinence was 50.2 (SD 12.2) years pre intervention and 48.7 (SD 12.0) years post intervention
Interventions	National guidelines for menorrhagia and urinary incontinence were adapted into local protocols at participating hospitals - two hospitals implemented protocols for menorrhagia and two hospitals implemented protocols for urinary incontinence. Protocols were introduced via staff education sessions. Protocols were placed in women's medical records prior to elective admission and displayed in wards
Outcomes	Objective outcomes for process of care were measured. Primary outcomes were compliance with recommendations for initial hospital assessment; compliance with recommendations on investigations; compliance with recommendations on first-line treatments; compliance with guidelines for pre-surgery assessment; rates of appropriate surgical treatment
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	No	CBA design.
Allocation concealment?	No	CBA design.
Blinding? All outcomes	No	CBA design.

Chadha 2000 (*Continued*)

Incomplete outcome data addressed? All outcomes	Yes	Comment: reason for missing outcome data unlikely to be related to the true outcome
Free of selective reporting?	Yes	Comment: all the pre-specified outcomes have been reported in the pre-specified way
Free of other bias?	Unclear	Comment: only 57% and 45% women returned the questionnaire at six and twelve months follow-up for the analysis of outcome of care Quote: *"Use of endometrial biopsy, were 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 significant 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."* Quote: *"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

Methods	*Individual randomized single-center controlled trial. Participants were randomized after meeting clearly defined inclusion criteria.* *Randomization method unclear (patient allocated "at random").* *Single blinding unclear. Objective patient outcomes used.* *Power calculation remains unclear.*
Participants	Asthmatic children (n = 42) recruited from a Taiwan medical children hospital. Setting seems to be regional and was reported as "Taiwan residents from Taipei County". Mean Age was 5,54 (SD 3,04) years for both groups. There was no statistical difference at baseline between the experimental and control participants. The mean age of the parents was 36,95 (SD 4,61) The experimental group consisted of 20 and the control group of 22 asthmatic children
Interventions	Complex CPW intervention (paper format): complex non-invasive CPW intervention for asthmatic children combined with teaching sessions for the parents and children, training & instructions and case management

Chen 2004 (*Continued*)

	Pathway intervention was based on an asthma care map and designed for appropriate patient management and cost containment. All CPW criteria met and highly (A) evidence-based implementation strategy used Control conditions: traditional or "usual care" for asthma management
Outcomes	Usage rate of the emergency room (surrogate outcome for in-hospital complications) and hospital readmissions (only reported as non significant). Follow-up period was 3 months
Notes	Protection against contamination of the control professionals remains unclear

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Comment: insufficient information about the sequence generation process to permit judgment of "yes" or "no"
Allocation concealment?	Unclear	Comment: insufficient information provided to permit judgment
Blinding? All outcomes	Unclear	Comment: insufficient information provided to permit judgment
Incomplete outcome data addressed? All outcomes	Yes	Comment: no missing outcome data.
Free of selective reporting?	Unclear	Comment: the study outcomes are not clearly defined in the article, making difficult to judge whether the results are free of selective reporting
Free of other bias?	Unclear	Comment: insufficient information to assess whether an important risk of bias exists

Choong 2000

Methods	Pseudo-randomized single-center controlled clinical trial. Participants were pseudo-randomized based on the patient unit record number, even numbers were allocated to the control group and odd numbers to the pathway group *Single blinding remains unclear. Objective patient outcomes used.* Appropriate power calculation used.
Participants	Hospitalized orthopadic patients (n = 111) with femural neck fracture. Patients were recruited from a orthopadic urban hospital setting in Melbourne, Australia The experimental group consisted of 55 and the control group of 56 patients with a mean age of 84 years for both groups. There was no statistical difference at baseline

Choong 2000 (*Continued*)

	between the experimental and control participants
Interventions	Invasive CPW Intervention (paper format): Stand-alone intervention for femural neck fracture including detailed care assessment and discharge planning on admission. Pathway intervention was "proactive care" protocol based and designed for appropriate patient management and cost containment. All CPW criteria met and low (C) evidence-based implementation strategy used Control conditions: traditional or "usual care" for femural neck fracture justified by a detailed protocol for control participants. Physician's driven management with discharge planning described as "begun postoperatively" and depending on patient progress
Outcomes	LOS (days), days to mobilisation, confusional status, in-hospital complications, post-discharge complications and readmission rates. Follow-up period was 28 days
Notes	Protection against contamination of the control professionals remains unclear

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	No	Comment: non-random sequence generation process used Quote: *"Patients were allocated on the basis on their unit record number, even numbers to the control group, and odd numbers to the clinical pathway group."*
Allocation concealment?	Unclear	Comment: the method used by the administrative clerk in charge of the allocation sequence is not described
Blinding? All outcomes	Yes	Comment: no blinding but the outcome and outcome measurement are not likely to be influenced by lack of blinding
Incomplete outcome data addressed? All outcomes	Yes	Comment: no data missing.
Free of selective reporting?	Yes	Comment: all the study pre-specified outcome have been reported in the prespecified way
Free of other bias?	Unclear	Comment: the study appears to be free of other bias.

Cole 2002

Methods	*Individual randomized single-center controlled trial. Participants were randomized after meeting clearly defined inclusion criteria.* Computer generated blocked randomization was employed and clearly justified by the authors. Blinded data assessment and objective patient outcomes used *Appropriate power calculation remains unclear.*
Participants	Geriatric medical patients presented to the ED (n = 227) with suspected delirium were recruited from a urban Canadian setting and admitted to the general medical units within the study hospital in Montreal 113 experimental patients with a mean age of 82,7 years (SD 7,5) were assessed and treated in accordance with the complex intervention reported and 114 patients with a mean age of 82 years (SD 7,1) received traditional or usual care. There was no statistical difference at baseline between the experimental and control participants
Interventions	Complex CPW intervention (paper format): complex non-invasive CPW intervention for the systematic detection and care of delirium in older medical patients combined with case management. Intervention include a complex confusional assessment and a detailed care protocol and was designed for appropriate patient management. All CPW criteria met and highly (A) evidence-based implementation strategy used Control conditions: traditional or "usual care" for older patients with suspected delirium. No confusional assessment used
Outcomes	LOS, mortality at 8 weeks, discharge destination at 8 weeks, less dependent at 8 weeks. Follow-up period was 8 weeks
Notes	Protection against contamination of the control professionals remains unclear

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Quote: *"Stratified randomization was used; that is, independent randomization was done within group of prevalent and incident cases respectively. Further more we performed blocking using blocks of different sizes to guarantee 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 help to maintain blinding as to treatment allocation."*
Allocation concealment?	Yes	Quote: *"Patients were randomly allocated by means of computer-generated random numbers to receive the intervention or usual care on the five medical units."*

Cole 2002 (*Continued*)

Blinding? All outcomes	Unclear	Comment: blinding was not possible in one of the 5 hospitals included in the study (investigator's unit)
Incomplete outcome data addressed? All outcomes	Yes	Comment: 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
Free of selective reporting?	Yes	Comment: all of the pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way
Free of other bias?	Yes	Comment: the study appears to be free of other biases.

Delaney 2003

Methods	*Individual randomized single-center controlled trial. Participants were randomized after consent to the CPW intervention or traditional care.* Computer generated randomization was employed and executed by the biostatistics department. Blinded data assessment remains unclear but objective patient outcomes used Appropriate power calculation used.
Participants	Surgical patients (n = 64) were recruited from a urban US setting and allocated to receive the complex CPW intervention (n = 31) or traditional care (n = 33). Participants were characterized by a mean age of 50,6 years for the experimental group and 41,9 years for the control patients. There was no statistical difference at baseline between the experimental and control participants
Interventions	Stand-alone CPW intervention (paper format): Invasive CPW intervention for laparotomy and intestinal resection. Surgical intervention was characterized by a proactive patient management led by a a colorectal nurse manager. Wall charts and early conversation from intravenous to oral analgesia employed. Intervention was designed for appropriate patient management and cost containment. All CPW criteria met and moderate (B) evidence-based implementation strategy used Control conditions: traditional or "usual care" for surgical patients with laparotomy reported and justified by the authors. Traditional care protocol reflects traditional means of surgical care, i.e. diet withheld until flatus or stool and late conversation to oral analgesia after diet tolerated
Outcomes	LOS, LOS including time spent in readmission, pain scores, QOL, hospital satisfaction, rehospitalization, complications until follow-up and happiness to be discharged. Follow-up period was 30 days

Delaney 2003 (*Continued*)

Notes	Protection against contamination of the control professionals remains unclear

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Quote: *"Randomization was performed with sealed envelopes prepared by the biostatistics department."*
Allocation concealment?	Yes	Comment: sealed envelopes used.
Blinding? All outcomes	Unclear	Comment: the study did not address this outcome.
Incomplete outcome data addressed? All outcomes	Yes	Comment: no missing outcome data.
Free of selective reporting?	Yes	Comment: all pre-specified outcomes have been reported in the pre-specified way
Free of other bias?	Unclear	Comment: insufficient information to assess the risk of bias due to contamination between intervention and control groups

Doherty 2006

Methods	Multi-center controlled before and after study (CBA). Authors used a cluster design and 8 hospitals were matched pair wise and one randomly allocated to the experimental group. Comparability was assessed using RRMA rating and hospital size (patients / beds) and justified by the authors. Medical units of the hospitals served as experimental or control sites. Timing of data collection was contemporaneous and reliable outcome measures used *Pre-intervention measures reported and no substantial differences detected.* Appropriate power calculation used. Allocation per cluster but only pooled results presented for both groups of patients (potential unit of analyses error)
Participants	Asthmatic patients (n = 187) recruited from 8 rural settings in Australia and presented to the ED. 98 patients were allocated to intervention hospitals and 89 to control hospitals. The mean age was reported elsewhere (see Doherty et al 2007) and ranged from 33 for interventional participants versus 37 years for control patients. There was no statistical difference in asthma severity at baseline between both groups of patients
Interventions	Stand-alone CPW intervention (paper format): Non invasive CPW intervention for Asthma care. Guideline based intervention for acute asthma, characterized by a proactive asthma severity assessment and short term asthma management plan (STAMP). Inter-

	vention was designed for appropriate patient management and 4 out of five CPW criteria met. Highly (A) evidence-based implementation strategy used Control conditions / hospitals: traditional or "usual care" for asthmatic patients without active implementation and adoption of national guidelines. Traditional care not justified by protocol and poorly described as traditional care for acute asthma
Outcomes	Assessment of severity of asthma, use of spirometry, overuse of ipratropium for mild asthma, use of systemic steroids, inappropriate use of antibiotics and use of a STAMP. Follow-up period was from index admission until discharge
Notes	Applicability due to rural setting and small Australian hospitals may be limited but robust cluster design and highly evidence based implementation strategy used

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	No	CBA design
Allocation concealment?	No	CBA design
Blinding? All outcomes	No	CBA design
Incomplete outcome data addressed? All outcomes	Unclear	Comment: number of patients differs between pre and post intervention. No reasons for missing data provided
Free of selective reporting?	Unclear	Comment: main outcome of the study not clearly defined in the methods section outcomes appears 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 weather the article is free of selective reporting or not
Free of other bias?	Unclear	Comment: insufficient information to assess whether an important risk of bias exists. Characteristics of intervention and control group at baseline not shown

Dowsey 1999

Methods	*Individual randomized single-center controlled trial. Participants were allocated to receive standardized orthopaedic care or usual care for postoperative care. Due to poor reporting, it remains unclear if the allocation refers to one ore more independent orthopedic wards or teams.* Computer generated randomization was employed and clearly justified by the authors. Data assessment by a blinded clerical assistant and objective patient outcomes used *Appropriate power calculation employed and justified by the authors.*
Participants	*Elective orthopaedic patients (n = 163) for hip and knee arthroplasty were* randomised *to the pathway intervention (n = 92) or usual care group (n = 71). The mean age reported was 64 years for experimental and 68 years for control patients. Participants were recruited from a tertiary referral hospital within an urban Australian setting.*
Interventions	Invasive "stand-alone" intervention (paper format): Pathway for hip and knee arthroplasty reported as "proactive and standardized orthopaedic care with predefined daily written goals. The Intervention was protocol based and includes a daily re-evaluated discharge plan and patient education.Intervention was designed for quality management and all CPW criteria met. Moderate (B) evidence-based implementation strategy used Control conditions: Poorly r*eported as "reactive orthopedic treatment"* whereby the treating team responded to the needs of the patient in providing postoperative care
Outcomes	LOS, days to sitting out of bed, days to ambulation, complications and hospital readmission until follow-up and matched / planned discharge destination. Follow-up period was 3 month
Notes	Protection against contamination of the control professionals remains unclear

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	*Quote: "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?	Unclear	Comment: insufficient information to permit judgment "yes" or "no"
Blinding? All outcomes	Unclear	Comment: the study did not address this outcome.
Incomplete outcome data addressed? All outcomes	Yes	Quote: *"Twelve patients were excluded by the criteria listed in the methods? Having revision arthroplasty, simultaneous bilateral joint arthroplasty, arthroplasty for acute trauma or complex tumour surgery."* Comment: reason for missing data unlikely to be related to the true outcome

Dowsey 1999 (*Continued*)

Free of selective reporting?	Yes	Comment: all of the study's pre-specified outcomes have been reported in the pre-specified way
Free of other bias?	Yes	Comment: the study appears to be free of other sources of bias

Falconer 1993

Methods	*Individual randomized single-center controlled trial. Participants were allocated to receive standardized multidisciplinary stroke rehabilitation or the traditional rehabilitation program. As reported and justified by the authors, experimental and control subjects were allocated to different treatment teams respectively different units or wards within the study hospital. Randomization method remains unclear (patient allocated "at random") and some irregularities occurred but more then 80% of randomized participants analyzed (121 finally analyzed out of 136 randomized). Irregularities within randomization reported due to bed availability. Blinded data assessment and objective patient outcomes used. Power calculation remains unclear.*
Participants	Stroke patients for rehabilitation (n = 121) recruited from a university teaching hospital. Urban US American setting characterized as hospitalized stroke patients with a with / black ratio (W/B) of 37/16 and a mean age of 68,6 years for the 53 experimental patients and a W/B ratio of 49/19 and a mean age of 67,6 years for the 68 patients received traditional rehabilitation for stroke There was no statistical difference at baseline between the experimental and control participants
Interventions	Non-Invasive "stand-alone" intervention (electronic format): Pathway for stroke rehabilitation reported as "multidisciplinary and standardized stroke rehabilitation with predefined daily written goals". The Intervention was based on daily team conferences, electronic protocols and includes a daily re-evaluated discharge plan and continuous feedback. Intervention was designed for appropriate management and cost containment. All CPW criteria met. Moderate (B) evidence-based implementation strategy used Control conditions: reported and justified by the authors with a protocol. Discipline orientated patient assessment and care with discharge planning at the direction of the physician in charge. No detailed care plan used
Outcomes	LOS, hospital charges, patient satisfaction and functional status. Secondary outcomes mortality and rehospitalization did not meet EPOC criteria. Follow-up period was 12 months
Notes	Allocation to different wards or units for both groups reported, but protection against contamination of the control professionals remains unclear. Possible ceiling effect reported: 1 year pilot study previously to the major study with a mean LOS reduction of 3.3 days

Risk of bias

Falconer 1993 (*Continued*)

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Comment: insufficient information about the sequence generation process to permit judgment "yes" or "no"
Allocation concealment?	Unclear	Comment: method of concealment not described.
Blinding? All outcomes	Unclear	Comment: insufficient information to permit judgment "yes" or "no"
Incomplete outcome data addressed? All outcomes	Yes	Quote: *"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."* Comment: reason for missing data unlikely to be related to true outcome
Free of selective reporting?	Yes	Comment: all of the pre-specified outcomes have been reported in the pre-specified way
Free of other bias?	Yes	Comment: the study appears to be free of other sources of contamination

Gomez 1996

Methods	*Individual randomized single-center controlled trial. Participants were randomized to receive accelerated diagnostic and clinical treatment for suspected myocardial infarction (MI) or traditional care reflecting the standard prior to the study. Experimental patients were allocated to a chest pain evaluation unit receiving standardized risk assessment and treatment whereas the control patients were allocated to a telemetry unit and were assessed and treated by traditional means.* Randomization was performed by sealed envelopes containing the treatment assignment and clearly justified by the authors. Blinded data assessment and objective patient outcomes used *Appropriate power calculation employed and reported by the authors.*
Participants	Medical patients with suspected MI (n = 100) recruited from a university hospital. Urban US American setting (Salt Lake City) characterized as patients presented to the ED with suspected MI. The 50 experimental patients had a mean age of 50 years and the corresponding 50 control subjects a mean age of 53 years There was no statistical difference at baseline between the experimental and control participants

Interventions	Minimaly invasive (PTCA) and non-invasive "stand-alone" intervention (paper format): Intervention was based on a accelerated diagnostic pathway and standardized treatment for low risk patients with suspected MI or acute chest pain. The diagnostic pathway included a Goldman algorithm to detect low risk patients and hospitalization for low risk patients was not mandatory. Intervention was designed for cost containment. All CPW criteria met. Moderate (B) evidence-based implementation strategy used Control conditions: patients allocated to the telemetry unit received clinical assessment and treatment for suspected MI by traditional means. Patients were managed by there attending physicians and no differentiation was made between low and high risk patients. Clinical assignment, therapy and discharge planning were at the direction of the physician in charge
Outcomes	LOS (hours), hospital charges and rehospitalization within 30 days. Follow-up period was 30 days
Notes	Protection against contamination of the control professionals remains unclear

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Quote: *"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?	Yes	Comment: sequentially envelopes have been used.
Blinding? All outcomes	No	Comment: participant and investigators not blinded. Quote: *"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 toward ordering briefer, more economic evaluations, which would have had the effect of reducing true differences between groups."*
Incomplete outcome data addressed? All outcomes	Yes	Comment: no missing outcome data.
Free of selective reporting?	Yes	Comment: all of the pre-specified outcomes have been reported in the pre-specified way

Gomez 1996 (*Continued*)

Free of other bias?	No	Quote: *"The relatively small sample size, low event rate and short follow-up period of this study (30 days) does 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."*

Johnson 2000

Methods	Individual-randomized controlled trial with allocation to a ward using the CPW or a ward providing usual care in the same hospital
Participants	Paediatric inpatients admitted for asthma aged 2 to 18 years (64% male). Total number of participants was 110 with 55 in the intervention group and 55 in the control group
Interventions	Asthma CPW implemented for one paediatric ward (intervention) and routine care at the other ward (control). Key features were nurse-driven decisions for weaning bronchodilators, frequent peak flow measurement, asthma teaching essentials, prescriptions for "home therapy" given pre discharge and early establishment of an asthma management plan
Outcomes	Objective primary outcomes measured were hours of hospitalization, number of nebulisations during hospitalization, number of unplanned interventions within two weeks of discharge and hospital charges
Notes	Protection against contamination of the control professionals remains unclear

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Comment: insufficient information to permit judgment "yes" or "no"
Allocation concealment?	Unclear	Comment: insufficient information to permit judgment "yes" or "no"
Blinding? All outcomes	Unclear	Comment: insufficient information to permit judgment "yes" or "no"
Incomplete outcome data addressed? All outcomes	Yes	Comment: number of patients excluded and reason of exclusion from analysis have been reported

Johnson 2000 (*Continued*)

Free of selective reporting?	Yes	Comment: all of the study pre-specified outcomes have been reported in the pre-specified way
Free of other bias?	No	Quote: *"The study was limited primarily by an inability to enrol some eligible patients because of bed shortages."* Comment: clinical and demographic characteristics of intervention and control groups not comparable at baseline Quote: *"Our intervention group had a higher number of patients who received steroids before their arrival to the ED."* Quote: *"Statistically significant difference in the mean age of our 2 groups".*

Kampan 2006

Methods	Individual randomized single-center controlled trial. Participants were randomized after eligibility confirmed
Participants	Patients admitted to Taksin Hopsital, Bangkok, with type 2 diabetes and hypoglycaemia between July and December 2005. 33 were randomized to the intervention and 32 to the control group (total n = 65). The majority were female (77%) and the mean age was 64.4 years (SD 11). Both groups had similar age, gender, mean serum glucose, number of chronic complications, concurrent illnesses and pattern of hypoglycaemic drugs on admission
Interventions	CPW and counselling were provided as the intervention. The three essential components of the CPW were evaluation of patient status, initiation of appropriate treatment and education or counselling with a discharge plan
Outcomes	Objective primary outcomes measured were LOS (days), mean cost, number of capillary blood tests, readmissions with recurrent hypoglycaemia within 3 months
Notes	Randomization process unclear.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Comment: insufficient information to permit judgment "yes" or "no"
Allocation concealment?	Unclear	Comment: insufficient information to permit judgment "yes" or "no"

Kampan 2006 (*Continued*)

Blinding? All outcomes	Unclear	Comment: insufficient information to permit judgment "yes" or "no"
Incomplete outcome data addressed? All outcomes	Yes	Comment: no missing outcome data.
Free of selective reporting?	Yes	Comment: all the pre-specified outcomes have been reported in the pre-specified way
Free of other bias?	Unclear	Comment: insufficient information to assess whether an important risk of bias exists

Kim 2002

Methods	Individual randomized controlled trial in an emergency department of an accelerated CPW. Randomization codes were assigned to consecutive patients prior to the study
Participants	Patients presenting to the emergency department with newly diagnosed or new-onset atrial fibrillation. Nine patients were randomized to the intervention and 9 to the control. Mean age was 48 years and baseline characteristics were reported as similar between the groups
Interventions	Particpants were allocated to an accelerated CPW with dalteparin and early cardioversion or for routine hospital admission
Outcomes	Objective primary outcomes measured were LOS (days) and hospital costs
Notes	Protection against contamination process unclear.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Comment: randomization process not clearly described. Quote: *"Patients were randomized after enrolment on the basis of the assigned code to either the traditional strategy of hospital admission or to an accelerated ED-based clinical pathway."*
Allocation concealment?	Unclear	Comment: insufficient information to permit judgment of "yes" or "no"
Blinding? All outcomes	Unclear	Comment: insufficient information to permit judgment of "yes" or "no"

Kim 2002 (*Continued*)

Incomplete outcome data addressed? All outcomes	Yes	Comment: no missing outcome data.
Free of selective reporting?	Yes	Comment: all of the study pre-specified outcomes have been reported in the pre-specified way
Free of other bias?	Yes	Comment: the study appears to be free of other sources of bias

Kiyama 2003

Methods	Individual-randomized controlled trial in a single hospital with patients randomly allocated to the main building or the east building depending
Participants	Patients admitted to Nippon Medical School Hospital from January to December 2001 for gastrectomy for cancer. Forty-seven patients were randomized to the intervention with 38 allocated to the control group. Mean age for the intervention group was 63 (SD 12.9) and 66.8 (SD 12.1) years for the control group
Interventions	Implementation of a CPW standardizing practice and incorporating printed order sets, such as drug and infusion protocols
Outcomes	Objective primary outcomes measured were length of pre-operative stay in hospital (days) , length of post-operative stay in hospital (days), in-hospital morbidity and complications rate, and rate of "target achievement" at 1, 4, 7 and 14 days. Examples of target achievements are tolerating diet and cessation of intravenous infusion
Notes	Randomization process was influenced by bed availability.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	No	Comment: patients allocation by availability of beds. Quote: *"The patients were randomly assigned to either the main building or the east building of the participating hospital, depending of the availability of beds."*
Allocation concealment?	Unclear	Comment: insufficient information to permit judgment of "yes" or "no"
Blinding? All outcomes	Unclear	Comment: the study did not address this outcome.

Incomplete outcome data addressed? All outcomes	Unclear	Comment: insufficient reporting of attrition's to permit judgment of "yes" or "no". No reason for missing data provided
Free of selective reporting?	Unclear	Comment: insufficient information to permit judgment "yes" or "no"
Free of other bias?	Unclear	Comment: insufficient information to assess whether an important risk of bias exists

Kollef 1997

Methods	Individual randomized controlled trial across two medical and two surgical intensive care units in two hospitals. Stratification according to ICU site was done to ensure similar distributions of allocations across the four sites
Participants	Patients requiring mechanical ventilation in the medical and surgical intensive care units of Barnes Hospital and Jewish Hospital (USA) between July and October 1995. A total of 357 patients participated with 179 in the intervention and 178 in the control group. Forty-seven percent of the sample was male and 62% were African-American. The mean age for the intervention was 62.3 (SD 17.3) years and 62.3 (SD 16.8) years for the control group. The intervention group had a higher percentage of participants with COPD (27. 9 V 18.5; P = 0.036) and a lower APACHE II score (16.4 [SD 5.9] V 17.7 [5.5]; P = 0. 026). No differences were measured between intervention and control groups for other baseline characteristics. including gender and reason for ICU
Interventions	The implementation of protocols for use by nurses and respiratory therapists to wean patients from mechanical ventilation versus traditional physician-directed weaning
Outcomes	The primary objective measures were duration of mechanical ventilation before and after commencement of weaning (hours), number requiring reintubation, hospital mortality and LOS in hospital (days)
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Quote: *"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*

Kollef 1997 (*Continued*)

		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?	Yes	Quote: *"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."*
Blinding? All outcomes	Unclear	Comment: the study did not address this outcome.
Incomplete outcome data addressed? All outcomes	Yes	Comment: reason for missing outcome data unlikely to be related to the true outcome Quote: *"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."*
Free of selective reporting?	Yes	Comment: all of the study's pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way
Free of other bias?	Yes	Comment: the study appears to be free of other sources of bias

Marelich 2000

Methods	Single-center individual randomized controlled trial in medical and surgical (trauma) intensive care units. Randomization was by opaque, sealed, numbered envelopes stratified by medical and surgical intensive care units
Participants	A total of 335 patients were enrolled at the University of California, Davis, Medical Centre between June 1997 and May 1998 One-hundred and seventy participants were enrolled in the Medical ICU (82 intervention and 82 control). Mean age for the intervention group was 56.6 (SD 16) years and 59% were male whilst the control group had a mean age of 54.5 (SD 17.1) years and 63% were male

	One-hundred and sixty-five participants were enrolled in the surgical intensive care unit (84 intervention and 81 control). Mean age for the intervention group was 41.5 (SD 18. 3) years and 68% were male whilst the control group had a mean age of 41.0 (SD 17.6) years and 75% were male
Interventions	Implementation of a ventilation management protocol in medical and surgical intensive care units versus usual care
Outcomes	Outcome measures were duration of mechanical ventilation and rate of ventilation associated pneumonia. Ventilator associated pneumonia was defined as initiation of antibiotics in association with two of the following (1) positive endotracheal tube aspirate or bronchoscopy cultures; (2) fever or rising leukocyte count; and (3) pulmonary opacities
Notes	Protection against contamination of the control professionals remains unclear

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Quote: *"Randomization was by opaque, sealed, numbered envelopes stratified for MICU and trauma services and for ICU."*
Allocation concealment?	Yes	Comment: sealed envelopes used.
Blinding? All outcomes	No	Comment: no blinding.
Incomplete outcome data addressed? All outcomes	Yes	Comment: reasons for patients' exclusion presented. Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups Quote: *"There were no differences in the proportions of patients censored within the combined treatment and control groups and MICU and trauma subgroups."*
Free of selective reporting?	Yes	Comment: the study protocol is available and all of the study's pre-specified (primary and secondary) outcomes have been reported in the pre-specified way
Free of other bias?	Yes	Comment: the study appears to be free of other sources of bias

Marrie 2000

Methods	Multi-center cluster-randomized controlled trial of 19 hospitals
Participants	A total of 1743 patients presenting with community-acquired pneumonia to emergency departments of participating Canadian hospitals between January 1 and July 31 1998. The nine intervention hospitals recruited 716 participants (53.9% male; mean age 64.1 [SD 3.5] years) whilst the ten control hospitals offering conventional care recruited 1027 participants (50.5% male; mean age 64.2 [SD 5.1] years). There were no significant differences between intervention and control groups in disease or disability severity
Interventions	Implementation of an emergency and inpatient CPW for community-acquired pneumonia including a clinic al prediction rule, antibiotic and practice guidelines. Education plans for implementation were developed at each intervention site
Outcomes	Objective outcome measures were quality of life (measured by SF-36) at six weeks and LOS (days)
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Quote: *"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?	Yes	Quote: *"Random assignment was generated by computer."*
Blinding? All outcomes	Yes	Quote: *"Separate investigators meetings, study protocols, and correspondence were used to ensure that health care personnel at the control sites remained unaware of critical pathway components."* Quote: *"All clinical outcomes were independently validated by two investigators who were unaware of the treatment assignment."*
Incomplete outcome data addressed? All outcomes	Unclear	Comment: uncertain risk of bias as they are insufficient details in the article to permit judgement of "yes" or "no"
Free of selective reporting?	Unclear	Comment: First outcome: The difference between the intervention hospitals and the controls is not clearly reported. The results are presented in a graph

Marrie 2000 (*Continued*)

		so we don't have the exact numbers (to be used in a meta-analysis for example) Second outcome: Baseline measurement not presented and P-values not shown for the control group
Free of other bias?	No	Comment: unit analysis error as the randomization unit (hospitals) is different from the unit of analysis (patients)

Philbin 2000

Methods	*Cluster-randomized multi-center (n = 10 hospitals) controlled trial. Medical units at the participating hospitals were randomized to employ a multifaceted quality improvement intervention for heart failure patients (5 study hospitals) or were assigned to traditional care hospitals (n = 5 hospitals) reflecting the standard prior to the study.* Cluster-randomization of the 10 hospitals was reported in detail elsewhere (Philbin 1996) and justified by the authors. Computer generated randomization was used and blinded data assessment done *Due to poor reporting, appropriate power calculation remains unclear.*
Participants	2906 medical patients with heart failure recruited from 10 cluster hospitals either allocated to a multifaceted quality improvement program including a critical pathway (n = 5 hospitals or 1602 participants) or to 5 traditional care hospitals (n = 1304 participants) from different US American settings. Patients were characterized by a mean age of 75/77 (baseline versus post-intervention) years for experimental patients and 74/76 years for control subjects. 97% of the experimental and 98% of the control patients were also described as Caucasian There was no statistical difference at baseline between the experimental and control participants
Interventions	A multifaceted quality improvement intervention was implemented to maximize the impact of a clinical pathway for heart failure. The implementation porcess included leadership by physicians, nurses and administrators; education sessions; and audit and feedback
Outcomes	LOS pooled, LOS per cluster, hospital charges pooled, in-hospital mortality, QOL, heart failure mortality, all cause mortality, readmission for heart failure and readmission for all causes, process of care indicators and ACE inhibitor use at discharge. Follow-up period was 6 month. Most results reported only as absolute change from baseline and some patients measures as well as post test measures
Notes	*Possible unit of analyses error except for LOS outcome. Only LOS measures were also reported per hospital (cluster).*

Risk of bias

Item	Authors' judgement	Description

Philbin 2000 (*Continued*)

Adequate sequence generation?	Unclear	Comment: randomization procedure not described.
Allocation concealment?	Unclear	Comment: insufficient information to permit judgment "yes" or "no"
Blinding? All outcomes	Unclear	Comment: the study did not address this outcome.
Incomplete outcome data addressed? All outcomes	Yes	Comment: no missing outcome data.
Free of selective reporting?	Yes	Comment: all of the study's pre-specified outcomes have been reported in the pre-specified way
Free of other bias?	Yes	Comment: difference between randomization unit (hospitals) and analysis unit (patients) were overcome using appropriate statistical methods Quote: *"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 postintervention) 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."*

Roberts 1997

Methods	*Individual randomized single-center controlled trial. Participants were randomized to receive accelerated diagnostic and clinical treatment for suspected myocardial infarction (AMI) or standard evaluation of chest pain reflecting the diagnostic and treatment standard prior to the study.* The intervention CPW consists of a accelerated diagnostic protocol (ADP possible MI) at the ED observation unit in which more than 50% of the patients were discharged at home after risk assessment versus a control group in which 100% of the patients were admitted to a hospital telemetry unit (usual care) at least for one day Randomization was performed by consecutively numbered sealed envelopes containing the treatment assignment and clearly justified by the authors. Blinded data assessment and objective patient outcomes used. Masking of the professionals not used because not realistic (two different professional treatment teams) *Appropriate power calculation employed and justified by the authors.*
Participants	Medical patients with suspected MI (n = 165) recruited from a public teaching hospital. Urban US American setting (Chicago) characterized as patients presented to the ED with suspected MI. The 82 experimental patients had a mean age of 47,3 years and

	the corresponding 83 control subjects a mean age of 48 years. Additionally, the authors described the included patients as African American 62.4%; Hispanic 10.9%; White 4. 8% and Others 21.8%. There was no statistical difference at baseline between the experimental and control participants
Interventions	Non-invasive "stand-alone" intervention (paper format): Intervention was based on an accelerated diagnostic protocol and standardized treatment for patients with suspected MI. The diagnostic pathway included a Goldman algorithm to differentiate low and high risk patients and hospitalization for low risk patients was not mandatory. Intervention was designed for appropriate management and cost containment. Four out of 5 CPW criteria met. Low (C) evidence-based implementation strategy used Control conditions: patients allocated to the telemetry unit received clinical assessment and treatment for suspected MI by traditional means. Patients were managed by their attending physicians and no differentiation was made between low and high risk patients. All management was at the discretion of the internal medicine attending physician
Outcomes	LOS (hours), hospital costs (full costing approach), hospital admission rate and rehospitalization at 8 weeks. Follow-up period was 8 weeks
Notes	Two different teams reported, but protection against contamination of the control professionals remains unclear

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Comment: insufficient information to permit judgment "yes" or "no"
Allocation concealment?	Unclear	Comment: insufficient information to permit judgment "yes" or "no"
Blinding? All outcomes	Unclear	Comment: the study did not address this outcome.
Incomplete outcome data addressed? All outcomes	Unclear	Comment: insufficient reporting of attrition / exclusion to permit judgment of "yes" or "no"
Free of selective reporting?	Unclear	Comment: insufficient information to permit judgment "yes" or "no"
Free of other bias?	Unclear	Comment: insufficient information to assess whether an important risk of bias exists

Smith 2004

Methods	Non-randomized multi-center controlled before and after study (CBA). Authors used a cluster design (4 cluster = 4 hospitals) and 2 intervention and 2 control public teaching hospitals were allocated. Medical units of the hospitals served as experimental or control sites and characteristics of the second sites were clearly justified and comparable. Timing of data collection was contemporaneous and reliable outcome measures used *Pre-intervention measures reported and no substantial differences detected.* Appropriate power calculation used. Allocation per cluster but only pooled results presented for both groups of patients. Non potential unit of analyses error due to a statistical calculation of infraclass cluster effects
Participants	Patients with chronic obstructive pulmonary disease (COPD) (n = 1230) recruited from 4 urban settings in South Australia (Woodville South Australia close to Adelaide) and presented to the ED. 839 patients were allocated to intervention hospitals and 391 to control hospitals. The mean age was only reported in strata and no differences detected
Interventions	Stand-alone CPW intervention (paper format): Non invasive CPW intervention for COPD. Guideline based intervention for chronic obstructive pulmonary disease, named as ACCORD management and discharge plan and characterized by a detailed clinical assessment, care and discharge plan based on specific criteria. Intervention was designed for appropriate patient management and all CPW criteria met. Highly (A) evidence-based implementation strategy used Control conditions / hospitals: traditional or "usual care" for COPD patients without active implementation and adoption of ACCORD guidelines. Traditional care not justified by protocol and poorly described as usual care for COPD
Outcomes	LOS, readmission and mortality rates. Follow-up from the first index admission until end of baseline or post-intervention phase
Notes	Robust cluster design and highly evidence based (A) implementation strategy used. Control conditions poorly described

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	No	CBA design.
Allocation concealment?	No	CBA design.
Blinding? All outcomes	No	CBA design.
Incomplete outcome data addressed? All outcomes	Yes	Quote: *"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."* Quote: *"Adjustment for potential confounding was undertaken by Poisson regression*

		analysis with allowance made for clustering by hospital, patient identifier and time on trial. " Quote: *"Participants who were in both the pre-intervention and intervention phases were omitted."*
Free of selective reporting?	Yes	Comment: results clearly presented. Study protocol available and all of the study's pre-specified (primary and secondary) outcomes that are of interest for the review have been reported in the pre-specified way
Free of other bias?	No	CBA design.

Sulch 2000

Methods	*Individual randomized single-center controlled trial. Participants were randomized in blocks of 10 to receive integrated care for stroke rehabilitation or conventional care reflecting the standard for stroke rehabilitation prior to the study.The study was carried out on a stroke rehabilitation unit which consisted of 2 separate bed areas managed by 2 separate teams of nurses.* Patients were randomized before transfer to the stroke rehabilitation unit when they were medically and neurologically stable. The responsible physician called the randomization office, which confirmed eligibility and allocated consecutive patients to intervention or control group on the basis of a computer-generated list of random numbers. Blinded data assessment and objective patient outcomes used. Masking of the professionals not used because not realistic (two different professional treatment teams) *Appropriate power calculation employed and justified by the authors.*
Participants	Stroke patients for rehabilitation (n = 152) recruited from a teaching hospital. British setting (London) characterized as patients reaching stability for stroke rehabilitation. The 76 experimental patients had a mean age of 75 years and the corresponding 76 control subjects a mean age of 74 years There was no statistical difference at baseline between the experimental and control participants
Interventions	Non-invasive "stand-alone" intervention (paper format): Multidisciplinary intervention for stroke rehabilitation. Intervention was guided by a senior nurse and contains a detailed care plan, which details the steps in the course of stroke rehabilitation. The standardized rehabilitation program was daily re-evaluated and includes time frames or criteria based progression. Intervention was designed for appropriate management. Four out of 5 CPW criteria met. High (A) evidence-based implementation strategy used Control conditions: patients allocated to the control unit and treated by traditional means. Conventional care was provided by means of the functional model of care. Patients were assessed comprehensively, and an individualized rehabilitation program was designed by members of the multidisciplinary team. In contrast to the ICP method, in which therapeutic activities, short-term goals, and the time taken to achieve these

Sulch 2000 (*Continued*)

	goals were defined in advance, these aspects were discussed in weekly multidisciplinary meetings and determined on the basis of patients' progress
Outcomes	LOS, mean duration of therapy input, Barthel index at 26 weeks, mortality at 26 weeks and discharge destination. Follow-up period was 26 weeks
Notes	Two different independent teams reported, but protection against contamination of the control professionals remains unclear

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Comment: patients allocation made on the basis of a computer-generated list of random numbers
Allocation concealment?	Unclear	Comment: insufficient information about the sequence generation process to permit judgment of "yes" or "no"
Blinding? All outcomes	Unclear	Comment: insufficient information to permit judgment of "yes" or "no"
Incomplete outcome data addressed? All outcomes	Yes	Comment: no missing outcome data.
Free of selective reporting?	Yes	Comment: all of the study's pre-specified outcomes have been reported in the pre-specified way
Free of other bias?	Yes	Comment: the study appears to be free of other sources of bias

Sulch 2002

Methods	Double publication, please see Sulch et al. (2000). More patient outcomes reported, therefore included
Participants	Please see Sulch et al. (2000).
Interventions	Please see Sulch et al. (2000).
Outcomes	Additional outcomes reported: Mobility at 6 months, self-care at 6 months, social activities at 6 months, pain at 6 months, psychological functioning at 6 months, process of care indicators and patient satisfaction. Follow-up period was 26 weeks or 6 months
Notes	Please see Sulch et al. (2000).

Sulch 2002 (*Continued*)

Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Comment: patients allocation made on the basis of a computer-generated list of random numbers
Allocation concealment?	Unclear	Comment: insufficient information about the sequence generation process to permit judgment of "yes" or "no"
Blinding? All outcomes	Unclear	Comment: insufficient information to permit judgment of "yes" or "no"
Incomplete outcome data addressed? All outcomes	Unclear	Comment: no missing outcome data.
Free of selective reporting?	Unclear	Comment: all of the study's pre-specified outcomes have been reported in the pre-specified way
Free of other bias?	Unclear	Comment: the study appears to be free of other sources of bias

Tilden 1987

Methods	The authors used an experimental time series design (ITS). Baseline and post-intervention measures were depicted graphically and the outcome measure used was the rate of "patients identified by nurses as battered". The number of health professionals (as target) were not differing between pre- and post-measures The number of measures (points in time) were justified by the authors and reliable outcome measures used. Statistical adjustment for serial correlation and power calculation remained unclear. Protection against detection bias remains unclear
Participants	Non-invasive intervention to increase "patients identified by nurses as potentially battered" with nurses and other professionals targeted (n = 22; 22 full time and 5 half time nurses pre- and post-intervention). Evaluation included 892 patient records with 447 records investigated before the implementation of the intervention and 445 post-intervention. Patients were recruited from a emergency department of a large university hospital from a urban US setting. The health professionals were characterized as full time and half time nurses. Age or professional qualification was not reported
Interventions	Stand-alone CPW Intervention with health professionals (nurses and physicians) in an emergency department targeted for better identification of battered woman and combined with an education program. Pathway intervention was based on a professional protocol and was designed for better detection of female patients targeted. Four out of five CPW criteria met and moderate (B) evidence-based implementation strategy used

	Baseline: baseline conditions or "usual care" representing the standard of care prior to the implementation of the intervention. Health professionals were not exposed to the intervention in the pre-intervention phase
Outcomes	The outcome of interest was the rate for documentation of battered woman. Follow-up from index admission until discharge
Notes	Blinded data assessment remains unclear due to poor reporting. Study outcomes reported only graphically and data (re-)analyzed and extracted with MS paint

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	No	ITS design.
Allocation concealment?	No	ITS design.
Blinding? All outcomes	No	Comment: no blinding. Quote: *"The intervention targeted the emergency room nursing staff."* Quote: *"Interview protocol was designed by the investigators in collaboration with nursing staff."*
Incomplete outcome data addressed? All outcomes	Yes	Comment: no missing outcome data.
Free of selective reporting?	Unclear	Comment: insufficient information to permit judgement of "yes" or "no"
Free of other bias?	No	Comment: the study has several potential sources of bias related to the specific study design used Quote: *"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 staffs 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."*

Usui 2004

Methods	Pseudo-randomized controlled trial that was carried out in a single center. Experimental patients received standardized treatment based on the e-CP for community-acquired pneumonia (CAP) versus usual care reflecting the standard of care prior to the intervention. Due to poor reporting process of pseudo-randomization remains unclear but there was no statistical difference at baseline between the experimental and control participants *Single blinding reported and justified by the authors. Objective patient outcomes used.* Power calculation not employed and study probably underpowered
Participants	The study sample (n = 61) consisted of 30 hospitalized patients who received treatment based on the e-CP for CAP (e-CP group). Another 31 patients who formed the control group received conventional treatment without the e-CP for CAP. The mean age of the patients was 44.0 years in the e-CP group and 51.4 years in the control group. The female-to-male ratio was 19:11 for the e-CP group and 15:16 for the control group. Patients were recruited from a urban Japanese secondary care setting in Tokyo. Patient in- and exclusion criteria clearly stated and justified by the authors
Interventions	Non-invasive CPW intervention (electronic format): stand-alone intervention "electronic clinical pathway (e-CP)" for community-acquired pneumonia (CAP) was examined. The pathway covered the management of medical procedures, including physical and laboratory examinations, medical care, prescriptions, diets, activities and patient education. Intervention was designed for appropriate patient management and cost containment. All CPW criteria met and low (C) evidence-based implementation strategy used Control conditions: The rationale for the choice of the comparator (standard treatment) was clear and was justified by the authors. However, the protocols for standard treatment were not described in detail in the paper, thus objective assessments of the validity of the comparator were not possible
Outcomes	LOS (days), duration of antibiotic infusion, treatment success rate and the direct costs used were for treatment (antibiotic infusions), laboratory and radiography tests. The costs and the quantities were not reported separately. Discounting was not reported. The cost data were based on health insurance points for the Japanese Health Care system. The period of follow-up was until hospital discharge. No loss to follow-up was reported
Notes	Protection against contamination of the control professionals remains unclear

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	No	Quote: *"This was a non-randomized controlled trial that was carried out in a single centre."*
Allocation concealment?	No	

Usui 2004 (*Continued*)

Blinding? All outcomes	Unclear	Comment: insufficient information to permit judgment "yes" or "no"
Incomplete outcome data addressed? All outcomes	Unclear	Comment: insufficient information to permit judgment "yes" or "no"
Free of selective reporting?	Unclear	Comment: insufficient information to permit judgment "yes" or "no"
Free of other bias?	Unclear	Comment: insufficient information to permit judgment "yes" or "no"

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 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 programme by comparing a historical control with a concurrent experimental group
Abisheganaden 2001	Did not meet EPOC study design criteria as investigators compared an asthma carepath 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 standardisation 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
Adrales 2002	Did not meet study design criteria as the investigators compared an implementation of a thoracostomy tube guideline with traditional thoracostomy management by employing a simple pre-post comparison
Akamatsu 2004	Time series study investigating the effects of introducing a pathway for MI. Did not meet ITS study design criteria as only three data points tested in total
Allen 2002	Did not meet inclusion criteria as investigators evaluated the effectiveness of a post-discharge care management model for stroke

(*Continued*)

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
Archer 1997	Did not meet EPOC study design criteria as investigators evaluated the effects of a pathway for total colectomy by employing a simple pre-post comparison
Arisawa 2005	Did not meet ITS quality criteria as a time series was used to study the usefulness of a clinical pathway for transurethral resection of the prostate with three measures tested in total
Arko 2001	Did not meet inclusion criteria as investigators compared two different operation technics for aneurysm repair and it was not a pathway study
Asano 2002	This study of the impact of a clinical pathway for Bengin Prostatic Hyper-plasia did not meet EPOC design criteria for a controlled before and after study as only a single sample pre and post intervention was tested.
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 study is investigating the effectiveness of an intervention designed to reduce ”door-to-antibiotic time“ in community-acquired pneumonia by using only one control group
Basse 2000	Did not meet inclusion criteria as case study reporting the experience with one cohort of patients suffering from stroke
Beaupre 2005	Did not meet EPOC study design criteria as investigators evaluated the effect of a pathway for hip fracture on in-hospital mortality by executing a simple pre-post comparison
Beaupre 2006	Double publication. Please see Beaupre 2005.
Becker 1997	Did not meet EPOC study design criteria as investigators employed a simple pre-post comparison to investigate the effect of a pathway for haemodialysis vascular access
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 2004	Did not meet intervention minimum criteria (content criteria) as only three out of five pathway criteria met
Berenholtz 2004a	Double publication. Please see Berenholtz 2004.
Bertges 2000	Did not meet EPOC study design criteria as case-control design used

(*Continued*)

Bhayani 2003	The investigators compared two different operation techniques for prostatectomy. Did not meet inclusion criteria as intervention only used for better standardization in both study arms
Bing 1997	Did not meet study design criteria as investigators compared standardized pathway care for MI versus traditional management for MI by employing a simple pre-post comparison
Bittinger 1995	PhD thesis investigating a CPW aiming to standardise the management of congestive heart failure. RCT design did not meet quality criteria as only 50% of study patient were followed-up after randomization
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 2000	Did not meet EPOC study design criteria as investigators compared the outcomes of two different studies (one RCT versus cohort study) evaluating the effectiveness of clinical pathways
Board 2000a	Randomized controlled study comparing in-hospital 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 is not hospital setting
Board 2000b	Publication is based on the article Board 2000a, double publication
Bowen 1994	Did not meet CBA study design criteria as investigators compared traditional care for stroke versus standardized care for stroke by employing a controlled before and after study with one control and one experimental group
Bradshaw 1998	Did not meet inclusion criteria as investigators compared the effects of a pathway for patients undergoing colorectal surgery versus traditional surgery care by employing a case-control design
Branney 1997	Did not meet EPOC study design criteria as study investigating the effectiveness of standardized pathway care for abdominal trauma versus standard care by using a simple pre-post comparison
Brattebo 2004	Please see included study Brattebo et al. 2002: Double publication
Braun 2005	Investigators compared two different anaesthesia procedures. Did not meet inclusion criteria as intervention only used for better standardization in both study arms
Brignole 2006	Did not meet pathway definition as it was not multidisciplinary
Brugler 1999	This study evaluated a malnutrition treatment program in a community hospital. Both controlled before and after and interrupted time series methodologies used but control site was inappropriate for comparison and less than three time periods post-intervention were tested
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

(*Continued*)

Buckley 2000	Did not meet inclusion criteria as investigators compared two surgical procedures by following the same clinical pathway for better comparability
Buckmaster 2006	Did not meet CBA quality criteria as investigators evaluated a pathway for patients with acute coronary syndromes versus usual care by employing a controlled before and after (CBA) study with only one control group
Bultema 1996	Investigators reported outcomes from an intervention to improve outcomes for geriatric patients with depression. The study did not meet inclusion criteria for a controlled before and after study as only a single sample pre and post intervention was tested
Burns 1998	Investigators compared a standardized approach to patients requiring prolonged mechanical ventilation versus traditional care. Did not meet EPOC design criteria as data collection was not contemporaneous
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
Capelastegui 2004	Did not meet minimum criteria for definition of a clinical pathway as only 3 out of 5 content criteria met
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
Chase 1983	Did not meet inclusion criteria as the intervention under consideration was the implementation of a Medical Information Management System (MIM) into an existing pathway
Chen 2000	Did not meet EPOC quality criteria as only 3 out of five pathway criteria met and case-control design used
Cheney 2005	Did not meet EPOC study design criteria as pathway investigation based on a simple pre-post comparison with a historical cohort
Christensen 1997	Study investigating carotid endarterectomy clinical pathway versus traditional care. Design at high risk of bias. CBA and ITS quality criteria not met as four yearly pathway cohorts used
Chu 2001	Did not meet inclusion criteria as not comparative and subjective experience with a computerized pathway tool reported
Chu 2001a	See Chu 2001. Double publication.
Chu 2001b	Investigators studied a computerised clinical pathway but did not meet inclusion criteria for a controlled before and after study as only a single-sample pre and post intervention was tested.
Conway 2003	The investigators studied the effect of cardiac troponin T (cTnT) measurement. Did not meet inclusion criteria as intervention protocol only used for better comparability of both study arms

(*Continued*)

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 less than three time periods pre and post intervention
Covinsky 1998	Did not meet minimum criteria for definition of a clinical pathway as it was not multidisciplinary
Crane 1999	Did not meet EPOC study design criteria as investigators evaluated the effectiveness of a critical pathway for diabetic foot infections by employing a case-control design and comparing it with a historical cohort
Criscione 1995	Study evaluating a primary care pathway for developmental disabilities. Did not meet inclusion criteria as not hospital setting
Crunden 2005	Did not meet EPOC study design criteria as investigators evaluated a standardized ventilator care bundle versus traditional ventilator management by using a simple pre-post comparison
D'Amato 1998	Authors presented results from the implementation of physician-driven protocols for hysterectomy that did not meet minimum criteria for definition of a clinical pathway as it was not multi-disciplinary
Dalcin 2007	Did not meet ITS quality criteria as authors evaluated the effect of clinical pathways on the management of acute asthma by employing a time series model by testing less than three time periods pre and post intervention
Danchaivijitr 1992	Study evaluating the effects of an indication sheet for urethral catheterization and did not meet minimum criteria for definition of a clinical pathway as it was not multidisciplinary
de Villiers 2007	Did not meet ITS quality criteria as investigators evaluated a standardized strategy for PTCA by employing time series measures only post intervention
Debrix 1999	This study into the impact of an intervention to manage use of antiemetics by cancer patients did not meet EPOC design criteria for an interrupted time series study as less than three time points were used pre and post intervention
DeLong 1998	Study evaluating a pathway intervention for congestive heart failure. Did not meet inclusion criteria as design used was a simple pre-post comparison
Dempsey 1995	Study evaluating a pneumonia pathway in a nursing home setting. Did not meet inclusion criteria as setting not hospital and ITS data not analyzed appropriately
Doherty 2007	Did not meet CBA design criteria as authors evaluated an asthma pathway by using a controlled before and after design with only one control group
Dranitsaris 1995	Study investigating guideline implementation for medical therapy. Did not meet minimum criteria for definition of a clinical pathway as it was not multidisciplinary
Du 1999	Did not meet inclusion criteria as investigators evaluated the effectiveness of an oncology pathway in a primary care setting. Not hospital

(*Continued*)

Durieux 2000	This intervention to reduce the incidence of venous thromboembolism did not meet minimum criteria for definition of a clinical pathway as it was directed at physicians and was not multidisciplinary
Eagle 1990	Did not meet minimum criteria for definition of a clinical pathway as it was not multidisciplinary
Eagle 2005	Did not meet minimum criteria for definition of a clinical pathway as study evaluating the effects of implementing a guideline based care for MI versus traditional management
East 1999	Investigators evaluated the effects of computerized decision support for mechanical ventilation. 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 definition of a clinical pathway
Eggimann 2000	Investigators measured the impact of a prevention strategy targeted at vascular-access care on incidence of infections acquired in intensive care. The study did not meet inclusion criteria for a controlled before and after study as only a single-sample pre and post intervention was tested
Emil 2006	Did not meet EPOC study design criteria as investigators explored the effects of a paediatric appendicitis clinical pathway by using a case-control design
Emond 1999	Authors reported on the effect of an emergency department asthma program on acute asthma care but the study did not meet EPOC design criteria for an interrupted time series study as only one time period was measured pre intervention
Fan 2006	Study investigated national Canadian guidelines called "Ottawa Ankle Rules". Study Intervention did not meet pathway definition as intervention only met 2 out of 5 content criteria
Fanslow 1998	This evaluation of an emergency department protocol of care on partner abuse did not meet EPOC design criteria for a controlled before and after study as the two sites that were not comparable
Ferrando 2005	This descriptive study of guidelines for preoperative assessment did not meet EPOC study inclusion criteria
Ferri 2006	This report on patient perceptions of a clinical pathway for laparoscopic surgery did not meet design criteria for a controlled before and after study as only a single-sample pre and post intervention was tested.
Fine 2003	Authors implemented and evaluated a medical practice guideline and discharge strategy for patients with community-acquired pneumonia by employing a cluster randomized study design. Did not meet minimum criteria for definition of a clinical pathway as it was not multidisciplinary. However, control professionals (MD) also received guideline intervention (educational mailing). Likely double publication, see Stone 2005
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
Fleisher 1995	Study investigating the effects of a care strategy for very-low-birth-weight premature infants versus traditional paediatric management. Did not meet inclusion criteria as pathway content criteria matched only 2 out of 5

(*Continued*)

Flickinger 1997	Did not meet EPOC quality design criteria as authors compared standardized pneumonia care versus traditional hospital management by using a concurrent pathway cohort versus a historical control
Frankel 1999	This report on compliance with guidelines did not meet minimum criteria for definition of a clinical pathway as it was not multidisciplinary
Fridlin 1996	This investigation of the use of severity-adjusted data to impact clinical pathways did not meet EPOC study design criteria for an interrupted time series study as only one time point was used pre intervention
Frutos 2007	Did not meet inclusion criteria as study represents a clinical report and not a comparative study
Garcia-Aymerich 2007	Authors evaluated an integrated care intervention for COPD. Did not meet inclusion criteria as setting was primary care and randomisation of participants after hospital discharge. RCT design
Gheiler 1999	This report on the results of a clinical care pathway for radical prostatectomy patients did not meet EPOC study design criteria for an interrupted time series study as only one time point was used pre intervention
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 less than three time periods pre and post intervention
Gorski 2000	Did not meet inclusion criteria as study investigating the effect of a home care pathway for treatment of deep vein thrombosis versus traditional home care Not hospital setting.
Gottlieb 1996	Did not meet EPOC study design criteria as the authors investigated the effects of a clinical pathway for pneumonia by employing a simple pre-post comparison
Gounder 2003	This multi-center 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
Graeber 2007	Investigators evaluated the effectiveness of a range of clinical pathways in general surgery by employing a simple pre-post comparison. EPOC study design criteria not met
Greenfield 1975	Did not meet inclusion criteria as investigators evaluated a headache protocol for nurses in primary care Not hospital setting.
Greenfield 1976	Please see Greenfield et al 1975, double publication.
Grimm 2006	This descriptive paper of a clinical pathway for acute coronary syndrome did not meet EPOC study inclusion criteria for RCTs, CCTs,CBAs or ITS
Grimshaw 1996	This evaluation of the impact of guidelines and local protocols for women with menorrhagia or urinary incontinence did not meet inclusion criteria as the setting was not in a hospital

(*Continued*)

Gunten 2005	This study of an intervention to manage antibiotic use did not meet minimum criteria for definition of a clinical pathway as it was not multidisciplinary
Hommel 2007	Did not meet EPOC study design criteria as investigators evaluated a management strategy for nutrition by employing a simple pre-post comparison
Joh 2003	This study into effects of the critical pathway for inguinal hernia repair did not meet EPOC study design criteria. Controlled before and after study where data collection was not contemporaneous between groups
Joiner 1996	This study of an intervention to reduce ventilator-associated pneumonia utilised an interrupted time series design did not meet EPOC study design criteria as seasonal modelling was not included
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
Katterhagen 1996	This study into physician compliance with outcome-based guidelines and clinical pathways in oncology used a single institution, single sample before and after design that did not meet EPOC study design criteria
Kaufman 2006	This study into a pathway for laparoscopic prostatectomy used an interrupted time series design that included a total of three five-months time periods and did not meet the minimum number of time periods required by the EPOC study design criteria
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.
Keetch 1998	This study into LOS impact of a pathway for decreasing hospital stay after radical prostatectomy utilised 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 2000	Investigators evaluated the effects of a paediatric hernia pathway. Study did not meet design criteria. Pre-post comparison used and data collection was not contemporaneous
Kelly 2000a	Investigators evaluated an asthma clinical pathway. Did not meet EPOC study design criteria as a pre-post comparison was used
Keogh 2003	This study of an intervention to guide weaning from ventilation in paediatric intensive care did not meet design criteria for an interrupted time series study as less than three time points were used pre and post intervention
Khoo 2007	Authors evaluated a cancer management protocol versus usual cancer care by using a randomized controlled trial. Did not meet pathway definition as only 3 out of five criteria matched
Khowaja 2006	Investigators evaluated a clinical pathway for TURP. Quasi-experimental design with non-equivalent groups that did not meet EPOC design criteria

(*Continued*)

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
Kim 2001	Investigators evaluated a clinical pathway for artrial fibrillation. Study did not meet EPOC design criteria as a single-sample pre and post comparison was used
Kinsman 2004	Investigators evaluated a clinical pathway for AMI. Did not meet EPOC study design criteria as only a single-sample pre-post comparison employed
Kinsman 2004a	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 for a pathway designed to guide AMI management
Kiyama 2003a	This publication duplicated the results previously published. These results were included in this review as Kiyama 2003
Knight 2002	This study into an intervention to guide weaning from ventilation in paediatric intensive care employed a controlled clinical trial design where physicians chose whether patients were allocated to clinical pathway. High risk of allocation bias
Kong 1997	Investigators evaluated a COPD practice guideline. Historical control compared with a pathway group. Investigators used time series analysis but study did not meet EPOC study design criteria as the time-point for the intervention was not clarified
Konishi 2001	Investigators evaluated a clinical pathway for gastric cancer. Study did not meet design criteria for a controlled before and after study as a pre-post comparison was used and data collection was not contemporaneous between groups
Kucenic 2000	Investigators evaluated a clinical pathway for MI. Insufficient time periods to meet minimum criteria for interrupted time series study.
Lagoe 1997	Investigators evaluated a number of clinical pathways for different conditions. Did not meet EPOC study design criteria as different yearly patient cohorts (94/95/96) were compared and data collection was not contemporaneous between groups
Landefeld 1992	Investigators evaluated the implementation of a guideline for anticoagulant therapy. Did not meet minimum criteria for definition of a clinical pathway as it was not multidisciplinary
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
Leibman 1998	Effects of a pathway for radical retropubic prostatectomy evaluated by employing a pre-post design with one group baseline and one control and one intervention group post intervention. Minimum criteria of two control groups post intervention not met
Lightbody 2002	Pathway for falls prevention program was not implemented in hospital
Little 1996	Qualitative study concerning implementation issues. Review inclusion criteria not met

(*Continued*)

Loeb 2006	Not hospital setting.
Macario 1998	Controlled before and after study of CPW for knee replacement surgery. Control groups post intervention were prostatectomy and hip replacement and did not meet criteria for comparative characteristics
Mamolen 2000	Evaluation of a burn wound pathway. Not hospital setting. Review inclusion criteria not met
Mandl 2000	Investigators evaluated the implementation of a pneumonia guideline. Retrospective interrupted time series of four time periods -3 before and one after. Did not meet design criteria for an interrupted time series study as less than three time points were used post intervention
Massie 2004	Authors evaluated a paediatric asthma guideline. Three cohorts -one baseline (pre intervention) and two intervention cohorts (post). Minimum design criteria for controlled before and after study not met
Masters 2001	Evaluation of an asthma management care plan. Before and after intervention study with unblinded, unmatched samples did not meet EPOC study design criteria
Matsumoto 2002	Investigators evaluated the implementation of a pathway for abdominal aortic aneurysms. Did not meet design criteria for a controlled before and after study as only a single-sample pre and post intervention was tested
Mazur 1996	This investigation into the process of paediatric asthma care did not meet design criteria for a controlled before and after study as only a single-sample pre and post intervention was tested
McAchran 1993	Pathway investigation for ureteral reimplantation. Case study designs were not included in this review
McAdam 1990	Computer aided diagnosis system was implemented and evaluated. Did not meet content criteria for definition of a clinical pathway as it was not multidisciplinary
McIlvoy 2001	Investigators evaluated a pathway for head injuries. Inadequate number of groups to meet EPOC design criteria
McKinley 2001	Study investigating the effects of computerized decision support versus physician directed guideline management. Did not meet pathway content criteria (1 out of five criteria met)
McKinsey 1999	Did not meet EPOC design criteria as authors compared clinical pathway care for uncomplicated MI patients versus traditional management by employing a simple pre-post comparison
McLean 2006	Did not meet EPOC quality criteria as investigators evaluated a ventilation weaning protocol for critically ill adults versus traditional ventilation management by employing a simple pre-post comparison
McManus 2005	Did not meet EPOC design criteria as authors compared pathway care for acute exacerbations of chronic obstructive pulmonary disease versus usual care by employing a simple pre-post comparison
Melbert 2002	Did not meet EPOC design criteria as investigators explored the effects of a critical pathway for colon resections versus traditional surgical management by using a case-control design

(*Continued*)

Metersky 2001	Did not meet EPOC quality criteria as investigators compared a pneumonia clinical pathway versus usual pneumonia management by employing a simple pre-post comparison
Miller 2002	Evaluation of a pathway for penetrating colon wounds. Did not meet EPOC design criteria as authors compared a pathway cohort with data from another study published elsewhere
Misset 2004	Investigators evaluated a quality improvement initiative. Intervention did not meet pathway definition as it was not multidisciplinary
Mizuki 2006	This evaluation of a clinical pathway protocol for patients with bleeding peptic ulcers utilised a single sample before and after design that did not meet EPOC study quality criteria
Mol 2005	Investigators evaluated the implementation of an antibiotic guideline. Intervention did not meet pathway definition as it was not multidisciplinary
Monesi 2003	Did not meet inclusion criteria as investigators evaluated the effects of a pathway for diabetic patients by employing a case-control design
Munoz 2006	Did not meet EPOC design criteria as authors compared standardized care for pneumonia versus traditional pneumonia management by employing a simple pre-post comparison
Naji 1994	Investigators evaluated an intervention for diabetic care. Intervention did not meet pathway definition as it was not multidisciplinary
Nanly 2005	Four types of pathways evaluated. Did not meet EPOC design criteria as evaluation used a simple pre-post comparison
O'Brien 2000	Did not meet EPOC quality criteria as investigators evaluated the impact of a care pathway-driven diabetes education strategy by using a pre-post comparison
Ogawa 2004	Did not meet EPOC design criteria as authors investigated the effects of a clinical pathway by employing a simple pre-post comparison
Okon 2004	Intervention did not meet pathway definition as it was not multidisciplinary
Ono 2003	Did not meet EPOC design criteria as investigators evaluated the effects of a clinical pathway for fast track recovery in children after cardiac surgery by employing a simple pre-post comparison
Otsuka 2003	Translation revealed intervention did not meet pathway definition
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 was not analyzed appropriately
Ozdas 2006	Did not meet EPOC quality criteria as authors evaluated the effects of "best of care" protocols into clinicians' workflow by using a simple pre-post comparison
Palmer 2000	Double publication, please see Marrie (2000).

(*Continued*)

Pearson 2001	Did not meet design inclusion criteria as it was only a report and pre-post comparison
Perez-Blanco 2004	Did not meet inclusion criteria as it is only a clinical report
Perlstein 2000	Cohort study investigating the effects of a guideline based strategy for bronchiolitis by comparing 3 yearly cohorts. Did not meet ITS and CBA design criteria as 3 different patient cohorts compared and tested
Perry 2003	Did not meet EPOC quality criteria as authors investigated the effects of a nutrition guideline for stroke patients by using a simple pre-post comparison
Pestian 1998	Did not meet EPOC design criteria as authors evaluated the effectiveness of a tonsillectomy and adenoidectomy clinical pathway by employing a simple pre-post comparison
Peter 2004	Did not meet EPOC design criteria as investigators evaluated the clinical effectiveness of an integrated care pathway for infants with bronchiolitis by using a simple pre-post comparison
Pilon 1997	Did not meet EPOC study design criteria as investigators evaluated a practice guideline for arterial blood gas measurement in the intensive care unit by comparing 3 patient cohorts with 3 historical cohorts
Piontek 2003	Did not meet inclusion criteria as study was an ACS Level II trauma center verification, not a pathway 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
Pritts 1999	Did not meet EPOC design criteria as investigators evaluated the effects of a clinical pathway for bowel resection by using a before and after study with one concurrent and one historical control group
Pronovost 2002	Authors evaluated the effects of a pathway for reducing failed extubations in the intensive care. Did not meet EPOC design criteria as it was a time series with one data point before and three after the intervention was implemented
Ranjan 2003	Did not meet EPOC design criteria as authors evaluated the effectiveness of a clinical pathway in the management of congestive heart failure by employing a case-control study design
Rasmussen 2002	Did not meet EPOC design criteria as authors evaluated an accelerated recovery program after hip fracture surgery by using a simple pre-post comparison
Ratnaike 1993	Investigators evaluated a chest pain intervention. Did not meet minimum criteria for definition of a clinical pathway as it was not multidisciplinary
Reilly 2002	Did not meet EPOC design criteria as authors tested a rule-out protocol for suspected acute cardiac ischemia by comparing 1 cohort pre- versus 1 cohort post-intervention
Renholm 2002	Inclusion criteria not met, review.

(*Continued*)

Roberts 1991	Did not meet EPOC design criteria as authors evaluated a strategy for eliminating needless testing in intensive care by using a simple pre-post comparison
Roberts 1993	Double publication, please see Roberts et al. (1991).
Roberts 2004	Did not meet EPOC design criteria as authors evaluated a pathway management strategy for femural neck fracture in older people by employing a before and after design with only one control and one experimental group
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
Roman 2001	Did not meet EPOC design criteria as authors evaluated a pathway strategy diabetes care by using a simple pre-post comparison
Ross 1997	Did not meet EPOC design criteria as authors evaluated a pathway strategy for stroke by employing 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
Rosswurm 1998	Did not meet EPOC design criteria as investigators evaluated the effects of standardized care and discharge planning for geriatric patients by employing a simple pre-post comparison
Rydman 1998	Investigators compared a fast track protocol for asthmatic patients versus hospitalization and usual care by employing a randomized controlled trial. Did not meet pathway content criteria as it was not multidisciplinary
Salinas 2006	Did not meet inclusion criteria as authors compared to different anaesthesia techniques by using a clinical pathway in each group only for better comparison
Sanders 2002	Did not meet EPOC design criteria as investigators evaluated a strategy for percutaneous endoscopic gastrostomy by employing 2 hospital cohorts
Schriger 1997	Intervention was a clinical guideline for clinical documentation andc did not meet minimum criteria for definition of a clinical pathway as it was not multidisciplinary
Scott 2004	Did not meet EPOC design criteria as authors evaluated a strategy for patients with acute cardiac disease versus usual care by employing a simple pre-post comparison
Selekman 1999	Did not meet EPOC design criteria as investigators evaluated a paediatric asthma pathway by employing a case-control design
Shepperd 2006	Inclusion criteria not met, Cochrane review not study.
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

(*Continued*)

Smith 1999	Authors compared standardised care managed by a clinical pathway for MI by employing a time series design. Did not meet EPOC design criteria as inappropriate ITS data analyses used
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
Spillane 1997	Intervention (care plan) did not meet inclusion criteria as CPW content criteria not met
Spranzo 1993	Did not meet pathway content criteria as intervention was not multidisciplinary. Investigators evaluated a computerized nurse care-planning strategy by using a RCT design at high risk of exclusion bias
Stoller 1998	Did not meet pathway content criteria as respiratory care intervention was not multidisciplinary. Authors compared respiratory therapist directed vs. physician directed respiratory care
Stone 2005	Authors implemented and evaluated a guideline for patients with community-acquired pneumonia by employing a randomized study design. Did not meet minimum criteria for definition of a clinical pathway as it was not multidisciplinary
Summers 1998	Did not meet EPOC design criteria as authors evaluated a stroke clinical pathway by using a time series. Design at high risk of bias. No statistical control used
Thilly 2003	Intervention does not meet multidisciplinary content criterion as it is a practice guideline for ACE inhibitor use. Inclusion criteria not met
Thomas 2003	Did not meet EPOC design criteria as authors investigated the effectiveness of a clinical pathway for hip and knee arthroplasty by using yearly patient cohorts
Tosun 2006	Did not meet EPOC design criteria as 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
Uchiyama 2003	Did not meet inclusion criteria as authors compared switch therapy for pneumonia versus usual care for pneumonia and pathway in both groups used only for better comparability
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
Vandamme 2006	This study into a pathway for oral healthcare was excluded due to a lack of information provided regarding the intervention tested. Minimum criteria for a clinical pathway was not met
Vanhaecht 2002	Evaluation reflects the first phase of a cohort study published in 2005. Please see Vanhaecht et al. (2005). Double publication

(*Continued*)

Vanhaecht 2005	Did not meet EPOC design criteria as authors evaluated the effectiveness of a clinical pathway for total knee arthroplasty by using a time series model at high risk of bias. Only 3 measures reported
Walsh 2001	Did not meet EPOC design criteria as investigators evaluated a critical pathway strategy for infrainguinal 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
Warner 2002	Did not meet ITS quality criteria as investigators evaluated a clinical pathway for acute appendicitis by using a time series at high risk of bias. ITS data not analyzed appropriately
Washington 1999	Only conference abstract available. Refers to the publication Washington et al (2000). Please see Washington et al. (2000).
Washington 2000	Did not meet inclusion criteria as paper reports only experience of developing a guideline for respiratory care
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. Study did not meet ITS design criteria
Weingarten 1993	Did not meet intervention content and inclusion criteria as authors evaluated the diagnostic accuracy of a diagnostic strategy for heart failure patients
Westvik 2006	Did not meet inclusion criteria. Pathway content criteria not met
Wiist 1999	Authors evaluated the effectiveness of an abuse assessment protocol versus usual care Did not meet intervention content criteria.
Wilson 2002	Did not meet EPOC design criteria as investigators evaluated a clinical pathway for bronchiolitis by employing a case-control design
Yamauchi 2003	Did not meet ITS quality criteria as authors evaluated a clinical pathway for inpatients with gastric ulcer by using time-series with 3 measures in total tested
Yueh 2003	Did not meet CBA design criteria as authors evaluated critical pathways in head and neck cancer settings by comparing one experimental cohort versus a control group of patients per pathway indication
Zeler 1992	Authors evaluated a nurse-led intervention after cardiac surgery. Did not meet minimum criteria for definition of a clinical pathway as it was not multidisciplinary
Zhang 2005	Authors evaluated a clinical pathway for patients suffering from depression. Did not meet minimum criteria for definition of a clinical pathway as it was not multidisciplinary
Zhang 2005a	The intervention designed to guide inpatient depression management did not meet minimum criteria for definition of a clinical pathway as it was not multidisciplinary

(*Continued*)

Zorn 1999	PhD thesis did not meet EPOC design criteria as 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

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

Cunningham 2008

Methods	C-RCT
Participants	13 intervention block-clusters and 13 control block-clusters which corresponds with 298 patients (163 on CPW vs. 135 off CPW)
Interventions	ICP on acute asthma/ wheeze in children attending hospital
Outcomes	LOS, prednisolone rate, hospital admission rate, rate of recovery, time to discharge, education provided and prescribing errors
Notes	Additional information (CPW) required. Email double checked and author contacted via email. Pending

Kiyama 2003b

Methods	Method remains unclear, economic evaluation
Participants	76
Interventions	clinical pathway for gastrectomy
Outcomes	Treatment costs
Notes	Pending, EPOC design criteria

Namiki 2004

Methods	Method not clear based on the brief translation. Possibly CBA design. Full text translation required to assess EPOC CBA criteria. Seems to be simple pre-post comparison
Participants	69
Interventions	Radical prostatectomy carepath
Outcomes	Number of encounters, diagnostic and therapeutic interventions, hospitalization and operative charges, and follow-up visits, diagnostic tests and interventions for 1 year
Notes	Waiting for author replay. Pending, EPOC design criteria

Rich-Ruiz 2006

Methods	RCT
Participants	122
Interventions	Pathway for transurethral resection of the prostate
Outcomes	LOS, patient satisfaction and complication rate
Notes	Email double checked and author contacted via email. Pending

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

Panella 2007

Trial name or title	A cluster randomized controlled trial of a clinical pathway for hospital treatment of heart failure: study design and population
Methods	C-RCT
Participants	14 hospitals
Interventions	clinical pathway for hospital treatment of heart failure
Outcomes	in-hospital mortality, LOS, readmissions, patient satisfaction and costs
Starting date	
Contact information	University of Piedmonte, Italy
Notes	author contacted, results pending

DATA AND ANALYSES

Comparison 1. Randomised vs non-randomized studies (studies)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 randomised vs non-randomised studies	17		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 Randomised studies	15	3386	Mean Difference (IV, Random, 95% CI)	-1.09 [-1.59, -0.60]
1.2 Non-randomised studies	2	172	Mean Difference (IV, Random, 95% CI)	-1.79 [-2.99, -0.60]

Comparison 2. Stand-alone clinical pathway vs usual care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 LOS: invasive versus non-invasive	14		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 Non-invasive studies	6	663	Mean Difference (IV, Random, 95% CI)	-1.14 [0.00, -0.28]
1.2 Invasive studies	8	1099	Mean Difference (IV, Random, 95% CI)	-1.39 [-2.17, -0.60]
2 LOS: hospital area	14		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 ED	2	183	Mean Difference (IV, Random, 95% CI)	-0.97 [-2.24, 0.30]
2.2 General acute	8	879	Mean Difference (IV, Random, 95% CI)	-1.49 [-2.14, -0.85]
2.3 Extended care	3	337	Mean Difference (IV, Random, 95% CI)	1.46 [-2.14, 5.05]
2.4 ICU	1	321	Mean Difference (IV, Random, 95% CI)	-5.90 [-10.51, -1.29]
3 LOS: implementation process	14		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 High evidence based cpw implementation	2	252	Mean Difference (IV, Random, 95% CI)	1.17 [-3.87, 6.22]
3.2 Moderately evidence based impl	8	903	Mean Difference (IV, Random, 95% CI)	-1.44 [-2.05, -0.83]
3.3 Low ebm	4	565	Mean Difference (IV, Random, 95% CI)	-1.92 [-3.53, -0.30]
4 LOS: country	14		Mean Difference (IV, Random, 95% CI)	Subtotals only
4.1 USA	7	910	Mean Difference (IV, Random, 95% CI)	-0.85 [-1.40, -0.29]
4.2 AUS	2	274	Mean Difference (IV, Random, 95% CI)	-1.45 [-2.29, -0.61]
4.3 UK	1	152	Mean Difference (IV, Random, 95% CI)	5.0 [-1.71, 11.71]
4.4 Canada	1	211	Mean Difference (IV, Random, 95% CI)	-1.40 [-1.94, -0.86]
4.5 Japan	3	215	Mean Difference (IV, Random, 95% CI)	-3.01 [-5.35, -0.67]
5 LOS: year	14		Mean Difference (IV, Random, 95% CI)	Totals not selected
5.1 Year	14		Mean Difference (IV, Random, 95% CI)	Not estimable
6 LOS: condition or intervention	6		Mean Difference (IV, Random, 95% CI)	Subtotals only
6.1 Stroke	2	273	Mean Difference (IV, Random, 95% CI)	3.99 [-0.29, 8.27]
6.2 Pneumonia	2	272	Mean Difference (IV, Random, 95% CI)	-1.67 [-2.73, -0.62]
6.3 Suspected MI	2	286	Mean Difference (IV, Random, 95% CI)	-0.90 [-1.98, 0.18]
7 Days to sitting out of bed	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
8 Duration of ventilation (TSA)	1		Change in level and slope (Fixed, 95% CI)	Totals not selected
8.1 Change in level	1		Change in level and slope (Fixed, 95% CI)	Not estimable

8.2 Change in slope	1		Change in level and slope (Fixed, 95% CI)	Not estimable
9 Duration of mechanical ventilation in hours	2	678	Mean Difference (IV, Random, 95% CI)	-33.72 [-55.73, -11.71]
10 Duration of antibiotic infusion	2	272	Mean Difference (IV, Random, 95% CI)	-1.70 [-2.01, -1.40]
11 Patient satisfaction	3		Mean Difference (IV, Random, 95% CI)	Totals not selected
12 Hospital costs / charges	6		Mean Difference (IV, Random, 95% CI)	Totals not selected
12.1 Hospital charges	2		Mean Difference (IV, Random, 95% CI)	Not estimable
12.2 Hospital costs	4		Mean Difference (IV, Random, 95% CI)	Not estimable
13 hospital costs	4		Mean Difference (IV, Random, 95% CI)	Totals not selected
14 SMD hospital cost data	8	965	Std. Mean Difference (IV, Random, 95% CI)	-0.52 [-0.78, -0.26]
14.1 non-invasive	3	189	Std. Mean Difference (IV, Random, 95% CI)	-0.69 [-0.99, -0.40]
14.2 invasive	5	776	Std. Mean Difference (IV, Random, 95% CI)	-0.44 [-0.77, -0.11]
15 Standardised hospital costs / charges / insurance points	8	965	Std. Mean Difference (IV, Random, 95% CI)	-0.52 [-0.78, -0.26]
16 Hospital insurance points (Japan: surrogate for hospital charges)	2	130	Mean Difference (IV, Random, 95% CI)	-8197.00 [-12357.33, -4040.66]
17 Complications up to 3 months	1	163	Odds Ratio (M-H, Fixed, 95% CI)	0.31 [0.13, 0.72]
18 Mortality rate	3	1187	Odds Ratio (M-H, Random, 95% CI)	0.84 [0.64, 1.11]
19 In-hospital complications	5	664	Odds Ratio (IV, Random, 95% CI)	0.58 [0.36, 0.94]
20 Hospital readmission up to 6 months	6	672	Odds Ratio (IV, Random, 95% CI)	0.60 [0.32, 1.13]
21 Process of care: documentation	2	241	Odds Ratio (M-H, Random, 95% CI)	11.95 [4.72, 30.30]
22 TSA ITS Level	1		level (Random, 95% CI)	18.58 [1.85, 35.30]
23 Process of care: documentation (TSA) ITS slope	1		slope (Fixed, 95% CI)	-0.68 [-4.32, 2.97]

Comparison 3. Multifaceted intervention including clinical pathway vs usual care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 LOS	3	1796	Mean Difference (IV, Random, 95% CI)	-0.86 [-2.52, 0.81]
1.1 Non-randomized studies	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
1.2 Randomized studies	3	1796	Mean Difference (IV, Random, 95% CI)	-0.86 [-2.52, 0.81]
2 Hospital costs / charges	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 Hospital charges	1	1504	Mean Difference (IV, Random, 95% CI)	-887.03 [-2779.38, 1005.32]
2.2 Hospital costs	2	371	Mean Difference (IV, Random, 95% CI)	-52.74 [-119.09, 13.60]
3 Standardised hospital costs / charges / insurance points	3	1875	Std. Mean Difference (IV, Random, 95% CI)	-0.06 [-0.15, 0.03]
4 Mortality rate	1	227	Odds Ratio (M-H, Random, 95% CI)	1.19 [0.62, 2.26]
5 Hospital readmission up to 6 months	2		Odds Ratio (IV, Random, 95% CI)	Totals not selected
6 LOS (sensitivity analysis + Bittinger RCT study 1995	4	1826	Mean Difference (IV, Random, 95% CI)	-0.59 [-1.66, 0.48]
6.1 comparison as 3.1.2 plus Bauer = Bittinger study	4	1826	Mean Difference (IV, Random, 95% CI)	-0.59 [-1.66, 0.48]

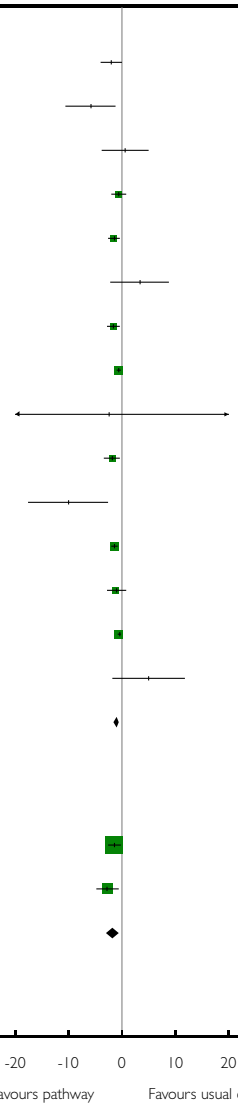
Analysis 1.1. Comparison 1 Randomised vs non-randomized studies (studies), Outcome 1 randomised vs non-randomised studies.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 1 Randomised vs non-randomized studies (Σ studies)

Outcome: 1 randomised vs non-randomised studies

Study or subgroup	clinical pathway N	Mean(SD)	usual care N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Randomised studies							
Aizawa 2002	32	12.7 (2.8)	37	14.7 (5.2)		4.9 %	-2.00 [-3.94, -0.06]
Brook 1999	162	14 (17.3)	159	19.9 (24.2)		1.1 %	-5.90 [-10.51, -1.29]
Cole 2002	113	19.7 (17.1)	114	19.1 (16.8)		1.2 %	0.60 [-3.81, 5.01]
Delaney 2003	31	5.2 (2.5)	33	5.8 (3)		8.1 %	-0.60 [-1.95, 0.75]
Dowsey 1999	92	7.1 (3.67)	71	8.6 (3.67)		9.8 %	-1.50 [-2.64, -0.36]
Falconer 1993	53	35.6 (15.5)	68	32.3 (15.4)		0.8 %	3.30 [-2.25, 8.85]
Gomez 1996	53	0.64 (0.51)	68	2.28 (5.25)		8.8 %	-1.64 [-2.90, -0.38]
Johnson 2000	50	1.68 (1.12)	50	2.24 (1.12)		17.5 %	-0.56 [-1.00, -0.12]
Kampan 2006	33	3.94 (1.03)	32	6.38 (404)		0.0 %	-2.44 [-142.42, 137.54]
Kim 2002	9	0.25 (0.15)	9	2.1 (2.3)		7.1 %	-1.85 [-3.36, -0.34]
Kiyama 2003	47	18.1 (9.5)	38	28.2 (22.3)		0.4 %	-10.10 [-17.69, -2.51]
Marrie 2000	87	8.2 (1.9)	124	9.6 (2.1)		16.3 %	-1.40 [-1.94, -0.86]
Philbin 2000	840	-1.8 (17.69)	664	-0.7 (17.69)		5.5 %	-1.10 [-2.90, 0.70]
Roberts 1997	82	1.38 (1.18)	83	1.87 (1.33)		18.1 %	-0.49 [-0.87, -0.11]
Sulch 2000	76	50 (19)	76	45 (23)		0.5 %	5.00 [-1.71, 11.71]
Subtotal (95% CI)	**1760**		**1626**			**100.0 %**	**-1.09 [-1.59, -0.60]**
Heterogeneity: Tau^2 = 0.32; Chi^2 = 30.79, df = 14 (P = 0.01); I^2 =55%							
Test for overall effect: Z = 4.32 (P = 0.000016)							
2 Non-randomised studies							
Choong 2000	55	6.6 (3.35)	56	8 (3.35)		70.7 %	-1.40 [-2.65, -0.15]
Usui 2004	30	8.03 (4.18)	31	10.77 (4.18)		29.3 %	-2.74 [-4.84, -0.64]
Subtotal (95% CI)	**85**		**87**			**100.0 %**	**-1.79 [-2.99, -0.60]**
Heterogeneity: Tau^2 = 0.12; Chi^2 = 1.16, df = 1 (P = 0.28); I^2 =14%							
Test for overall effect: Z = 2.94 (P = 0.0033)							



Analysis 2.1. Comparison 2 Stand-alone clinical pathway vs usual care, Outcome 1 LOS: invasive versus non-invasive.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 2 Stand-alone clinical pathway vs usual care

Outcome: 1 LOS: invasive versus non-invasive

Study or subgroup	Clinical pathway N	Mean(SD)	Usual care N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Non-invasive studies							
Falconer 1993	53	35.6 (15.5)	68	32.3 (15.4)		2.3 %	3.30 [-2.25, 8.85]
Marrie 2000	87	8.2 (1.9)	124	9.6 (2.1)		32.7 %	-1.40 [-1.94, -0.86]
Johnson 2000	50	1.68 (1.12)	50	2.24 (1.12)		34.3 %	-0.56 [-1.00, -0.12]
Sulch 2000	76	50 (19)	76	45 (23)		1.6 %	5.00 [-1.71, 11.71]
Kim 2002	9	0.25 (0.15)	9	2.1 (2.3)		17.5 %	-1.85 [-3.36, -0.34]
Usui 2004	30	8.03 (4.18)	31	10.77 (4.18)		11.6 %	-2.74 [-4.84, -0.64]
Subtotal (95% CI)	**305**		**358**			**100.0 %**	**-1.14 [-2.00, -0.28]**
Heterogeneity: Tau^2 = 0.51; Chi^2 = 15.10, df = 5 (P = 0.01); I^2 =67%							
Test for overall effect: Z = 2.59 (P = 0.0095)							
2 Invasive studies							
Gomez 1996	53	0.64 (0.51)	68	2.28 (5.25)		15.5 %	-1.64 [-2.90, -0.38]
Roberts 1997	82	1.38 (1.18)	83	1.87 (1.33)		24.1 %	-0.49 [-0.87, -0.11]
Brook 1999	162	14 (17.3)	159	19.9 (24.2)		2.6 %	-5.90 [-10.51, -1.29]
Dowsey 1999	92	7.1 (3.67)	71	8.6 (3.67)		16.7 %	-1.50 [-2.64, -0.36]
Choong 2000	55	6.6 (3.35)	56	8 (3.35)		15.6 %	-1.40 [-2.65, -0.15]
Aizawa 2002	32	12.7 (2.8)	37	14.7 (5.2)		10.0 %	-2.00 [-3.94, -0.06]
Kiyama 2003	47	18.1 (9.5)	38	28.2 (22.3)		1.0 %	-10.10 [-17.69, -2.51]
Delaney 2003	31	5.2 (2.5)	33	5.8 (3)		14.6 %	-0.60 [-1.95, 0.75]
Subtotal (95% CI)	**554**		**545**			**100.0 %**	**-1.39 [-2.17, -0.60]**
Heterogeneity: Tau^2 = 0.63; Chi^2 = 18.60, df = 7 (P = 0.01); I^2 =62%							
Test for overall effect: Z = 3.45 (P = 0.00055)							

Analysis 2.2. Comparison 2 Stand-alone clinical pathway vs usual care, Outcome 2 LOS: hospital area.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 2 Stand-alone clinical pathway vs usual care

Outcome: 2 LOS: hospital area

Study or subgroup	Clinical pathway N	Mean(SD)	Usual care N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 ED							
Kim 2002	9	0.25 (0.15)	9	2.1 (2.3)		35.1 %	-1.85 [-3.36, -0.34]
Roberts 1997	82	1.38 (1.18)	83	1.87 (1.33)		64.9 %	-0.49 [-0.87, -0.11]
Subtotal (95% CI)	**91**		**92**			**100.0 %**	**-0.97 [-2.24, 0.30]**
Heterogeneity: Tau² = 0.61; Chi² = 2.94, df = 1 (P = 0.09); I² =66%							
Test for overall effect: Z = 1.49 (P = 0.14)							
2 General acute							
Aizawa 2002	32	12.7 (2.8)	37	14.7 (5.2)		7.9 %	-2.00 [-3.94, -0.06]
Choong 2000	32	12.7 (2.8)	37	14.7 (5.2)		7.9 %	-2.00 [-3.94, -0.06]
Dowsey 1999	92	7.1 (3.67)	71	8.6 (3.67)		14.9 %	-1.50 [-2.64, -0.36]
Gomez 1996	53	0.64 (0.51)	68	2.28 (5.25)		13.5 %	-1.64 [-2.90, -0.38]
Johnson 2000	50	1.68 (1.12)	50	2.24 (1.12)		24.7 %	-0.56 [-1.00, -0.12]
Kiyama 2003	47	18.1 (9.5)	38	28.2 (22.3)		0.7 %	-10.10 [-17.69, -2.51]
Marrie 2000	87	8.2 (1.9)	124	9.6 (2.1)		23.2 %	-1.40 [-1.94, -0.86]
Usui 2004	30	8.03 (4.18)	31	10.77 (4.18)		7.1 %	-2.74 [-4.84, -0.64]
Subtotal (95% CI)	**423**		**456**			**100.0 %**	**-1.49 [-2.14, -0.85]**
Heterogeneity: Tau² = 0.39; Chi² = 17.57, df = 7 (P = 0.01); I² =60%							
Test for overall effect: Z = 4.53 (P < 0.00001)							
3 Extended care							
Delaney 2003	31	5.2 (2.5)	33	5.8 (3)		55.8 %	-0.60 [-1.95, 0.75]
Falconer 1993	53	35.6 (15.5)	68	32.3 (15.4)		24.8 %	3.30 [-2.25, 8.85]
Sulch 2000	76	50 (19)	76	45 (23)		19.5 %	5.00 [-1.71, 11.71]
Subtotal (95% CI)	**160**		**177**			**100.0 %**	**1.46 [-2.14, 5.05]**
Heterogeneity: Tau² = 5.55; Chi² = 4.17, df = 2 (P = 0.12); I² =52%							
Test for overall effect: Z = 0.79 (P = 0.43)							

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Study or subgroup	Clinical pathway N	Mean(SD)	Usual care N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
4 ICU							
Brook 1999	162	14 (17.3)	159	19.9 (24.2)		100.0 %	-5.90 [-10.51, -1.29]
Subtotal (95% CI)	**162**		**159**			**100.0 %**	**-5.90 [-10.51, -1.29]**
Heterogeneity: not applicable							
Test for overall effect: Z = 2.51 (P = 0.012)							

Analysis 2.3. Comparison 2 Stand-alone clinical pathway vs usual care, Outcome 3 LOS: implementation process.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 2 Stand-alone clinical pathway vs usual care

Outcome: 3 LOS: implementation process

Study or subgroup	Clinical pathway N	Mean(SD)	Usual care N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 High evidence based cpw implementation							
Johnson 2000	50	1.68 (1.12)	50	2.24 (1.12)		68.9 %	-0.56 [-1.00, -0.12]
Sulch 2000	76	50 (19)	76	45 (23)		31.1 %	5.00 [-1.71, 11.71]
Subtotal (95% CI)	**126**		**126**			**100.0 %**	**1.17 [-3.87, 6.22]**
Heterogeneity: Tau^2 = 9.58; Chi^2 = 2.63, df = 1 (P = 0.10); I^2 =62%							
Test for overall effect: Z = 0.45 (P = 0.65)							
2 Moderately evidence based impl							
Aizawa 2002	32	12.7 (2.8)	37	14.7 (5.2)		8.2 %	-2.00 [-3.94, -0.06]
Choong 2000	32	12.7 (2.8)	37	14.7 (5.2)		8.2 %	-2.00 [-3.94, -0.06]
Delaney 2003	31	5.2 (2.5)	33	5.8 (3)		14.3 %	-0.60 [-1.95, 0.75]
Dowsey 1999	92	7.1 (3.67)	71	8.6 (3.67)		17.9 %	-1.50 [-2.64, -0.36]
Falconer 1993	53	35.6 (15.5)	68	32.3 (15.4)		1.2 %	3.30 [-2.25, 8.85]

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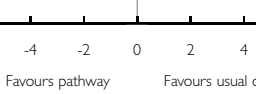
Study or subgroup	Clinical pathway N	Mean(SD)	Usual care N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Gomez 1996	53	0.64 (0.51)	68	2.28 (5.25)		15.7 %	-1.64 [-2.90, -0.38]
Kiyama 2003	47	18.1 (9.5)	38	28.2 (22.3)		0.6 %	-10.10 [-17.69, -2.51]
Marrie 2000	87	8.2 (1.9)	124	9.6 (2.1)		33.9 %	-1.40 [-1.94, -0.86]
Subtotal (95% CI)	**427**		**476**			**100.0 %**	**-1.44 [-2.05, -0.83]**
Heterogeneity: $Tau^2 = 0.21$; $Chi^2 = 10.05$, df = 7 (P = 0.19); $I^2 = 30\%$							
Test for overall effect: Z = 4.61 (P < 0.00001)							
3 Low ebm							
Brook 1999	162	14 (17.3)	159	19.9 (24.2)		9.3 %	-5.90 [-10.51, -1.29]
Kim 2002	9	0.25 (0.15)	9	2.1 (2.3)		29.1 %	-1.85 [-3.36, -0.34]
Roberts 1997	82	1.38 (1.18)	83	1.87 (1.33)		38.1 %	-0.49 [-0.87, -0.11]
Usui 2004	30	8.03 (4.18)	31	10.77 (4.18)		23.5 %	-2.74 [-4.84, -0.64]
Subtotal (95% CI)	**283**		**282**			**100.0 %**	**-1.92 [-3.53, -0.30]**
Heterogeneity: $Tau^2 = 1.74$; $Chi^2 = 11.89$, df = 3 (P = 0.01); $I^2 = 75\%$							
Test for overall effect: Z = 2.33 (P = 0.020)							

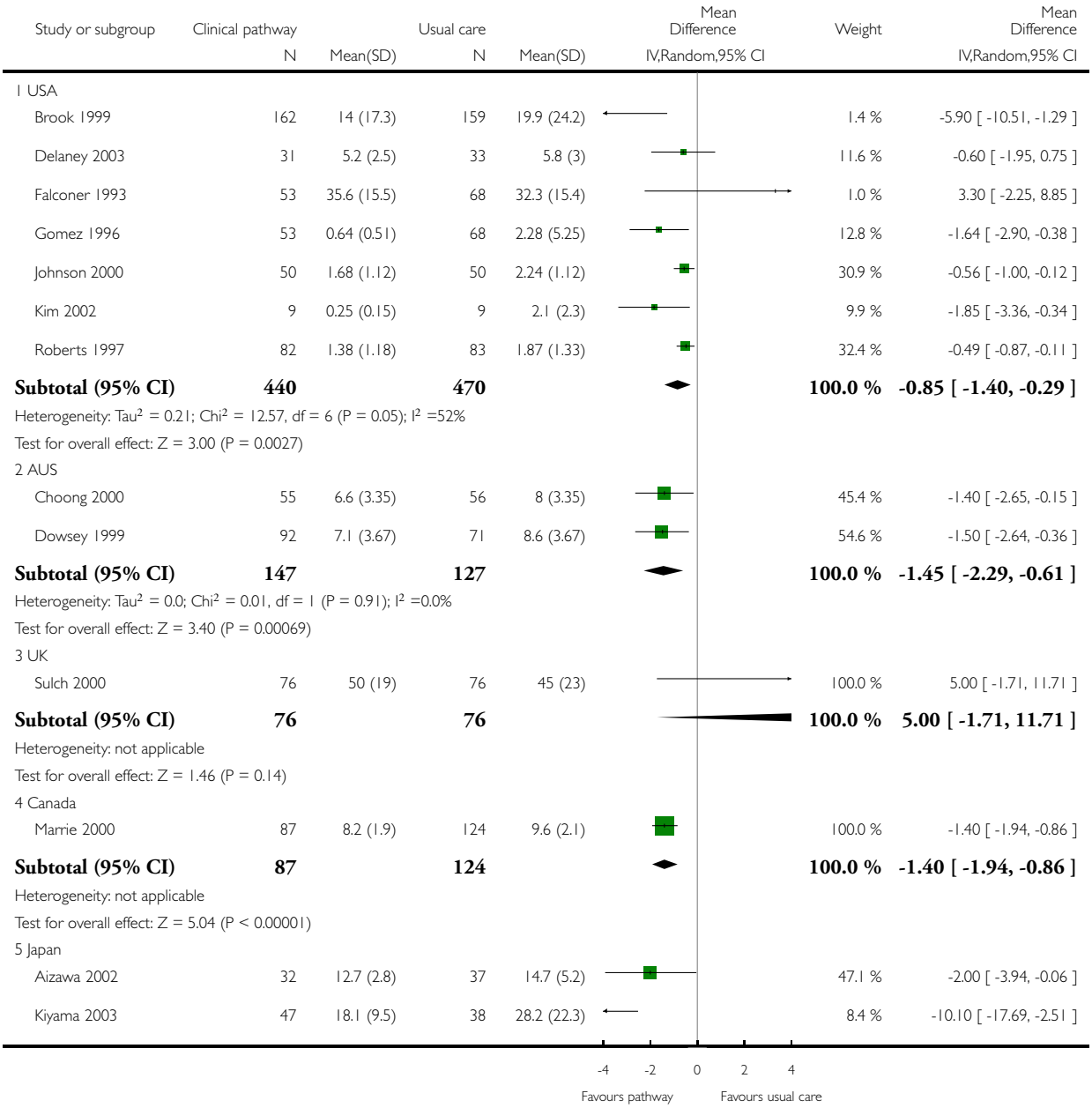


Analysis 2.4. Comparison 2 Stand-alone clinical pathway vs usual care, Outcome 4 LOS: country.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 2 Stand-alone clinical pathway vs usual care

Outcome: 4 LOS: country



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Study or subgroup	Clinical pathway N	Mean(SD)	Usual care N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Usui 2004	30	8.03 (4.18)	31	10.77 (4.18)		44.6 %	-2.74 [-4.84, -0.64]
Subtotal (95% CI)	**109**		**106**			**100.0 %**	**-3.01 [-5.35, -0.67]**

Heterogeneity: $Tau^2 = 2.05$; $Chi^2 = 4.13$, df = 2 (P = 0.13); $I^2 = 52\%$

Test for overall effect: Z = 2.52 (P = 0.012)

Analysis 2.5. Comparison 2 Stand-alone clinical pathway vs usual care, Outcome 5 LOS: year.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 2 Stand-alone clinical pathway vs usual care

Outcome: 5 LOS: year

Study or subgroup	Clinical pathway N	Mean(SD)	Usual care N	Mean(SD)	Mean Difference IV,Random,95% CI	Mean Difference IV,Random,95% CI
1 Year						
Falconer 1993	53	35.6 (15.5)	68	32.3 (15.4)		3.30 [-2.25, 8.85]
Gomez 1996	53	0.64 (0.51)	68	2.28 (5.25)		-1.64 [-2.90, -0.38]
Roberts 1997	82	1.38 (1.18)	83	1.87 (1.33)		-0.49 [-0.87, -0.11]
Dowsey 1999	92	7.1 (3.67)	71	8.6 (3.67)		-1.50 [-2.64, -0.36]
Brook 1999	162	14 (17.3)	159	19.9 (24.2)		-5.90 [-10.51, -1.29]
Choong 2000	55	6.6 (3.35)	56	8 (3.35)		-1.40 [-2.65, -0.15]
Marrie 2000	87	8.2 (1.9)	124	9.6 (2.1)		-1.40 [-1.94, -0.86]
Sulch 2000	76	50 (19)	76	45 (23)		5.00 [-1.71, 11.71]
Johnson 2000	50	1.68 (1.12)	50	2.24 (1.12)		-0.56 [-1.00, -0.12]
Kim 2002	9	0.25 (0.15)	9	2.1 (2.3)		-1.85 [-3.36, -0.34]
Aizawa 2002	32	12.7 (2.8)	37	14.7 (5.2)		-2.00 [-3.94, -0.06]

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Study or subgroup	Clinical pathway N	Mean(SD)	Usual care N	Mean(SD)	Mean Difference IV,Random,95% CI	Mean Difference IV,Random,95% CI
Delaney 2003	31	5.2 (2.5)	33	5.8 (3)		-0.60 [-1.95, 0.75]
Kiyama 2003	47	18.1 (9.5)	38	28.2 (22.3)		-10.10 [-17.69, -2.51]
Usui 2004	30	8.03 (4.18)	31	10.77 (4.18)		-2.74 [-4.84, -0.64]

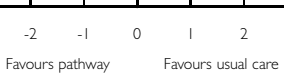
Analysis 2.6. Comparison 2 Stand-alone clinical pathway vs usual care, Outcome 6 LOS: condition or intervention.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 2 Stand-alone clinical pathway vs usual care

Outcome: 6 LOS: condition or intervention

Study or subgroup	Clinical pathway N	Mean(SD)	Usual care N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Stroke							
Falconer 1993	53	35.6 (15.5)	68	32.3 (15.4)		59.4 %	3.30 [-2.25, 8.85]
Sulch 2000	76	50 (19)	76	45 (23)		40.6 %	5.00 [-1.71, 11.71]
Subtotal (95% CI)	**129**		**144**			**100.0 %**	**3.99 [-0.29, 8.27]**
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.15, df = 1 (P = 0.70); I^2 =0.0%							
Test for overall effect: Z = 1.83 (P = 0.067)							
2 Pneumonia							
Marrie 2000	87	8.2 (1.9)	124	9.6 (2.1)		79.8 %	-1.40 [-1.94, -0.86]
Usui 2004	30	8.03 (4.18)	31	10.77 (4.18)		20.2 %	-2.74 [-4.84, -0.64]
Subtotal (95% CI)	**117**		**155**			**100.0 %**	**-1.67 [-2.73, -0.62]**
Heterogeneity: Tau^2 = 0.29; Chi^2 = 1.47, df = 1 (P = 0.23); I^2 =32%							
Test for overall effect: Z = 3.10 (P = 0.0019)							
3 Suspected MI							
Gomez 1996	53	0.64 (0.51)	68	2.28 (5.25)		35.9 %	-1.64 [-2.90, -0.38]



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Study or subgroup	Clinical pathway		Usual care		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
Roberts 1997	82	1.38 (1.18)	83	1.87 (1.33)		64.1 %	-0.49 [-0.87, -0.11]
Subtotal (95% CI)	**135**		**151**			**100.0 %**	**-0.90 [-1.98, 0.18]**

Heterogeneity: $Tau^2 = 0.44$; $Chi^2 = 2.95$, df = 1 (P = 0.09); $I^2 = 66\%$

Test for overall effect: Z = 1.64 (P = 0.10)

Analysis 2.7. Comparison 2 Stand-alone clinical pathway vs usual care, Outcome 7 Days to sitting out of bed.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 2 Stand-alone clinical pathway vs usual care

Outcome: 7 Days to sitting out of bed

Study or subgroup	Clinical pathway		Usual care		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
Choong 2000	55	1.6 (1.44)	56	2.2 (1.44)			-0.60 [-1.14, -0.06]
Dowsey 1999	92	1.94 (2.8)	71	3.42 (2.8)			-1.48 [-2.35, -0.61]
Subtotal (95% CI)	**0**		**0**				**0.0 [0.0, 0.0]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.0$, df = 0 (P<0.00001); $I^2 = 0.0\%$

Test for overall effect: Z = 0.0 (P < 0.00001)

Analysis 2.8. Comparison 2 Stand-alone clinical pathway vs usual care, Outcome 8 Duration of ventilation (TSA).

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 2 Stand-alone clinical pathway vs usual care

Outcome: 8 Duration of ventilation (TSA)

Study or subgroup	Change in level and slope (SE)	Change in level and slope IV,Fixed,95% CI	Change in level and slope IV,Fixed,95% CI
1 Change in level			
Brattebo 2002	-0.115 (0.246)		-0.12 [-0.60, 0.37]
2 Change in slope			
Brattebo 2002	0.031 (0.145)		0.03 [-0.25, 0.32]

Analysis 2.9. Comparison 2 Stand-alone clinical pathway vs usual care, Outcome 9 Duration of mechanical ventilation in hours.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 2 Stand-alone clinical pathway vs usual care

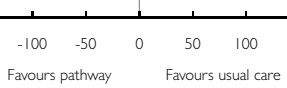
Outcome: 9 Duration of mechanical ventilation in hours

Study or subgroup	Clinical pathway N	Mean(SD)	Usual care N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Brook 1999	162	89.1 (133.6)	159	124 (153.6)		48.8 %	-34.90 [-66.42, -3.38]
Kollef 1997	179	69.4 (123.7)	178	102 (169.1)		51.2 %	-32.60 [-63.35, -1.85]
Total (95% CI)	**341**		**337**			**100.0 %**	**-33.72 [-55.73, -11.71]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.01$, df = 1 (P = 0.92); $I^2 = 0.0\%$

Test for overall effect: Z = 3.00 (P = 0.0027)

Test for subgroup differences: Not applicable



Analysis 2.10. Comparison 2 Stand-alone clinical pathway vs usual care, Outcome 10 Duration of antibiotic infusion.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 2 Stand-alone clinical pathway vs usual care

Outcome: 10 Duration of antibiotic infusion

Study or subgroup	Clinical pathway		Usual care		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
Marrie 2000	87	4.6 (0.9)	124	6.3 (1.4)		97.0 %	-1.70 [-2.01, -1.39]
Usui 2004	30	6.47 (3.53)	31	8.22 (3.53)		3.0 %	-1.75 [-3.52, 0.02]
Total (95% CI)	**117**		**155**			**100.0 %**	**-1.70 [-2.01, -1.40]**

Heterogeneity: Tau² = 0.0; Chi² = 0.00, df = 1 (P = 0.96); I² =0.0%

Test for overall effect: Z = 10.90 (P < 0.00001)

Test for subgroup differences: Not applicable

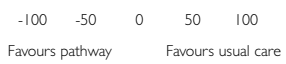
Analysis 2.11. Comparison 2 Stand-alone clinical pathway vs usual care, Outcome 11 Patient satisfaction.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 2 Stand-alone clinical pathway vs usual care

Outcome: 11 Patient satisfaction

Study or subgroup	Clinical pathway		Usual care		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI	IV,Random,95% CI
Delaney 2003	31	8.2 (2.2)	33	8.4 (1.6)		-0.20 [-1.15, 0.75]
Falconer 1993	53	7.7 (2.6)	68	8.8 (1.7)		-1.10 [-1.91, -0.29]
Marrie 2000	87	30.3 (1.5)	124	29.9 (1.6)		0.40 [-0.02, 0.82]



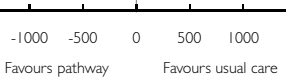
Analysis 2.12. Comparison 2 Stand-alone clinical pathway vs usual care, Outcome 12 Hospital costs / charges.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 2 Stand-alone clinical pathway vs usual care

Outcome: 12 Hospital costs / charges

Study or subgroup	Clinical pathway		Usual care		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI	IV,Random,95% CI
1 Hospital charges						
Gomez 1996	50	1417.03 (1857.99)	50	6336.21 (16251.01)	-4919.18 [-9452.99, -385.37]	
Johnson 2000	55	2522.69 (1151.9)	55	3265.77 (1151.9)		-743.08 [-1173.60, -312.56]
2 Hospital costs						
Kim 2002	9	870 (394)	9	1706 (1512)		-836.00 [-1856.81, 184.81]
Kiyama 2003	47	9695.05 (1822.69)	38	12466.99 (5072.65)	-2771.94 [-4466.87, -1077.01]	
Kollef 1997	179	30052 (29122)	178	29791 (28090)		261.00 [-5674.42, 6196.42]
Roberts 1997	82	1728.88 (1145.04)	83	2370.42 (919.88)		-641.54 [-958.69, -324.39]



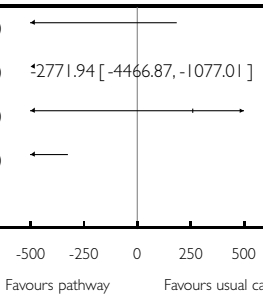
Analysis 2.13. Comparison 2 Stand-alone clinical pathway vs usual care, Outcome 13 hospital costs.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 2 Stand-alone clinical pathway vs usual care

Outcome: 13 hospital costs

Study or subgroup	Clinical pathway N	Mean(SD)	Usual care N	Mean(SD)	Mean Difference IV,Random,95% CI	Mean Difference IV,Random,95% CI
Kim 2002	9	870 (394)	9	1706 (1512)		-836.00 [-1856.81, 184.81]
Kiyama 2003	47	9695.05 (1822.69)	38	12466.99 (5072.65)	-2771.94 [-4466.87, -1077.01]	
Kollef 1997	179	30052 (29122)	178	29791 (28090)		261.00 [-5674.42, 6196.42]
Roberts 1997	82	1728.88 (1145.04)	83	2370.42 (919.88)		-641.54 [-958.69, -324.39]

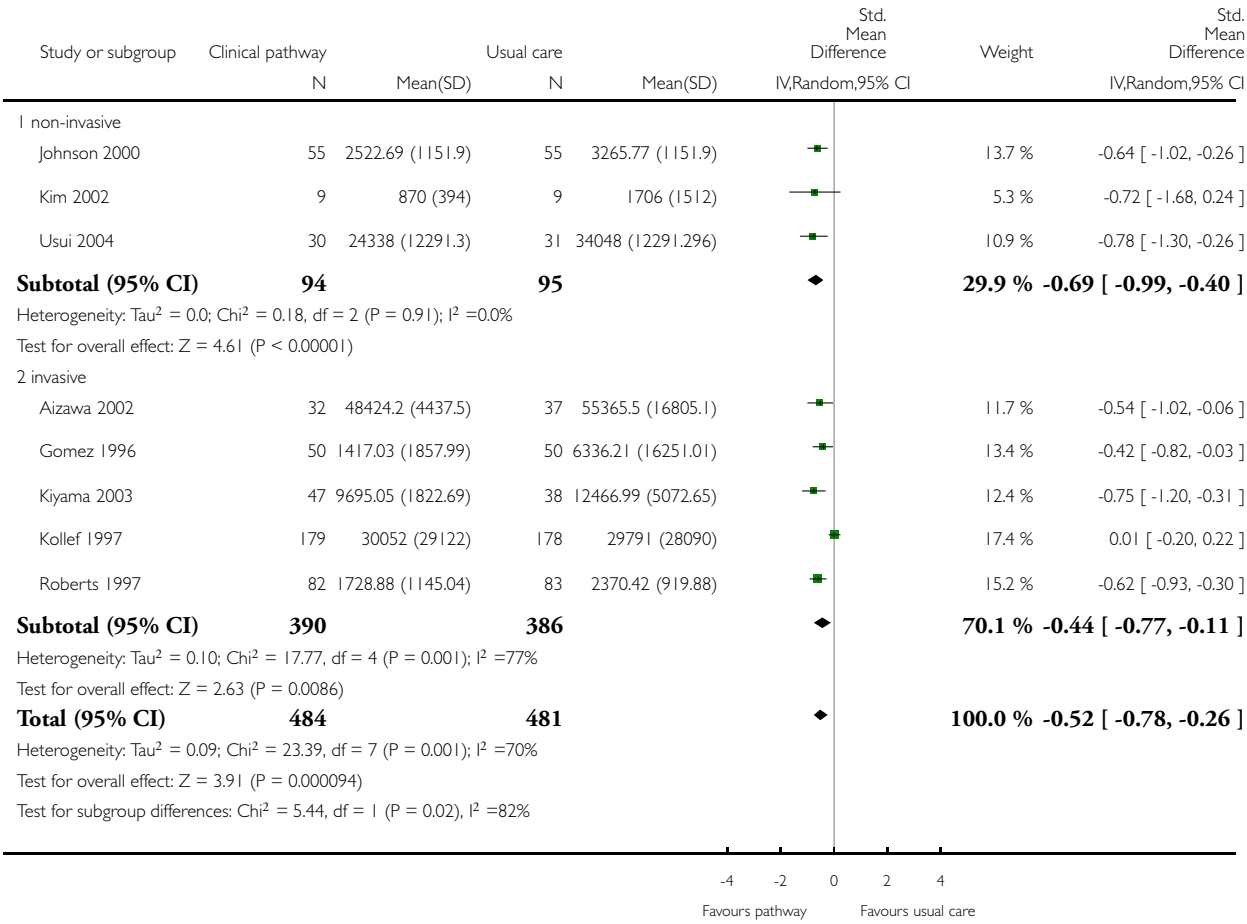


Analysis 2.14. Comparison 2 Stand-alone clinical pathway vs usual care, Outcome 14 SMD hospital cost data.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 2 Stand-alone clinical pathway vs usual care

Outcome: 14 SMD hospital cost data



Analysis 2.15. Comparison 2 Stand-alone clinical pathway vs usual care, Outcome 15 Standardised hospital costs / charges / insurance points.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 2 Stand-alone clinical pathway vs usual care

Outcome: 15 Standardised hospital costs / charges / insurance points

Study or subgroup	Clinical pathway N	Mean(SD)	Usual care N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Aizawa 2002	32	48424 (4438)	37	55366 (16805)		11.7 %	-0.54 [-1.02, -0.06]
Gomez 1996	50	1417.03 (1857.99)	50	6336.21 (16251.01)		13.4 %	-0.42 [-0.82, -0.03]
Johnson 2000	55	2522.69 (1151.9)	55	3265.77 (1151.9)		13.7 %	-0.64 [-1.02, -0.26]
Kim 2002	9	870 (394)	9	1706 (1512)		5.3 %	-0.72 [-1.68, 0.24]
Kiyama 2003	47	9695.05 (1822.69)	38	12466.99 (5072.65)		12.4 %	-0.75 [-1.20, -0.31]
Kollef 1997	179	30052 (29122)	178	29791 (28090)		17.4 %	0.01 [-0.20, 0.22]
Roberts 1997	82	1728.88 (1145.04)	83	2370.42 (919.88)		15.2 %	-0.62 [-0.93, -0.30]
Usui 2004	30	24338 (12291.3)	31	34048 (12291.296)		10.9 %	-0.78 [-1.30, -0.26]
Total (95% CI)	**484**		**481**			**100.0 %**	**-0.52 [-0.78, -0.26]**

Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 23.39$, df = 7 (P = 0.001); $I^2 = 70\%$

Test for overall effect: Z = 3.91 (P = 0.000094)

Test for subgroup differences: Not applicable

Analysis 2.16. Comparison 2 Stand-alone clinical pathway vs usual care, Outcome 16 Hospital insurance points (Japan: surrogate for hospital charges).

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 2 Stand-alone clinical pathway vs usual care

Outcome: 16 Hospital insurance points (Japan: surrogate for hospital charges)

Study or subgroup	Clinical pathway N	Mean(SD)	Usual care N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Aizawa 2002	32	48424.2 (4437.5)	37	55365.5 (16805.1)		54.6 %	-6941.30 [-12570.22, -1312.38]
Usui 2004	30	24338 (12291.3)	31	34048 (12291.296)		45.4 %	-9710.00 [-15879.77, -3540.23]
Total (95% CI)	**62**		**68**			**100.0 %**	**-8199.00 [-12357.33, -4040.66]**

Heterogeneity: Tau² = 0.0; Chi² = 0.42, df = 1 (P = 0.52); I² =0.0%

Test for overall effect: Z = 3.86 (P = 0.00011)

Test for subgroup differences: Not applicable

Analysis 2.17. Comparison 2 Stand-alone clinical pathway vs usual care, Outcome 17 Complications up to 3 months.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 2 Stand-alone clinical pathway vs usual care

Outcome: 17 Complications up to 3 months

Study or subgroup	Clinical pathway n/N	Usual care n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Dowsey 1999	10/92	20/71		100.0 %	0.31 [0.13, 0.72]
Total (95% CI)	**92**	**71**		**100.0 %**	**0.31 [0.13, 0.72]**

Total events: 10 (Clinical pathway), 20 (Usual care)

Heterogeneity: not applicable

Test for overall effect: Z = 2.74 (P = 0.0062)

Test for subgroup differences: Not applicable

Analysis 2.18. Comparison 2 Stand-alone clinical pathway vs usual care, Outcome 18 Mortality rate.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 2 Stand-alone clinical pathway vs usual care

Outcome: 18 Mortality rate

Study or subgroup	Clinical pathway n/N	Usual care n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Brook 1999	49/162	57/159		36.0 %	0.78 [0.49, 1.24]
Kollef 1997	40/179	42/178		32.2 %	0.93 [0.57, 1.53]
Smith 2004	49/334	30/175		31.8 %	0.83 [0.51, 1.37]
Total (95% CI)	**675**	**512**		**100.0 %**	**0.84 [0.64, 1.11]**

Total events: 138 (Clinical pathway), 129 (Usual care)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.28$, df = 2 (P = 0.87); $I^2 = 0.0\%$

Test for overall effect: Z = 1.21 (P = 0.23)

Analysis 2.19. Comparison 2 Stand-alone clinical pathway vs usual care, Outcome 19 In-hospital complications.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 2 Stand-alone clinical pathway vs usual care

Outcome: 19 In-hospital complications

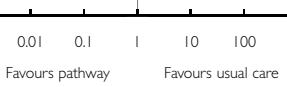
Study or subgroup	Clinical pathway n/N	Usual care n/N	Odds Ratio IV,Random,95% CI	Weight	Odds Ratio IV,Random,95% CI
Aizawa 2002	1/32	2/37		3.9 %	0.56 [0.05, 6.53]
Choong 2000	10/55	14/56		27.9 %	0.67 [0.27, 1.66]
Delaney 2003	7/31	10/33		18.5 %	0.67 [0.22, 2.06]
Kiyama 2003	3/47	5/38		10.3 %	0.45 [0.10, 2.02]
Marelich 2000	11/166	20/169		39.4 %	0.53 [0.24, 1.14]
Total (95% CI)	**331**	**333**		**100.0 %**	**0.58 [0.36, 0.94]**

Total events: 32 (Clinical pathway), 51 (Usual care)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.32$, df = 4 (P = 0.99); $I^2 = 0.0\%$

Test for overall effect: Z = 2.20 (P = 0.028)

Test for subgroup differences: Not applicable



Analysis 2.20. Comparison 2 Stand-alone clinical pathway vs usual care, Outcome 20 Hospital readmission up to 6 months.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 2 Stand-alone clinical pathway vs usual care

Outcome: 20 Hospital readmission up to 6 months

Study or subgroup	Clinical pathway n/N	Usual care n/N	Odds Ratio IV,Random,95% CI	Weight	Odds Ratio IV,Random,95% CI
Aizawa 2002	1/32	0/37		3.8 %	3.57 [0.14, 90.78]
Choong 2000	2/55	6/56		14.7 %	0.31 [0.06, 1.63]
Delaney 2003	3/31	6/33		18.2 %	0.48 [0.11, 2.13]
Dowsey 1999	4/92	9/71		26.8 %	0.31 [0.09, 1.06]
Gomez 1996	3/50	3/50		14.7 %	1.00 [0.19, 5.21]
Roberts 1997	5/82	4/83		21.9 %	1.28 [0.33, 4.96]
Total (95% CI)	**342**	**330**		**100.0 %**	**0.60 [0.32, 1.13]**

Total events: 18 (Clinical pathway), 28 (Usual care)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 4.51$, df = 5 (P = 0.48); $I^2 = 0.0\%$

Test for overall effect: Z = 1.58 (P = 0.11)

Test for subgroup differences: Not applicable

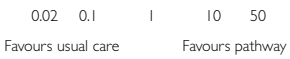
Analysis 2.21. Comparison 2 Stand-alone clinical pathway vs usual care, Outcome 21 Process of care: documentation.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 2 Stand-alone clinical pathway vs usual care

Outcome: 21 Process of care: documentation

Study or subgroup	Clinical pathway n/N	Usual care n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Doherty 2006	29/47	6/42		79.2 %	9.67 [3.40, 27.50]
Sulch 2002	75/76	56/76		20.8 %	26.79 [3.49, 205.58]
Total (95% CI)	**123**	**118**		**100.0 %**	**11.95 [4.72, 30.30]**
Total events: 104 (Clinical pathway), 62 (Usual care)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.84$, df = 1 (P = 0.36); $I^2 = 0.0\%$					
Test for overall effect: Z = 5.23 (P < 0.00001)					



Analysis 2.22. Comparison 2 Stand-alone clinical pathway vs usual care, Outcome 22 TSA ITS Level.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 2 Stand-alone clinical pathway vs usual care

Outcome: 22 TSA ITS Level

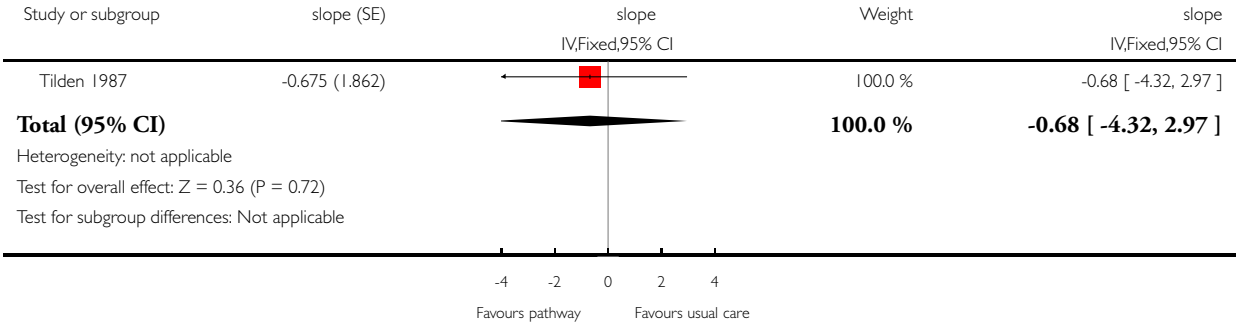
Study or subgroup	level (SE)	level IV,Random,95% CI	Weight	level IV,Random,95% CI
Tilden 1987	18.575 (8.533)		100.0 %	18.58 [1.85, 35.30]
Total (95% CI)			**100.0 %**	**18.58 [1.85, 35.30]**
Heterogeneity: not applicable				
Test for overall effect: Z = 2.18 (P = 0.029)				

Analysis 2.23. Comparison 2 Stand-alone clinical pathway vs usual care, Outcome 23 Process of care: documentation (TSA) ITS slope.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 2 Stand-alone clinical pathway vs usual care

Outcome: 23 Process of care: documentation (TSA) ITS slope



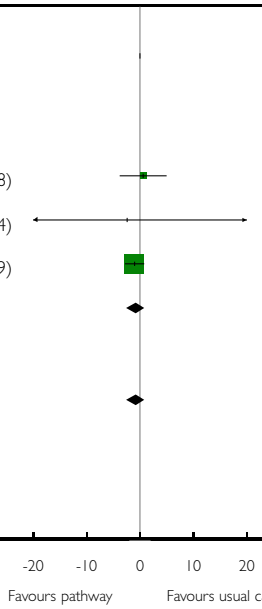
Analysis 3.1. Comparison 3 Multifaceted intervention including clinical pathway vs usual care, Outcome 1 LOS.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 3 Multifaceted intervention including clinical pathway vs usual care

Outcome: 1 LOS

Study or subgroup	Clinical pathway N	Mean(SD)	Usual care N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Non-randomized studies							
Subtotal (95% CI)	**0**		**0**				**Not estimable**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
2 Randomized studies							
Cole 2002	113	19.7 (17.1)	114	19.1 (16.8)		14.3 %	0.60 [-3.81, 5.01]
Kampan 2006	33	3.94 (1.03)	32	6.38 (404)		0.0 %	-2.44 [-142.42, 137.54]
Philbin 2000	840	-1.8 (17.69)	664	-0.7 (17.69)		85.7 %	-1.10 [-2.90, 0.70]
Subtotal (95% CI)	**986**		**810**			**100.0 %**	**-0.86 [-2.52, 0.81]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.49$, df = 2 (P = 0.78); $I^2 = 0.0\%$							
Test for overall effect: Z = 1.01 (P = 0.31)							
Total (95% CI)	**986**		**810**			**100.0 %**	**-0.86 [-2.52, 0.81]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.49$, df = 2 (P = 0.78); $I^2 = 0.0\%$							
Test for overall effect: Z = 1.01 (P = 0.31)							
Test for subgroup differences: Not applicable							

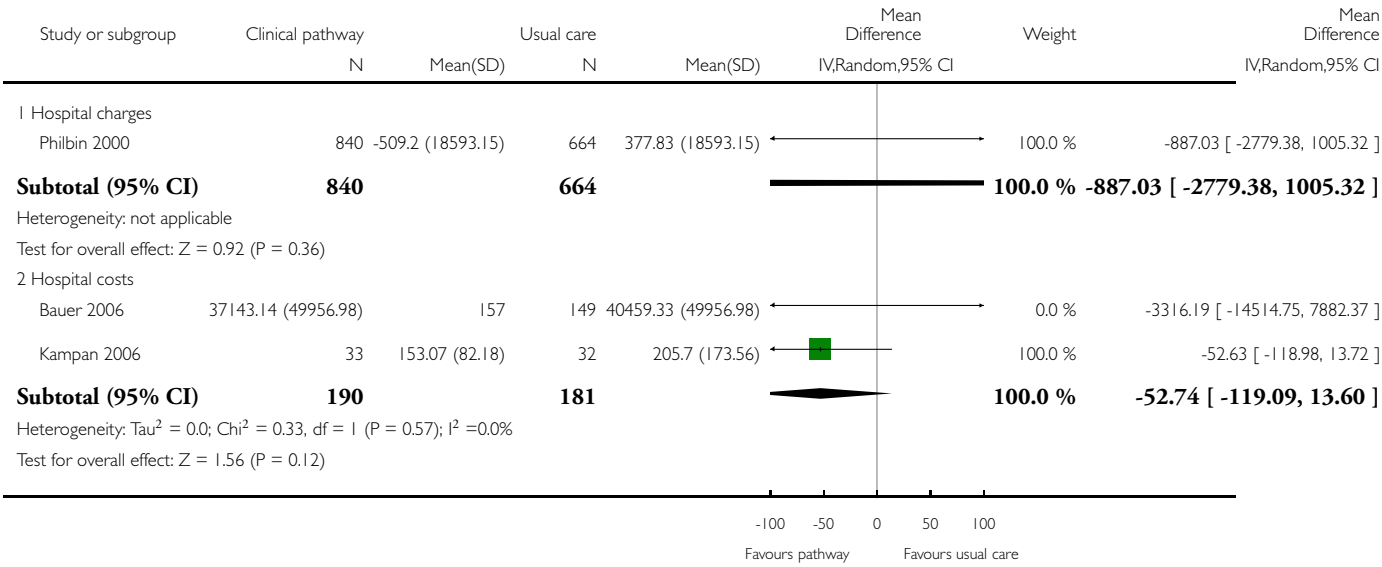


Analysis 3.2. Comparison 3 Multifaceted intervention including clinical pathway vs usual care, Outcome 2 Hospital costs / charges.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 3 Multifaceted intervention including clinical pathway vs usual care

Outcome: 2 Hospital costs / charges



Analysis 3.3. Comparison 3 Multifaceted intervention including clinical pathway vs usual care, Outcome 3 Standardised hospital costs / charges / insurance points.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 3 Multifaceted intervention including clinical pathway vs usual care

Outcome: 3 Standardised hospital costs / charges / insurance points

Study or subgroup	Clinical pathway N	Mean(SD)	Usual care N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Bauer 2006	37143.14 (49956.98)	157	149	40459.33 (49956.98)		16.5 %	-0.07 [-0.29, 0.16]
Kampan 2006	33	153.07 (82.18)	32	205.7 (173.56)		3.4 %	-0.38 [-0.88, 0.11]
Philbin 2000	840	-509.2 (18593.15)	664	377.83 (18593.15)		80.1 %	-0.05 [-0.15, 0.05]
Total (95% CI)	**1030**		**845**			**100.0 %**	**-0.06 [-0.15, 0.03]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.74$, df = 2 (P = 0.42); $I^2 = 0.0\%$

Test for overall effect: Z = 1.34 (P = 0.18)

Test for subgroup differences: Not applicable

Analysis 3.4. Comparison 3 Multifaceted intervention including clinical pathway vs usual care, Outcome 4 Mortality rate.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 3 Multifaceted intervention including clinical pathway vs usual care

Outcome: 4 Mortality rate

Study or subgroup	Clinical pathway n/N	Usual care n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Cole 2002	25/113	22/114		100.0 %	1.19 [0.62, 2.26]
Total (95% CI)	**113**	**114**		**100.0 %**	**1.19 [0.62, 2.26]**

Total events: 25 (Clinical pathway), 22 (Usual care)

Heterogeneity: not applicable

Test for overall effect: Z = 0.53 (P = 0.60)

Analysis 3.5. Comparison 3 Multifaceted intervention including clinical pathway vs usual care, Outcome 5 Hospital readmission up to 6 months.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 3 Multifaceted intervention including clinical pathway vs usual care

Outcome: 5 Hospital readmission up to 6 months

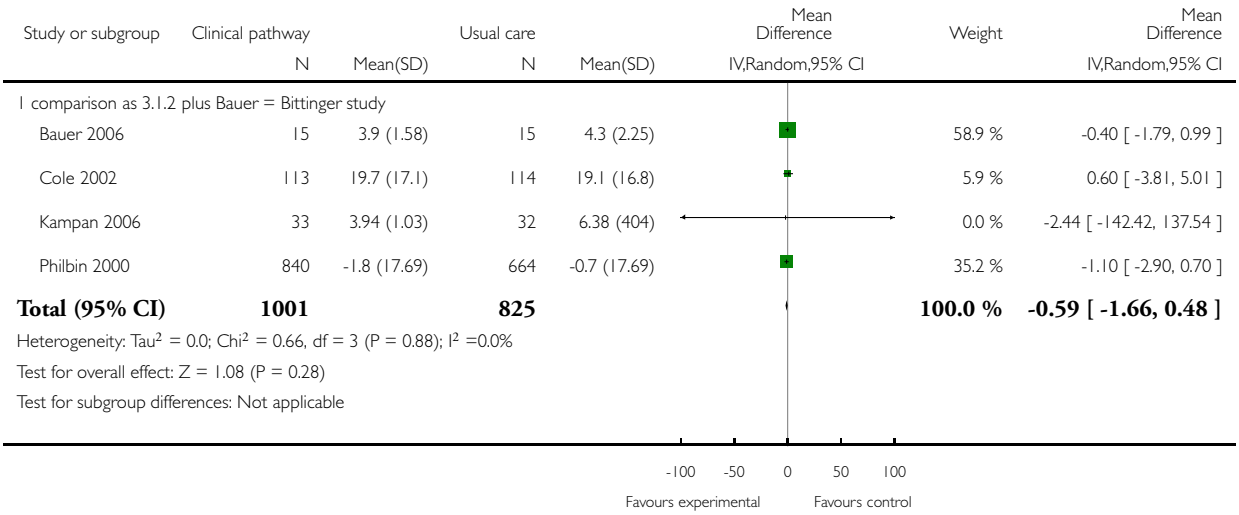
Study or subgroup	Favours pathway n/N	Usual care n/N	Odds Ratio IV,Random,95% CI	Odds Ratio IV,Random,95% CI
Kampan 2006	2/33	11/32		0.12 [0.02, 0.61]
Philbin 2000	169/840	141/664		0.93 [0.73, 1.20]

Analysis 3.6. Comparison 3 Multifaceted intervention including clinical pathway vs usual care, Outcome 6 LOS (sensitivity analysis + Bittinger RCT study 1995.

Review: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs

Comparison: 3 Multifaceted intervention including clinical pathway vs usual care

Outcome: 6 LOS (sensitivity analysis + Bittinger RCT study 1995



ADDITIONAL TABLES

Table 1. Original reported costs / charges data

Study ID	Country	Price year / study period	Cost / charges measure	Original currency	Experimental	E-SD	E-N	Control	C-SD	C-N
Comparison 1: single CPW intervention versus usual care										
Aizawa 2002	Japan	2000	hospital charges (insurance points)	insurance points	48424	4438	32	55366	16805	37
Falconer 1993	USA	87-91	(median) hospital charges bed days	US $	14440	missing	53	14420	missing	68

Table 1. Original reported costs / charges data (*Continued*)

Falconer 1993	USA	87-91	(median) hospital charges services	US $	11249	missing	53	9579	missing	68
Falconer 1993	USA	87-91	(median) hospital charges drugs	US $	1130	missing	53	1015	missing	68
Falconer 1993	USA	87-91	(median) hospital charges; other charges	US $	2397	missing	53	1871	missing	68
Gomez 1996	USA	1994	hospital charges initial stay	US $	1279	1677	50	5719	14668	50
Gomez 1996	USA	1994	hospital charges at 30 days	US $	1424	1735	50	5860	14638	50
Johnson 2000	USA	95-97	hospital room charges	US $	2407	1099	55	3116	1099	55
Johnson 2000	USA	95-97	hospital medication charges	US $	129	107	55	153	107	55
Johnson 2000	USA	95-97	hospital lab tests charges	US $	21	66	55	42	66	55
Johnson 2000	USA	95-97	hospital charges respiratory therapy	US $	42	322	55	250	322	55
Kim 2002	USA	2000	direct variable mean hos-	US $	870	394	9	1706	1512	9

Table 1. Original reported costs / charges data (*Continued*)

			pital costs (excluding professional fees)							
Kiyama 2003	Japan	2001	direct variable mean hospital costs (including medication and professional fees)	Jen	1502587	282489	47	1932197	786185	38
Kiyama 2003	Japan	2001	direct variable mean costs medication	Jen	190339	112760	47	270631	176643	38
Kiyama 2003	Japan	2001	direct variable mean daily costs	Jen	58383	8575	47	55651	15573	38
Kollef 1997	USA	1995	hospital costs (poor reporting: seems to be direct variable costs	US $	27680	26823	179	27439	25873	178
Roberts 1997	USA	1993	total hospital costs (doctors & nurses fees included)	US $	1528	1012	82	2095	813	83
Usui 2004	Japan	2002/ 2003	hospital charges (insur-	insurance points	24338	12291	30	34048	12291	31

Table 1. Original reported costs / charges data (*Continued*)

			ance points)							
Usui 2004	Japan	2002/ 2003	hospital charges antibiotic infusion	insurance points	3285	2027	30	3928	2027	31
Usui 2004	Japan	2002/ 2003	hospital charges laboratory costs	insurance points	3220	3097	30	5785	3097	31
Usui 2004	Japan	2002/ 2003	hospital charges radiology costs	insurance points	1438	1194	30	2471	1194	31
Comparison 2: Multifaceted intervention including a CPW versus usual care										
Bauer 2006	USA	2004	3 years mean intervention costs (direct variable costs)	US $	61398	63129	157	64379	58118	149
Bauer 2006	USA	2004	direct outpatient costs (direct variable costs)	US $	20740	15825	157	20091	15825	149
Bauer 2006	USA	2004	hospital inpatient costs (direct variable costs)	US $	40658	54684	157	44288	54684	149
Bauer 2006	USA	2004	psychiatric inpatient costs (direct variable	US $	27428	41440	157	30665	41440	149

Table 1. Original reported costs / charges data (*Continued*)

			costs)							
Bauer 2006	USA	2004	medical surgical inpatient costs (direct variable costs)	US $	13230	28798	157	13523	28798	149
Kampan 2006	Thailand	2005	hospital costs (poor reporting: seems to be total hospital costs	BAHT	2744	1473	33	3687	3111	32
Philbin 2000	USA	1995	hospital charges	US $	-469	17125	840	348	17125	664

Table 2. Cost / charges data, standardized to the year 2000 (CCEMG EPPI tool used)

Study ID	Cost / charges measure	Price year used	Deflator used	Exchange rates	Target currency	Experimental	E-SD	E-N	Control	C-SD	C-N
Comparison 1: single CPW intervention versus usual care											
Aizawa 2002	hospital charges (insurance points)	2000	NON	insurance points	NON	48424	4438	32	55366	16805	37
Falconer 1993	(median) hospital charges bed days	median (87-91)	GDPD values (IMF)*	PPP values*	US $ year 2000	18320	missing	53	18295	missing	68
Falconer 1993	(median) hospital charges services	median (87-91)	GDPD values (IMF)*	PPP values*	US $ year 2000	14272	missing	53	12153	missing	68

Table 2. Cost / charges data, standardized to the year 2000 (CCEMG EPPI tool used) (*Continued*)

Falconer 1993	(median) hospital charges drugs	median (87-91)	GDPD values (IMF)*	PPP values*	US $ year 2000	1434	missing	53	1288	missing	68
Falconer 1993	(median) hospital charges; other charges	median (87-91)	GDPD values (IMF)*	PPP values*	US $ year 2000	3041	missing	53	2374	missing	68
Gomez 1996	hospital charges initial stay	1994	GDPD values (IMF)*	PPP values*	US $ year 2000	1417	1858	50	6336	16251	50
Gomez 1996	hospital charges at 30 days	1994	GDPD values (IMF)*	PPP values*	US $ year 2000	1578	1922	50	6492	16218	50
Johnson 2000	hospital room charges	1997	GDPD values (IMF)*	PPP values*	US $ year 2000	2523	1152	55	3266	1152	55
Johnson 2000	hospital medication charges	1997	GDPD values (IMF)*	PPP values*	US $ year 2000	135	112	55	160	112	57
Johnson 2000	hospital lab tests charges	1997	GDPD values (IMF)*	PPP values*	US $ year 2000	22	70	55	44	70	55
Johnson 2000	hospital charges respiratory therapy	1997	GDPD values (IMF)*	PPP values*	US $ year 2000	44	338	55	262	338	55
Kim 2002	direct variable mean hospital costs (exclud-	2000	GDPD values (IMF)*	PPP values*	US $ year 2000	870	394	9	1706	1512	9

Table 2. Cost / charges data, standardized to the year 2000 (CCEMG EPPI tool used) (*Continued*)

	ing professional fees)										
Kiyama 2003	direct variable mean hospital costs (including medication and professional fees)	2001	GDPD values (IMF)*	PPP values*	US $ year 2000	9695	1823	47	12467	5073	38
Kiyama 2003	direct variable mean costs medication	2001	GDPD values (IMF)*	PPP values*	US $ year 2000	1228	728	47	1746	1140	38
Kiyama 2003	direct variable mean daily costs	2001	US $	PPP values*	US $ year 2000	377	55	47	359	100	38
Kollef 1997	hospital costs (poor reporting: seems to be direct variable costs	1995	US $	PPP values*	US $ year 2000	30052	29122	179	29791	28090	178
Roberts 1997	total hospital costs (doctors & nurses fees included)	1993	GDPD values (IMF)*	PPP values*	US $ year 2000	1729	1145	82	2370	920	83
Usui 2004	hospital charges (insurance	2002/ 2003	NON	insurance points	NON	24338	12291	30	34048	12291	31

Table 2. Cost / charges data, standardized to the year 2000 (CCEMG EPPI tool used) (*Continued*)

	points)										
Usui 2004	hospital charges antibiotic infusion	2002/2003	NON	insurance points	NON	3285	2027	30	3928	2027	31
Usui 2004	hospital charges laboratory costs	2002/2003	NON	insurance points	NON	3220	3097	30	5785	3097	31
Usui 2004	hospital charges radiology costs	2002/2003	NON	insurance points	NON	1438	1194	30	2471	1194	31
Comparison 2: Multifaceted intervention including a CPW versus usual care											
Bauer 2006	3 years mean intervention costs (direct variable costs)	2004	GDPD values (IMF)*	PPP values*	US $ year 2000	56090	57672	157	58813	53094	149
Bauer 2006	direct outpatient costs (direct variable costs)	2004	GDPD values (IMF)*	PPP values*	US $ year 2000	18947	14457	157	18354	14457	149
Bauer 2006	hospital inpatient costs (direct variable costs)	2004	GDPD values (IMF)*	PPP values*	US $ year 2000	37143	49957	157	40459	49957	149
Bauer 2006	psychiatric inpatient	2004	GDPD values (IMF)*	PPP values*	US $ year 2000	25057	37857	157	28014	37857	149

Table 2. Cost / charges data, standardized to the year 2000 (CCEMG EPPI tool used) (*Continued*)

	costs (direct variable costs)										
Bauer 2006	medical surgical inpatient costs (direct variable costs)	2004	GDPD values (IMF)*	PPP values*	US $ year 2000	12086	26308	157	12354	26308	149
Kampan 2006	hospital costs (poor reporting: seems to be total hospital costs	2005	GDPD values (IMF)*	PPP values*	US $ year 2000	153	82	33	206	174	32
Philbin 2000	hospital charges	1995	GDPD values (IMF)*	PPP values*	US $ year 2000	-509	18593	840	378	18593	664

Table 3. Continuous primary study results (pre-intervention) baseline measures

STUDY ID	Baseline outcome measure	E-Mean baseline	E-Median baseline	E-N baseline	C-Mean baseline	C-Median baseline	C-N baseline
Comparison 1: single CPW intervention versus usual care							
Chadha 2000	Compliance with five recommendations for initial hospital assessment (menorrhagia)	3.7		472	3.4		416
Chadha 2000	Compliance with five recommendations for initial hospital as-	3.1		416	3.0		472

Table 3. Continuous primary study results (pre-intervention) baseline measures (*Continued*)

	sessment (urinary incontinence)						
Smith 2004	LOS days (no values reported)			505			216
Smith 2004	Readmission rate per 100 participant days	0.59			0.56		
Smith 2004	Deaths per 100 patient days	0.20			0.19		
Sulch 2000	Barthel index		5	152 (total both groups)		6	152 (total both groups)
Comparison 2: Multifaceted intervention including a CPW versus usual care							
Philbin 2000	LOS (days) all hospitals pooled	8.0		762	7.7		640

Table 4. Continuous primary study results post-intervention measures

study ID	Outcome	Experimental-mean	E-SD	E-N	Control-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		
Aizawa 2002	Duration of catheterization	4.75	1.10	32.00	5.40	2.10	37.00		
Brook 1999	Duration of mechanical ventilation (in hours)	89.10	133.60	162.00	124.00	153.60	159.00		

Table 4. 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	2.84	1.40	162.00	2.90	1.50	159.00		
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 - 0.9)
Choong 2000	LOS (days)	6.60	3.35	55.00	8.00	3.35	56.00	0.0300	
Choong 2000	Days to mobilisation (days)	1.60	1.44	55.00	2.20	1.44	56.00	0.0300	
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		
Delaney 2003	Pain score at 2 days post-op	3.30	1.90	31.00	3.40	1.50	33.00		

Table 4. Continuous primary study results post-intervention measures (*Continued*)

Delaney 2003	QOL at 10 days post-op	5.60	1.80	31.00	6.30	2.10	33.00		
Delaney 2003	Satisfaction with hospital stay at 30 days	8.20	2.20	31.00	8.40	1.60	33.00		
Delaney 2003	Happiness to be discharged	8.00	1.90	31.00	8.00	1.90	33.00		
Dowsey 1999	Los (days)	7.10	3.67	92.00	8.60	3.67	71.00		(1.03-1.30)
Dowsey 1999	Days to 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 to 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		
Falconer 1993	Patient satisfaction	7.70	2.60	53.00	8.8	1.70	68.00		
Falconer 1993	Functional status	40.90	15.80	53.00	40.2	17.40	68.00		
Gomez 1996	LOS (days)	0.64	0.51	53.00	2.28	5.25	68.00		
Gomez 1996	LOS (hours)	15.40	12.20	50.00	54.6	126.00	50.00		
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	

Table 4. Continuous primary study results post-intervention measures (*Continued*)

Johnson 2000	Number of nebulisations during hospitalisation every 2 hours	4.50	4.44	55.00	6.5	4.44	55.00	0.0200	
Johnson 2000	Number of nebulisations during hospitalisation every 3 hours	3.70	3.64	55.00	5.9	3.64	55.00	0.0020	
Johnson 2000	Number of nebulisations during hospitalisation every 4 hours	3.50	3.09	55.00	4.7	3.09	55.00	0.0440	
Johnson 2000	Number of nebulisations during hospitalisation every 6 hours	1.40	1.60	55.00	2.2	1.60	55.00	0.0100	
Johnson 2000	Number of nebulisations during hospitalisation every 8 hours	0.10	-0.52	55.00	0	-0.52	55.00	0.3200	
Kim 2002	Los (days)	0.25	0.15	9.00	2.1	2.30	9.00		
Kiyama 2003	Los (days) pre-operative hospital stay	9.00	3.20	47.00	12.6	6.00	38.00	0.0010	

Table 4. Continuous primary study results post-intervention measures (*Continued*)

Kiyama 2003	Los (days) post-operative 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	
Marrie 2000	SF-36 2 weeks after cessation of antibiotics	16.00	3.70	716.00	16.50	4.70	1027.00		
Marrie 2000	SF-36 6 weeks after cessation of antibiotics	30.30	1.50	716.00	29.9	1.60	1027.00		
Marrie 2000	Bed days per patient managed (product of average LOS/admission rate) surrogate for direct costs	4.4	1.50	716.00	6.1	2.10	1027.00	0.0400	
Marrie 2000	LOS (days)	8.20	1.90	716.00	9.60	2.10	1027.00		
Marrie 2000	Duration intravenous antibiotics (days)	4.60	0.90	716.00	6.30	1.40	1027.00		

Table 4. Continuous primary study results post-intervention measures (*Continued*)

Marelich 2000	Duration of mech ventilation (medical ICU) median values reported	3.25	11.32	82.00	9.67	11.32	88.00	0.0003	
Marelich 2000	Duration of mech ventilation (combined ICUs) median values reported	2.83	5.42	166.00	5.17	5.42	169.00	0.0001	
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		
Sulch 2000	LOS (days)	50.00	19.00	76.00	45	23.00	76.00		
Sulch 2000	Physiotherapy: Mean duration of therapy input at 12 weeks	38.00	28.80	76.00	34.8	27.80	76.00		
Sulch 2000	Physiotherapy: Mean duration of therapy input at 26 weeks	42.80	41.20	76.00	39.4	36.40	76.00		
Sulch 2000	Physiotherapy: Mean duration of therapy per patient day	0.80	0.60	76.00	0.7	0.60	76.00		

Table 4. Continuous primary study results post-intervention measures (*Continued*)

Sulch 2000	Occupational Therapy: Mean duration of therapy input at 12 weeks	8.00	6.00	76.00	7.5	7.00	76.00		
Sulch 2000	Occupational Therapy: Mean duration of therapy input at 26 weeks	8.50	7.50	76.00	8	705.00	76.00		
Sulch 2000	Occupational Therapy: Mean duration of therapy per patient day	0.20	0.40	76.00	0.2	0.20	76.00		
Usui 2004	LOS (days)	8.03	4.18	30.00	10.77	4.18	31.00	0.0130	
Usui 2004	Duration of antibiotic infusion (days) surrogate outcome for costs	6.47	3.53	30.00	8.22	3.53	31.00	0.0580	
Comparison 2: Multifaceted intervention including a CPW versus usual care									
Chen 2004	Usage rate of the emergency room (surrogate outcome for in-hosp. compl.)	0.15	0.37	20.00	0.59	0.50	22.00		

Table 4. Continuous primary study results post-intervention measures (*Continued*)

Cole 2002	LOS days	19.70	17.10	113.00	19.10	16.80	114.00		
Kampan 2006	LOS (days)	3.94	1.03	33.00	6.38	4.04	32.00		
Kampan 2006	Number of capillary blood glucose tests	10.03	5.04	33.00	12.34	5.96	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)

Table 5. Continuous primary study outcome (>more than two study groups/ hospitals): experimental groups/ hospitals

Study ID	Experimental groups baseline outcome	E-N baseline	E-Mean baseline	Experimental groups postintervention	E-N post-intervention	E-Mean post-intervention	pre-post change	P value
Comparison 1: single CPW intervention versus usual care								
Philbin 2000	Hospital A LOS (days)	18	9.2	Hospital A LOS (days)	37	5.8		P= 0.42
Philbin 2000	Hospital B LOS (days)	243	9.1	Hospital B LOS (days)	217	6.9		P= 0.02
Philbin 2000	Hospital C LOS (days)	159	7.2	Hospital C LOS (days)	126	5.2		P= 0.01
Philbin 2000	Hospital D LOS (days)	168	9.0	Hospital D LOS (days)	225	7.5		P= 0.07
Philbin 2000	Hospital E LOS (days)	174	5.7	Hospital E LOS (days)	235	5.7		P= 0.09
Bookbinder 2005	Palliative ward Symptoms assessed	20	7.6	Palliative ward Symptoms assessed	55	10.2	2.6	P<0.001
Bookbinder 2005	Oncology & geriatric wards	41	6	Oncology & geriatric wards	51	10.5	4.5	p<0.001

Table 5. Continuous primary study outcome (>more than two study groups/ hospitals): experimental groups/ hospitals (*Continued*)

	Symptoms assessed			Symptoms assessed				
Bookbinder 2005	Palliative ward Problematic Symptoms identified	20	4.8	Palliative ward Problematic Symptoms identified	55	3.7	1.1	p=0.014
Bookbinder 2005	Oncology & geriatric wards Problematic Symptoms identified	41	3.5	Oncology & geriatric wards Problematic Symptoms identified	51	3.9	0.4	p=0.386
Bookbinder 2005	Palliative ward Number of Interventions	20	5.1	Palliative ward Number of Interventions	55	4.1	1	p=0.021
Bookbinder 2005	Oncology & geriatric wards Number of interventions	41	4.1	Oncology & geriatric wards Number of interventions	51	4.4	0.3	p=0.484
Bookbinder 2005	Palliative ward Number inpatient consultations	20	1.6	Palliative ward Number inpatient consultations	55	2.2	0.6	p=0.062
Bookbinder 2005	Oncology & geriatric wards Number inpatient consultations	41	4	Oncology & geriatric wards Number inpatient consultations	51	5.1	1.1	p=0.037

Table 6. Continuous primary study outcome (>more than two study groups/ hospitals): control groups/ hospitals

Study ID	Control groups baseline outcome	Control-N baseline	C-Mean baseline	Control post-intervention outcome	C-N post-intervention	C-Mean post-intervention	pre-post change	P value
Comparison 1: single CPW intervention versus usual care								

Table 6. Continuous primary study outcome (>more than two study groups/ hospitals): control groups/ hospitals (*Continued*)

Philbin 2000	Hospital F LOS (days)	152	5.7	Hospital F LOS (days)	134	5.2		P= 0.48
Philbin 2000	Hospital G LOS (days)	117	8.0	Hospital G LOS (days)	152	7.3		P= 0.34
Philbin 2000	Hospital H LOS (days)	125	9.4	Hospital H LOS (days)	104	6.7		P= 0.001
Philbin 2000	Hospital I LOS (days)	25	6.5	Hospital I LOS (days)	5	6.8		P= 0.08
Philbin 2000	Hospital J LOS (days)	221	8.9	Hospital J LOS (days)	269	8.9		P= 0.94
Bookbinder 2005	General Medical Wards Symptoms assessed	50	7.9	General Medical Wards Symptoms assessed	50	9.5	1.6	P<0.001
Bookbinder 2005	General Medical Wards Problematic Symptoms identified	50	3.4	General Medical Wards Problematic Symptoms identified	50	2.7	0.7	p=0.124
Bookbinder 2005	General Medical Wards Number of interventions	50	3.9	General Medical Wards Number of interventions	50	3.1	0.8	p=0.109
Bookbinder 2005	General Medical Wards Number inpatient consultations	50	3.3	General Medical Wards Number inpatient consultations	50	4.3	1	p=0.068

Table 7. Dichotomous primary study outcomes (pre-intervention) baseline

Study ID	Dichotomous outcome baseline measure	Experimental-events	E-N	%	Control-events	C-N	%
Comparison 1: single CPW intervention versus usual care							
Chadha 2000	Appropriate use of hospital investigations (menorrhagia)	208	472	44%	175	416	42%
Chadha 2000	Appropriate use of hospital investigations (urinary incontinence)	92	416	22%	212	472	45%
Chadha 2000	Inappropriate use of hospital investigations (menorrhagia)	127	472	27%	125	416	30%
Chadha 2000	Inappropriate use of hospital investigations (urinary incontinence)	116	416	28%	38	472	8%
Chadha 2000	Appropriate first-line treatments (menorrhagia)	382	472	81%	345	416	83%
Chadha 2000	Appropriate first-line treatments (urinary incontinence)	262	416	63%	340	472	72%
Chadha 2000	Appropriate pre-surgery assessment (menorrhagia)	90	472	19%	62	416	15%

Table 7. Dichotomous primary study outcomes (pre-intervention) baseline (*Continued*)

Chadha 2000	Appropriate pre-surgery assessment (urinary incontinence)	29	416	7%	99	472	21%
Doherty 2006	Assessment of severity of asthma	4	52	8%	5	46	11%
Doherty 2006	Use of spirometry	6	52	12%	1	46	2%
Doherty 2006	Overuse of ipratropium for mild asthma	16	36	44%	15	31	48%
Doherty 2006	Use of systemic steroids	31	51	61%	22	46	48%
Doherty 2006	Use of STAMP (Short-term Asthma Management Plan)	4	44	9%	0	32	0%
Doherty 2006	Inappropriate use of antibiotics	9	43	21%	11	41	27%
Doherty 2006	Aggregate measures	99	278	36%	74	242	31%

Table 8. 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	In-hospital complications	1	32	3%	2	37	5%

Table 8. Dichotomous primary study results post-intervention measures (*Continued*)

Aizawa 2002	Rehospitalisation within 6 months	1	32	3%	0	37	0%
Brook 1999	In-hospital mortality	49	162	30%	57	159	36%
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%
Chadha 2000	Inappropriate use of hospital investigations (urinary incontinence)	58	416	14%	64	427	15%
Chadha 2000	Appropriate first-line treatments (menorrhagia)	378	472	80%	324	416	78%
Chadha 2000	Appropriate first-line treatments (urinary incontinence)	241	416	58%	359	472	76%
Chadha 2000	Appropriate pre-surgery assessment (menorrhagia)	203	472	43%	46	416	11%

Table 8. Dichotomous primary study results post-intervention measures (*Continued*)

Chadha 2000	Appropriate pre-surgery assessment (urinary incontinence)	133	416	32%	127	472	27%
Choong 2000	Confusional status (yes-no)	23	55	42%	31	56	55%
Choong 2000	In-hospital complications	10	55	18%	14	56	25%
Choong 2000	Post-discharge complications	3	55	5%	6	56	11%
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	In-hospital complications	7	31	23%	10	33	30%
Doherty 2006	Assessment of severity of asthma	29	47	62%	6	42	14%
Doherty 2006	Use of spirometry	29	47	62%	3	42	7%
Doherty 2006	Overuse of ipratropium for mild asthma	9	30	30%	13	42	31%
Doherty 2006	Use of systemic steroids	33	46	72%	8	38	21%
Doherty 2006	Use of STAMP	10	38	26%	1	38	3%
Doherty 2006	Inappropriate use of antibiotics	9	42	21%	5	39	13%

Table 8. Dichotomous primary study results post-intervention measures (*Continued*)

Doherty 2006	Aggregate measures	155	250	62%	71	231	31%
Dowsey 1999	Match/ planned discharge destination	64	92	70%	43	71	61%
Dowsey 1999	hospital readmission at 3 month follow up	4	92	4%	9	71	13%
Dowsey 1999	complication until 3 month	10	92	11%	20	71	28%
Gomez 1996	Rehospitalisation within 30 days	3	50	6%	3	50	6%
Johnson 2000	Number of unplanned interventions within 2 weeks of discharge	1	55	2%	4	55	7%
Kiyama 2003	Morbidity rate in hospital	3	47	6%	5	38	13%
Kiyama 2003	In-hospital complications until discharge	3	47	6%	5	38	13%
Kiyama 2003	Target achievements day 1	41	47	87%	21	38	54%
Kiyama 2003	Target achievements day 4	46	47	98%	30	38	78%
Kiyama 2003	Target achievements day 7	43	47	91%	26	38	68%
Kiyama 2003	Target achievements	43	47	91%	19	38	50%

Table 8. Dichotomous primary study results post-intervention measures (*Continued*)

	day 14						
Kollef 1997	Hospital mortality	40	179	22%	42	178	24%
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%
Roberts 1997	Hospital admission rate	37	82	45%	83	83	100%
Roberts 1997	Rehospitalisation after 8 weeks	5	82	6%	4	83	5%
Smith 2004	Hospital mortality	49	334	15%	30	175	17%
Sulch 2000	Mortality at 26 weeks	10	76	13%	6	76	8%
Sulch 2000	Discharge to home	56	76	74%	54	76	71%
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	68	76	89%	53	76	70%

Table 8. Dichotomous primary study results post-intervention measures (*Continued*)

	death / follow-up)						
Sulch 2002	Process of care (communication with GP)	61	76	80%	34	76	45%
Usui 2004	Treatment success rate	27	30	90%	28	31	90%
Comparison 2: Multifaceted intervention including a CPW versus usual care							
Cole 2002	Mortality at 8 weeks	25	113	0.22	22	114	19%
Cole 2002	Discharged at 8 weeks	65	113	0.58	77	114	68%
Cole 2002	Less dependent at 8 weeks	4	65	0.06	6	77	8%
Kampan 2006	Readmissions with hypoglycaemia within 3 months	2	33	6%	11	32	34%
Philbin 2000	In-hospital mortality	44	840	5%	25	664	4%
Philbin 2000	QOL following discharge	7	840	1%	7	664	1%
Philbin 2000	QOL (functional)	2	840	0%	2	664	0%
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%

Table 8. Dichotomous primary study results post-intervention measures (*Continued*)

Philbin 2000	Readmission - all causes (6 month)	363	840	43%	293	664	44%
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	Process of care - diet counselling	613	840	73%	518	664	78%
Philbin 2000	ACE inhibitor use at discharge	529	840	63%	438	664	66%

Table 9. ITS studies data

Study ID	Tilden, VP (**Tilden 1987**)	Brattebo, G (**Brattebo 2002**)
Outcome measure	Documented identification by nurses of female victims of domestic violence	Ventilation patient days per month
N-baseline	447	147
N-post-intervention	445	138
Number of measures baseline	4	11
Number of measures post-intervention	4	11
time-interval between measures	4 weeks	4 weeks
Outcome results	Increased documentation of female victims of domestic violence (p = 0.03)	No change in number of ventilation days (p = 0.834).

APPENDICES

Appendix 1. Appendix A: Medline search strategy

We searched MEDLINE using the following search strategy:
Database: Ovid MEDLINE(R) <1950 to April Week 4 2008>

1	Critical Pathways/
2	((clinical or critical or care) adj path$).tw.
3	(care adj (map$ or plan$)).tw.
4	exp Guideline/
5	Health Planning Guidelines.tw.
6	Guideline Adherence/
7	(compliance adj (protocol? or policy or guideline?)).tw
8	(guideline? adj2 (introduc$ or issu$ or impact or effect? or disseminat$ or distribut$ or implement$)).tw
9	nursing protocol?.tw.
10	professional standard$.tw.
11	(practice guidelin$ or practice protocol$ or clinical practice guidelin$).tw
12	Guideline.pt.
13	or/1-12
14	exp Hospitalization/
15	(in-patient or hospitali?ed or hospitali?ation or acutely ill patient?).tw
16	exp Outpatient Clinics, Hospital/
17	in-hospital.tw.
18	exp Hospital Units/
19	(patient adj (admission or re-admission or readmission or discharge)).tw
20	exp *Emergency Service, Hospital/
21	or/14-20

(*Continued*)

22	13 and 21
23	randomise controlled trial.pt.
24	random$.tw.
25	control$.tw.
26	intervention$.tw.
27	evaluat$.tw.
28	or/23-27
29	Animal/
30	Human/
31	29 not (29 and 30)
32	28 not 31
33	22 and 32

Appendix 2. Appendix B: Study assessment and data collection form

Data Collection Form (version 28/03/08)
Study ID number
STUDY STATUS
Pending
Included
Excluded

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

EndNote citation:

Primary Author Email Address for correspondence: Email address i.e.

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**
3. Does it details the steps in a course of treatment or care in a plan, pathway, algorithm, guideline, protocol or other "inventory of actions"?	**YES** **NO** **Can't tell**
4. Do the steps in the pathway have time-frames or criteria-based progression (ie. steps are taken if designated criteria are met)?	**YES** **NO** **Can't tell**
5. Does it aim to standardize care for a specific clinical problem, procedure or episode of care?	**YES** **NO** **Can't tell**
Source of information for minimum criteria for a clinical pathway (CPW) (page numbers):	
Eligibility: **Criterion 1 must be "yes"** **PLUS** **"Yes" to 3 out of the 4 other criteria to meet definition of a CPW.** **Eligibility: EXCLUDE / CONTINUE**	

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

(*Continued*)

TION	
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 above design, or have selected NOT DONE then EXCLUDE **Reason for exclusion:_____** **or CONTINUE**	

SETTING & PARTICIPANTS		
Geographic location of the hospital Where was/were 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** _____

(*Continued*)

Description of health professionals targeted Which health professionals were expected to utilise the CPW? **Provide description here:** (page no.)		**Specialists/Surgeons** **Nurses** **Allied Health** **Multidisciplinary** **Others (specify)** _____ **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 health care professionals who were the target of the CPW provided?		**Gender mix (% male):** **Age range:** **Not stated**
Section of hospital where intervention took place What specific ward or unit was the CPW introduced in to?		**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**

(*Continued*)

Number of patients included How many patients were included in the study? How many in intervention and control groups?		**Number of groups**	
	Intervention		
	Control		
	Number of participants		
	Intervention		**n =**
	Control		**n =**
	Total number of participants		**n =**
Characteristics of patients included. What were the demographic characteristics of the patients who were recruited?		**Gender mix (% male):** **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 effects of clustering?** E.g., do they mention intracluster correlation co-efficient?		**Done** **Not clear** **Not done** **Yes** **No** **Not applicable**	
ELIGIBILITY: If 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 vs usual care** **Intervention including CPW vs intervention without CPW** **Intervention including CPW usual care** **Other (specify)** _____

(*Continued*)

Description of intervention: (page no.)	
Invasive or non-invasive intervention targeted? INVASIVE examples = CPW for gastrectomy; PTCA; laparoscopic cholecystectomy; hip and knee arthroplasty NON-INVASIVE examples = CPW for stroke; pneumonia; asthma	**Invasive** **Non-invasive**
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 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 hardcopy 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	**Done** **Not clear** **Not done**

(*Continued*)

users / clinicians on format of CPW	
Was there clinician involvement in development of CPW? DONE = clearly stated that clinicians were involved in 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 implementation of the CPW? DONE = gaps identified by local audit NOT CLEAR = anecdotal or evidence not local NOT DONE = no audit or identifying of evidence-practice gaps	**Done** **Not clear** **Not done**
Were barriers to change identified? DONE = barriers clearly stated NOT CLEAR = barriers may have been identified NOT DONE = barriers to change not stated	**Done** **Not clear** **Not done**
Were reminder systems incorporated into implementation? DONE = formal reminder system described e.g., posters, computer reminders NOT CLEAR = reminder system may have been used NOT DONE = reminder system not described	**Done** **Not clear** **Not done**
Was audit and feedback incorporated into implementation? DONE = audit and feedback process clearly stated NOT CLEAR = audit and feedback may have been used NOT DONE = no description of audit and feedback provided	**Done** **Not clear** **Not done**
Were education sessions used to implement CPW? DONE = education sessions attended by majority of users / clinicians NOT CLEAR = education sessions may have been provided and may have been	**Done** **Not clear** **Not done**

(*Continued*)

attended by users / clinicians NOT DONE = no education sessions provided or attended by users / clinicians	
Were local opinions leaders used to implement CPW? DONE = clear identification and utilisation of local opinion leaders NOT CLEAR = local opinion leaders may have been involved NOT DONE = no evidence of utilisation of local opinion leaders	**Done** **Not clear** **Not done**
Evidence-based implementation strategy: A = 7-10 criteria checked as "Done" B = 2-6 criteria checked as "Done" C = 0-1 criteria checked as "Done"	**A (high)** **B (moderate)** **C (low)**
What was the source of funding for the study? Who funded the study?	**Nil** **Govt** **Commercial** **Health service** **Voluntary body** **Charity** **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	

(*Continued*)

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 their a possible ceiling effect? (i.e. little room for improved outcomes)	
Ceiling effect identified by investigator:	**Yes (specify)** **_____** **No** **Not relevant**
Ceiling effect identified by reviewer:	**Yes (specify)** **_____** **No** **Not relevant**
Were outcomes measured in a clinical (i.e. not test) situation?	**Done** **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**	

STUDY QUALITY			Quality Criteria for RCT or CCT:			What was the randomization process? (page no.)	
	Was their allocation concealment to reduce chance of selection bias? DONE = random process described (e.g. , random number table, coin flips, sealed opaque envelopes) NOT DONE = alternation such as reference to case record numbers, dates of birth, day of week, etc	**Done Not clear Not done**		**Was follow-up of participants appropriate to reduce exclusion bias?** DONE = outcome measures for 80-100% of subjects randomised. NOT DONE = outcome measures for < 80% of subjects randomised	**Done Not clear Not done**		
Were outcomes assessed blindly or objectively (to reduce detection bias)? DONE = authors explicitly state that primary outcome measures were assessed blindly OR outcome variables are objective e.g., LOS, drug level		**Done Not clear Not done**	**Were baseline results reported for each group / cluster?** DONE = measured prior to intervention and no substantial differences between groups NOT DONE = differences likely to undermine post results		**Done Not clear Not done**		**Were reliable primary outcome measures used?** DONE = automated outcome (e.g., mortality, LOS) NOT DONE = subjective measures such as satisfaction

(*Continued*)

assessed by a standardized test NOT CLEAR = not specified in the paper NOT DONE = if outcomes not assessed blindly											
	Done Not clear Not done			**Protection against contamination:** DONE = control subject unlikely to receive intervention NOT CLEAR = possible that control subjects received intervention. Communication between experimental and control professionals could have occurred NOT DONE = control subjects likely to have received intervention		**Done Not clear Not done**			**Risk of bias:** Low risk = all criteria checked as "Done" Moderate risk = all criteria checked as "Done" or "Not clear" High risk = one or more criteria checked as "Not done"		**A (low) B (moderate) C (high)**

(*Continued*)

		Source of information for quality criteria: (page no.)			**Is follow-up with authors required?**		**Yes / No**			**Study still eligible?** NB: Studies at "C high" risk of bias to be excluded
Included ? Excluded ?				**Did both reviewers agree on inclusion / exclusion and study quality?**		**Yes / No**			**If no, what was the source(s) of disagreement?**	

Quality criteria for CBA:	
Were baseline results reported? DONE = measured prior to intervention and no substantial differences between groups NOT DONE = differences likely to un-	**Done** **Not clear** **Not done**

(*Continued*)

dermine post results	
Characteristics for studies using second site as control: DONE = site characteristics reported and similar NOT DONE = not reported or reported and substantial differences	**Not appropriate** **Done** **Not clear** **Not done**
Were outcomes assessed blindly or objectively (to reduce detection bias)?	**Done** **Not clear** **Not done**
Protection against contamination: DONE = control subject unlikely to receive CPW NOT CLEAR = possible that control subjects received CPW NOT DONE = control subjects likely to have received CPW	**Done** **Not clear** **Not done**
Were reliable primary outcome measures used? DONE = automated outcome (e.g., mortality, LOS) NOT DONE = subjective measures such as satisfaction	**Done** **Not clear** **Not done**
Follow-up of participants (exclusion bias): DONE = outcome measures for 80-100% of subjects randomised. NOT DONE = outcome measures for < 80% of subjects randomised	**Done** **Not clear** **Not done**
Risk of bias: Low risk = all criteria checked as "Done" or "Not appropriate" Moderate risk = all criteria checked as "Done" or "Not clear" High risk = one or more criteria checked as "Not done"	**A (low)** **B (moderate)** **C (high)**
Source of information for quality criteria: (page no.)	
Study still eligible? NB: Studies at "C high" risk of bias to be excluded	**Included** **Excluded**

(*Continued*)

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

Quality criteria for ITS:	
Protection against secular changes: DONE = intervention occurred independent of other changes NOT DONE = intervention was not independent of other changes	**Done** **Not clear** **Not done**
Data analyzed appropriately: DONE = ARIMA or time series regression model(s) and adjusted for serial correlation NOT DONE = above conditions not met	**Done** **Not clear** **Not done**
Reason for number of points pre and post intervention given: DONE = rationale for number of points stated (e.g., anticipated term of effects) or sample size calculation performed NOT DONE = above conditions not met	**Done** **Not clear** **Not done**
Shape of intervention effect specified: DONE = rationale for shape of effect given NOT DONE = no rationale provided	**Done** **Not clear** **Not done**
Protection against detection bias: DONE = data collection unchanged pre and post intervention NOT DONE = source or method of data collection changed	**Done** **Not clear** **Not done**
Outcomes assessed blindly or objectively (detection bias):	**Done** **Not clear** **Not done**
Completeness of data set: DONE = data set covers 80-100% of participants or care episodes	**Done** **Not clear** **Not done**

(*Continued*)

NOT DONE = data set < 80% of participants or care episodes	
Were reliable primary outcome measures used? DONE = automated outcome (e.g., mortality, LOS) NOT DONE = subjective measures such as satisfaction	**Done** **Not clear** **Not done**
Risk of bias: Low risk = all criteria checked as "Done" Moderate risk = all criteria checked as "Done" or "Not clear" High risk = one or more criteria checked as "Not done"	**A (low)** **B (moderate)** **C (high)**
Source of information for quality criteria: (page no.)	
Study still eligible? NB: Studies at "C high" risk of bias to be excluded	**Included** **Excluded**

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

RESULTS FOR RCT / CCT / CBA	
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	
Outcome measure 1:	

(*Continued*)

	Intervention (E) **n =**	Control (C) **n =**	
Baseline			
Post-intervention			
Pre-post change			
Difference in change (?E - ?C)			
Positive finding	**Yes / No**		
For cluster trials, did analysis account for clustering?	**Yes / No**		
Outcome measure 2:			
	Intervention (E) **n =**	Control (C) **n =**	
Baseline			
Post-intervention			
Pre-post change			
Difference in change (?E - ?C)			
Positive finding	**Yes / No**		
For cluster trials, did analysis account for clustering?	**Yes / No**		

(*Continued*)

Outcome measure 3:		
	Intervention (E) **n =**	Control (C) **n =**
Baseline		
Post-intervention		
Pre-post change		
Difference in change (?E - ?C)		
Positive finding	**Yes / No**	
For cluster trials, did analysis account for clustering?	**Yes / No**	

Outcome measure 4:		
	Intervention (E) **n =**	Control (C) **n =**
Baseline		
Post-intervention		
Pre-post change		

(*Continued)*

Difference in change (? E - ?C)		
Positive finding	**Yes / No**	
For cluster trials, did analysis account for clustering?	**Yes / No**	
Outcome measure 5:		
	Intervention (E) **n =**	Control (C) **n =**
Baseline		
Post-intervention		
Pre-post change		
Difference in change (? E - ?C)		
Positive finding	**Yes / No**	
For cluster trials, did analysis account for clustering?	**Yes / No**	

Have you attached additional pages of results? Yes No

Data extraction is now complete. Choose next path:

Pass on to second reviewer **Forward for data entry into RevMan**

Date actioned:.....

RESULTS FOR ITS		
Outcome measure 1:		
Number of points	Pre	
Number of measurement units in whole series		
Time interval between points		
Means	Pre	
Absolute change		
Percentage relative change		
Model used		
Statistical significance		
Only reported graphically?	Yes / No	
Positive finding?	Yes / No	
Outcome measure 2:		
Number of points	Pre	
Number of measurement units in whole series		
Time interval between points		

(*Continued*)

Means	Pre	
Absolute change		
Percentage relative change		
Model used		
Statistical significance		
Only reported graphically?	Yes / No	
Positive finding?	Yes / No	

Outcome measure 3:		
Number of points	Pre	
Number of measurement units in whole series		
Time interval between points		
Means	Pre	
Absolute change		
Percentage relative change		
Model used		
Statistical significance		

(*Continued*)

Only reported graphically?	Yes / No	
Positive finding?	Yes / No	

Outcome measure 4:		
Number of points	Pre	
Number of measurement units in whole series		
Time interval between points		
Means	Pre	
Absolute change		
Percentage relative change		
Model used		
Statistical significance		
Only reported graphically?	Yes / No	
Positive finding?	Yes / No	

Have you attached additional pages of results? Yes No
Data extraction is now complete. Choose next path:
Pass on to second reviewer Forward for data entry into RevMan
Date actioned:.....

WHAT'S NEW

Last assessed as up-to-date: 19 June 2009.

Date	Event	Description
15 June 2010	New search has been performed	"minor changes to text to remove inconsistencies in the text"
6 August 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 3, 2007

Review first published: Issue 3, 2010

CONTRIBUTIONS OF AUTHORS

All review authors have contributed to the production of the protocol. TR lead the writing of the protocol, all other protocol authors provided comment and feedback. For the full review: TR developed and ran the search strategy, AM and TR screened records for eligibility for length of stay (LOS) and hospital costs. LK or TR acted as abitrators in the case of disagreement. LK and EJ developed and ran the search strategy and screened records for eligibility for professional practice and patient outcomes. All review authors abstracted data, undertook analysis and wrote up the review. In particular HG, AM, JK and TR took the leadership regarding to the analysis and the interpretation of results relating to LOS and hospital costs. LK, EJ, JW and PS led the analysis and interpretation of professional practice and patient outcome results.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- Institut of Public Health / Medical Statistics Dresden, Germany.
- School of Rural Health, Monash University, Melbourne, Australia.
- Centre for Health Research and Psycho-oncology (CHeRP), University of Newcastle, Australia.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The definition of what constituted a CPW evolved during the search strategy. Post-hoc, a check-list was developed to define an intervention as a CPW for inclusion in this review. The following five criteria for a CPW were assessed:

1. The intervention was a structured multi-disciplinary plan of care
2. The intervention was used to channel the translation of 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"
4. The intervention had time-frames or criteria-based progression (ie. steps were taken if designated criteria were met)
5. The intervention aimed to standardize care for a specific clinical problem, procedure or episode of care

An intervention was defined as a CPW if point one (the intervention was a structured multi-disciplinary plan of care) was met and in addition, three out of the remaining four criteria were also met.

In the protocol we had planned the following comparisons:

(1) Patients managed according to CPW compared to usual care. Impact on patient outcomes, professional practice, length of hospital stay and hospital costs.

(2) Patients managed within a multifaceted intervention with a CPW compared to the same intervention without a CPW.

However, once the studies were retrieved it became evident that there were no studies in the second group. Instead we compared:

(1) Patients managed according to CPW compared to usual care. Impact on patient outcomes, professional practice, length of hospital stay and hospital costs.

(2) Patients managed within a multifaceted intervention including a CPW compared to usual care.

In the protocol we had planned to categorise the setting of the CPW in to the following categories: inpatient, outpatient, medical, surgical, critical care, emergency, rehabilitation, aged care). However, once the 28 studies were obtained these categories were revised to: general acute, ICU, ED, extended care, other.

Previous studies (including EPOC reviews) have demonstrated that implementation of interventions to improve professional practice benefit from being multifaceted and including the following features: 1) evidence based content; was 2) adaption for local use; 3) clinicians involved 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; 9) use of education sessions, and 10) use of local opinions leaders as part of the process (Cluzeau 1999; Doherty 2006; Grimshaw 1998; Grimshaw 2001; Kinsman 2004a; Stone 2002). In order to gauge how evidence informed the development and implementation of the CPW was information pertaining to each of these ten possible criteria were extracted from each included study. Initially we planned to extract information on all ten criteria and to score each study according to how many of the ten possible criteria had been completed. However, reporting of design and implementation characteristics was very poor in the included studies in particular for the following three indicators: identification of potential barriers to change, incorporation of reminder systems and use of local opinions leaders. Even though we believe these to be important we did not include them in the implementation quality assessment as they would not discriminate between studies.

The search strategy defined in the protocol was used for the initial search and was refined to be more sensitive for update searches. Since both strategies employed differ in terms of the estimated sensitivity, we additional present the first electronic search strategies employed for electronic searches until February 2007.

Database: Ovid MEDLINE(R) <1950 to February Week 4 2007>

Search Strategy:

1 Critical Pathways/

2 ((clinical or critical or care) adj path$).tw.

3 (care adj (map$ or plan$)).tw

4 exp Guideline/

5 Health Planning Guidelines.tw

6 Guideline Adherence/

7 (compliance adj (protocol? or policy or guideline?)).tw.

8 (guideline? adj2 (introduc$ or issu$ or impact or effect? or disseminat$ or distribut$ or implement$)).tw.

9 nursing protocol?.tw.

10 professional standard$.tw.

11 (practice guidelin$ or practice protocol$ or clinical practice guidelin$).tw.

12 Guideline.pt.

13 or/1-12

14 exp Hospitalization/

15 (in-patient or hospitali?ed or hospitali?ation or acutely ill patient?).tw.

16 exp Outpatient Clinics, Hospital/

17 in-hospital.tw.

18 exp Hospital Units/

19 (patient adj (admission or re-admission or readmission or discharge)).tw.

20 exp *Emergency Service, Hospital/

21 or/14-20

22 13 and 21

23 randomized controlled trial.pt.

24 controlled clinical trial.pt.

25 Intervention Studies/

26 experiment$.tw.

27 (time adj series).tw.

28 (pre test or pretest or post test or posttest).tw.

29 Random Allocation/

30 impact.tw.

31 intervention?.tw.

32 Evaluation Studies/

33 Comparative Study.pt.

34 or/23-33

35 Animal/

36 Human/

37 35 not (35 and 36)

38 34 not 37

39 22 and 38

40 limit 39 to review

41 39 not 40

42 meta-analysis.pt.

43 41 not 42

INDEX TERMS

Medical Subject Headings (MeSH)

*Critical Pathways [economics; organization & administration; standards]; *Hospital Costs; *Length of Stay; *Outcome and Process Assessment (Health Care) [organization & administration; standards]; *Professional Practice [economics; organization & administration; standards]

MeSH check words

Humans