Clinical pathways in hospitals: Evaluating effects and costs

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Clinical Pathways in Hospitals: Evaluating effects and costs

Zorgpaden in ziekenhuizen: evaluatie van effecten en kosten

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CHAPTER 1

General Introduction

1 General Introduction

1.1 The changing health care environment: The role of clinical pathways in evidence-based practice and patient safety

In the past there was little incentive for hospital providers to monitor patient safety and resource utilization. Hospital systems were simply not receptive to concepts related to quality of care and process management [1]. This has changed dramatically throughout the last century. National and international attention to quality problems such as substandard care, variations in care, and waiting times has made hospital management and medical specialists aware that the way hospital care is delivered needs to be reorganised.

Despite the fact that considerable resources have been devoted to evidence-based medicine, the transfer of research findings into hospital practice is often a slow and hindering process [2]. This means that patients do not get treatment of proven benefit because the time it takes for research to become available at the patient's bedside is unacceptably long. Two investigations conducted in the United States and the Netherlands revealed, that 30% to 45% of patients are not receiving evidence-based care and that approximately 25% of care processes are unnecessary or even harmful [3, 4].

These problems can be avoided if clinical pathways are applied to the patient care delivery process by defining a timeline of the expected flow of services for a group of patients with a particular diagnosis or undergoing a particular procedure. Clinical pathways are one example of healthcare management aimed at standardizing clinical processes, therefore maximizing patient safety and clinical efficiency. Clinical pathways (CPWs) have been promoted by Lord Darzi in recent Governmental health policy reports in England, and pathway implementation is likely to become more prevalent, especially in Australia and Canada [5-8]. Variation is a problematical element in health care systems and CPWs may serve as an evidence-based intervention to reduce variations in hospital practice and improve patient outcome. Determining factors of variation include the different settings of health care services, the sparse use of medical evidence, and the phenomena of schools of belief [9]. In particular, professional variation and the limited use of the best available evidence seem to be the key elements in many problems dealing with health care variations.

However, like many clinical procedures and despite 30 years of research in the area of CPWs, we still lack a robust, generalizable evidence base to support decisions about the effectiveness of CPWs in hospitals [10]. Moreover, it is not known how CPWs should be implemented effectively into a hospital's organisation. The litera-

ture only suggests that multifaceted implementation strategies which are tailored to the hospital context are more likely to be effective [10].

This thesis aims to improve the understanding of clinical pathways in hospitals by testing the primary hypothesis: ***What are the effects of clinical pathways on professional practice, patient outcomes, length of stay and hospital costs?*** We will focus on the rigorous investigation of the international evidence regarding the effectiveness of CPWs, including the definition of clinical pathways, the quality of the evidence base for pathway effectiveness and a case study to implement and evaluate CPWs in rural Australian hospitals. The case study aims to fill some of the gaps in terms of the evidence base for CPW effectiveness because clinical pathways in rural emergency departments have not been adequately tested.
The scope of this thesis is limited to hospitals. Hence, other sectors of the health care system (such as primary care) are not taken into account.

In this introduction, attention is firstly paid to the example of the WHO surgical checklist and the possible role of clinical pathways in evidence-based medicine and patient safety. Then we will discuss the principals of evidence-based medicine and quality improvement as the theoretical base and context of this dissertation. This introduction ends with an overview of the thesis and a summary of the research questions.

1.2 Organizational changes in hospitals can be beneficial: The example of the WHO surgery checklist

In 2007, the World Health Organization (WHO) launched the Safe Surgery Saves Lives campaign. The aim was to improve consistency of surgical care and adherence to safety practices. The investigators developed and trialled a 19-item surgical protocol intended to be transferable to different hospital settings worldwide. The WHO surgical safety checklist is a two-minute tool consisting of a series of checks that occur firstly before the delivery of anaesthesia, secondly before any incision is made and last but not least before the patient leaves the operating room [11]. The results of a pilot-study conducted in eight different international hospitals (in Canada, India, Jordan, New Zealand, Philippines, Tanzania, England and America) showed a relationship between substandard care processes and the rate of major surgical complications. In-hospital complications declined from 11.0% at baseline to 7% ($p< 0.001$) after implementation of the surgical checklist, and in-hospital mortality, which was 1.5% before the checklist was introduced, decreased to 0.8% afterward

(p=0.003) [12]. Moreover preventing in-hospital complications is a desired outcome even when it does not reduce hospital costs significantly.

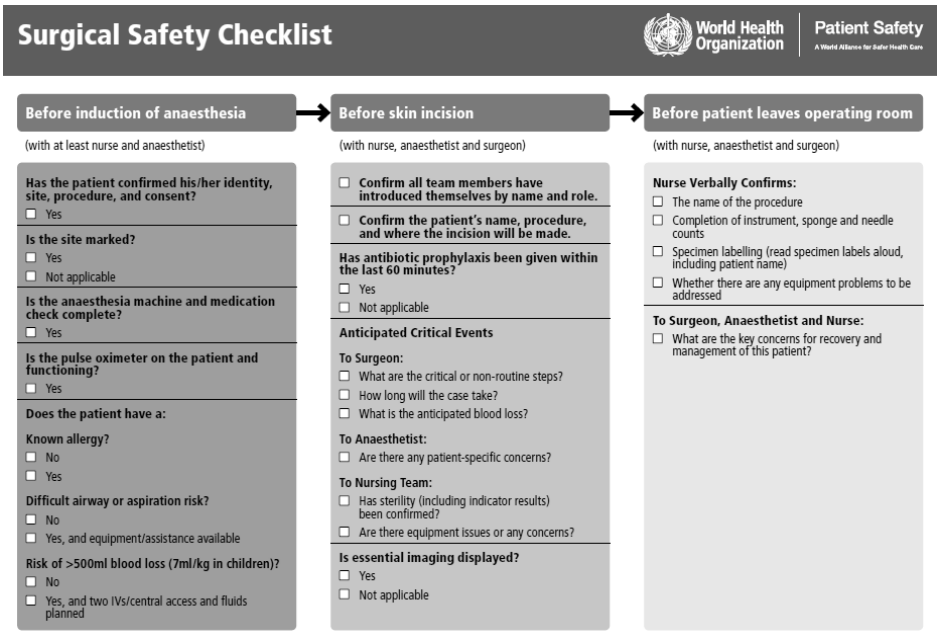

Figure 1: WHO Surgical Safety Checklist, Source: World Health Organization [http://whqlibdoc.who.int/publications/2009/9789241598590_eng_checklist.pdf]

Other researchers also tested the WHO checklist and reported improved patient outcomes after implementation in European hospital settings in France, Finland and the Netherlands [13-15]. The implementation manual of the WHO suggests that the checklist has to be adapted to the local context and that surgical departments must follow the implementation strategy. This theory and evidence-based surgical checklist has already caught the attention of practitioners in other countries, and a considerable number have begun or will begin to implement similar approaches. The "horse race" in terms of the WHO checklist dissemination and implementation has just started and is expected to continue globally. This experience could also stimulate more research in the field of clinical pathways in hospitals, the context of this PhD thesis. Both interventions are similar, but differ in scope. The pathway approach usually covers all essential steps needed in the care of patients with a specific clinical problem compared with the narrow scope of the surgical safety checklist approach.

1.3 Theoretical context of the research

The concept of pathways originated in the construction and engineering fields where it proved a valuable tool to manage large and complex projects. They have been in use in all fields of business for many years [1]. In industry, processes occupy a central place in the management of a product line. Most of the methods are based on quality improvement and refer to Donabedian in the 1960s and Deming's principles of quality management. The growing awareness that evident findings are not translated into practice in a timely fashion, linked with the ongoing focus on evidence-based practice, has stimulated interest in improving ways to minimize what can be described as the knowledge to action gap. However, the field of health quality improvement science might be described as badly conceptualized because a systematic review identified 29 terms used to refer to the concept of knowledge to action [16]. However, the so called "knowledge to action loop" suggests that planned processes are more likely to achieve changes in praxis. Figure 2 presents the quality improvement concept in form of the knowledge to action loop.

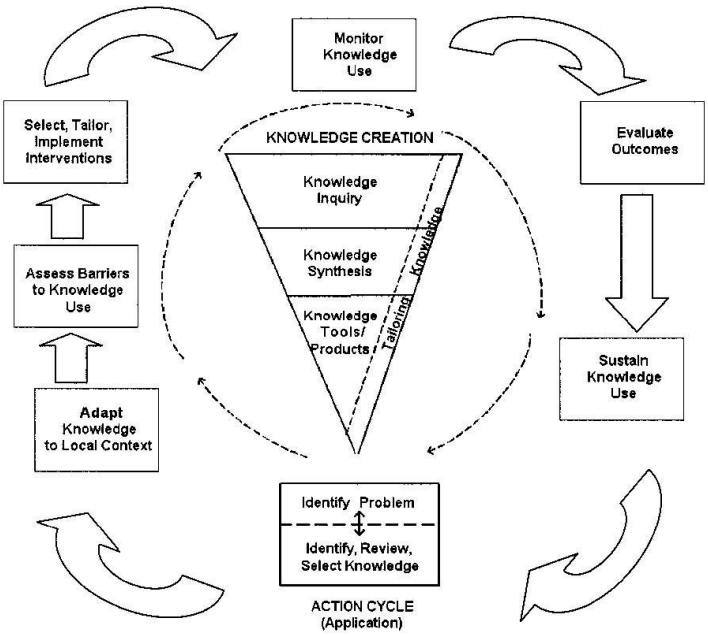

Figure 2: Knowledge to action cycle: Graham ID et al. Lost in Knowledge Translation: Time for a Map? Journal of Continuing Education in the Health Professions, 2006

1.4 Theoretical base of the research

The principles of evidence-based medicine

Evidence-based medicine (EBM) is an approach to medical practice in which the clinicians critically appraise the available evidence and use it in the best clinical practice for the patient [17]. The formal evaluation process of the evidence refers to the relationship between a certain method or design of a study and the confidence that can be placed in the reported results. In Figure 3, we present the hierarchy of evidence in form of a pyramid.

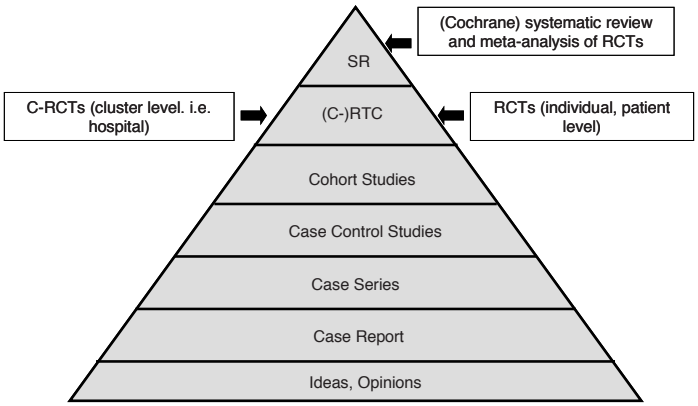

Figure 3: Hierarchy of evidentiary rigor in evidence-based medicine
Source: SUNY (State University of New York). 2004. Guide to research methods: The evidence pyramid, http://library.downstate.edu/EBM2/2100.htm (accessed April 2, 2012), adapted by the author

Well conducted systematic reviews are increasingly seen as providing the best evidence to guide the choice of patient management strategies [18]. In terms of primary studies, the randomized controlled trial (RCT), is considered as principal in the EBM pyramid and represents the highest quality level. An RCT is a powerful, rigorous research design to explore the efficacy of a clinical intervention under controlled 'experimental' conditions. Whilst experimental methods such as randomized trials are recommended they may be considered beyond the capacity of many clinicians and researchers. The next quality level is considered as evidence from well designed trials without randomization (i.e. cohort, time series etc.).
While there are many well developed and well accepted critical appraisal criteria for experimental studies, validated criteria for non-experimental studies such as controlled before and after studies (CBAs) and interrupted time series (ITS) are only available from the Cochrane Effective Practice and Organisation of Care (EPOC) Group module and website [19]. Both non-randomized designs are subject to a lack of control and high risk of bias so EPOC developed criteria to facilitate their application in clinical research and systematic reviews. Table 1 depicts the Cochrane EPOC

standard [20] of randomized and non-randomized studies to evaluate clinical pathways in hospitals.

Table 1: Cochrane EPOC study design criteria

Type of study	Study characteristics
Patient randomized controlled trials (P-RCT):	The individual patients are allocated by random to the intervention or control group. Individual randomisation facilitates equally distributed patient characteristics and comparability. The exposure to the intervention should be the only factor that distinguishes between both groups.
Cluster randomized controlled trials (C-RCT):	Robust study design that prevents contamination of professionals by randomising groups of professionals (i.e. different practices, wards or hospitals). However, this means the fundamental assumption of independence is violated because patients within a cluster are more likely to respond in a similar manner (intra-cluster correlation). The lack of independence, statistically called "intra-cluster correlation", also means a specific adjustment for clustering effects is required to assure comparability with individually randomized trials.
Non-randomized controlled trials (CCTs):	Patient or cluster trials where allocation to experimental and control groups was quasi-random (i.e. alternated allocation).
Controlled before and after studies (CBAs):	CBAs are experimental studies with two or more control groups compared with one or more experimental groups but where the allocation is not randomized. 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. The reliability of the intervention effect is questionable because there may be unidentified differences between the experimental intervention and control groups which may have modified the observed effect. Note: EPOC has recently changed the policy about inclusion of CBA studies with only one intervention site. Specific details about design criteria can be found at the website (www.epoc.cochrane.org)
Interrupted time series designs (ITS):	ITS represent a robust method of measuring the effect of an intervention as a trend over time. It is a useful design when recruitment of a control cohort is impractical. Three or more data points are collected before and after the intervention as a minimum standard. The intervention effect is measured against the pre-intervention trend.

Source: Bero L, Eccles M, Grimshaw J, Gruen RL, Mayhew A, Oxman AD, Tavender E, Zwarenstein M, Shepperd S, Paulsen E, Pantoja T, Lewin S, Ballini L. Cochrane Effective Practice and Organisation of Care Group (Cochrane Group Module). About The Cochrane Collaboration (Cochrane Review Groups (CRGs)). The Cochrane Library. Oxford: John Wiley, 2009; adapted by the author

The traditional EBM approach has been criticized because evidence gathered from RCTs may too narrowly defined and too severely constrained. For this reason the Cochrane EPOC sub-group and other prominent quality improvement experts like Berwick DM, et al. (2008) have called for a wider range of scientific methodologies to evaluate complex interventions such as clinical pathways [21]. This important issue will be discussed and elaborated in more detail in the general discussion at the end of this dissertation.

Hospital systems

Hospitals are institutions which provide medical care to patients [19]. As a direct result of specialization, hospitals are traditionally organized in a functional structure, which means the processes of care are usually built around the different medical specializations in hospitals, such as surgery, internal medicine, neurology, and other disciplines [22].

In terms of hospital characteristics, another picture appears. In a traditional approach, hospital are often categorized as General Hospitals, University Hospitals and Specialized Hospitals [23, 24]. General hospitals usually concentrate on a broad range on treatments and nursing. University hospitals also focus on research and education as well as the development of medical innovations. Last but not least, specialized hospital care typically focuses on a few clinical indications with a high number of cases per year. Therefore hospital care can be described as highly complex clinical processes but the hospital categories do not always match the complexity of the treatment provided (e.g. when specialized cataract operations or complex stroke treatment are provided in a general hospital).

This thesis does not focus on factors like the ownership of hospitals (private vs. governmental or state owned hospitals) or economic issues like non-for-profit vs. for-profit organizations, although this factors can imply significant differences on the organization of care processes in hospitals [25].

1.5 The clinical pathway approach to improve patient outcomes and hospital costs. The evidence base on CPW effectiveness.

For the purpose of this thesis CPWs are defined as structured multidisciplinary care plans which detail essential steps in the care of patients with a specific clinical problem. A simplified surgical pathway is displayed in figure 4.

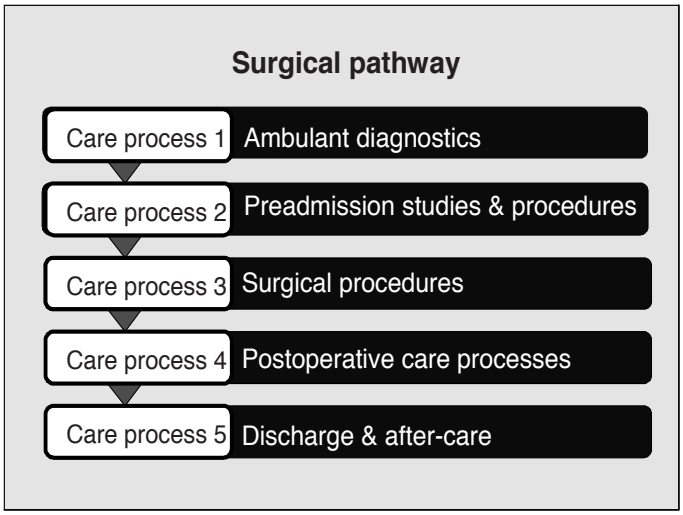

Figure 4: Schematic surgical pathway

In 2003, it was reported that CPWs had been implemented in more than 80% of hospitals in the United States [26]. This reflects an enormous resource commitment in the development and implementation of pathways in hospitals. In this era of evidence informed practice, it is therefore problematic that individual studies of the impact of CPW are varied and contradictory and that there is still no standardized definition of what a 'clinical pathway' actually constitutes. The overall quality and scope of studies investigating CPWs has not been adequately analyzed and we still lack a robust, generalizable evidence base to support decisions about the effectiveness of CPWs in hospitals [10, 26, 27].

Organizational approaches in hospitals and CPWs

In addition CPWs have an impact beyond clinical outcomes and are in fact complex organizational interventions as well. They affect the management of patient flows, professional resources, and empowerment of staff. Reported improved hospital outcomes [27-31] trigger the question “what kind of organizational invention is it grounded upon?”. From an organizational science perspective we know that we have an option of only a managerial or a complete organizational intervention [32].

Although this insight is based on the "law of the requisite variety" of pathologist and psychiatrist Willem Ross Ashby [33, 34], it is barely known in the medical and clinical world. This explains why accounts of CPWs do not stress this fundamental perspective. It is, however, important to distinguish the difference as managerial interventions are "symptom" driven and organizational interventions are "cause-eliminating" driven [35]. Figure 5 graphically depicts the different organizational approaches.

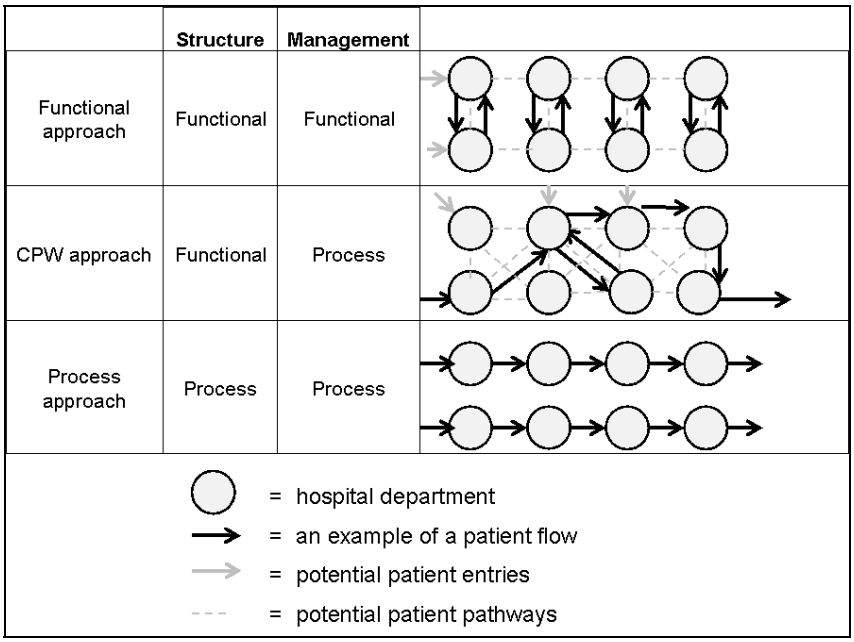

Figure 5: Organizational approaches in hospitals
Source: Vos, L: Towards process-oriented care delivery in hospitals. PhD thesis. Maastricht University, 2010; adapted by the author

A managerial intervention on its own, for instance, changes the way patient flows and resources are coordinated without questioning how patients flow between organized resources and departments. From organizational science we know that most hospitals are organized in a functionally differentiated manner; clinical and administrative functions are organized by discipline [22]. This creates a complex organization which is difficult to manage [36] leading to substandard care, long-stay and staff issues in hospitals. A managerial intervention "accepts" this complex hospital footprint and focuses on improving the coordination of the patient flows and

resources within a hospital. A complete organizational intervention (see figure 5; full process oriented approach), in contrast, first reduces the complexity of a hospital's footprint to create a simpler structure where coordination is easier, before actually improving the management of it [35, 36].
In clinical practice, the CPW approach as a managerial intervention is the principal approach with a high prevalence in hospitals [26] because of the inherent limitations of a full process oriented patient flow. Hospital policy and planning, ownership of hospitals (private vs. state owned) or legal barriers are just a few hindering factors to implement a full patient and process oriented approach. Reducing the complexity of an existing hospital enterprise requires extensive investments in construction and medical infrastructure. However, the German hospital chain Roehn Klinikum AG follows a patient oriented flow principle which has been successfully applied for many years [37]. In-patient treatment in acute care is organized in standard-care, intermediate-care and maximum-care facilities by multidisciplinary teams, depending on how severe the condition is. A multidisciplinary team of doctors (e.g. Surgeon, Anesthetist & Neurologist), nurses and other professionals provide standardized care for a highly selected range of indications. Nevertheless, the Roehn Klinikum care model has been criticized as cream picking, since this for-profit hospital chain has a strategic focus on a few economically interesting conditions or procedures such as percutaneous transluminal coronary angioplasty (PTCA).

1.6 Aims of the thesis and research approach

The main question for this thesis is: ***What are the effects of clinical pathways on professional practice, patient outcomes, length of stay and hospital costs?***

The primary research question is elaborated in chapter 3 and 4.

The secondary research questions are:
(1) "What is a clinical pathway?"
(2) "What is the standard of clinical pathway research in hospitals and is there a need for improvement in the design of evaluation trials?"
(3) "Do clinical pathways enhance access to evidence-based acute myocardial infarction (AMI) treatment in rural emergency departments?"

Sub-question 1 is addressed in chapter 2, sub-question 2 in chapter 5, and sub-question 3 in chapter 6.

The thesis starts in chapter 2 with the question "What is a clinical pathway" and focuses on the concept of CPWs in hospitals. Then in chapters 3 & 4 we describe the

process and findings of a systematic review on clinical pathway effectiveness. The published evidence had not previously been rigorously catalogued, screened, analysed and summarized. In this PhD thesis we conduct a systematic review of the impact of clinical pathways in hospitals following the Cochrane methodology. Chapter 5 deals with the quality of the evidence base for pathway effectiveness and the room for improvement in the design of evaluation trails.

Finally, chapter 6 presents a case study with the aim of filling some of the gaps in terms of the evidence base for CPW effectiveness in rural hospital settings. We focus on a CPW for the emergency treatment of acute myocardial infarction (AMI) because rural Australians are more likely to die of an AMI than those living in urban areas and clinical pathways in rural emergency departments have not been adequately tested. The pressure to make effective and evidence-based clinical decisions is even more an issue in rural Australia with the need to support relatively isolated hospital professionals with limited resources.

This thesis aims to improve the evidence base in the field of integrated care in hospitals.

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CHAPTER 2

What is a clinical pathway? Development of a definition to inform the debate.

This chapter was published as:
Kinsman L, Rotter T, James E, Snow P, Willis J: **What is a clinical pathway? Development of a definition to inform the debate.** In *BMC Medicine*, vol. 8; 2010.

2.1 Background

In 2003, it was reported that clinical pathways had been implemented in more than 80% of hospitals in the United States. This represents an enormous resource commitment both in the development of pathways, the training of staff, and in the ongoing implementation of pathways in the hospital setting. In this era of evidence informed practice, it is therefore problematic that individual studies of the impact of clinical pathways are varied and contradictory [1] and that there is still no standardized definition of what a 'clinical pathway' actually constitutes. In fact, a recent literature review identified 84 different terms that may mean a clinical pathway. These included (amongst others) care map, care pathway, critical pathway, integrated care pathway, protocol and guideline [2].

This lack of a uniformly accepted definition of what constitutes a clinical pathway impacts on capacity to empirically test the evidence base and compromises planning, resourcing, development and implementation of clinical pathways. A lack of consensus regarding research outcomes is not surprising given the lack of agreement regarding what defines a clinical pathway.

Our team of researchers faced this issue when devising the protocol for a Cochrane systematic review of the impact of clinical pathways in hospitals [3]. The development of minimum criteria to define a clinical pathway was required to ensure that appropriate studies were sourced and included in the review. The aim of this paper is to describe the developmental process undertaken and the resulting criteria so that other researchers who are developing and evaluating clinical pathways or attempting to synthesise the existing literature can consider the usefulness of these criteria for their studies.

2.2 Method

We undertook a four stage process aiming to develop 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. Synthesize previously suggested components and derive draft criteria for testing

3. Pilot test the level of agreement between review authors when applying criteria to identified studies

4. Modify criteria to maximize agreement between review authors

2.3 Results

Literature

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 et al. (1998), De Bleser et al. (2006) and Vanhaecht et al. (2006) [2, 4, 5]. De Bleser et al. (2006) surveyed the multiple terms used to describe a clinical pathway via a comprehensive review of the literature and derived key characteristics in attempting to address international confusion regarding the definition of a clinical pathway [2]. Campbell et al. (1998) described clinical pathways in the context of their relationship to clinical guidelines [4], whilst Vanhaecht et al. (2006) summarized previous studies to determine whether their review of audit tools elicited common characteristics of clinical pathways [5]. A summary of the characteristics identified by these studies is provided in Table 1.

Table 1: Characteristics of clinical pathways derived from sentinel articles

De Bleser et al. [2]	*Campbell et al. [4]*	*Vanhaecht et al. [5]*
• Guides care management for a well defined group of patients for a well-defined period of time • States goals and key elements of care based on evidence and best practice • Sequences the actions of a multidisciplinary team	• Structured multidisciplinary care plan • Detail essential steps in care of patients with a specific clinical problem • Facilitate translation of national guidelines into local protocols • Help communication with patients by providing a clearly written summary of care	• Facilitate variance management • Support multidisciplinary care • Support evidence-based clinical practice

- Allow documenting, monitoring and evaluating of variances

Criteria

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 or 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 health-care in a specific population

Level of agreement and final criteria

These criteria were tested by three of the team on five papers. If the intervention described in the paper met all five criteria then it was considered a clinical pathway. This resulted in agreement between reviewers on only two out of the five papers. It was apparent that the main obstacle to agreement on all five criteria was the poor reporting of the intervention. To address this issue the criteria were unchanged but their relative importance was adjusted. 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). This amended schedule of essential criteria was then tested by applying them to a further five papers. Following the application of the amended schedule of criteria, there was 100% agreement between the three review authors regarding whether an intervention was a clinical pathway. This schedule was then

adopted by the review group and applied to studies identified by the search strategy for the systematic review.

Application of criteria

The weighted criteria were applied to 248 full-text articles. Two review authors independently screened articles to assess which studies met the criteria for a clinical pathway and the Cochrane methodological quality criteria. The Cochrane methodological criteria relates to minimum quality standards for quantitative studies using randomized controlled trial, controlled clinical trial, controlled before and after and interrupted time series study designs [6]. Unresolved disagreements on inclusion were referred to a third review author. Sixty-three papers were excluded as they did not meet the criteria defining a clinical pathway. Only two studies needed to be referred to a third review author because of disagreement on a study meeting the minimum definition criteria.

Twenty-eight studies were included on both definition and methodological criteria in the final review. Fifteen studies termed their intervention a clinical pathway whilst eight others referred to their intervention as a "protocol". No other term was used more than once. The remaining terms used for what we included as a clinical pathway were "care model", "care map", "multidisciplinary care", "evidence-based care" and "guideline".

2.4 Discussion

The criteria developed in this study were derived from a critical analysis of existing literature and pilot testing to ensure the practicality of their use. Though broadly inclusive, they were designed to have clear parameters in order to allow development of objective inclusion criteria. The search strategy utilized in the Cochrane review was also deliberately inclusive so that all possible literature was screened for inclusion. Subsequently the individual empirical studies included in the review often included interventions described by the primary authors as something other than a clinical pathway. This was borne out by the fact that only 15 out of the final 28 included studies used the term 'clinical pathway' to describe their intervention. The existence of interventions called something other than a clinical pathway that meet the same criteria is evidence of confusion around what constitutes a clinical pathway. This strongly suggests that the development of an acceptable, objective and applicable definition would overcome much confusion about what constitutes a clinical pathway. The criteria described here provide a sound basis for further dis-

cussion amongst researchers and clinicians with the desire being to move towards an internationally acceptable definition.

There was a high level of agreement between authors when criteria were applied as evidenced by only two studies being referred to a third author due to disagreement, whilst there was agreement on the exclusion of 63 other studies. Therefore, these criteria demonstrate strong potential to be clear and objective enough for broad agreement and utilization by publishers, researchers, clinicians and anyone else interested in the investigation of clinical pathways in health care.

The criteria developed for this review could be used as a framework for describing interventions that may be considered a clinical pathway. This would strengthen the capacity of clinicians, researchers, educators and policy-makers to locate and apply relevant evidence regarding the use of clinical pathways.

2.5 Conclusion

This paper described the developmental process undertaken to devise criteria to define a clinical pathway. Researchers who are developing and evaluating clinical pathways or attempting to synthesize the existing literature should consider the usefulness of these criteria for their studies. It is also recommended that these criteria be used as a basis for ongoing development of a standardized, internationally accepted definition of a clinical pathway.

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CHAPTER 3

The scope of the systematic review. Pilot search to develop the review inclusion criteria

The full version of this chapter was published as: Rotter T, Kugler J, Koch R, Gothe H, Twork S, van Oostrum J M: **A systematic review and meta-analysis of the effects of clinical pathways on length of stay, hospital costs and patient outcomes.** In *BMC Health Serv Res 8(1), 2008*

3.1 Background

Clinical pathways represent a form of "cookbook medicine" that many perceive as an appropriate tool that contributes to quality management, cost-cutting and patient satisfaction. For the aim of this review, clinical pathways are defined as complex interventions consisting of a number of components based on the best available evidence and guidelines for specific conditions [1]. A clinical pathway defines the sequencing and timing of health interventions and should be developed through the collaborative effort of physicians, nurses, pharmacists, and other associated health professionals [2]. Clinical pathways aim to minimize delays and maximize resource utilization and quality of care [1]. They are also referred to as "integrated care pathways", "critical pathways", "care plans", "care paths", "care maps" and "care protocols".

The effectiveness of clinical pathways is under debate. However, especially in the US, up to 80 percent of hospitals already use clinical pathways for at least some indications [3]. A number of primary studies considered the effectiveness of clinical pathways, but results are inconsistent and suffer from various biases [4-7]. Only one systematic review has been performed, specifically for stroke patients [8]. Narrative reviews are more common, which often rely on "expert opinions" [9-11].

We perform a systematic review and a random effects meta-analysis to assess whether clinical pathways improved the outcome measures "length of stay (LOS)", "hospital costs" and "quality of care" when compared to standard care. By performing a systematic review and meta-analysis we are able to present the available evidence in a substantiated and concise way, in order to provide a framework for local healthcare organizations considering the effectiveness of clinical pathways.

3.2 Methods

We followed the methods of the Cochrane Collaboration [12] with some modifications, mainly concerning presentation of meta-analytic results.

Study selection criteria

As potential patient samples we considered hospitalized children and adults of every age and indication, whose treatment involved the management strategy "clinical pathways". Given the problem that there are variations in the terminology used in the current research [13], we defined minimum "inclusion criteria" for meeting our clinical pathway definition (see Table 1). Based on our definition (see background), we developed a pre-specified, three operational pathway criteria as follows: 1) multidisciplinary (two or multiple clinical professions involved), 2) protocol or algorithm based (i.e. structured care plan/ treatment-protocol or algorithm) and finally, 3) evidence based (pathway components were minimally based on one RCT or best

practice guidelines). Every pathway characteristic could be met as (1) "yes" criterion; (2) "not sure" because of poor reporting and the failure to contact the principal author or (3) "criterion not met." If one or more pathway criteria selected is not met, then we excluded the study.

Please note, additional information relating to the included studies that matched these requirements or differ from each other, are given in the results section of this review.

Table 1 - Pathway characteristics and quality outcome measures of studies included

Pathway	Characteristics			Quality Measure	Pathway [n/N]	Control [n/N]
Study-ID	**multi-disciplinary**	**evidence-based**	**protocol/ algorithm based**		**Counts and rates are presented in natural units and as percentages as far as reported**	**N = numer of participants n = number of events (%) = percentage**
Invasive Care						
Grines, CL 1998	X	X	X	In-hospital complications Re-hospitalisation (6 months)	20/237 (8.4%) 10/237 (4.2%)	20/234 (8.5%) N.S. 9/234 (3.9%) N.S.
Swanson, CE 1998	X	Not sure	X	Hospital mortality Mean Modified Barthel Index	2/38 (5.2%) 92.8	2/33 (6.1%) N.S. 85.6 (p<0.05)
Dowsey, MM 1999	X	X	X	In-hospital complications Re-hospitalisation (3 months)	10/92 (10.8%) 1/92 (1.1%)	20/71 (28.1%) (p<0.05) 0/71 (0%) N.S.
Choong, PF 2000	X	X	X	In-hospital complications Re-hospitalisation (28 days)	10/55 (18.2%) 2/55 (3.6%)	14/56 (25.0%) N.S. 6/56 (10.7%) N.S.
Aizawa, T 2002	X	X	X	In-hospital complications Re-hospitalisation (6 months)	1/32 (3.1%) 1/32 (3.1%)	2/37 (5.4%) N.S. 0/37 (0%) N.S.
Kiyama, T 2003	X	X	X	In-hospital complications	3/47 (6.4%)	5/38 (13.2%) N.S.
Hirao, M 2005	X	X	X	In-hospital complications Re-hospitalisation (6 months)	19/53 (35.8%) 0/53 (0%)	17/50 (34.0%) N.S. 0/50 (0%)
Non-Invasive Care						
Falconer, JA 1993	X	Not sure	X	Mortality (12 months) Re-hospitalisation (12 months) Cognitive and functional scores (0-100) Patient satisfaction	N.S. N.S. N.S. 7.7 (SD 2.6)	N.S. N.S. N.S. 8.8 (SD 1.7) (p<0.05)
Gomez, MA 1996	X	X	X	Complete and graded exercise test	44/50 (88.0%)	15/50 (30.0%)
Roberts, RR 1997	X	X	X	Hospitalised patients as % Re-hospitalisation (8 weeks)	(45.1%) 5/82 (6.1%)	(100%) 4/83 (4.8%) N.S.
Johnson, KB 2000	X	X	X	Unscheduled clinic visits; no hospital re-admission (2 weeks)	0/55 (0%)	2/55 (3.6%)
Kollef, HM 2000	X	X	X	In-hospital complications Hospital mortality	9/239 (3.8%) 5/239 (2.1%)	13/250 (5.2%) N.S. 8/250 (3.2%) N.S.
Marrie, TJ 2000	X	X	X	Absolute difference in rates (ARR) between pathway and control In-hospital complications Re-hospitalisation (6 weeks) Mortality (6 weeks)	 (0.6%) (0.7%) (-0.1%)	1-sided 95% CI upper limit: (4.6%) N.S. (3.6%) N.S. (2.5%) N.S.
Sulch, D 1999	X	X	X	Median Barthel Index Score (26 weeks) Mortality (26 weeks)	17 10/76 (13.2%)	17 N.S. 6/76 (7.9%) N.S.
Kim, MH 2002	X	X	X	Complications until follow-up (27 days) Re-hospitalisation (27 days)	1/9 (11.1%) 2/9 (22.2%)	1/9 (11.1%) N.S. 0/9 (0%) N.S.
Chen, SH 2004	X	X	X	Emergency room usage (not comparable with in-hospital complications) Re-hospitalisation (3 months)	3/20 (15.0%) N.S.	13/22 (59.1%) (p<0.05) N.S.
Usui, K 2004	X	X	X	Not reported		

Legend: Every pathway characteristic could be met as (1) "yes" criterion; (2) "not sure" because of poor reporting and the failure to contact the principal author or (3) "criterion not met." If one or more pathway criteria selected is/are not met, then we excluded the study. Due to poor reporting some quality measures are presented only as percentages or mean scores with or without associated standard deviations (SD). Some quality measures were only reported as statistical significant (i.e. p<0.05) or not significant (N.S.) and any other data were missing.

The setting definition covered the whole range of services offered by the clinical (out- and in-patient) as well as in the in-patient rehabilitation sector. We only gathered robust evidence and limited our study selection to randomized controlled trials (RCT) and controlled clinical trials (CCT) including methodological quality criteria (please see "quality assessment and data analyses").
We considered every objective economic and patient outcome for inclusion. We pre-defined (1) in-hospital complications as a secondary disease or adverse medical occurrence during hospitalization [14] and (2) we defined re-hospitalization as a readmission within a specified follow up period of an index admission.

Data sources and search strategy

We performed specialized searches of the Medline database (1966-2006), Embase (1980-2006), Cinahl (1982-2006), Global Health (1973-2006), and the specialized Cochrane register (including NHS EED and HTA Database; last update: 13.11.06), not restricted by language or country. We used free text words (tw), medical subject headings (MeSH terms -/-) or exploded MeSH terms for our MEDLINE literature search. This controlled vocabulary was adapted (as much as possible) to the indexation (thesaurus) of all other databases included in this review. We demonstrate our "clinical pathway search strategy" with the MEDLINE inquiry (Table 2).
Furthermore, we employed citation tracking, which examines included studies and previous reviews and contacted investigators to identify any study missed by the electronic searches.

Table 2 - Clinical pathway search strategy Ovid Medline: 1966 to November Week 2 2006

1.	Critical Pathways/
2.	(clinical path$ or critical path$ or care path$ or care map$).tw.
3.	exp Guidelines/
4.	Health Planning Guidelines/
5.	Guideline Adherence/
6.	(guideline? adj2 introduc$ or issu$ or impact or effect? or disseminat$ or distribut$)).tw.
7.	nursing protocol$.tw.
8.	(professional standard$ or professional protocol or professional care map).tw.
9.	(practice guidelin$ or practice protocol$ or clinical practice guideline$).tw.
10.	guideline.pt.
11.	or/1-10
12.	exp Hospitalization/
13.	(in-patient or hospitalized or hospitalised or hospitalisation or hospitalization).tw.
14.	exp Outpatient Clinics, Hospital/
15.	in-hospital.tw.
16.	exp Hospital Units/
17.	(Patient Admission or patient readmission or patient readmission or discharge).tw.
18.	or/12-17
19.	11 and 18
20.	randomized controlled trial.pt.
21.	controlled clinical trial.pt.
22.	intervention studies/
23.	experiment$.tw.
24.	pre test or pretest or (posttest or post test)).tw.
25.	random allocation/
26.	or/20-25
27.	18 and 26

Quality assessment and data analysis

For quality of studies, we adhered to the Effective Organisation of Care Group (EPOC) module [15] and defined three risk classes: Class I (low risk of bias), Class II (moderate risk of bias) and Class III (high risk of bias). Two reviewers independently assessed and abstracted data, on the intervention criteria, study characteristics and methodological quality. Any disagreement was discussed with a third reviewer. Studies with a high risk of bias were excluded from the review after documentation. If a primary study did not provide information about the standard deviation, we used the approximate or direct algebraic connection between the stated confidence intervals, or p-values, and the standard deviation and calculated the inverse transformation to the individual or pooled standard deviation [12]. Prior to the actual statistical pooling of the singular effects, an adjustment of the data regarding costs due to inflation and price adjustment (OECD Health Care Price Index) was carried out [16]. We chose the US Dollar (USD) as the basic currency. The year 2000 was chosen as a representative year for inflation and price adjustments or exchange rates.

We used Review Manager (RevMan) of the Cochrane Collaboration to calculate a pooled effect estimate, called weighted mean difference (WMD) [17]. We used a random effects model since this model estimates the effect with consideration to

the variance between studies, rather than ignoring heterogeneity by employing a fixed effect model. The effect sizes were generated using a model fitting inverse variance weights [17].

Heterogeneity and meta-analysis

Despite the expected clinical heterogeneity (clinical variability of the included pathway interventions) within the review, it is important to assess the comparability of the results from individual studies. A useful statistic for quantifying inconsistency is I^2= [(Q df)/Q] x 100%, where Q is the chi-squared statistic and df is its degrees of freedom [12]. This quantifies the total variance explained by the heterogeneity as a percentage. We considered an overall test-value greater than 60% to serve as evidence of substantial heterogeneity of a magnitude were statistical pooling is not appropriate.

Sensitivity analysis

In a sensitivity analysis, both fixed effects and random effects models were employed to determine the causes of heterogeneity and test the confidence that can be placed in both estimates. Only robust estimations of the pooled effects with similar results in fixed effects and random effects models are included in the meta-analysis and discussed. Furthermore, sensitivity analyses were performed to test whether the effect size varied by the countries where the study was carried out (adjusting for market forces) and the year of publication, adjusting for temporal trends.

Assessing publication bias

We used a funnel plot analysis to assess publication bias, i.e. the bias caused by a lower likelihood of publication for non-significant studies. The funnel plot is a scatter-plot with the x-axis representing the effects estimated from the primary studies, and the y-axis representing a measure of the sample size in each study (SE; standard error of the mean) [18]. If publication bias is absent, the diagram shows an inverted symmetrical funnel.

3.3 Results

Search strategy and intervention characteristics

The specialized search strategy led to the initial selection of 2,386 studies, whereas only 17 matched our methodical requirements (see Figure 1 & 2). For the first stage of the study assessment, we scanned all of the 2,386 titles and abstracts for inclusion, the remaining 256 possibly relevant studies were retrieved as full text articles. Based on the full text assessment, we excluded 190 studies out of 256 because they failed to meet our pathway definition. The majority of the excluded studies failed to meet the multidisciplinary pathway criterion, i.e. it was a therapy guideline issued by a medical association or it was a uni-professional nursing care plan. Others did not meet the “algorithm or protocol based” criterion because there was no struc-

ture and detailed care plan. For example a poster with issued guidelines was posted in the Emergency Department.
Evidence for meeting the minimal criterion "pathway content is minimally based on one RCT" was reported in 15 studies out of 17, which were included in the review. The study from Falconer et al. and Swanson at al. met the evidence criterion, "not sure" because we failed in contacting the principal investigators [19, 20].

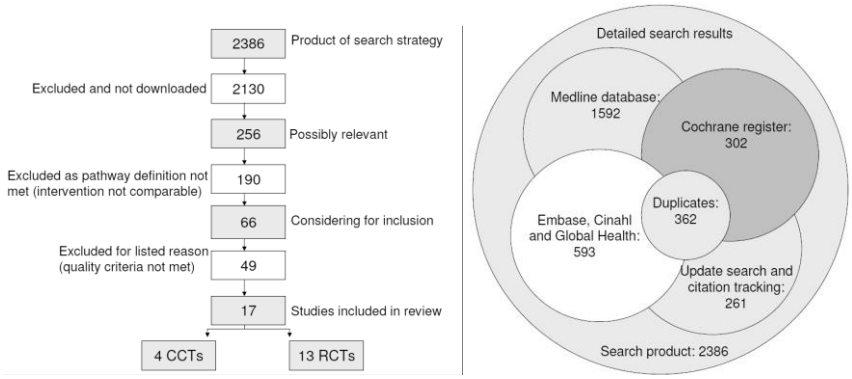

Figure 1 & 2

Intervention characteristics

The reported pathway strategies can be described as complex pathway interventions versus a "non-intervention" control group or often poorly, described as "usual or traditional care" group. Most of the experimental interventions were combined with other types of interventions like audit and feedback, educational meetings, and reminders. For 8 out of the 17 (47%) included studies, it was clear that the structured care plan was combined with a "clinical diagnostic or assessment protocol" [19, 21-27].
The evidence base for two (12%) pathway interventions was "not sure," whereas the remaining 15 interventions were minimally based on one randomized study or good evidence. The reported purpose of the pathway strategies was appropriate management or cost containment.
The hospital setting was in two studies a multi-center study comprising a range of hospitals included in the investigation [22, 26]. From the 15 remaining single center studies, 8 studies (53%) were carried out in a university (teaching) hospital setting [20, 23-25, 28-31] and 7 studies (46%) in a non-university hospital setting [19, 21, 27, 32-35].

Details of the intervention characteristics are given in Table 3.

Table 3 - Characteristics of studies included

Study-ID	Study Quality	Country	Sample Size [N]	Mean Age [Years]	Diagnosis/Intervention
Invasive Care					
Grines, CL 1998	Class I	USA*	471	56	Primary Angioplasty in Myocardial Infarction
Swanson, CE 1998	Class II	Australia	67	55	Femoral Fractures
Dowsey, MM 1999	Class II	Australia	163	66	Hip and Knee Arthroplasty
Choong, PF 2000	Class II	Australia	111	81	Fractured Neck of Femur
Aizawa, T 2002	Class II	Japan	69	71	Transurethral Resection of the Prostate
Kiyama, T 2003	Class II	Japan	85	63	Gastrectomy
Hirao, M 2005	Class II	Japan	103	61	Gastrectomy
Non-Invasive Care					
Falconer, JA 1993	Class II	USA*	121	68	Stroke Rehabilitation
Gomez, MA 1996	Class I	USA*	100	52	Myocardial Ischemia
Roberts, RR 1997	Class II	USA*	165	48	Chest Pain
Johnson, KB 2000	Class II	USA*	110	7	Paediatric Asthma
Kollef, HM 2000	Class II	USA*	489	60	Respiratory Care
Marrie, TJ 2000	Class I	USA*	19***	64	Community-Acquired Pneumonia
Sulch, D 2000	Class II	UK**	152	75	Stroke Rehabilitation
Kim, MH 2002	Class II	USA*	18	48	Artrial Fibrillation
Chen, SH 2004	Class II	Taiwan	42	8	Paediatric Asthma
Usui, K 2004	Class II	Japan	61	48	Community-Acquired Pneumonia

Quality assessment

To summarize, we examined the design and study quality of 66 studies, excluding 49 out of the 66 studies because of the high risk of bias (see trail flow, Figure 1).

The patient was randomized to the experimental or control group in 12 out of 13 (92%) RCTs. The randomization process was clear in all such studies and justified by the authors. Referring to the individually randomized and single-center studies, the assessment of protection against contamination of the control professionals remained unclear due to poor reporting. None of the investigators reported protection against contamination (communication between experimental and control professionals) and it is possible that control subjects received the intervention. Only the investigation from Marie et al. used a robust cluster randomized design, with 19 hospitals as unit of allocation [26]. To avoid "unit of analysis error," we conducted the meta-analysis at the same level as the allocation (19 cluster-hospitals = 19 patients).

Poor reporting also lead to difficulties in determining the assessment of the power calculations. For instance, sample-size calculation was unclear for over 60% of the included studies; hence the study sample may not have been sufficiently large. Another problem, due to poor reporting was the selection of comparators. The choice of the comparator (i.e. the control and intervention units were located either in the

main building or the east building of the participating hospital) was stated and justified by the authors of the 17 primary studies. However, a clear description of what was meant by traditional care or usual care (control group) would have helped in assessing the relevance of the study to other settings.
Primary studies reporting economic data, can be described by a very limited scope of evaluation, focusing on direct hospital LOS and costs effects, rather than on a full economic evaluation [16]. In Table 3 the quality assessment and characteristics of the 17 studies included in the review and meta-analysis are shown in detail.

Effects on LOS

Out of the 16 studies (12 randomized and four non-randomized studies representing a study population of 4,028 patients) examining the effect of clinical pathways on the length of stay, 12 showed significant effects [19, 20, 22-35]. However, heterogeneity between studies reporting on LOS was substantial (I^2 = 80 %) and may refer to both the statistical inconsistency as well as to the varying clinical pathway interventions that were included. As a result, the estimation of an overall pooled effect is not appropriate and in Figure 3, the differences from the individual studies in LOS are depicted together with the corresponding confidence intervals without totals. The reported LOS in Kiyama 2003 was calculated from the day of surgery to the day of discharge [35]. All other studies included in this analysis considered the total LOS.

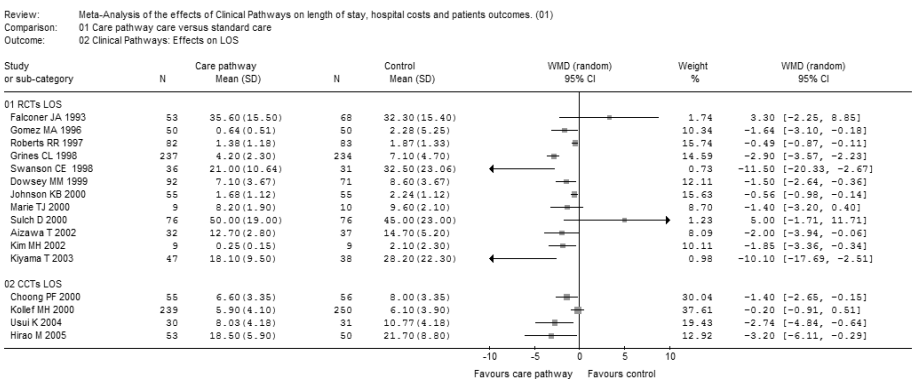

Figure 3

Effects on patient outcomes

Out of 17 trials reporting effects on quality outcome measures (see Table 1); six measures were comparable in terms of re-hospitalization and seven in terms of in-hospital complications [19-31, 33-35]. In total, nine primary studies were included in the Meta-analysis (representing a study population of 1,674 patients), examining the effect of clinical pathways on quality patient outcomes. The pooled Odds Ratio (OR) for re-admission was 1.1 (95% CI: 0.57 to 2.08) and for in-hospital complications the overall OR was 0.7 (95% CI: 0.49 to 1.0). Statistical heterogeneity was not present among the studies and there was no evidence of difference in readmission to hospitals or in-hospital complications. The effects of clinical pathways on clinical

outcomes in the individual studies are depicted together with the pooled OR (see Figure 4 & 5). There was clinical variance in the range of follow-up periods that were used by the investigators measuring re-hospitalization (follow up periods ranged from 27 days to 6 month, see Table 1) as well as the investigators used varying definitions of the term in-hospital complications (included in-hospital complications were cardiac events, infections, thrombosis, re-operation, sepsis and empyema.) Obviously, this implies that any time element in the patient outcome data is lost through this approach and it was not possible to compute a series of dichotomous outcomes, i.e. at least one event during the first year of follow up.

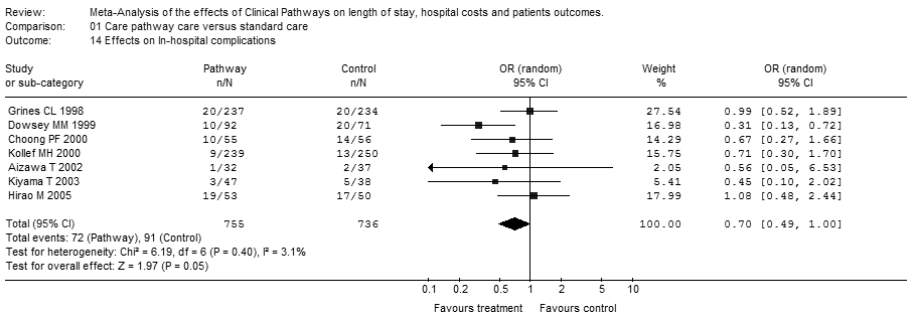

Figure 4

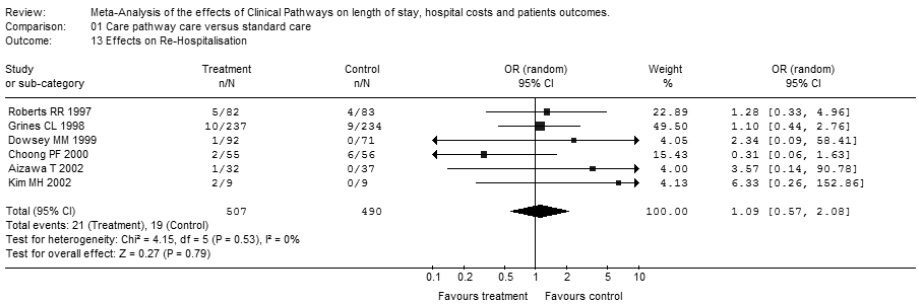

Figure 5

Effects on hospital costs

Six of the included studies (five randomized and one non-randomized), representing a sample of 1328 treated patients, reported on cost effects (22, 24, 27, 29, 30, 35). Four out of the five randomized studies found significantly lower hospitalization costs for pathway groups. The statistical heterogeneity was substantial (I^2 = 88 %) and compromised the estimation of a pooled effect. Additionally, we also observed a considerable methodological variation which refers to the different methods of cost calculation used by the investigators. Some investigators used a full cost ap-

proach (fix and variable costs included), whereas others calculated only direct hospital costs. Table 4 describes the costs differences in detail.

Study ID	Country	Currency	Experiment	SD	Control	SD
Kiyama, T 2003	Japan	US$	$14013	$2634	$18020	$7332
Kim, MH 2002	USA*	US$	$879	$394	$1706	$1512
Kollef, HM 2000	USA*	US$	$922	$1614	$1120	$1430
Grines, CL 1998	USA*	US$	$11430	$6257	$13733	$7249
Roberts, RR 1997	USA*	US$	$1877	$1243	$2574	$999
Gomez, MA 1996	USA*	US$	$1535	$1985	$6768	$17359

Table 4 - Cost data, standardized to the year 2000

Sensitivity analyses

The LOS effects were robust in terms of the sensitivity analysis concerning the different statistical calculation models (fixed versus random effects model) and the Year of publication, adjusting for temporal trends. However, we observed a trend toward greater reported LOS effects from Japanese studies with a reduction of approximately three days (WMD – 2.7), followed by studies carried out in Australia (WMD – 1.5), Canada (WMD – 1.4) and the USA (WMD – 0.8). Subsequently, we tested the hypotheses, that different market forces (reported effect sizes per country) are possibly confounding the conclusions of these review and meta-analysis. After exclusion (stepwise/ iterative and all of the primary Japanese studies) of the subgroup of Japanese studies, the (calculative) overall LOS effect remained robust and statistically significant, but tended to be smaller (WMD – 1.2; subgroup "Japanese studies excluded" versus WMD – 1.5; subgroup "all primary studies" included). This applies also to the subgroup Analysis "Invasive versus non-invasive LOS effects", after exclusion of the subgroup of Japanese studies (WMD -0.6 conservative versus -2.2 invasive).
In addition, the overall odds ratios (OR) for re-admission and in-hospital complications were robust in all terms of the sensitivity analysis, indicating reliable pooled results.

Publication bias and other sources of systematic error

The funnel plot showed a relatively symmetric distribution (Figure 6), but the point cloud does not have a distinctive funnel form. The deficient funnel form of the funnel plot can also be due to the relatively high heterogeneity with respect to the different pathway indications of the primary studies included in these review (cross-indicational methodology of the primary studies). Furthermore, the number of studies was relatively small.

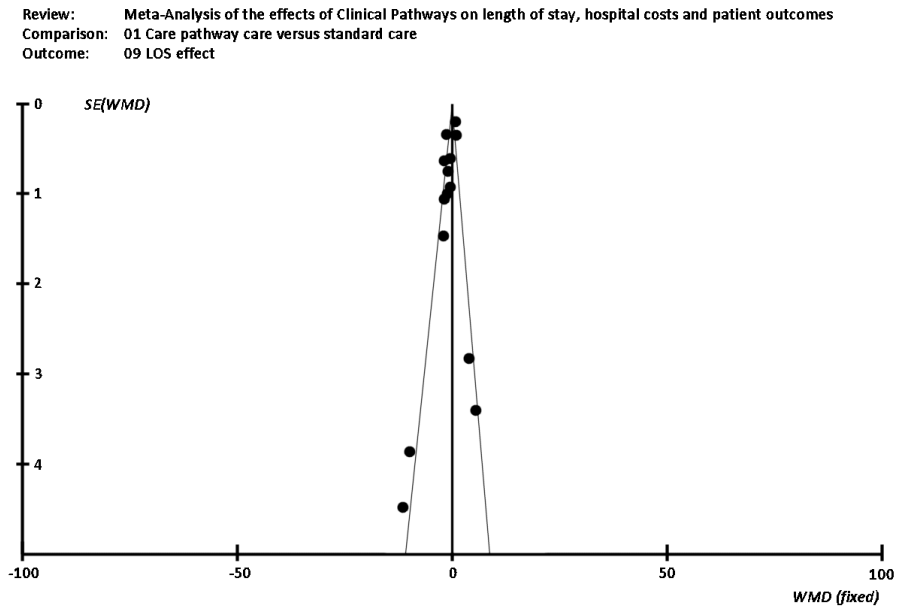

Figure 6

3.4 Discussion

In general, the majority of studies reporting economic data (LOS and hospital costs) showed a positive impact. Clinical pathways appeared to be effective in reducing LOS and costs. These results may not be applied for acute rehabilitation for stroke, where reverse effects were reported (see effects on LOS, Figure 3) [19, 34]. Both trends were not statistically significant but they were in contrast to the majority of pathway effects reported in the present review. However, the question of comparability may rise as a reflection of the differing pathway components included in this review and also applies to the kind and number of providers included in the primary studies.

We did not publish our review protocol prior to the study. The review protocol for the follow-up study will be published as a Cochrane review to prevent any doubt about the comparison to be data-driven instead of protocol-driven. We determined the scope of this review question on a pilot analysis of existing primary study data resulting in a diverse set of included studies. As it is an explanatory analysis, the pooled results of the meta-analyses may only apply for the majority of included pathway conditions reporting positive effects or trends. Another limitation refers to the poorly described control conditions reported in the primary studies and implied both, the risk of contamination, and the masking of effects. It should be noted that

the development and implementation of clinical pathways consumes a considerable amount of resources. This corresponds to the fact that truly achievable costs savings depend on the number of cases (volume). This has to be included in the costs analysis. The inflation-adjusted costs for implementation (without maintenance and further development) of the pathway indication "Caesarian section" amounted to nearly $20,000 [36]. However, since normally 20 percent of the diagnoses cover 80 percent of the cases [37], a considerable percentage of medical services can be dealt with using a relatively small number of clinical pathways. Therefore, the expenditures will amortize rapidly.

It is very important not to look too far into these results, as there were some limitations. Moreover, it has to be emphasized that evidence determined by meta-analysis is always exploratory in nature and should be considered with caution.
Due to the result of the relatively small number of studies meeting inclusion criteria, this evidence base is not conclusive enough to provide a replicable framework for all pathway strategies. The likely benefits and costs need to be considered by the local healthcare providers when implementing clinical pathways under different circumstances. This review has shown that there is not one, singular strong evidence base. Accordingly, decision-makers should also consider some limitations in relation to the generalization of these findings. Replicating the results of this review in other settings could be problematic (e.g. ceiling effects such as market forces).
The heterogeneity in design and outcomes of the studies was large and refers to the statistical heterogeneity in addition to the clinical variability of the included studies. This precluded the overall pooling of LOS and cost data, although the order of magnitude of effects indicated that there are considerable implications of using clinical pathways.
It is unavoidable that some studies will have been overlooked, despite our electronic search strategy. Studies meeting our clinical pathway definition (see Table 1 & 4) were included, regardless of the fact that the term pathway was mentioned in the study and was done to avoid subjectivity. Also, studies were independently assessed and data extracted by two with any disagreement discussed with a third reviewer.

Finally, should be emphasized that the standard of the primary studies included pose a threat to the validity of the results. While the overall quality of the included studies was moderate, most demonstrated methodological weaknesses such as a small sample size available for analysis.

3.5 Conclusions

With respect to the totality of available evidence, the knowledge about the mechanisms through which pathways work is insufficient. Future research should focus on a better understanding of the key elements of clinical pathways that have impact on economic and patient outcomes. It is also surprising that more studies do not consider any cost effects other than those of treatment. Health-economic research should therefore concentrate on costs of development and implementation of clinical pathways.

This investigation is the first systematic review regarding the effects of clinical pathways on process and patient outcomes. We explicitly decided to expand this review and will also include less restrictive study designs in addition to randomized and quasi-randomized trials, to provide a comprehensive theoretical basis. The character of non-experimental studies makes them even more difficult to critically assess and moreover, due to the lack of MeSH terms the search results cannot be as sensitive as those for purely RCT/ CCT-based reviews. Another future direction is a more comprehensive, patient-centered approach, concentrating more on patient-outcomes rather then health-economic study endpoints. The next scheduled update for this review is planned for the End of 2009.

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CHAPTER 4

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

Section 4.1

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

(Protocol)

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4.1.1 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 [1]. 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 [2].

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 [3]. 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 [4], inguinal hernia repair [5], laparoscopic surgery [6], pancreaticoduodenectomy [7], and the management of fractured neck of femur [8], 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 [9-13]. Conversely, there are studies reporting no benefit regarding LOS and total costs. These include CPWs implemented for femoral neck fracture in older people [14], acute exacerbations of bronchial asthma [15], carotid endarterectomy [16] , and head and neck cancer [17]. 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 [3]. A systematic review and meta-analysis is required to reconcile CPW studies with differing results.

4.1.2 Objectives

This review addresses the following question:

What is the effect of CPWs on professional practice, patient outcomes, LOS or hospital costs?

The specific objectives of this review are:
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 summarise included studies narratively and qualitatively.
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 will be categorised as:

- Setting (inpatient, outpatient, medical, surgical, critical care, emergency, rehabilitation, aged care)
- Implementation process (multifaceted, local consensus)
- Invasive or non-invasive nature of patient management guided by CPW (e.g. CPW for gastrectomy; PTCA; laparoscopic cholecystectomy; hip and knee arthroplasty etc. versus CPW for stroke; pneumonia; asthma etc)
- 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 are planned:

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. Impact on patient outcomes, professional practice, length of hospital stay and hospital costs.

We will also explore the effects of the following characteristics of the intervention on the magnitude of effect across studies (sub-group-analysis):

1. Effect of high quality studies versus low quality studies (Sub-group-analysis re-

garding the study design)
2. Country(s) where the study was carried out.
3. The date of study / year of publication (adjusting for temporal trends).

4.1.3 Criteria for considering studies for this review

Types of studies
Randomised controlled trials (RCTs), controlled clinical trials (CCTs), controlled before and after studies (CBAs) and interrupted time series analysis (ITS) will be included after meeting EPOC methodological quality criteria.

Types of participants
Health professionals, including doctors, nurses, physiotherapists, pharmacists, occupational therapists, social workers, dietitians, psychologists, psychiatrists and dentists involved in CPW utilisation in the hospital setting.
Any hospitalized patients (in-patient and out-patient settings) with conditions managed on a CPW, irrespective of diagnosis.
Hospitals evaluating the impact of CPWs.

Types of interventions
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 [1]. For the purposes of this review, the intervention of interest is 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 expect that most studies will compare CPW intervention with usual care in the same setting. Studies of multifaceted interventions will be included if the CPW aspect can be separately assessed from other elements of the intervention. For example, a multifaceted intervention may include 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 multi-faceted intervention incorporating a CPW compared to the same intervention without a CPW element will be included.

Types of outcome measures
Objectively measured patient outcomes, professional practice, LOS and hospital costs.

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

Professional practice outcomes include quality measures appropriate to the specific

aim of the CPW (for example, time to mobilisation post surgery), staff satisfaction and adherence to evidence-based practice.

Length of stay (LOS) includes the duration of hospital stay measured in hours or days that have been reported in the included studies.

Hospital costs include 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 pathology and haematology tests ordered.

Search strategy for identification of studies

See: Effective Practice and Organisation of Care Group methods used in reviews.
The Database of Abstracts of Reviews of Effectiveness (DARE) will be searched for related reviews

The following electronic databases will be searched for primary studies:

a) The EPOC Register (and the database of studies awaiting assessment) will be reviewed (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) Hand searching of those high-yield journals and conference proceedings which have not already been hand searched on behalf of the Cochrane Collaboration.
e) Reference lists of all papers and relevant reviews identified.
f) Authors of relevant papers will be contacted regarding any further published or unpublished work.
g) Authors of other reviews in the field of effective professional practice will be contacted regarding relevant studies of which they may be aware.
h) We will search ISI Web of Science for papers which cite studies included in the review

Electronic databases will be searched 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 will be translated into the other databases using the appropriate controlled vocabulary as applicable. We will not use language restrictions.

We will search MEDLINE using the following search strategy:

Database: Ovid MEDLINE(R) <1950 to February Week 4 2007>
Search Strategy:
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1 Critical Pathways/
2 ((clinical or critical or care) adj path$).tw.
3 (care adj (map$ or plan$)).tw.
4 exp Guidelines/
5 Health Planning Guidelines/
6 Guideline Adherence/
7 (compliance adj (protocol? or policy or guideline?)).tw.
8 (guideline? adj2 (introduc$ 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

4.1.4 Methods of the review

Screening

All titles and abstracts will be screened independently by 2 reviewers (LK and EJ for professional practice and patient outcomes; TR and RK for relevance regarding LOS and hospital costs) to assess which studies meet the inclusion criteria. All titles and abstracts will be pooled and duplicates deleted. Full text copies of all potentially relevant papers will be retrieved. Unresolved disagreements on inclusion will be referred to a third reviewer, and if consensus cannot be reached, the EPOC contact editor.

Data management

Searches

Details on the number of retrieved references, the number of obtained full-text-papers and the number of included and excluded articles will be recorded and reported. This data will be managed in RevMan and the reason for excluding retrieved studies will be stated.

Data Abstraction

Data will be extracted using a standardised data extraction sheet and extracted directly from trial reports. When necessary, additional information will be sought from the authors of the primary studies. The relevant data will be entered into the RevMan software.

Quality assessment and analysis

Two reviewers (LK and EJ for patient outcomes and professional practice; TR and RK for LOS and hospital costs) will assess the methodological quality of all included studies and categorise them into three classes: A (low risk of bias), B (moderate risk of bias) and C (high risk of bias), using the EPOC checklist for the assessment of methodological quality of studies (see EPOC module). Unresolved disagreements on risk of bias classification will be referred to a third reviewer, and if consensus cannot be reached, the EPOC contact editor. Studies classified as high risk of bias will be excluded.

Data will be reported in natural units. In the case of missing standard deviation, the appropriate transformation will be undertaken. For continuous outcome measures a summary effect size, the weighted mean difference with 95% confidence levels, will be estimated.

Hospital costs will be assessed and calculated in the individual studies. We will only consider reported hospital cost data as direct costs, based on costs rather then on fees. Pilot study results indicated insufficient reported data to synthesise full eco-

nomic evaluations. We will investigate the direct cost-effects of CPWs (cost-analysis) not the cost-effectiveness. Cost data will be presented in US $ for the common price year 2000. Costs will be adjusted for inflation applying country-specific discount rates published by the OECD or using government recommended rates and providing a sensitivity analysis with a common discount rate recommended in the literature [18]. Additionally, we will provide the undiscounted cost data to allow readers to recalculate the results using any discount rate. Studies reporting cost data in other currencies will be converted to US $ using the average exchange rate (cash quotation interbank) for the base year 2000.

Combining Studies

We will present the results of studies in tabular form and make an assessment of the effects of studies, based upon the quality, the size and direction of effect observed. Studies will be grouped, and vote counts made on the following outcomes: effective/no difference/harm.

We expect to find both statistical and contextual heterogeneity, given the range of disparate outcomes measured, the many different settings in which care will be delivered, and the wide range of diagnoses and types of patients included in different study designs. This makes it unlikely that statistical pooling will be feasible, but if there appears to be a body of studies amenable to meta-analysis, then their results will be displayed graphically, and viewed to assess heterogeneity. Both fixed and random effects meta-analysis will be undertaken to assess the robustness of the results. Any study that appears to be an outlier will have its influence on meta-analysis assessed by excluding it. In comparisons of homogeneous groups of studies with different outcome measures, we will consider using a single effect size measure (standardized mean differences). Funnel plots will be considered only if more than five trials can be pooled for meta-analysis.

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

Ongoing Studies

On-going studies identified will be described, where available, detailing the primary author, research question(s), methods and outcome measures together with an estimate of the reporting date.

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Section 4.2

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

(Cochrane Review)

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4.2.1 Introduction

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 and have been implemented internationally since the 1980's [1]. Clinical pathways have the potential to align with the case-mix model of health care delivery and to support cost minimization [2]. In 2003, it was reported that CPW had been implemented in more than 80% of hospitals in the United States. This reflects an enormous resource commitment in the development and implementation of pathways in hospitals. In this era of evidence informed practice, it is therefore problematic that individual studies of the impact of CPW are varied and contradictory [3]. The plethora of study designs, settings and proposed pathway interventions make the relevance of individual studies very difficult to evaluate and apply to particular clinical settings. This is further complicated by the varying perceptions of what constitutes a CPW. A recent literature review identified 84 different terms that may mean a CPW. These included (amongst others) care map, care pathway, critical pathway, integrated care pathway, protocol and guideline [4]. Thus, it was timely to objectively define a CPW and catalogue and analyze the existing literature via a rigorous systematic review in order to provide a framework for doctors, nurses, physiotherapists and other health care professionals considering the effectiveness of CPWs. We summarized the evidence and assessed the effect of CPW on professional practice (e.g. quality of documentation), patient outcomes (e.g. mortality, complications), length of hospital stay and hospital costs.

4.2.2 Methods

We followed the Cochrane systematic review methodology for considering and analysing studies [5].

Review eligibility criteria

We included randomized controlled trials (individual or cluster level), controlled clinical trials (CCTs), controlled before and after studies (CBAs), and studies using interrupted time series analysis (ITS) designs were included after meeting Effective Practice and Organisation of Care (EPOC) methodological design and quality criteria. The study population included (1) Hospitalized patients (in-patient and out-patient settings) with conditions managed on a CPW, irrespective of diagnosis. (2) Health professionals, i.e. doctors, nurses, physiotherapists, pharmacists, occupational therapists, social workers, dieticians, psychologists, psychiatrists, speech pathologists and dentists involved in CPW utilization in the hospital setting, (3) Hospitals evaluat-

ing the impact of CPWs. An intervention was defined as a CPW if it was a multidisciplinary plan of care and met three out of the following four criteria:

1. The intervention was used to translate guidelines or evidence into local structures;
2. The intervention detailed the steps in the course of treatment or care in a plan, pathway, algorithm, guideline, protocol of other 'inventory of actions';
3. The intervention had time-frames or criteria-based progression; and
4. The intervention aimed to standardize care for a specific clinical problem, procedure or episode of healthcare in a specific population.

After meeting the minimum criteria for defining a CPW we included studies comparing (1) patients managed according to CPWs compared to usual care and (2) patients managed within a multifaceted intervention including a CPW compared to usual care. Patient outcome measures included inpatient mortality, mortality at longest follow-up, hospital readmissions, in-hospital complications, adverse events, ICU admissions and duration of mechanical ventilation. Professional practice outcomes included quality measures appropriate to the specific aim of the CPW, staff satisfaction and adherence to evidence-based practice, e.g. 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 hospitalization and any appropriate resource utilization data as a surrogate measure for studies that did not report primary hospital-cost-data.

We searched the Database of Abstracts of Reviews of Effectiveness (DARE), the EPOC register, the Cochrane Central Register of Controlled Trials (CENTRAL) and bibliographic databases such as MEDLINE, EMBASE, PUBMED, CINAHL, NHS EED and Global Health using identified terms that may relate to use of a CPW in a hospital environment. Hand-searching of high yield journals and conference proceedings, screening reference lists and contacting authors of included studies, searching of the ISI Web of Science and contact with professional associations, e.g. the European Pathways Association were performed to identify potentially relevant studies. No language limitations were imposed. The MEDLINE search strategy is presented in chapter 7 and can be found in the full version of the EPOC review, recently published in the Cochrane Library [6]. Two review authors independently screened all titles and abstracts. Unresolved disagreements were referred to a third review author. The same review authors independently assessed full-text articles for inclusion against criteria for defining a CPW and study quality using a validated and standardized data extraction form. Details on the number of retrieved references, the number of obtained full text papers and the number of included and excluded articles are presented in detail in the full version of the EPOC review, recently published in the Cochrane Library [6]. When necessary, we sought additional information from the authors of the primary studies. The methodological quality of all included studies was also assessed independently by two review authors using the EPOC risk of bias tool [5] and categorized them as low, moderate or high risk. We referred unre-

solved disagreements on risk of bias classification to a third review author. We excluded studies classified as high risk of bias. A summary of the risk of bias assessment is given in Table 1.

Table 1: key characteristics of included primary studies

Study ID	CPW condition	Type of ward	Type of hospital	Sample size	Study type	Country	Risk of bias
Comparison 1: single CPW intervention versus usual care							
Aizawa, T 2002	TURP	Surgical / Urology unit	Acute	69	P-RCT	Japan	Moderate risk (B)
Brook, AD 1999	Mechanical ventilation	Medical ICU	ICU	321	P-RCT	USA	Moderate risk (B)
Chadha, Y 2000	menorrhagia and urinary incontinence	Gynaecological unit	Acute	946	CBA	UK	Moderate risk (B)
Choong, PFM 2000	femural neck fracture	Orthopadic unit	Acute	111	CCT	AUS	Moderate risk (B)
Delaney, CP 2003	CPW Laparotomy and Intestinal Resection	Surgical Rehabilitation	Extended care	64	P-RCT	USA	Moderate risk (B)
Doherty, SR 2006	Asthma care	Medical units of the hospitals	Acute	187	CBA	AUS	Moderate risk (B)
Dowsey, MM 1999	Hip and knee arthroplasty	Orthopadic unit	Acute	163	P-RCT	AUS	Moderate risk (B)
Falconer, JA 1993	Stroke Rehabilitation	Stroke Rehabilitation	Extended care	121	P-RCT	USA	Moderate risk (B)
Gomez, MA 1996	Suspected MI	Coronary Care unit/ Chest pain evaluation unit	Acute	100	P-RCT	USA	Moderate risk (B)
Johnson KB 2000	Asthmatic children	Emergency and Paediatric wards	Acute	110	P-RCT	USA	Moderate risk (B)
Kim MH 2002	Atrial fibrillation	Emergency Department	ED	18	P-RCT	USA	Moderate risk (B)
Kiyama T 2003	Gastrectomy	Surgical ward	Acute	85	P-RCT	Japan	Moderate risk (B)
Kollef MH 1997	Mechanical ventilation	Medical & Surgical ICU	ICU	357	P-RCT	USA	Low risk (A)
Marelich GP 2000	Mechanical ventilation	Medical ICU	ICU	253	P-RCT	USA	Low risk (A)
Marrie TJ 2000	Pneumonia	Emergency Department	Acute	1743	C-RCT	Canada	Moderate risk (B)
Roberts, RR 1997	CPW Chest Pain/ possible MI	Emergency/ telemetry oservational units	ED	165	P-RCT	USA	Moderate risk (B)
Smith, BJ 2004	CPW COPD	Medical Units	Acute	1230	CBA	AUS	Low risk (A)
Sulch, D 2000	Stroke Rehabilitation	Stroke Rehabilitation	Extended care	152	P-RCT	UK	Moderate risk (B)
Sulch, D 2002	Stroke Rehabilitation	Stroke Rehabilitation	Extended care	152	P-RCT	UK	Moderate risk (B)
Tilden, VP 1987	Identification of battered woman	Emergency Department	ED	892	ITS	USA	Moderate risk (B)
Usui, K 2004	Pneumonia	Medical Units/ respiratory medicine	Acute	61	CCT	Japan	Moderate risk (B)
Comparison 2: Multifaceted intervention including a CPW versus usual care							
Bauer, MS 2006	Bipolar disorder	Mental health outpatient clinic VAMC	Other	306	P-RCT	USA	Low risk (A)
Bookbinder, M 2005	Palliative care	Palliative Care	Extended care	267	CBA	USA	Moderate risk (B)
Brattebo, G 2002	Mechanical ventilation	Surcigal ICU	ICU	285	ITS	Norway	Moderate risk (B)

(Table 1 cont.)

Chen, SH 2004	asthmatic children	Pediatric unit	Acute	42	P-RCT	Taiwan	Moderate risk (B)
Cole, MG 2002	Care of delirium in older medical patients	Medical units	Acute	227	P-RCT	Canada	Low risk (A)
Kampan P 2006	Diabetic patients admitted with hypoglycaemia	Medical unit	Acute	65	P-RCT	Thailand	Moderate risk (B)
Philbin, EF 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

4.2.3 Data analysis and statistical pooling of studies

Statistical pooling was conducted when studies were sufficiently clinically similar and the statistical test of heterogeneity was low to moderate (I squared test). A Cochrane web-based program, Review Manager (RevMan), was used to calculate a pooled estimate of the combined intervention effect [7]. 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 [8, 9]. Costs / charges were adjusted for inflation by applying Gross Domestic Product deflators as 'GDPD values' or using government recommended rates and providing a sensitivity analysis with a common discount rate recommended in the literature [10]. Additionally, we provide the un-discounted cost data to allow readers to recalculate the results using any discount rate.
Both tables are presented as additional tables in the full version of the EPOC review recently published in the Cochrane Library [6].

4.2.4 Results

A final inclusion sample of 27 studies (see table 1) was derived from the 3214 abstracts identified by the search strategy. A summary of the key characteristics of included studies is provided in Table 1. Results from the study by Sulch were reported in two separate publications (2000 and 2002).

Included study characteristics

Of the 27 included studies 19 were RCTs [11-30], four were CBAs [31-34], two were CCTs [35, 36] and two were ITS [37, 38]. Out of the 19 RCTs, two were cluster-randomized studies [14, 15].
Included studies targeted a large range of conditions (Please see table 1 for a brief description). Across the 27 studies there were 19 different conditions targeted. Please see also effects of pathway interventions, subgroup analysis by condition. Thirteen of the studies were conducted in the United States [13, 14, 16, 17, 19, 21-23, 25, 28, 29, 31, 38] four in Australia [24, 33-35], three in Japan [18, 30, 36], two each in the United Kingdom [11, 12, 32], and Canada [15, 26] and one each in Thailand [20], Taiwan [27] and Norway [37]. Fifteen studies were conducted in general acute wards (e.g. medical, surgical, paediatrics, gynaecology) [14, 15, 18, 20-22, 24, 26, 27, 30, 32-36], four in an extended stay facility (e.g. rehabilitation) [11, 12, 23, 25, 31], four in an ICU [16, 17, 28, 37], three in an Emergency Department (ED) [13, 19, 38], and one [29] in a mental health outpatient clinic. In nine studies the CPW was designed for an invasive procedure [16-18, 24, 25, 28, 30, 35, 37] . Sixteen described CPWs for a non-invasive procedure, e.g. diabetes, stroke, asthma [11, 12, 14, 15, 19-21, 23, 26, 27, 29, 31, 33, 34, 36, 38] and two described CPWs for combined invasive / non-invasive procedures, e.g. for suspected MI with or without PTCA [22, 32].

Intervention characteristics and comparison

Twenty studies compared a stand-alone CPW to usual care [11-13, 15-19, 21-25, 28, 30, 32-36, 38] and seven compared a multifaceted intervention including a CPW to usual care [14, 20, 26, 27, 29, 31, 37]. Multifaceted pathway interventions were combined with case management elements [20, 26, 27, 29, 31] or with complex quality improvement programs [14, 31]. Five studies were assessed as at low risk of bias with the remaining 22 rated as moderate. Table 1 presents a summary of the quality assessment.

Effects of pathway interventions

Comparison 1: Single CPW intervention vs. usual care.

In-hospital complications were measured in five invasive pathway studies and all reported improved outcomes for the CPW group [16, 18, 25, 30, 35]. The invasive CPW conditions included were TURP [30], femoral neck fracture [35], laparotomy and intestinal resection [25], gastrectomy [18] and mechanical ventilation. The combined odds ratio (OR) for in-hospital complications was 0.58 (95% CI 0.36, 0.94) in favour of invasive CPWs and statistically significant. The effect of CPWs on in-hospital complications in the individual studies are depicted together with the

pooled OR in Figure 1. Statistical heterogeneity was not present among the studies, indicating reliable pooled (in-hospital complications) results. There was clinical variance in the range of follow-up periods that were used as well as varying definitions of the term (in-hospital) complications. The in-hospital complications included in the primary studies were post-operative infections, thrombosis, bleeding and pneumonia.

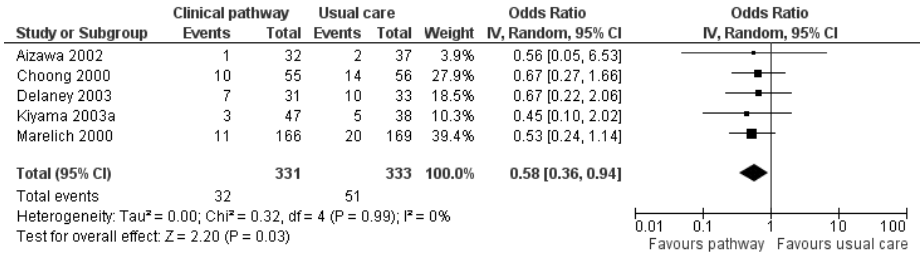

Figure 1: Stand-alone clinical pathway vs. usual care, outcome: OR in-hospital complications. Source: Review-Manager

Six measures were comparable in terms of hospital readmission reported for all causes and characterized with follow-up periods up to six months [13, 22, 24, 25, 30, 35]. 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 OR for readmission was 0.6 (95% CI 0.32, to 1.13) in favour of clinical pathways but was not statistically significant.

Within the subgroup of single pathway interventions, three studies were clinically and statistically comparable and reported in-hospital mortality rates. The pooled OR for in-hospital mortality was 0.84 (95% CI: 0.61 to 1.11) in favour of CPWs but did not reach a statistically significant level.

Three studies measured the impact of CPWs on quality and quantity of documentation in medical records and two reported positive findings [12, 38, 39]. Doherty (2006) reported on the documentation of severity of asthma and Sulch (2002) measured the documentation of team goals for stroke patients. Tilden (1987) measured documented identification of female victims of domestic violence in the emergency department and found no statistically significant change when time series analysis was utilized. The studies by Doherty (2006) and Sulch (2002) were clinically and statistically comparable, resulting in a substantial and significant result (OR 11.95: 95%CI 4.72 to 30.30, see Figure 2) favouring improved documentation with CPWs.

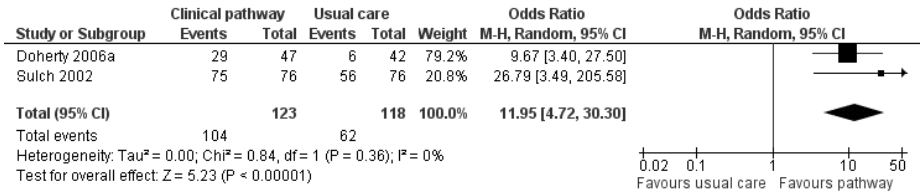

Figure 2: Stand-alone clinical pathway vs. usual care, outcome: OR professional documentation. Source: Review-Manager

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, 14 (70%) primary studies examined the effect of CPWs on LOS [11, 13, 15, 18, 19, 21-25, 28, 30, 34-36], with 11 showing significant reductions [13, 15, 18, 19, 21, 22, 24, 28, 30, 35, 36]. The LOS reported by Kiyama (2003) was calculated from the day of surgery to the day of discharge [18]. All other studies included in this analysis considered the total LOS from admission to discharge. Heterogeneity within this subgroup analysis of studies reporting on LOS was substantial (I = 62%) and the estimation of a pooled effect was not appropriate.

Subgroup analysis

Primary studies were ordered in forest plots by country to examine possible different market effects. We observed greater reported LOS effects from Japanese studies with a pooled reduction of approximately three days weighted mean difference (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.

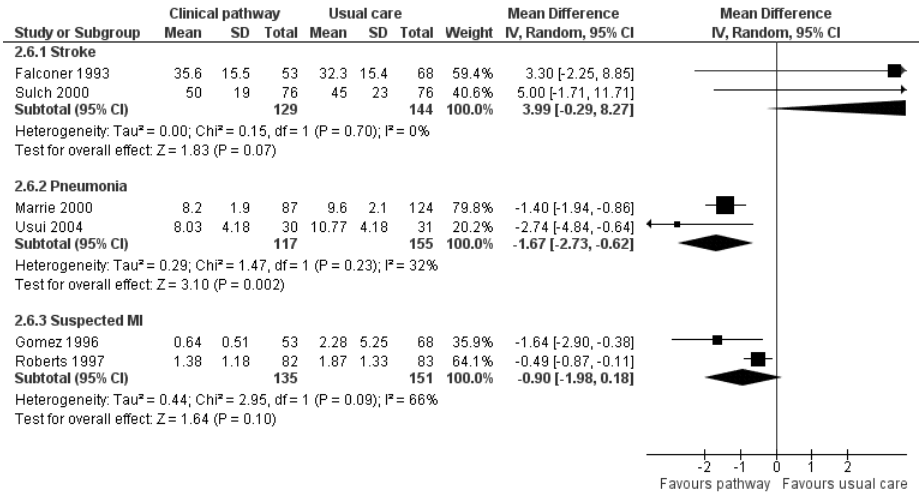

Figure 3: Stand-alone clinical pathway vs. usual care, outcome: LOS grouped by CPW condition. Source: Review-Manager

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 [11, 12, 23], pneumonia [15, 36], suspected myocardial infarction [13, 22] and mechanical ventilation [17, 28]. Further conditions within this subgroup of single pathway interventions were transurethral resection of the prostate [30], menorrhagia and urinary incontinency [32], femoral neck fracture [35], laparotomy and intestinal resection [25], asthma care [33], hip and knee arthroplasty [24], asthma in children [21], atrial fibrillation [19], gastrectomy [18], chronic obstructive pulmonary disease or COPD [34] and a pathway instrument designed for the better identification of female victims of domestic violence [38]. Significant clinical and statistical heterogeneity prevented the estimation of an overall pooled effect where studies were grouped according to condition. Therefore we concentrated on sub-group analysis per pathway condition without a total estimate, please see Figure 3. Falconer (1993) and Sulch (2000) both reported non-significant increased LOS associated with CPWs in stroke rehabilitation units (see Figure 3). The combined OR 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 ($p < 0.001$).

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). 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 was 1.67 days (95% CI -2.73, -0.62) less and intravenous antibiotic duration was 1.70 days less (95% CI -2.01, -1.40) in the CPW group. Gomez (1996) and Roberts (1997) both reported decreases in LOS for CPWs implemented in emergency departments for suspected myocardial infarction (see figure 3). The combined LOS for the Gomez (1996) and Roberts' (1997) studies was WMD -0.90 days (95% CI -1.98, 0.18) but did not reach statistical significance. 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%).

Three studies [16, 17, 28] reported similar reductions in the total time patients required mechanical ventilation in ICU when a CPW was implemented. The combined WMD for the Brook (1999) and Kollef (1997) studies was -33.72 hours (95% CI -55.73 to -11.71)(see Figure 4). Marelich (2000) also 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). The different reporting of Marelich's data prevented this study being combined in meta-analysis with other mechanical ventilation studies [16]. However, the findings of Marelich's study were consistent with the findings from the other studies measuring the impact of CPWs on mechanical ventilation.

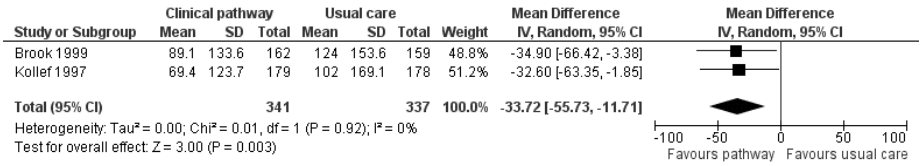

Figure 4: Stand-alone clinical pathway vs. usual care, outcome: duration of mechanical ventilation. Source: Review-Manager

Out of 20 primary investigations grouped as single pathway interventions, eight 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 [13, 18, 21, 22, 30, 36]. 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. Please see Table 2 for a detailed description of the costing methods used and cost measures included in the primary evaluations. Furthermore, hospital costs and charges are presented in the full version of the EPOC review in tabular form as reported in the primary evaluations and adjusted to $US dollars standardized to the year 2000 [6].

Table 2: Overview of costing methods used and costs measures included in the primary studies

Study ID	Costs measure	Country	Costing methode	Costs included	Costs 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 fees)	Fixed costs
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

Comparison 2: Multifaceted intervention including a CPW versus usual care

Of the seven primary studies categorized as multifaceted interventions including a CPW element, three studies [14, 20, 27] measured the impact of a CPW on rate of hospital re-admission and two studies used mortality as a study endpoint and reported no statistically significant difference following implementation of the CPW [14, 26]. Three investigations reported LOS measures for statistical comparison [14, 20, 26] and no significant between group differences were seen. Three studies reported on hospital costs / charges [14, 20, 29]. None of these three studies reported statistically significant differences in costs / charges outcomes.

In summary, multifaceted interventions did not differ from usual care for mortality, length of hospital stay or hospital costs/ charges. One (n = 65) out of 3 randomized studies found that multifaceted interventions reduced hospital readmissions more than usual care, but only a very small sample size was available for analysis and the study was underpowered [20]. The study by Kampan (2006) reported in particular a significant reduction in six month readmissions for hypoglycaemia in patients with diabetes (6% versus 34%; p = 0.04).

Subgroup analysis

Seven separate conditions were analyzed in this group and subgroup analysis was not possible. The different pathway indications were bipolar disorder [29], palliative care [31], mechanical ventilation [37], asthma in children [27], delirium in older medical patients [26], diabetic patients admitted with hypoglycaemia [20] and heart failure [14].

4.2.5 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 world-wide. The breadth of the review also introduced a degree of clinical and statistical heterogeneity that made 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.

A major finding was the significant reduction in in-hospital complications associated with the introduction of CPWs. All seven studies [16, 18, 24, 25, 30, 31, 35] 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 CPW corresponds to prevention of one complication for every 18 patients treated (NNT = 18). This strongly suggests that CPWs have a substantial role to play in patient safety.

Documentation appears to improve with the implementation of a CPW. 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. 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 [40].

Multiple studies measured the impact of CPWs on pneumonia [15, 36], myocardial infarction [13, 22] and mechanical ventilation[16, 17, 28, 37]. 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.

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 [11, 12, 23]. 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 organized multidisciplinary care [41]. 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 optimizing stroke management without the introduction of a CPW.

Despite being utilized in healthcare since the 1980s, no clear definition for CPWs has been widely accepted. Subsequently, minimum content criteria were developed for this review based on previous attempts to empirically describe CPWs and pilot tested for reliability. This approach maximized 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 CPW is adopted in order for current literature to be easily and widely accessed and compared.

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 and 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. Poor reporting was also 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 randomized 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 relatively few resources. Our screening and appraising of studies indicate that a large amount of resources are being used on studies that do not contribute to the evidence base regarding CPWs because of their low study design quality.

Studies were ordered in forest plots by country and major 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. As an example, it could be highly difficult 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 [42] indicate also a country-specific estimate for the potential LOS impact of CPW strategies and are evidenced by the observed LOS patterns from the present review if grouped or sorted by country. LOS in hospital as 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.

While the design and content of a CPW were recognized as important, it was not possible to assess these aspects as the CPW document was rarely provided in the

journal article. Future evaluations should therefore follow the SQUIRE guidelines to increase the standard of reporting on design, content and implementation criteria. Moreover, design and content attributes of successful CPWs require further exploration for which document review could be incorporated to elicit characteristics associated with CPW effectiveness.

4.2.6 Implications for practice

This review has established that CPWs are 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 [35], intestinal resection [25], gastrectomy , mechanical ventilation [16], transurethral resection of the prostate [30] and hip or knee arthroplasty [24].

4.2.7 Implications for research

Studies measuring the impact of CPWs should incorporate EPOC standards into design to maximize the quality of evidence underpinning this model that is being utilized in a vast array of healthcare settings. 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 reviews should focus on grouping and comparing within pathway conditions, for example, CPWs for pneumonia. This strategy is highly supported by the low level of heterogeneity observed by grouping per condition.

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CHAPTER 5

The quality of the evidence base for clinical pathway effectiveness: room for improvement in the design of evaluation trials

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5.1 Background

What are clinical pathways?

Clinical pathways (CPWs) are evidence-based multidisciplinary care plans which describe the essential steps needed in the care of patients with a specific clinical problem. They are used to translate clinical guidelines into local protocols and clinical practice [1]. Whereas clinical guidelines provide generic recommendations, CPWs are specifically tailored to the local hospital structures, systems and time-frames used. Clinical pathways have been proposed as a strategy to optimise resource allocation in a climate of increasing healthcare costs [2]. Other terms used to describe clinical pathways include 'integrated care pathways,' 'critical pathways,' 'care plans,' 'care paths' and 'care maps.'

Objectives

The first objective of this article is to report on the methodological quality of the existing evidence base regarding the effectiveness of CPW research in the hospital setting. An international, multidisciplinary team of researchers conducted a systematic review of the effectiveness of CPWs in hospitals, with the findings recently published in the Cochrane library [3]. The second objective is to test the hypothesis that simple pre-post studies tend to overestimate CPW effects reported.

5.2 Method

We followed the validated Cochrane Effective Practice and Organisation of Care Group (EPOC) methodology for considering and analyzing studies [4]. The primary systematic review aimed to catalogue the international evidence to assess the effect of clinical pathways on professional practice, patient outcomes, length of hospital stay and hospital costs. We searched the Database of Abstracts of Reviews of Effectiveness, the Effective Practice and Organisation of Care Register, the Cochrane Central Register of Controlled Trials and bibliographic databases including MEDLINE, EMBASE, CINAHL, NHS EED and Global Health. Details of the electronic search strategy for the identification of studies are presented in detail in the EPOC review, recently published in the Cochrane Library [3]. Our team developed and validated five minimum criteria to define a CPW to ensure that only appropriate studies were sourced and included in the review [5]. An integral component of the review process was a rigorous appraisal of the study designs and methodological quality of all

relevant CPW evaluations. This allowed the identification of strengths and limitations of the evidence base for CPW effectiveness with regard to the first study objective.

Assessment of study design

For the purpose of the systematic review on CPWs in hospitals, four study designs were considered for inclusion: randomized controlled trials (RCTs), controlled clinical trials (CCTs), controlled before and after studies (CBAs) and interrupted time series analysis (ITS).

While there are many well developed and well accepted critical appraisal criteria for experimental studies, fewer exist for non-experimental studies such as CBAs and ITS. Both designs are subject to a lack of control and high risk of bias so EPOC developed criteria to facilitate their quality assessment and inclusion (where appropriate) in systematic reviews. For example, CBAs are required to have more than one control group and ITS require at least three time points before and after an intervention. Validated criteria for the assessment of these designs have been developed by EPOC and are available from the EPOC website [6] and the four different study designs are briefly outlined in table 1. In addition, the simplified EPOC gold standard of study designs considered for inclusion in the present review are depicted in figure 1 [4].

Table 1: EPOC study designs considered for inclusion

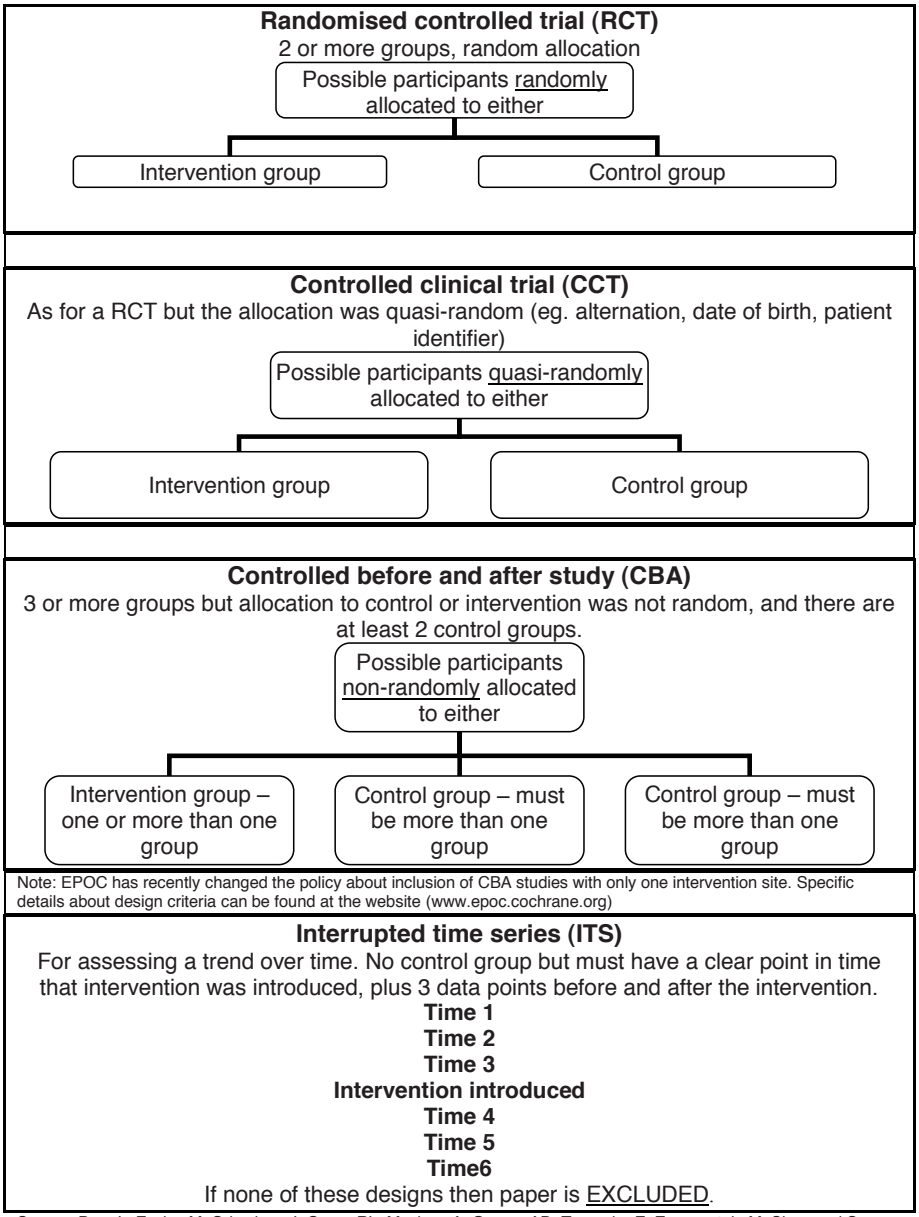
Patient randomized controlled trials (P-RCT):	The individual patients are allocated by random to the intervention or control group. Individual randomization facilitates equally distributed patient characteristics and comparability. Only the exposure to the intervention should be the factor that distinguishes between both groups.
Cluster randomized controlled trials (C-RCT):	This is a robust study design that prevents contamination of professionals by randomizing groups of professionals (i.e. different practices, wards or hospitals). However, this means the fundamental assumption of independence is violated because patients within a cluster are more likely to respond in a similar manner. This lack of independence, statistically called “intracluster correlation,” also means a specific adjustment for clustering effects is required to

	assure comparability with individually randomized trials.
Non-randomized controlled trials (CCTs):	Patient or cluster trials where allocation to experimental and control groups is quasi-random (i.e. alternated allocation).
Controlled before and after studies (CBAs):	CBAs are experimental studies with two or more control groups compared with one or more experimental groups but allocation is not random. 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. The reliability of the intervention effect is questionable because there may be unidentified differences between the experimental intervention and control groups which may have modified the observed effect. Note: EPOC has recently changed the policy about inclusion of CBA studies with only one intervention site. Specific details about design criteria can be found at the website (www.epoc.cochrane.org)
Interrupted time series designs (ITS):	This represents a robust method of measuring the effect of an intervention as a trend over time. It is a useful design when recruitment of a control cohort is impractical, e.g. due to changes in hospital policy. Three or more data points are collected before and after the intervention as a minimum standard. The intervention effect is measured against the pre-intervention trend.

Source: Bero L, Eccles M, Grimshaw J, Gruen RL, Mayhew A, Oxman AD, Tavender E, Zwarenstein M, Shepperd S, Paulsen E, Pantoja T, Lewin S, Ballini L. Cochrane Effective Practice and Organisation of Care Group (Cochrane Group Module). *About The Cochrane* Collaboration (Cochrane Review Groups (CRGs)). The Cochrane Library. Oxford: John Wiley, 2009; adapted by the authors

Risk of bias assessment

We developed a quality assessment and data abstraction instrument incorporating the EPOC risk of bias criteria [4]. Quality assessment was conducted on full-text articles once initial literature searching and screening indicated that articles were research-based and referred to a CPW and were, subsequently, potentially relevant. The EPOC approach for judging risk of bias of randomized and non-randomized studies is a two-part assessment tool, concerning specific domains and quality criteria (i.e. RCTs: sequence generation, allocation concealment, blinding, et cetera). The validated risk of bias criteria can be found in the Cochrane EPOC Group module [4].



Source: Bero L, Eccles M, Grimshaw J, Gruen RL, Mayhew A, Oxman AD, Tavender E, Zwarenstein M, Shepperd S, Paulsen E, Pantoja T, Lewin S, Ballini L. Cochrane Effective Practice and Organisation of Care Group (Cochrane Group Module). *About The Cochrane* Collaboration (Cochrane Review Groups (CRGs)). The Cochrane Library. Oxford: John Wiley, 2009; adopted by the authors

Figure 1: Simplified EPOC standard of study designs considered for inclusion in the present review

Comparison of CPW interventions

We compared patients managed according to CPW to those managed by usual care, and patients treated within a multifaceted intervention including a CPW compared to usual care.

Secondary analysis

The aim of the secondary analysis was to determine whether pre-post study design was associated with an overestimate of the effects of CPW. Other researchers also compared the findings of randomized evaluations vs. non-randomized study designs and concluded that such studies potentially overestimate the effects reported and there were systematic differences between effects estimated [7-9]. To test the hypothesis, we compared 14 primary studies [10-23], included in the Cochrane review, grouped into category 1 (patients managed according to CPW compared to usual care), and reporting on length of stay (LOS) as the most commonly employed outcome measure with a randomly selected sample of 14 excluded pre-post CPW evaluations also reporting LOS [24-37]. The selection of a random sample of studies was taken from those studies excluded on the basis of a simple pre-post design not meeting EPOC quality criteria (see table 2). We used a computer generated random sample (RAND function in Excel) [38] of 14 excluded pre-post studies reporting LOS as a primary study outcome [24-37].

Table 2 Reasons for exclusion stage one (n = 2954)

Reason	Number	%
Not CPW	2335	79.1
Not study	253	8.6
Not hospital	246	8.3
EPOC minimum study design criteria not met	89	3.0
Other (e.g. qualitative study)	31	1.0
Total	2954	100

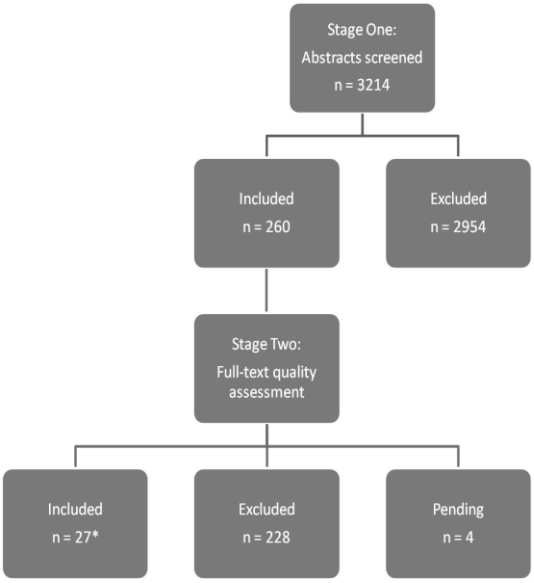
Statistical pooling (meta-analysis)

A Cochrane web-based program, Review Manager (RevMan), was used to calculate a pooled estimate of the combined intervention effect on LOS, called weighted mean difference (WMD) [39]. We used a random effects model since this model estimates the effect with consideration to the variance between studies, rather

than ignoring heterogeneity by employing a fixed effect model [40]. Statistical inconsistency within both subgroups was assessed by calculating a test of heterogeneity (I square (I^2)).

5.3 Results

All potentially relevant studies were assessed using the CPW definition [5] and EPOC review inclusion criteria for acceptable study designs [4]. Using two independent reviewers, we rejected 2954 of the 3214 potential papers and only 260 primary studies were initially identified as potentially relevant and full text copies were retrieved. Fig. 2 illustrates the described trial flow.



*NB: The results of one study were reported across two publications (Sulch 2000 & 2002).

Figure 2 Trial flow

The majority (79.1%) of the rejected studies (2335 out of 2954) had to be excluded because they failed to meet our definition of CPW. Table 2 illustrates the reasons for exclusion following title and abstract review. Out of the 260 primary studies meeting CPW content criteria following review of the full text, only 27 studies met the EPOC study design and risk of bias criteria.

Assessment of study design

Out of 27 CPW evaluations included, nineteen of the included studies were randomised controlled trials (RCTs) [10, 11, 13-22, 41-48], including two cluster randomised trials (C-RCT) [20, 47]. Four studies were CBAs [49-52], two were CCTs [12, 23] and two ITS [53, 54].

Of the original studies which met the CPW content criteria, more than 70% were excluded from the review as they were simple pre-post evaluations, mostly comparing two or more yearly patient cohorts (see Table 3).

Risk of bias assessment

Out of the 228 studies excluded in phase two following full text review (see Table 3) only four non-randomized studies [55-58] and one randomised clinical study (RCT) [59] were excluded because of high risk of bias. The RCT from Bittinger (1995) did not meet EPOC quality criteria as only 50% of study patients were followed up after randomization and there was a high risk of attrition bias. Four time series studies were excluded as data was not analyzed appropriately. The studies from Joiner (1996), Smith (1999), Summers (1998) and Warner (2002) had a high risk of bias because no statistical control was used [55-58].

Table 3 illustrates the reasons for exclusion in stage two after meeting CPW content criteria in stage one.

Table 3 Reasons for exclusion following full text review (n = 228)

Reason	Number	%
Not CPW	38	16.7
Simple pre-/post evaluations	160	70.2
High risk of bias	5 (1RCT)	2.2
Not study	14	6.1
Not hospital	11	4.8
Total	228	100

Secondary analysis

In figure 3 we provide the detailed results of the methodological comparison of the 14 included primary studies which utilised Cochrane EPOC study design quality

criteria [4] and reporting on LOS [10-23] vs. 14 randomly selected pre-post studies excluded from the review and reporting on LOS as a primary outcome [24-37]. We observed considerable statistical inconsistency within both subgroups of CPW studies, so the calculated estimates in LOS per subgroup should be treated with caution (I^2 = 62% Cochrane EPOC subgroup vs. 98% randomly selected subgroup.)

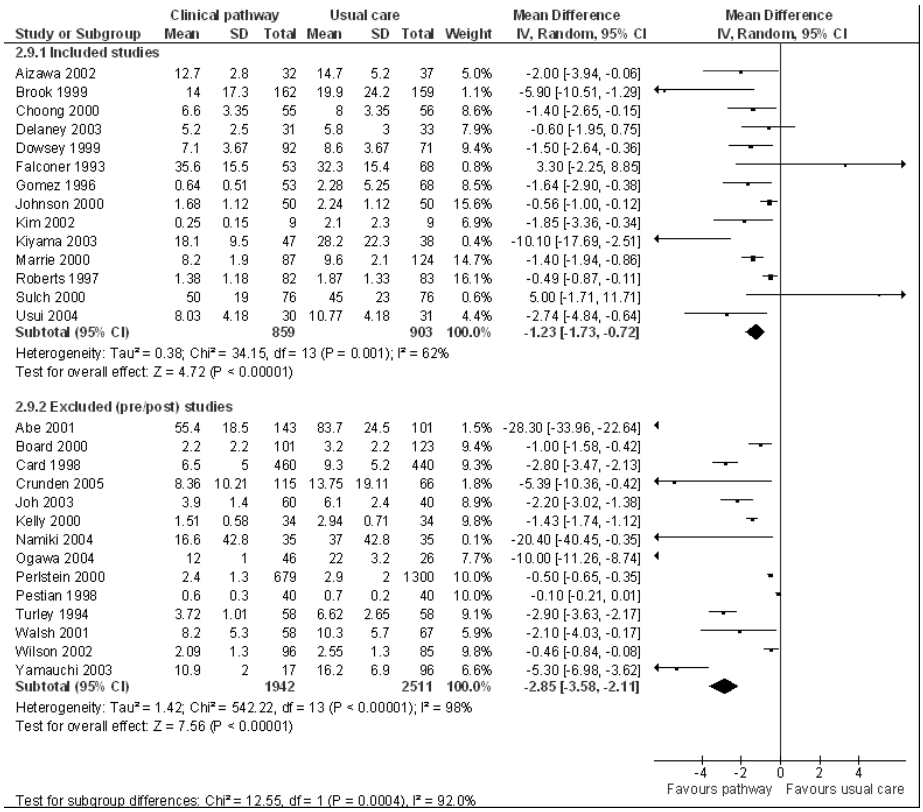


Figure 3 Comparison meta analysis LOS COCHRANE vs. Excluded pre-post studies

We observed greater reported LOS effects within the random subgroup of excluded pre-post studies after meeting CPW content criteria (WMD – 2.85 (95%CI: – 3.58 to – 2.11)), versus the pooled LOS data recently published in the Cochrane library (group 1 clinical pathway vs. usual care WMD – 1.23 (95%CI – 1.73 to – 0.72)) [3]. Moreover, the pre-post studies in the randomly selected subgroup tend to report more consistently on significant reductions in LOS (see figure 3). Statistically, the chi-squared test for subgroup differences also reached a significant level (P= 0.0004).

5.4 Discussion

Why is it important to critically appraise study designs in a systematic review?

We followed the validated Cochrane EPOC criteria for randomized and non-randomized CPW evaluations [4, 6]. The finding that the vast majority of studies failed to meet methodological quality criteria strongly indicates that low quality study designs are too often used to evaluate CPWs and contribute very little to the evidence base regarding CPWs.

Many of such excluded CPW evaluations claimed to provide evidence for the effectiveness of the pathway intervention under consideration but, with a methodologically weak study design, it remains unclear if the reported effect was really attributable to the CPW effectiveness or any other unknown factors. Possible confounding factors might have been the case-mix introduction, hospital quality improvement initiatives or changes in hospital policy [2]. The uncontrolled nature and exposure to bias convey that such studies contribute very little to the evidence-base.

Implications of including weak study designs

Based on our review experience, we reaffirm that uncontrolled pre-post designs are commonly used to evaluate the effectiveness of CPWs. Such designs are likely to be misleading and contribute little to understanding the reported effects of pathways. Considering the second objective of this article, the meta-analytic comparison supports other evidence [7-9] that simple pre-post study designs tend to overestimate intervention effects reported.

There is a place for well designed process-evaluations also referred to as interrupted time series (ITS) to explore and provide more insights into the varying pathway components and their causal effectiveness to determine how CPW interventions actually work. Carefully designed time series studies are less resource-intensive than RCTs, do not require a control group, and allow for the use of retrospective data. While requiring more advanced statistical techniques than simple pre-post studies, ITS supports research outcomes that are more likely to contribute to the evidence base, including systematic reviews. Better designed, conducted and reported CPW evaluations will contribute to a better understanding of the key elements of CPWs that impact on patient, provider and economic outcomes.

Limitations

The majority of included studies employed LOS as a performance measure. Hence, we compared the magnitudes of CPW effects on length of stay (n= 14 primary studies) rather than patient outcomes such as mortality (n=4 studies) or in-hospital complications (n=5 studies) [3]. The low number of primary CPW evaluations included in the review which reported on patient outcomes prevented further testing of the robustness of this methodological comparison.

5.5 Conclusion

Cochrane EPOC methodological inclusion criteria should be considered for quantitative evaluations into the impact of CPWs in hospitals. Based on our review experience, the EPOC methodological gold standard is infrequently transferred into research practice. Future evaluators could hereby contribute significantly to the understanding of factors associated with the reported effects of clinical pathways in hospitals by incorporating EPOC criteria into study design. Whilst experimental methods such as randomized trials are recommended they may be considered beyond the capacity of many clinicians and researchers. A well designed evaluation such as ITS or CBA that meets the EPOC gold standard methodological criteria can produce meaningful, rigorous results with the use of relatively few resources. In terms of the second study objective, the methodological comparison of Cochrane vs. non Cochrane study designs (see figure 3) also support the finding that simple pre-post study designs tend to overestimate CPW effects reported.

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CHAPTER 6

Do clinical pathways enhance access to evidence-based AMI treatment in rural emergency departments?

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Do clinical pathways enhance access to evidence-based AMI treatment in rural emergency departments?

6.1 Background

Clinical pathways (CPWs) are a strategy promoted as supporting evidence-based practice and the optimization of clinical efficiency by providing locally oriented guidance for the management of specific conditions [1]. CPWs have been used extensively in hospitals since the 1980s and more than 80% of hospitals in the USA use CPWs [2]. Intuitively, they should support the quality, safety and efficiency of healthcare. However, single studies into the impact of CPWs in hospitals have produced contradictory results for both economic [3-11] and patient outcomes [12-16]. These disparities may be explained by many factors, including assorted study designs or quality, divergent clinical settings, differences in compliance with CPWs and confusion around what a CPW is [17-19].

A wide-ranging Cochrane systematic review [1] concluded that CPWs were associated with reduced in-hospital complications and improved documentation. Additionally, it was found that a large majority of studies used methods that had an unacceptably high risk of bias (e.g. simple before and after design) and could not be generalized or included in a systematic review. Cluster randomized controlled trials were recommended for investigating the effect of complex interventions such as CPWs. The reviewers also sought to identify CPW characteristics that were associated with user compliance and successful outcomes [20], but stated that implementation strategies were too poorly reported to determine key characteristics. Only one included study [21] was conducted in a rural setting, making it difficult to interpret the review's findings into rural health service context.

The emergency treatment of acute myocardial infarction (AMI) in rural emergency departments is one area where there is much to be gained by reducing the evidence-practice gap. AMI is the leading cause of sudden death in the Australian

population accounting for one in ten deaths [22, 23]. People living in rural Australia are less likely to survive an AMI than people in major cities due to time to access emergency care, limited treatment options and a reported failure to receive recommended emergency treatment [24, 25]. This is an area where a well-integrated CPW could have a beneficial impact.

An essential component of rural AMI management is reperfusion therapy via intravenous administration of a thrombolytic agent which improves mortality for patients with an ST-elevation myocardial infarction (STEMI) [26, 27]. Thrombolysis best practice guidelines developed by the National Heart Foundation of Australia (NHFA), the Cardiac Society of Australia and New Zealand (CSANZ) and Australian College of Emergency Medicine (ACEM) come with the recommendation that their guidelines be incorporated into local health service policies [28]. The eligibility criteria for reperfusion therapy are provided in table 1.

Table 1: Eligibility criteria for thrombolysis for STEMI

Patients presenting within 12 hours of onset of ischaemic symptoms. ECG changes: ST elevation ≥ 1mm in two contiguous limb leads ST elevation ≥ 2mm in two contiguous chest leads New left bundle branch block Plus, absence of contraindications.

Key recommendations include performing an electrocardiograph (ECG) within ten minutes of arrival to an emergency department, and administering a thrombolytic drug within 30 minutes (so-called “door-to-needle time”) [28]. Studies have shown varying results in meeting this benchmark with a major USA audit of 62,470 cases indicating that door-to-needle time was within 30 minutes on 47% of occasions [29]

whilst the result was 58% (n = 101) and 24% (n = 140) in two smaller Canadian audits [30, 31]. Mean door-to-needle times of 64 and 58 minutes have been reported in rural and metropolitan settings [24, 31].

Studies of compliance with thrombolytic guidelines by measuring the proportion of those that meet criteria (including absence of contraindications) and receive a thrombolytic agent have been widely reported. A nationwide USA review indicated that 33% of eligible patients miss out on recommended reperfusion therapy [32]. Previous work in rural Australia indicated that 32% of eligible rural AMI patients missed out on delivery of a thrombolytic agent, that delays were common-place and that health professionals did not comply with the contents of CPWs [33]. This reinforced the finding of the Cochrane review that successful implementation processes enhancing clinician ownership and compliance need to be identified, developed and trialed [1].

Proven strategies to improve compliance with guidelines are active and multifaceted but have not been tested in CPWs. Active approaches include a combination of audit and feedback, reminder systems, engaging clinicians and targeted education [34, 35].

6.2 Methods

The aim of this study was to determine whether a five-step multifaceted implementation process of CPWs for STEMIs improved the proportion of eligible patients receiving a thrombolytic drug, and reduced door-to-needle and electrocardiogram times in rural Victorian emergency departments.

Study Design

A cluster RCT was conducted involving six rural hospitals that treat and do not immediately transfer AMI patients. All hospitals offered 24 hour on-site medical cover and each treated between 14,000 and 45,000 ED patients per year. Pairs of hospi-

tals were matched according to the anticipated number of eligible patients and on the basis of geographical separation, in order to minimize the risk of a control hospital being influenced by procedures at an intervention hospital and vice-versa. The distance between matched hospitals ranged from 118 to 452 kilometres. Randomization within pairs to either the intervention (n=3) or control (n=3) groups occurred by a simple coin toss.

Sample size

A 20-minute reduction in time to thrombolytic administration represents a modest improvement based on a previous local study reporting mean door-to-needle time of 70 minutes [24]. A post-intervention sample size of 90 patients was required to detect a 20-minute reduction in thrombolytic delivery time (significance level of 5%, power of 0.8, and intra-cluster correlation coefficient of 0.283) [36]. Available ED data indicated 15 eligible patients per month and that sample size should be reached in six months, so we conservatively planned for nine months pre and nine months post intervention data collection [24].

Intervention

The three intervention hospitals participated in the five-step implementation process described below. This process was a combination of evidence-based proposals by Doherty and Jones [37] and Kinsman et al. [24]. In brief, the three month implementation process entailed:

1. Engaging clinicians

   A senior clinician was recruited as a Research Assistant (RA) at each intervention site and facilitated discussions in ED to identify barriers to CPW implementation.

2. Clinical pathway development

Hospital-specific CPWs were based on NHFA guidelines and developed by RAs in collaboration with clinicians at each emergency department.

3. Reminders

Reminder visits by the first author occurred following implementation to liaise with clinical staff. RAs consistently reminded medical and nursing staff about the CPW.

4. Education

The RA and first author facilitated education sessions during implementation to review evidence underpinning the clinical pathway.

5. Audit and feedback

Performance results were communicated to emergency department clinicians once during the implementation project.

Data Collection

AMI medical records were identified by an International Classification of Diseases (ICD 10) report and audited using a specifically-designed data protocol. Initial data included type of infarct, gender and age. Electrocardiograms (ECGs) and clinical notes were checked against NHFA criteria for thrombolytic delivery (see table 1). ECGs were initially interpreted by a nurse educator who teaches ECG interpretation, then double-checked by a senior ED physician. A co-investigator reviewed 10% of the medical records to confirm accuracy of data extraction. Minor discrepancies were corrected and re-checked throughout the dataset. There was 100% agreement on ECG interpretation. Data collectors were not blinded to allocation of the service to intervention or control.

Baseline data were collected from February 1 to October 31 2008, whilst post-intervention data were collected between April 1 and December 31 2009. The implementation process for the intervention hospitals was carried out between November 2008 and March 2009.

Data Analysis

Use of thrombolytic drugs was categorized as yes/no for each eligible patient, and differences within and between intervention and control groups were compared at baseline and follow-up using a standard Chi-squared test. A Mann-Whitney U test was used to compare median door-to-needle and ECG times between and within intervention and control groups at baseline and follow-up. An independent sample t-test was used to compare mean time to thrombolytic delivery and ECG between and within intervention and control groups at baseline and follow-up. Chi-square analysis was used to compare proportions being administered a thrombolytic within 30 minutes and for proportions receiving an ECG within ten minutes. ANOVA and independent sample t-tests were used to assess demographic differences between and within intervention and control groups at baseline and follow-up. Results were compared by group (intervention or control) and matched samples.

Ethics approval was obtained from Monash University and relevant hospital committees. The ANZCTR code is 12608000209392.

6.3 Results

Sample

Overall, 915 medical records were audited across the six hospitals. Application of inclusion criteria produced a final sample of 108 (see Figure 1).

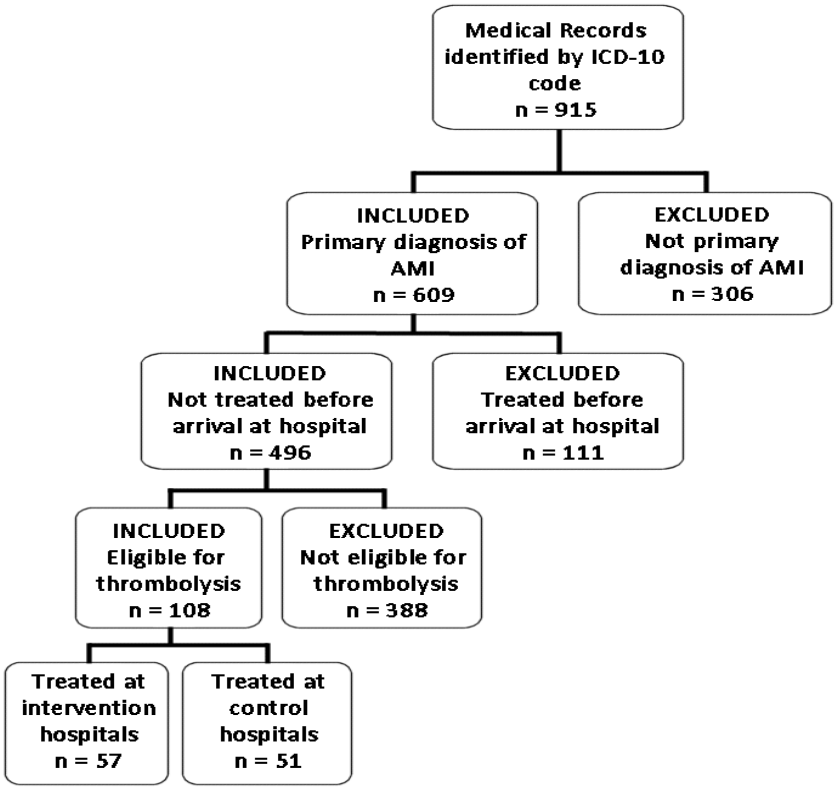

Figure 1: Derivation of final sample

The mean age of the sample was 62.7 (SD 12.8) years, 81% (87/108) were male and 61% (66/108) were diagnosed with an inferior AMI. All Design Effect measurements were less than one, indicating each cluster was acting independently and that individuals within clusters were acting independently. This substantiated the use of conventional measures to analyze data. There were no significant differences detected between baseline and post-intervention groups and intervention and control groups when compared on age, gender and type of AMI (see Table 2)

Table 2: Participant demographics

Characteristic	Intervention		Control		*P* value
	Baseline n = 25	Postintervention n = 32	Baseline n = 26	Postintervention n = 25	
Male gender	20 (80%)	23 (72%)	21 (81%)	23 (92%)	0.428[a]
Mean age (years) (SD)	63.5 (9.1)	64.7 (15.9)	64.2 (10.5)	57.6 (13.2)	0.450[b]
Type of AMI					
Inferior	16 (64%)	17 (53%)	18 (69%)	15 (60%)	0.730[a]
Anterior	8 (32%)	13 (41%)	8 (31%)	9 (36%)	
Other	1 (4%)	2 (6%)	0	1 (4%)	

[a] P value for the difference between groups calculated using Chi-square.
[b] P value for the difference between groups calculated using one-way ANOVA.

Matched pairs

Reasonably equal numbers of patients were included at matched sites (7 v 9; 37 v 28; 14 v 13). No significant differences between matched sites were found for any measures.

Time to thrombolysis and ECG

There were no statistically significant differences between intervention and control groups on any of the indicators measured at baseline or post-intervention (see Table 3). Overall, 84% (91/108) of those eligible for a thrombolytic drug received that treatment with a median door-to-needle time of 34 minutes and mean door-to-needle time of 43.5 (SD 35.3) minutes. Forty-seven percent received the thrombolytic agent within 30 minutes of arrival at ED. Median arrival to ECG time was six minutes, mean time from arrival to ECG was 8.2 (SD 11.0) minutes and 76% (77/101) of ECGs were taken within ten minutes.

Table 3: Thrombolytic administration and ECG measures: baseline and post intervention

	Intervention				Control			
Variable	Baseline n = 25	Post intervention n = 32	95% Confidence Interval	*p* value	Baseline n = 26	Post intervention n = 25	95% Confidence Interval	*p* value
Thrombolysis								
Percentage eligible and receiving drug	80%	78%		0.863[a]	96%	84%		0.191[a]
Mean door-to-needle time (minutes) (SD)	46.6 (37.7)	47.2 (40.5)	0 to 23.4	0.960[b]	43.8 (33.6)	35.9 (29.6)	0 to 26.9	0.404[b]
Range	12 to 150	7 to 166			1 to 133	12 to132		
Median	39	29		0.226[c]	37	29		0.226[c]
Interquartile range	18.5 to 58.0	16.2 to 65.7			15.5 to 58.5	20.0 to 44.0		
Percentage receiving thrombolytic within 30 mins	40%	37%[d]		0.360[a]	36%	62%		0.072[a]
ECG								
Mean door-to-ECG time (minutes) (SD)	6.4 (7.2)	11.4 (17.1)	0 to 2.8	0.205[b]	7.0 (8.4)	7.4 (4.9)	0 to 3.5	0.817[b]
Range	0 to 28	0 to 80			0 to 41	0 to 23		
Median	4	7		0.313[c]	5	6		0.802[c]
Interquartile range	0 to12.2	1 to 11			0.7 to 10.2	4.7 to 10.0		
Percentage having ECG within 10 mins[e]	73%	72%		0.980[a]	77%	83%		0.571[a]

6.4 Discussion

The five-step process for implementation of CPWs for chest pain appeared to have no impact on the delivery of thrombolytic drugs or time to ECG for AMI in this study. One likely explanation is that the results represent a ceiling effect. The complexities of clinical practice - for example, patients of advanced age or dementia within congested EDs - mean that 100% compliance with thrombolytic criteria is unrealistic and not every patient can receive a thrombolytic within 30 minutes of arrival. In addition, this study's results of overall eligible proportion receiving a thrombolytic (84%) is vastly superior to other published findings (67% [32], 68% [24]) as is the

mean door-to-needle time (43.5 minutes versus 64 mins [24] and 58 mins [31]). It is highly likely that there was no room for statistically significant improvements in either the intervention or control groups.

Moreover, comparison with international findings indicates that quality of care delivered in these rural EDs is at least as good as that delivered in metropolitan settings and that unfavourable mortality rates for rural AMI patients are not explained by lower quality of emergency care. Further investigation of access to services, pre-hospital treatment and in-hospital management is required to understand the relatively high mortality reported in rural Australia.

Another contributing factor is that the trial was underpowered to detect the success or failure of the CPW, evidenced by the high standard of care measures prior to CPW implementation. Final sample size was smaller than anticipated for the trial period as there was a dramatic reduction in proportion of patients eligible for thrombolysis since the previous audit conducted in 2004. The factors contributing to this reduction were that, proportionately, fewer AMI patients met the criteria for thrombolysis, and more patients were administered thrombolytic agents elsewhere (including smaller hospitals) and were not eligible for inclusion in the study.

6.5 Conclusions

Neutral findings always warrant careful exploration [38]. This study clearly illustrates the complexity involved in the evaluation of a complex intervention in rural hospital settings. Given the comprehensive and evidence-based CPW implementation strategy employed, we believe that the limited fidelity of the cluster randomized evaluation in detecting real differences between experimental and control hospitals as well as the high standard of care prior to implementation resulted in a failure to report on significant improvements rather than a failure of the CPW intervention itself.

AMI treatment was provided in an efficient manner by the participating EDs in this study. In an environment of well-coordinated, timely care a CPW is not likely to produce measurable improvements in process measurements, especially when an undersized sample make detection of small or subtle changes improbable. Further investigation of factors contributing to the high AMI mortality for rural Australians is required.

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CHAPTER 7

General discussion and conclusions

7.0 General discussion and conclusions

7.1 Introduction

Systematic reviews, knowledge syntheses and clinical pathways (CPWs) have emerged as rigorous means to translate and make research more accessible for health professionals. However, the gap between available evidence and hospital practice is well documented and the implementation of strategies to address this problem remains a challenge [1-6]. Clinical decisions are often not evidence-based and patients are not involved in the decision-making process. This leads to variations in the care provided and professional variation [7-9] is frequently associated with an increase in in-hospital complications. However, we know very little about potentially effective implementation strategies [10] and local barriers to implementing CPWs.

A clinical pathway is a complex clinical intervention that operationalizes best practices and clinical guidelines in an accessible format and brings evidence to the bedside for all the health professionals involved [11, 12]. CPWs represent a potentially important strategy for effective knowledge translation [13]; they have the capacity to promote safe, evidence-based care in hospitals by providing locally oriented guidance for the management of specific health conditions [14-18]. While CPWs have the potential to link evidence to hospital practice, their true impact has been limited by the lack of a robust, generalizable evidence base on CPW effectiveness [19], poorly reported implementation strategies and sub-optimal research designs.

Therefore, this thesis aimed to test the hypothesis that clinical pathways support evidence-based practice and maximize patient safety and clinical efficiency***. The main question for this thesis is: What are the effects of clinical pathways on professional practice, patient outcomes, length of stay and hospital costs?*** *According to the studies described in the previous chapters (2, 5 and 6), the following sub-questions were addressed:*

(1) "What is a clinical pathway?"

(2) "What is the standard of clinical pathway research in hospitals and is there a need for improvement in the design of evaluation trials?"

(3) "Do clinical pathways enhance access to evidence-based acute myocardial infarction (AMI) treatment in rural emergency departments?"

7.2 Main findings

7.2.1 What is a CPW?

In chapter 2, we focused on the varying terms used to describe CPWs and the development of minimum inclusion criteria to clearly define and identify clinical pathway interventions. A major problem in the protocol stage for the Cochrane review was the development of objective inclusion and exclusion criteria to clearly identify and catalog all available evidence about CPWs used in hospitals.

The first aim of this study was to design a sensitive electronic search strategy in order to select all relevant CPW investigations. The second aim was to develop objective content criteria to clearly describe a clinical pathway despite the varying terms used in the literature. Subsequently, an inclusive electronic search strategy with a high sensitivity had to be developed and pilot tested to include all possible terms used in the field of clinical pathway research in hospitals. The search filter was developed and pilot tested by the authors of the review and validated by the EPOC search coordinator to assure a comprehensive and robust search. This work has contributed to a high quality evidence base on CPW effectiveness but the low specificity of the electronic search filter was a challenge. The Cochrane EPOC search filter for CPWs in hospitals is depicted in table 1.

TABLE 1: Electronic search strategy for Medline

Database: Ovid MEDLINE(R) <1950 to April Week 4 2008> Search Strategy:	
1	Critical Pathways/
2	((clinical or critical or care) adj path$).tw.
3	(care adj (map$ or plan$)).tw.
4	exp Guidelines/
5	Health Planning Guidelines/
6	Guideline Adherence/
7	(compliance adj (protocol? or policy or guideline?)).tw.
8	(guideline? adj2 (introduc$ 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$).tw.
12	Guideline.pt.
13	or/1-12
14	exp Hospitalization/
15	(in-patient or hospitali?ed or hospitali?ation or acutely ill patient?).tw.
16	exp Outpatient Clinics, Hospital/
17	in-hospital.tw.
18	exp Hospital Units/
19	(patient adj (admission or readmission or readmission or discharge)).tw.
20	exp Emergency Service, Hospital/
21	or/14-20
22	13 and 21
23	randomized controlled trial.pt.
24	random$.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
Legend: and/or/not = Boolean operators tw = (free) text words / = explode function (exp) using MeSH terms pt = search syntax for RCTs in Medline via Ovid $; ? = truncation symbols in Ovid adj2 = searching for adjacent terms in Ovid (an additional number is indicating the maximum number of words between adjacent terms	

Source: Rotter T, Kinsman L, James E et al.: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs. Cochrane Database Syst Rev 2010:CD006632, amended by the author

Development of CPW content criteria

The second aim of this study was to develop objective content criteria to clearly describe a clinical pathway despite confusion about what constitutes a clinical pathway and the varying terms used in the literature [12]. A key issue in the protocol stage of the systematic review was to standardize minimum inclusion criteria for clinical pathway interventions. A recent literature review identified 84 different terms that have been used to describe a CPW, including care map, integrated care pathway, check list, and protocol [20]. It was necessary to identify, synthesize, and generate reproducible inclusion criteria to reach consensus between reviewers about decisions on including and excluding potentially relevant CPW interventions.

Method

The four stage process comprised (1) the identification of relevant CPW characteristics in terms of scope and objectivity; (2) a synthesis of the draft CPW criteria; (3) a pilot test of the criteria; and (4) final amendments of the CPW content criteria to maximize agreement between the reviewers [12]. The following five criteria were derived from the literature:

1. The intervention was based on a structured multidisciplinary care plan
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 (i.e. steps were taken if designated criteria were met)
5. The intervention had time-frames or criteria-based progression (i.e. steps were taken if designated criteria were met)

Three blinded reviewers assessed 10 possibly relevant CPW studies until a 100% agreement was reached. For the aim of the systematic review, an intervention was defined as a clinical pathway if it met the first multidisciplinary criteria and any three of the remaining four criteria [12].

Results and context
Many of the primary studies which finally met our standardized definition and were included in the review were not described as clinical pathways although many other terms were used in the literature such as check list, critical pathway or protocol. Other reviews in the field of clinical pathway research in hospitals did not attempt to develop standardized CPW content criteria and this may have biased their conclusions [21-25]. This work contributes to a better understanding about clinical pathways and paved the way towards an objective and internationally agreed CPW terminology

7.2.2 Do clinical pathways support evidence-based practice and maximize patient safety and clinical efficiency?

Pilot search.
In chapter 3 we determined the scope of the systematic review question on a pilot search of existing primary CPW studies. We included only randomized controlled trials (RCT) and controlled clinical trials (CCT) in the searches. The pilot study revealed a relatively small number of high quality studies used to evaluate the success or failure of a CPW intervention and the pilot analysis also indicated a low standard of CPW research in hospitals. As a direct result, we decided to expand the Cochrane review to include less restrictive study designs in addition to randomized and quasi-randomized trials in order to provide a comprehensive evidence base.

The Cochrane systematic review in chapter 4 describes the experience of conducting and reporting the effects of CPWs in hospitals. The review has a broad scope and outcomes reported were in-hospital complications, in-hospital mortality, hospital readmission, length of stay, and hospital costs [19]. Out of the 3214 studies identified, twenty-seven studies involving 11,398 participants met the Effective Practice and Organisation of Care (EPOC) eligibility and study quality criteria for inclusion. Twenty studies compared clinical pathways with usual care and seven studies compared clinical pathways as part of a multifaceted intervention with usual care. 19 RCTs and 8 non-RCTs met the selection criteria and many different hospital settings are included in the systematic review. This contributed to a high level of clinical and statistical heterogeneity so length of stay (LOS) and hospital cost data were not suitable for pooling due to the high variability (I square) among those studies.

Main results and context
Table 2 depicts the main results of the statistical pooling (meta-analysis) of primary studies, which compared CPWs that guide patient management with usual care.

Table 2: Main results

Outcomes	Number of studies (patients)	Event rates CPW vs usual care (%)	Odds Ratio for CPW vs usual care (95% confidence interval)	Number needed to treat (95% confidence interval)
In-hospital complications	5 (664)	9,3% vs 15%	0.58 (0.36 to 0.94)	18 (12 to 130)
In-hospital mortality at 26 weeks	3 (1187)	22% vs 25%	0.84 (0.64 to 1.11)	NS
Hospital readmission	6 (672)	5.5% vs 8.5%	0.6 (0.32 to 1.13)	NS
Professional documentation	2 (240)	84% vs 52%	11.95 (4.72 to 30.3	NA
*NS = not significant, NNT and CI calculated from review data				

Source: Rotter T, Kinsman L, James E, Machotta A, Gothe H, Willis J, Snow P, Kugler J: Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs. Cochrane Database Syst Rev 2010:CD006632, amended by the author

Despite the varying settings and investigations included in the review, it was striking that the majority of studies reported reductions in LOS and hospital costs for the experimental CPW group(s) compared with usual care.
Meta-analysis showed that CPWs decrease the number of in-hospital complications and two studies reported on improved professional documentation (see table 2).

In-hospital complications were measured in five invasive pathway studies and all reported improved outcomes for the CPW group [14-18]. Aizawa et al. (2002) tested a clinical pathway for the transurethral resection of the prostate (TURB), Choong et al. (2000) trailed a CPW for femoral neck fracture, Delaney et al. (2003) tested a CPW for laparotomy and intestinal resection, Kiyama et al. (2003) a CPW for gastrectomy, and Marelich et al. (2000) a clinical pathway for mechanical ventilation. In-hospital complications assessed were wound infections, bleeding and pneumonia.

However, both groups did not differ for in-hospital mortality and hospital readmission within 6 month (the longest follow up period reported.) Significant variations across studies prevented further meta-analysis and limited further conclusions. In terms of the transferability and generalizability of the review results, 4 RCTs were conducted in medical units and 3 RCTs in surgical units, 3 RCTs in medical or surgical

intensive care, 2 RCTs in emergency departments, 2 RCTs in stroke rehabilitation wards and 5 RCTS were conducted in other hospital settings.

The international review team followed a rigorous Cochrane EPOC protocol [26] (see chapter 4) and methodology to critically assess and report about the quality and reliability of the study results reported in the literature. This approach included the application of study design and risk of bias (study quality) criteria, if agreement was reached by at least two independent reviewers. This included data recalculations, statistical analysis and checking of the primary study data extracted. Statistical calculations were supervised by colleagues from the Cochrane EPOC satellite centre in Melbourne, Australia and CPW experts and professional associations were contacted and further information retrieved. After a comprehensive peer-review process, the EPOC review on CPWs was published in early 2010. To our knowledge, this was the first attempt to critically analyze the overall quality and scope of studies investigating clinical pathways in hospitals.
These efforts contributed to a very solid evidence base on CPW effectiveness in hospitals and the review represents the most comprehensive empirical data base in terms of the available quantitative literature. Many professional associations and professional bodies appreciated the usefulness of the review by publishing comments and brief summaries, for example the summary of Cruz-Flores, S. et al (2010) published in the American College of Physicians (ACP) Journal Club which can be found in an appendix to this chapter [27]. Another Cochrane systematic review has been performed for stroke patients, investigating several complex interventions including clinical pathways for standardized stroke care. The Review reports improved outcomes for stroke patients in dedicated units and provides valuable insight to elements that optimize stroke outcomes [27].
Grimshaw et al. critically assessed the international literature in terms of the effectiveness of clinical practice guidelines (CPG) and possible implementation strategies [28]. The comprehensive review on CPG effectiveness had a broad scope (hospitals, primary care and rehabilitation facilities) and more than 200 primary studies were included. Grimshaw and colleagues concluded that the majority of the primary studies investigating the effects of clinical practice guidelines reported on modest to moderate improvements in care. However the results are far from providing a comprehensive evidence base for deciding which guideline strategies are likely to be most efficient [28].

Narrative reviews are more common and the conclusions are often based on weak and bias-prone study designs [21, 23, 25].

7.2.3 What is the standard of clinical pathway research in hospitals?

Quality of the evidence-base

The methodological article in Chapter 5 focused on the quality of the existing evidence base for clinical pathway effectiveness and the room for improvement in the design of CPW evaluations.

Method

The analysis was based on the experience of conducting a Cochrane EPOC review (see chapter 4) on the effects of clinical pathways in hospitals. The aims of this article were twofold.

The first objective was to report about the rigorous assessment of the quality of published CPW evaluations [29]. For the purpose of the Cochrane EPOC review, four study designs were included. Randomized controlled trials (RCTs), controlled clinical trials (CCTs), controlled before and after studies (CBAs) and interrupted time series analysis (ITS).

The second objective (secondary analysis) of this paper was to test the hypotheses that weak pre-post evaluations tend to overestimate the CPW effects reported [29].

Assessment of study design and risk of bias

A major finding was that of the original studies which met CPW content criteria, more than 70% were excluded from the review as they were simple pre-post evaluations. Most of the studies published in the literature compared two or more yearly patient cohorts whilst it remained unclear if the reported CPW effects were really attributable to the CPW intervention or to other confounding factors. A possible confounder might have been the case-mix introduction (i.e. DRGs) or other quality improvement interventions. Such bias prone pre-post evaluations with their uncontrolled nature may inform knowledge users and hospital stakeholders locally but contribute very little to the international evidence-base for CPW effectiveness.

Risk of bias in individually randomized trials (RCTs)

Another methodological problem was the potential risk of contamination of health professionals. This problem was broadly discussed in the primary Cochrane review (see chapter 4, risk of bias of included studies) and refers to the processes used for protection against contamination of the health professionals in the control arms. Out of the 17 individually randomized evaluations (RCTs), only two investigations (11%) reported sufficient protection against contamination of the professionals. The remaining 15 primary studies remain unclear if any protection against contamination of the control professionals (masking of the effect of the intervention) was achieved.

Table 3 gives an overview about the reasons for exclusion in stage two after meeting CPW content criteria in stage one.

Table 3: Reasons for exclusion following full text review (n=228)

Reason	Number	%
Not CPW	38	16.7
Simple pre-/post evaluations	160	70.2
High risk of bias	5 (1RCT)	2.2
Not study	14	6.1
Not hospital	11	4.8
Total	228	100

Source: Rotter T, Kinsman L, James E, Machotta A, Steyerberg EW: The quality of the evidence base for clinical pathway effectiveness: Room for improvement in the design of evaluation trials. BMC Med Res Methodol 2012, 12:80.

Secondary analysis

The meta-analytic comparison supports previous findings: that pre-post evaluations may overestimate intervention effects reported and such studies tend to report more consistently on significant reductions in LOS. An overestimation of the effects reported in form of publication bias seems to be also a serious concern in the field of CPW research in hospitals. This is way the Cochrane EPOC sub-group also facilitates the application of non-randomized study designs to evaluate complex clinical interventions such as CPWs.

Main results and context

The article concluded that weak and bias-prone study designs are frequently used to test CPW effectiveness which decreases the number of reliable studies as well as the reliability of the review conclusions. The EPOC methodological gold standard is infrequently used in the field of CPW research. Validated design and risk of bias criteria are only available from the EPOC website [30].

In terms of the meta-analytic comparison, the secondary analysis also supports other findings that simple pre-post investigations tend to overestimate CPW effects reported [31-33] and these should not be used to evaluate quality improvement interventions such as clinical pathways.

7.2.4 *"Do clinical pathways enhance access to evidence-based acute myocardial infarction (AMI) treatment in rural emergency departments?"*

Clinical pathways for rural AMI patients.
In chapter 6 we presented the outcomes of a cluster-randomized CPW implementation study to evaluate the impact of CPWs for rural AMI patients. The aim of this investigation was to fill some of the gaps in terms of the evidence base for CPW effectiveness. Some important lessons were learned from the systematic Cochrane EPOC review, such as relatively few CPW investigations were conducted in a rural hospital setting and only one non-randomized rural CPW investigation met the strict Cochrane EPOC inclusion criteria [19].

Setting:
A CPW for the emergency treatment of acute myocardial infarction (AMI) in rural settings was introduced because rural Australians are 25% more likely to die of an AMI than those living in urban areas [34].

Method
CPW development
The CPW development was based on best clinical practice guidelines from the Australian Heart Foundation (NHFA), from the Cardiac Society of Australia and New Zealand (CSANZ) and the Australian College of Emergency Medicine (ACEM). CPW recommendations include an electrocardiogram (ECG) performed within 10 minutes of arrival and a thrombolysis administrated within 30 minutes (so called door to needle time) [35]. Figure 1 depicts the CPW for chest pain tested in rural emergency departments (ED)

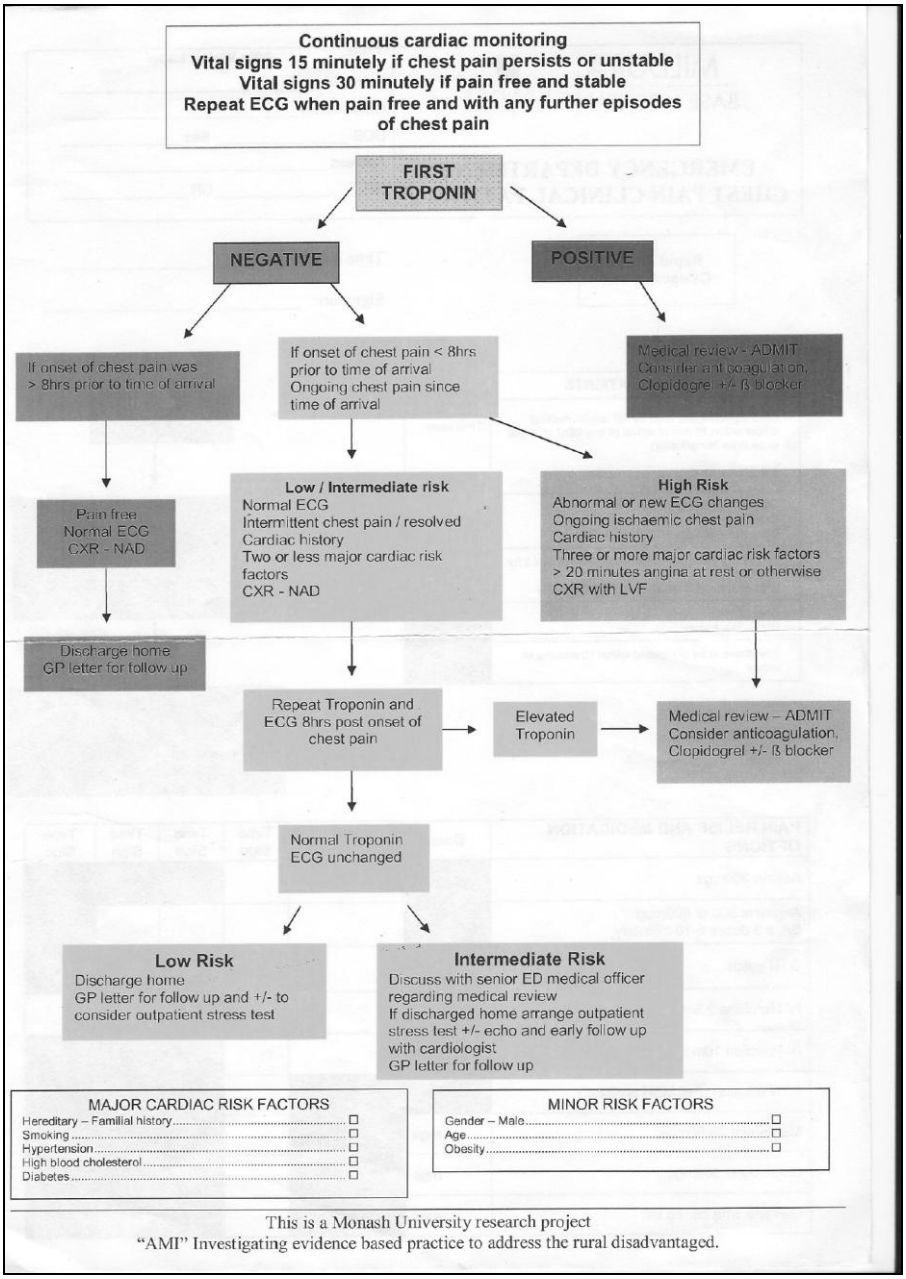

FIGURE 1: CPW for chest pain (rural CPW for AMI patients), Source: Kinsman LD, Buykx P, Humphreys JS, Snow PC, Willis J: A cluster randomised trial to assess the impact of clinical pathways on AMI management in rural Australian emergency departments. BMC Health Serv Res 2009, 9:83.

CPW implementation

Six rural Victorian EDs participated in the study and a five-step CPW implementation strategy was used to increase the number of eligible AMI patients receiving a thrombolytic drug. The five steps of the evidence-based CPW implementation process comprised (1) engaging ED clinicians, (2) evidence-based CPW development tailored to the specific hospital context, (3) reminders, (4) education sessions and (5) audit and feedback.

Outcome measures

Compliance was measured by the number of eligible patients which received reperfusion therapy via intravenous administration of a thrombolytic agent. Other outcome measures were time to thrombolysis and ECG.

Study design

Three pairs (n= 6) of rural hospitals were matched and randomized to either the intervention or control group. Randomization at a hospital level was chosen to prevent contamination of health professionals. A post-intervention sample size of 90 patients with an intra-cluster correlation coefficient of 0.283 [35, 36] was estimated to detect any meaningful differences between experimental and control hospitals in rural Victorian ED settings .

Main results and context

In the final study sample, 108 patients were eligible for thrombolysis, 51 patients in the pre-intervention phase and 57 post-intervention. There were no statistically significant differences between both groups of hospitals on the proportion of eligible AMI patients receiving a thrombolytic, mean or median door-to-needle time and time from arrival to ECG. Due to high baseline compliance to AMI clinical practice guidelines and changes in terms of AMI referrals to rural EDs, the trial was underpowered for detecting the success or failure of a CPW for chest pain. Thrombolytic agents were delivered at baseline in a timely and appropriate manner and measured as proportion of patients' eligible and receiving a thrombolytic drug (80% vs. 96%). Based on previous work in rural Victoria [37] we had anticipated a percentage of approximately 30% of eligible rural AMI patients missed out on delivery of a thrombolytic agent. Thus the high adherence to evidence-based recommendations for chest pain patients in rural Victoria left very little room for improvement.

In a previous study conducted in Australia, Kinsman et al. failed to report on improved outcomes when investigating guideline implementation for rural AMI patients to improve thrombolytic administration [37]. Conversely, Doherty at al. tested a CPW for acute asthma in rural Australian EDs and the investigators reported on significant improvements in the quality of care at the study hospitals but no change

at the control hospitals [38]. In summary, the results of individual studies into the impact of CPWs in rural hospital settings vary considerably.

7.3 Discussion of the main findings

7.3.1 What is a CPW?

It was imperative to focus on the conceptualization of CPWs and to address the lack of specificity and objectivity. The previously described definition based on five objective criteria will generate a higher level of agreement regarding what defines a CPW.

Several definitions identified through our literature searches could not be employed for this study because of the varying content criteria described. For instance, De Bleser et al. investigated the different terms used to describe a clinical pathway in the literature and derived multiple characteristics regarding a possible definition of a CPW [20] and Vanhaecht et al. evaluated clinical pathway audit tools and also described common CPW characteristics [39]. However both studies lack specificity and objectivity because the CPW information variously refers to a clinical pathway as a care pathway, care map, critical pathway or integrated care pathway. Only the CPW definition developed by Campbell et al. was useful because he describes clinical pathways in the context of their relationship to and differences from clinical practice guidelines [11]. A summary of the characteristics described in the literature are provided in Table 4.

Table 4: Characteristics of clinical pathways identified in the literature

Campbell et al. [11]	**De Bleser et al. [20]**	**Vanhaecht et. al. [39]**
Structured multidisciplinary care plan	Care management for a well defined group of patients for a well defined period of care	Multi-professional care plan
Detail essential steps in care for a specific problem	States goals of care based on evidence	Supports variance analysis
Knowledge translation of clinical practice guidelines into clinical practice	Describes the actions of a multi-professional team	Facilitates evidence-based practice
Improves communication with patients	Documenting, monitoring and evaluating variances	

Source: Kinsman L, Rotter T, James E, Snow P, Willis J: What is a clinical pathway? Development of a definition to inform the debate. BMC Medicine 2010, 8:DOI: 10.1186/1741-7015-1188-1131, amended by the author

The European Pathway Association (EPA)
The comprehensive definition published on the EPA website is manly based on the study by De Bleser et al. and could not be used for the development of objective content criteria [20, 40] (see description above). Thus the EPA information about what constitutes a CPW does not contribute to an internationally agreed terminology in the field of clinical pathway research.

The five empirically developed CPW content criteria for our literature searches should be used as discussion basis in developing an international consensus definition using a common CPW terminology [12]. Despite a liaison and several meetings with EPA representatives recently, we failed to collaborate effectively with the world's largest CPW organization in order to develop an internationally agreed consensus definition.
In summary, we still do not really know what we are speaking about because of the varying terms used in CPW research to describe a care pathway. There is still a lot of room for the development of an internationally agreed CPW terminology and definition.

7.3.2 CPW effectiveness

It was time to critically appraise and catalog the available evidence on CPW effectiveness. This systematic review is the most extensive and up-to-date review of the effects of clinical pathways in hospitals. Highly sensitive search strategies were developed and the included studies are considered to be a relatively complete set of studies for the period from the 1950s to mid 2008 [19]. The comprehensive searches detected more studies than previous comparable reviews, indicating an effective search strategy. Detailed data abstraction was conducted on the quality and characteristics of the studies and the weaknesses of the primary studies have been made more explicit for the reader.

We concluded that clinical pathways are associated with reduced in-hospital complications and CPWs could play an important role in patient safety [19]. Moreover, the interest shown by several professional and governmental bodies indicates the usefulness of the systematic review on CPW effectiveness.

However the quantitative Cochrane methodology also has limitations.

Low number of included studies

The most important limitation is the low number (n=27) of included studies and the quality of included studies. Due to the relatively small number of studies meeting inclusion criteria, this evidence base is insufficient in providing a replicable framework for all pathway strategies. The likely benefits and costs need to be considered by the local healthcare providers when implementing clinical pathways under different circumstances. This review has shown that there is not one single strong evidence base. Accordingly, decision makers should consider limitations in relation to the generalization of the review findings.

Quantitative Cochrane EPOC methodology

The quantitative Cochrane methodology has also limitations which do not allow qualitative CPW investigations (see also chapter 7.4 future research and conclusions). The evidence base on the effects of CPWs is currently lacking in explaining how and why specific CPW strategies were effective in one context and not in another. Exclusive quantitative approaches are not designed to explore reasons for this variation in effectiveness. Qualitative approaches can compliment quantitative outcome measures and are particular helpful in understanding the internal dynamics of complex interventions such as clinical pathways [41, 42].

Limitations of applying summary review results to individual patients.
Another limitation of the review methodology is that the summary results of systematic reviews might not apply to individual patients due to the lack of risk stratified analyses [43]. In a randomized clinical trial, differences in baseline characteristics between patients in the experimental and control arms can significantly affect the likely benefits of a clinical intervention such as CPWs. This is especially the case in small (underpowered) randomized evaluations because of chance fluctuations [43]. However, risk-based analyses in primary investigations are rarely performed because of the high number of participants required in each subgroup. With a reasonable number of patients included, risk-based analyses has enough statistical fidelity to detect variation of treatment effect rather than to report on an arithmetical mean or median outcome which can not be applied in a straightforward way to individual patients [43].

In contrast, most of the included randomized CPW evaluations had a small sample size and were probably underpowered. Thus we used a meta-analysis to statistically pool the primary study outcomes in order to increase power and precision by combining small study samples. However, the lack of risk stratified analysis in primary studies is problematic because it directly affects the transferability and generalizability of the summary results [43]. Assuming a high number of primary clinical trials with a risk-based subgroup analyses this approach could help to allocate patients by risk groups and summary results could be applied to the relevant patients effectively.

7.3.3 Standard of CPW research in hospitals

Why is it important to critically appraise study designs in a systematic review?

Pre-post comparisons
Cochrane EPOC criteria were used for the assessment of randomized and non randomized CPW studies. It was noticeable that the vast majority of studies failed to meet the minimum requirements of the study *design* criteria [29]. More than 70% of the studies meeting the CPW content criteria were excluded from the review as they were simple pre-post evaluations. The review indicates that uncontrolled pre-post comparisons are too often used to investigate the effectiveness of clinical pathways in hospitals. In addition, the meta analytic comparison revealed that pre-post studies also tend to overestimate CPW effects reported.

Individually randomized trials (RCTs)

In terms of the quality of included studies, many individually (patient) randomized evaluations had methodological weaknesses such as unclear protection against contamination of the control professionals [19]. We conclude that randomization at an individual level is not suitable in investigating changes in professional behaviour within the same team. A nurse or a doctor can not follow two different care regimens or recommendations for the experimental CPW patients vs. the usual care patients without professional contamination occurring in the control arm. This is especially the case if patients were randomized and allocated to the same ward or department.

Implications of using weak study designs

The Cochrane EPOC review represents a relatively complete set of CPW studies from the 1950s to 2008. However, the low number of included primary studies (27) is a serious limitation and a direct result of the low standard of clinical pathway research in hospitals. Uncontrolled pre-post comparisons are commonly used in hospital practice. Such weak study designs are likely to be biased and misleading and should not be applied in the field of CPW research. Weak pre-post designs are bias prone, tend to overestimate study effects reported and contribute little to the evidence base on understanding clinical pathways in hospitals.

This is why the Cochrane EPOC group advocates validated study design criteria for randomized and non-randomized studies (see figure 2) to investigate complex clinical interventions such as CPWs. Concerning randomized trials, the EPOC gold-standard is the cluster-randomized trial (C-RCT) because randomization is occurring on an institutional or cluster level and contamination of health professionals is unlikely. Experimental C-RCTs represent a robust design to evaluate CPW interventions but they may be considered beyond the capacity of many clinicians and researchers [44].

There are other approaches recommended by EPOC, such as statistically advanced process-evaluations also referred to as interrupted time series (see figure 2, ITS) to evaluate clinical pathways in hospitals [30, 45, 46]. Process evaluations are less resource-intensive and do not require a control group. In addition, multiple ITS evaluations can be employed to control for contemporary confounders or modifiers such as the case-mix introduction [47]. Another useful design that is more likely to contribute to a comprehensive evidence base on CPW effectiveness is the controlled before and after design (see figure 2, CBAs). CBAs are experimental approaches but allocation is not random. Because it is a non-randomized evaluation, two or more control groups are required and compared with one or more experimental groups at baseline and post-intervention [30, 46].

7.3.4 Clinical pathways for rural AMI patients

The aim of the rural CPW investigation was to fill some of the gaps in terms of the evidence base for CPW effectiveness. Only one controlled-before and after study conducted in a rural Australian hospital setting met the strict EPOC inclusion and study design criteria. The study concluded that thrombolytic agents were delivered in a timely and appropriate standard in the six participating emergency departments. A small sample size and a high compliance to AMI guidelines during the trial period left too little room for improvement in terms of the outcome measures compliance to AMI practice guidelines, use of thrombolytic drugs (door-to needle time) and time to ECG. Therefore, the trial results also emphasize the need for measuring compliance to clinical practice guidelines (CPG) prior to CPW development and implementation in order to improve clinical practice. In this study, baseline adherence with the evidence-based recommendations for AMI treatment was much higher than estimated in a rural study conducted in 2004 [37]. Reconsidering the comprehensive and evidence-based CPW implementation strategy used [35, 48], we believe that the limited fidelity of the cluster randomized trial in detecting statistically significant differences between experimental and control hospitals as well as the high standard of care prior to CPW implementation resulted in a failure to report on improved AMI outcomes rather than a failure of the CPW for chest pain itself.

Clinical pathways in rural emergency departments have not been adequately tested and evidence on CPW effectiveness in rural settings remains scarce. In addition, professional adherence to clinical practice guidelines should always have been evaluated prior to CPW development. Ootherwise CPW implementation and based on previously published professional adherence estimates from the literature should not be considered.

Considering the low prevalence of AMI patients in rural setting, small patient samples should be always taken with caution and trial periods should be extended accordingly to allocate a reasonable number of patients and to increase the power and precision of the effect estimates. The evidence-practice gap regarding CPW effectiveness for chest pain patients in rural hospitals remains a challenge as we were unable to report on improved AMI outcomes after CPW implementation.

In contrast, a complementary investigation in The Netherlands called 'Sneller Beter' ('Faster Better') with the aim of redesigning care processes by implementing CPWs concluded, that the clinical pathway concept is most beneficial when larger patient groups are involved. Twenty-four Dutch hospitals participated in the comprehensive quality improvement initiative and many clinical conditions, mainly invasive and diagnostic procedures, were included [49, 50].

7.4 Future research

7.4.1 CPW definition and concept

Future investigators should address the lack of specificity and objectivity in order to clearly define what constitutes a clinical pathway. The five empirically developed content criteria (see table2, CPW minimum criteria) should be used as a cornerstone for future CPW research. Objective and internationally agreed CPW content criteria are required and should be advocated by the EPA and other researchers to reach an international consensus definition with a common CPW terminology.

7.4.2 CPW effectiveness

The broad scope of the systematic review on CPW effectiveness was a direct result of the low number of high quality studies available in the literature rather than an objective choice or research strategy. Recent publications and reports from governmental bodies indicate that pathway implementation is likely to increase globally [3, 51, 52]. If rigorous approaches are used, this could contribute significantly to a higher number of primary studies becoming available for inclusion in systematic reviews on CPW effectiveness, leading towards a comprehensive evidence base. This is why the Cochrane collaboration recommends an update of systematic reviews every two years. We have therefore scheduled an update of the EPOC review on CPWs in hospitals in autumn 2012.

Grouping and comparing primary studies within pathway conditions

Subgroup analysis revealed the largest decrease in statistical heterogeneity when grouped per pathway condition, such as a CPW for hip replacement. This has implications for future reviews on the effects of CPWs in hospitals. Assuming a higher number of primary investigations meeting the study design criteria, future review methods should focus on grouping and comparing within pathway conditions.

Cost-effectiveness and economic CPW evaluations

Primary studies reporting on economic evaluations tend to have a very limited scope of evaluation, mostly focusing on CPW effects on hospital costs, rather than on a full economic evaluation [53, 54]. Future CPW interventions should also be investigated in terms of cost-effectiveness or value-for money. In a cost-effectiveness analysis, the marginal costs of the pathway intervention should be compared to the estimated benefit (cost savings).

Mixed-methods

Quantitative studies are not always suitable in explaining how and why CPW interventions were effective in one hospital and not in another. Solely quantitative approaches with baseline measures compared with post-intervention outcomes are not powerful enough, lacking, in terms of the fidelity of the evaluation process, the ability to determine the reasons for the success or failure of a clinical pathway intervention. Future CPW investigations should use a mixed-method approach to overcome this limitation and to understand reasons for varying research outcomes [41].

CPW implementation strategies

Most CPW evaluations focused on effectiveness measures rather than on CPW uptake or adherence to the evidence-based recommendations. A huge problem during the review phase of the systematic review was poor reporting of the CPW implementation strategy used. Due to this lack of study information, we failed to report on possibly successful implementation strategies for clinical pathways, so evidence on successful CPW implementation strategies remains scarce. Future research in the field of clinical pathways should therefore follow the SQUIRE framework to describe and report about CPW implementation [55-57]

The SQUIRE standard could also help to explain neutral findings clearly: were they a failure of the CPW intervention itself or were they attributable to poor implementation?

In summary, subsequent CPW implementation studies should focus on facilitators and barriers to implementing clinical pathways [58].

7.4.3 Room for improvement in the design of quantitative CPW evaluation trials

The EPOC methodological gold standard is infrequently used in the field of CPW research and validated design and risk of bias criteria are only available from the EPOC website [30]. Cochrane EPOC study design and risk of bias criteria for randomized and non-randomized investigations should always be used for the evaluation of CPWs in hospitals. Besides experimental approaches, EPOC also recommends rigorous process-evaluations, also called interrupted time series (ITS) to investigate clinical pathway interventions in hospitals [30, 45]. An area of uncertainty in ITS studies is the inability of this approach to assess the impact of simultaneously occurring events or ‘interventions’ such as quality improvement initiatives. The multiple baseline approach can overcome those problems; a study to minimize the impact of this methodological problem [47] (see Figure 2) provides more details about this helpful approach which requires less resources and statistical expertise in comparison to randomized evaluations. This study increases the confidence that can be placed in the scientific rigor of a multiple baseline design.

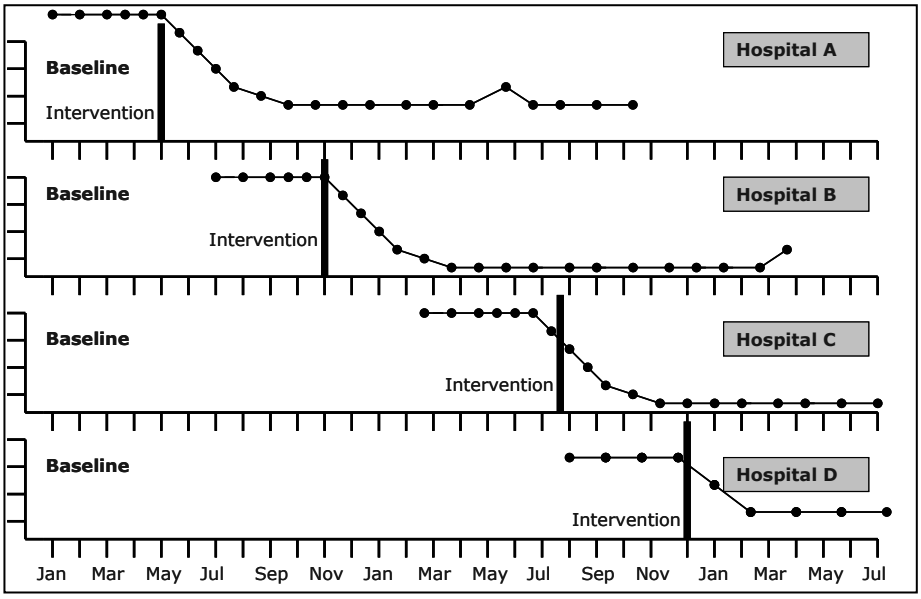

Figure 2: The multiple baseline approach
Source: Hawkins NG, Sanson-Fisher RW, Shakeshaft A, D'Este C, Green LW. The Multiple Baseline Design for Evaluating Population-based approaches. Am J Prev Med. 2007 Aug;33(2):162-8. Review, adapted by the author

7.4.4 CPW effectiveness for rural AMI patients

The implementation of a CPW for chest pain in rural Australian EDs showed no significant impact on study outcomes for AMI patients. The gap between the available evidence conducted in the Cochrane EPOC review and rural settings remain a challenge and the evidence-based management of AMI patients should be carefully investigated in the future. Typical characteristics of rural settings such as a low prevalence of eligible patients emphasizes the need for carefully designed quantitative studies to evaluate the effectiveness of clinical pathway interventions as cluster-randomized investigations might not always have enough fidelity for gaining a better understanding about the possible effects. Moreover, an important lesson learned from the Dutch Quality Improvement Initiative ‘‘Sneller Beter’ (‘Faster Better’) was that the clinical pathway concept is most beneficial when larger patient groups are involved. These results clearly suggest that CPWs should be implemented preferably for large groups of patients. Mixed methods could also help to explain

why specific clinical pathways were effective and contribute to patient safety and effectiveness in one (rural) hospital and not in another. Qualitative investigations should always compliment quantitative study designs in rural settings as an aid to understanding facilitators and barriers to CPWs implementation. The complex and dynamic characteristics of rural hospital settings require carefully designed approaches in order to improve clinical practice. The multiple baseline design is recommended to gain more insight in possibly effective CPW interventions as one intervention group serves as a 'control' for the other group of patients, which increases the power and precision of the effect estimate [47]. The accumulated evidence in Australia could then be tested and validated in comparable hospital settings in Canada and Scandinavia.

7.5 Conclusions

CPW implementation

We still know very little about possibly effective implementation strategies and we often do not really know if neutral study findings can be attributed to a failure of the implementation or a failure of the CPW intervention itself [10, 44, 54, 59]. This is a serious problem in the field of clinical pathway research and possibly effective strategies to successfully implement CPWs could also be adopted from complimentary studies investigating clinical practice guidelines or surgical checklists [60]. There is still a lot of room for implementation research and even the European Pathway Association does not primarily focus on CPW implementation research. This research gap remains a huge challenge but also provides a huge range of research opportunities. Multidisciplinary CPW research should be used to bridge between the different research groups, associations and professions in order to learn more about possibly successful implementation. Based on our experience, personal attitudes and competitive thinking represent one of the biggest barriers to a better understanding in the field of implementation research.

CPW evaluation and effectiveness

The EPOC gold standard to evaluate complex clinical interventions should be applied to all quantitative CPW investigations and complimentary qualitative studies could help researchers and clinicians to a better understanding of clinical pathway strategies in different clinical realities [30, 41, 46]. The reported effects on in-hospital complications are promising and the pathway concept seem to be effective for large groups of patients especially in invasive care, but much more research is needed to fully understand and transfer this evidence base into the varying clinical settings.

The choice of implementing clinical pathway strategies should be also based upon considerations of the likely costs and benefits of pathway interventions. It should be

noted that the development and implementation of clinical pathways consumes a considerable amount of resources. This corresponds to the fact that truly achievable cost savings depend on the number of cases (volume). According to a cost analysis from Comried et al. (1996), the inflation adjusted costs for the development and implementation of the pathway indication "Caesarian section" amounted to more than US$26,000 while the costs for the development and implementation of an additional care map for "normal vaginal delivery" were estimated at approximately US$10,000 [61]. However, since normally 20 percent of the diagnoses cover 80 percent of the cases [62], a considerable percentage of medical services can be dealt with using a relatively small number of clinical pathways.

CPW interventions often remain a 'black box' because of serious limitations in the field of research. In many clinical situations, the review findings are not directly transferable and a comprehensive evidence base on CPW effectiveness is still required. The current systematic review on the effects of clinical pathways is insufficient in supporting all CPW interventions, especially in rural and pediatric hospital settings [6, 8, 48]. Last but not least, more patient involvement in the clinical decision-making process in terms of CPW guided hospital care is strongly recommended because the patient should play a central role in this process [63]. By definition, clinical pathways support the involvement of patients in clinical practice but this aspect was rarely reported in over 3000 primary studies claiming to investigate CPW implementation and effectiveness.

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Appendix

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ACP ONLINE
ACP Products & Services

Quality Improvement

Review: Clinical pathways reduce in-hospital complications but not in-hospital mortality or readmissions

Emergency Med	★★★★★☆	Hospitalists	★★★★★★
Cardiology	★★★★★★	Endocrinology	★★★★★☆
Geriatrics	★★★★★★	Infectious Disease	★★★★★★
Neurology	★★★★★★	Phys Med & Rehab	★★★★★☆

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ACP Journal Club. 2010 Aug 17;153:JC2-12.
Rotter T, Kinsman L, James E, et al. **Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs.** Cochrane Database Syst Rev. 2010(3):CD006632. [20238347]

Question

Do clinical pathways (CPWs) that guide patient management improve patient outcomes more than usual care?

Review scope

Included studies compared CPWs, alone or as part of multifaceted interventions if CPWs could be assessed separately, with usual care and had low or medium risk for bias (Effective Practice and Organisation of Care [EPOC] risk for bias tool). CPWs were structured multidisciplinary care plans that included ≥ 3 of the following: guidelines or evidence translated for local use, detailed steps for care, timeframes for criteria-based progression, and standardized care for specific clinical problems in specific populations. Outcomes included in-hospital mortality, in-hospital complications, hospital readmissions, and length of hospital stay.

Review methods

MEDLINE (to Apr 2008), EMBASE/Excerpta Medica, CINAHL, NHS EED, Global Health, EPOC Register, Cochrane Central Register of Controlled Trials, ISI Web of Science, high-yield journals, conference abstracts, and reference lists were searched for randomized controlled trials (RCTs), controlled clinical trials, controlled before-and-after studies, and interrupted time series. The Database of Abstracts of Reviews of Effectiveness was searched for reviews. Experts were contacted. 19 RCTs and 8 non-RCTs met the selection criteria. 14 RCTs (n = 3721, 2 with low risk for bias) evaluated CPWs alone, and 5 (n = 3546, 2 with low risk for bias) evaluated multifaceted interventions with CPWs. 4 RCTs were conducted in medical units, 3 in medical or surgical intensive care units, 3 in surgical units, 2 in emergency departments, 2 in stroke rehabilitation wards, and 5 in other settings or a mix of settings.

Main results

Meta-analysis showed that CPWs alone reduced in-hospital complications more than usual care; groups did not differ for in-hospital mortality or hospital readmissions within 6 months (Table). Data for length of hospital stay were heterogeneous and not suitable for pooling. 9 of 12 RCTs found that CPWs alone reduced length of stay more than usual care. Multifaceted interventions did not differ from usual care for mortality (2 RCTs) or length of hospital stay (3 RCTs); 1 (n = 65) of 3 RCTs found that multifaceted interventions reduced hospital readmissions more than usual care at ≤ 6 months.

Conclusion

Clinical pathways are better than usual care for reducing in-hospital complications but not in-hospital mortality or hospital readmissions.

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Clinical pathways (CPWs) alone vs usual care (UC) for patient management*

Outcomes	Number of RCTs (n)/non-RCTs (n)	Weighted event rates	RRR (95% CI)	NNT(CI)
In-hospital mortality	2 (678)/1 (509)	22% vs 25%	13% (−8 to 32)	NS
In-hospital complications	4 (553)/1 (111)	9.3% vs 15%	38% (5 to 60)	18 (12 to 130)
Hospital readmission at ≤ 6 mo	5 (561)/1 (111)	5.3% vs 8.5%	38% (−12 to 66)	NS

*NS = not significant; RCT = randomized controlled trial; other abbreviations defined in Glossary. RRR, NNT, and CI calculated from data in article.

Commentary

CPWs were developed to translate evidence into practice, optimize processes of care and make them more efficient, and limit errors. The expected final product is improved clinical outcomes. Intuitively, this systematic approach to care makes sense; however, CPWs have yet to prove that they improve patient health outcomes. The systematic review by Rotter and colleagues showed that CPWs decrease the number of in-hospital complications associated with mainly invasive surgical procedures but do not reduce hospital readmissions or in-hospital mortality. Variations across studies in clinical settings, interventions, and countries, particularly in the analysis of length of stay, limit conclusions about generalizability of the results to clinical practice.

It is important to consider the choice of endpoints in the selected studies. First, length of hospital stay may represent a quality indicator but does not necessarily indicate better health outcomes for patients. Second, mortality is a hard endpoint that is easy to measure but might not be relevant for some disease processes treated in hospital. Third, readmissions up to 6 months may reflect efficacy of outpatient care rather than in-hospital CPWs. Finally, although in-hospital complications may seem to be a sensible health endpoint, its usefulness depends on the definition of complications and the clinical setting.

Rotter and colleagues' results are far from proving the efficacy of CPWs in every medical condition, but they support the notion that CPWs may improve outcomes by optimizing processes of care. More important, they point to gaps in knowledge and can guide future research.

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Summary

Clinical pathways in hospitals: Evaluating effects and costs

CPWs aim to standardize clinical processes of care within the unique culture and environment of the health care institution, thereby maximizing patient safety and clinical efficiency.

Many countries and professional bodies embrace the clinical pathway concept, such as in the United Kingdom, Canada, and Australia but as with any other intervention in health care delivery organization, the question is whether CPWs achieve what they aim for and whether they ultimately contribute to improve the outcomes of health care and at what costs. Therefore the main question for this thesis is: ***What are the effects of clinical pathways on professional practice, patient outcomes, length of stay and hospital costs?***

Chapter 1 explains the background of this thesis, the theoretical context of the research and lists the main research questions.

Chapter 2 illustrates the widespread confusion as to what constitutes a clinical pathway and the lack of agreement regarding an internationally agreed CPW terminology and definition. Independently of the terminology used, the concept of CPW is defined by the characteristics and contents of the strategy. Based on a synthesis of published definitions and descriptions we proposed an operational definition of CPWs. This work hence contributes to a better understanding about clinical pathways and paves the way towards an objective and internationally agreed CPW terminology.

Chapters 3 & 4 describe the process and findings of a Cochrane systematic review on clinical pathway effectiveness. In **chapter 3** the scope of the systematic review question was determined in a pilot search of existing primary CPW studies. The pilot study revealed a relatively small number of high quality studies used to evaluate the success or failure of a CPW intervention and the pilot analysis also indicated a low standard of CPW research in hospitals. As a direct result, the Cochrane review was expanded to also include less restrictive study designs in addition to randomized and quasi-randomized trials, in order to provide a comprehensive evidence base. **Chapter 4** tests the main research question: ***What are the effects of clinical pathways on professional practice, patient outcomes, length of stay and hospital costs?*** The international review team followed a rigorous Cochrane Effective Practice and Organisation of Care (EPOC) Group protocol and methodology to critically

assess and report about the quality and reliability of the study results reported in the literature. The comprehensive searches (from the 1950s to mid 2008) detected more studies than previous comparable reviews, indicating an effective search strategy. A main finding of the systematic review was that clinical pathways are associated with reduced in-hospital complications. Five invasive pathway studies reported on improved outcomes for the CPW groups (Odds Ratio 0.58; 95% confidence interval 0.36 to 0.94) and complications assessed were wound infections, bleeding and pneumonia. However, both groups did not differ for in-hospital mortality and hospital readmission and significant variations across studies prevented further meta-analysis and limited further conclusions.

The methodological article in **Chapter 5** focused on the quality of the existing evidence base for clinical pathway effectiveness and the room for improvement in the design of CPW evaluations. It was noticeable that the vast majority of studies failed to meet the minimum requirements of the study design criteria. More than 70% of the studies meeting the CPW content criteria were excluded from the review as they were simple pre-post evaluations. Such weak study designs are likely to be biased and misleading and should not be applied in the field of CPW research. Weak pre-post designs are bias prone, tend to overestimate study effects reported and contribute little to the evidence base on understanding clinical pathways in hospitals.

Chapter 6 presents the outcomes of a cluster-randomized study to evaluate the impact of CPWs for rural AMI patients. The implementation of a CPW for chest pain in rural Australian EDs showed no significant impact on study outcomes. The gap between the available evidence conducted in the Cochrane EPOC review and rural settings remain a challenge and the evidence-based management of AMI patients should be carefully investigated in the future. Typical characteristics of rural settings, such as a low prevalence of eligible patients, emphasizes the need for carefully designed quantitative studies to evaluate the effectiveness of clinical pathway interventions. Cluster-randomized investigations might not have enough fidelity for gaining a better understanding about the possible effects. In addition, mixed methods designs could help to explain why specific clinical pathways were effective and contribute to patient safety and effectiveness in one (rural) hospital and not in another.

Chapter 7 summarizes the main findings of this thesis and provides a critical discussion. Gaps in our current knowledge are discussed and suggestions for future research are provided. The research in terms of clinical pathways in hospitals reconfirms a common problem in the field of Health Quality Improvement Science. The CPW concept lacks in terms of specificity and objectivity and an internationally

agreed definition and terminology is needed. The Cochrane review on CPW effectiveness in hospitals represents an imperfect evidence-base for clinicians and decision makers because of the low number (n=27) of included studies and the modest quality of some of the included studies. Due to the relatively small number of studies meeting inclusion criteria, this evidence base is insufficient in providing a replicable framework for all pathway strategies. Despite the popularity of the clinical pathway concept worldwide this thesis is far from providing a single strong evidence base of CPWs in every medical condition, but the review findings support the hypothesis that CPWs may improve outcomes by optimizing care processes. The low standard of CPW research and the use of weak study designs have contributed to these serious limitations on understanding clinical pathways in hospitals. A higher standard of clinical pathway research in hospitals could contribute to a comprehensive and transferrable evidence base for improving clinical practice and patient safety. Last but not least, a significant knowledge-to-practice gap remains in rural settings and the evidence-based management of AMI patients should be rigorously investigated in the future.

Curriculum Vitae

Thomas Rotter was born in Ichenhausen, Germany, on the 14th of February 1969. He qualified as a Mental Health Nurse in 1995, and worked for more than 8 years in acute and long-term psychiatric hospitals. In 1997 he started studying Nursing Management and Health Economics at the University of Applied Sciences in Osnabrueck, Germany and graduated in 2002 (Dipl. Kfm.).
After two years in hospital management, he was awarded a Public Health Studies Scholarship at the Technical University of Dresden , completing his MPH in 2006. In 2007 he was awarded a PhD Research Scholarship and started a Doctorate at the Department of Public Health in Dresden which he completed in February 2010 with magna cum laude. During his studies, he moved to the Netherlands (in July 2007) and started another PhD at the Department of Public Health in Rotterdam, resulting in this thesis.

Thomas worked from September 2010 as Assistant Professor of European Public Health at the Faculty of Health, Medicine and Life Sciences, in Maastricht, The Netherlands. In September 2012, he was appointed as Research Chair in Health Quality Improvement Science at the University of Saskatchewan in Saskatoon, Canada.

Publications

Rotter T, Kinsman L, Machotta A, Zhao F and Van der Wijden T: Clinical pathways for primary care: effects on professional practice, patient outcomes, care processes, and costs. (Protocol) Cochrane Database of Systematic Reviews. (revised version submitted for publication in September 2012) (impact factor [IF] 2009: 5.65)

Van Hees M, Rotter T, Evers S. The effectiveness of individual interpersonal psychotherapy compared to usual care as a treatment for major depressive disorder in adult outpatients: a systematic review. BMC Psychiatry 2013, 13:22 (IF 2009: 2.55)

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Kinsman L, Rotter T, Willies J, Snow P, Buykx P, Humphreys J. Do clinical pathways enhance access to evidence-based AMI treatment in rural emergency departments? A cluster randomised controlled trial. Australian Journal of Rural Health. 04/2012; 20(2):59-66. DOI:10.1111/j.1440-1584.2012.01262.x (IF 2009: 0.78)

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Rotter T, Kugler J, Koch R, Gothe H, Twork S, et al. A systematic review and meta analysis of the effects of clinical pathways on length of stay, hospital costs and patient outcomes. BMC Health Serv. Res. 8: 265. (IF 2009: 1.66)

Twork, S, Rotter, T., Kugler, J. Immunmodulierende Therapie bei Multipler Sklerose: Health Technology Assessment und Leitlinien / Immunomodulating therapy for patients with multiple sclerosis: health technology assessment and guidelines. Akt. Neurol. 35(2): 70-80. doi: 10.1055/s-2007-986247 (IF 2009: 0.311)

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and hospital costs. (Protocol) Cochrane Database of Systematic Reviews 2007, Issue 3. Art. No.: CD006632. DOI: 10.1002/14651858.CD006632. (IF 2009: 5.65)

Kugler J, Rotter T, Chudak B, Klitzing C, Lischka D, Mytych D, Perduta J, Schöne, J, Twork S. EU-Projekt: EU-MED-EAST Regional networking in the health and social sector (2004-2006). Final report in German. Abschlussbericht & Abschlussevaluation des trilateralen grenzüberschreitenden Projektes EU-MED-EAST. Dresden: Landeshauptstadt Dresden, Amt für Presse- und Öffentlichkeitsarbeit. 2007

Textbooks:

Meyer zu Wendischhoff J, Rotter T.: “Psych” Kompakt / Diagnostic and therapeutic registration for inpatient psychiatric, psychosomatic and psychotherapeutic services in Germany. Textbook in German. ID Information

und Dokumentation im Gesundheitswesen GmbH, ID Verlag Berlin, 2010. ISBN 978-3-926436-96-2

Busse R, Klazinga N, Røttingen JA, Velasco Garrido M, Rotter T, et al. European Observatory on Health Systems and Policies' Study "Improving quality in European health systems – a comprehensive framework approach." Chapter II-8 "Clinical Pathways in Europe." European Observatory on Health Systems and Policies, Brussels (submitted for editorial review in October 2012)

PhD PORTFOLIO

Summary of PhD training and teaching activities
Name PhD student: Thomas Rotter
PhD period: 2007-2013
PhD supervisor: Prof. dr. E.W. Steyerberg

	Year	Workload(ECTS)
1. Courses		
Program Design and Tutoring Skills, Medical Faculty Carl Gustav Carus, Dresden, Germany	2007	12
Cochrane Workshop Systematic Reviews in Medicine, Amsterdam, Medical Centre Amsterdam, The Netherlands	2007	6
Sources of Heterogeneity in Analysis of Randomized Clinical Trials, Competence Centre for Clinical Trials Bremen	2007	5
Workshop Grading Evidence and Recommendations, Freiburg i. Br., Germany	2008	6
Review Completion Workshop, Australasian Cochrane Centre Melbourne, Australia	2009	7
Introduction to Problem Based Learning, Maastricht University, The Netherlands	2010	9
Blended Learning and PBL educational approaches, Maastricht University, The Netherlands	2011	12
2. Teaching activities		
Tutor and Lecturer in Evidence Based Practice for medical students, Medical Faculty Carl Gustav Carus, Dresden, Germany	2007	8
Module Coordinator (MSc) European Public Health Studies, Modules EPH 4003 & 4006, Maastricht University, The Netherlands	2010-2012	12
Student Supervision (Bachelor's, Master, Co-supervision Doctorate)	2010-2012	15

3. Conferences and presentations

Europe

International Conference 10 Years of Care Pathways, Catholic University Leuven, Belgium, keynote speech, do pathways work?	2009	5
Integrated Care Pathways Conference 2009, Preliminary Results Cochrane Review on Clinical Pathways, Portland Place, London, UK	2009	9
Hauptstadtkongress Berlin 2010, Effekte Klinischer Pfade, Berlin, Germany	2010	7
Klinikpfadworkshop: Prozessmanagement in der perioperativen Medizin, Universitaetsmedizin Mannheim, Germany	2010	8
Klinikpfadworkshop: Klinische Pfade, Kosten und Personal, Universitaetsmedizin Mannheim, Germany	2011	8
Klinikpfadworkshop: Evaluierung Klinische Pfade, Universitaetsmedizin Mannheim, Germany	2012	8
Hauptstadtkonferenz: Chirurgie ist mehr als Operieren, Effekte Klinischer Pfade, Berlin, Germany	2012	7

Canada

Children's Hospital Vancouver: Clinical Pathways in Pediatric Hospitals, University of British Columbia, Vancouver, Canada	2010	10
Canadian Institutes of Health Research (CIHR): Effects of clinical pathways in hospitals, Speech at the PHSI Partnership Meeting, Westin Hotel Ottawa, Canada	2011	10