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Evidence-Based Interventions to Reduce Adverse Events in Hospitals: A Systematic Review of Systematic Reviews

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ABSTRACT

Objective: To provide an overview of effective interventions aimed at reducing rates of adverse events in hospitals.

Design: Systematic review of systematic reviews.

Data sources: PubMed, CINAHL, PsycINFO, the Cochrane Library and EMBASE were searched for systematic reviews published up until October 2015.

Study selection: English-language systematic reviews of interventions aimed at reducing adverse events in hospitals, including studies with an experimental design and reporting adverse event rates were included. Two reviewers independently assessed each study's quality and extracted data on the study population, study design, intervention characteristics and adverse patient outcomes.

Results: Sixty systematic reviews with moderate to high quality were included. Statistically significant pooled effect sizes were found for 14 interventions, including: 1) multicomponent interventions to prevent delirium; 2) rapid response teams to reduce cardiopulmonary arrest and mortality rates; 3) pharmacist interventions to reduce adverse drug events; 4) exercises and multicomponent interventions to prevent falls; and 5) care bundle interventions, checklists and reminders to reduce infections. Most (82%) of the significant effect sizes were based on five or fewer primary studies with an experimental study design.

Conclusion: The evidence for patient safety interventions implemented in hospitals worldwide is weak. The findings address the need to invest in high-quality research standards in order to identify interventions that have a real impact on patient safety. Interventions to prevent delirium, cardiopulmonary arrest and mortality, adverse drug events, infections and falls are most effective and should therefore be prioritized by clinicians.

Strengths and limitations of this study

- This review offers a unique overview of effective patient-safety interventions based on data from systematic reviews, thereby producing a stronger evidence-based oversight of effective interventions compared to the outcomes of a systematic review of primary studies.

- For several patient-safety interventions that are implemented worldwide, there is a lack of high- quality studies in which these interventions are evaluated.

- The found estimates of effectiveness of patient safety interventions might vary across contexts, such as small versus large hospitals, academically affiliated hospitals versus those that are not, and the availability of factors that stimulate successful implementation of interventions.

INTRODUCTION

Improving patient safety is an ongoing concern for healthcare providers, managers and policy makers. Worldwide, the prevalence of patient harm and death as a result of adverse events is about 10% among hospitalized patients. Half of these adverse events are considered avoidable.[1] Despite the widespread implementation of interventions to reduce patient harm, patient safety is not improving.[2-4]

Although substantial effort has been invested into developing and implementing safety improvements, evidence for the effectiveness of interventions to reduce adverse events is limited.[5-7] Patient safety improvement interventions have been defined as: practices, strategies, structures, procedures, behavior or actions to prevent or mitigate unintended patient harm resulting from the healthcare process across a range of diseases and procedures.[8-11] Several reviews have studied the nature and effectiveness of a broad range of these patient safety interventions.[5 12-15] However, the findings of these reviews need to be seen in the light of several limitations. The reviews included studies with weak designs, lacking a systematic approach or conducted more than one decade ago. Most importantly, none of the reviews reviewed or prioritized patient safety interventions based on their effects on adverse event and mortality rates. So far, patient safety interventions have not been reviewed or prioritized based on effect measures.

Better insight into the effectiveness of interventions aimed to reduce adverse events and preventable deaths within hospitals is needed in order to assist managers and healthcare providers with deliberately selecting patient safety interventions based on available evidence [16] and to disseminate effective patient safety improvement interventions into routine practice.[3] Therefore, the aim of this study is to systematically review systematic reviews of interventions aimed at improving patient safety in hospitals by evaluating interventions, the studies they were tested in and the effect sizes found.

METHODS

We conducted this systematic review with a pre-specified protocol (**Appendix 1**), in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) and the AMSTAR checklist for systematic reviews (**Appendices 2 and 3**).[17 18]

Data Sources and Searches

We searched for systematic reviews from inception to 22 July 2013, using the following scientific databases: PubMed (including MEDLINE), CINAHL, PsycINFO, the Cochrane Library, and EMBASE. We used the filters for searching papers on patient safety developed by Tanon and colleagues [19] to maximize the sensitivity of our literature search. The search terms used are described in detail in **Appendix 4**. We updated the search until 6 October 2015 (see Flow Chart in **Figure 1**).

Additional hand searches were conducted in high-impact journals and online databases in the field of patient safety, including *Systematic Reviews Journal*, *Annals of Internal Medicine*, *BMJ*, *BMJ Quality and Safety in Healthcare* and *the International Journal of Quality in Healthcare*. Finally, references from the included systematic reviews and bibliographies of published and unpublished reviews related to our study objective were scanned to identify relevant systematic reviews.

Systematic Review Selection

Two researchers (MZ, GH) independently assessed the inclusion eligibility of the retrieved systematic reviews according to a standardized format (**Appendix 1**). The initial selection for inclusion was based on the title and abstract of the systematic reviews. A full-text copy of the article was retrieved and reviewed, in case the title and abstract provided insufficient information to determine its relevance. For the final selection, a full-text copy of the systematic reviews was examined to determine whether it fulfilled the inclusion criteria. Disagreement about inclusion was solved by discussion. When no consensus could be achieved, a third reviewer (HW) made the final decision.

Each systematic review had to meet the following criteria (**Appendix 1**):

1) English-language, full-text published and unpublished systematic reviews;

2) including randomized controlled trials (RCTs), non-randomized controlled trials (NRCTs), controlled before-after (CBA) studies and interrupted time series (ITS) (Cochrane Effective Practice and Organisation of Care (EPOC) review group methodological criteria);[20]

3) focusing on population of hospitalized patients across a range of diseases and procedures;

4) regarding patient safety interventions (aimed at changing healthcare processes, structures, strategies, behavior or actions) targeted at reducing adverse events; and

5) reporting quantitative effect measures.

Systematic reviews that met any of the flowing criteria were excluded from the review:

1) observational studies;

2) pharmacological studies;

3) psychiatric, obstetric patients or neonates as the study population/sample; and

4) only including process errors or consequences of adverse events (e.g., readmission and length of stay).

Data Extraction and Quality Assessment

One researcher (WG) extracted the data from the included systematic reviews using a standardized form (**Appendix 1**). The extracted data were checked by a second researcher (GH). Disagreement was resolved through discussion, and a third person (MZ) was consulted if needed. We limited the data extraction to the pre-specified elements, including the intervention components, design and number of included studies, study sample (nature and size) and effect measures. Of all of the studies in a systematic review, only data from studies that met our selection criteria (called 'relevant studies') were extracted and analyzed.

Three reviewers (MZ, GH, WG) independently assessed the likelihood that the design of a systematic review would generate unbiased results, using a quality assessment form (**Appendix 1**) that included the eleven AMSTAR quality criteria (A MeaSurement Tool to Assess systematic Reviews).[18] Systematic reviews scored 1 point for each fulfilled criterion, and a total score for each systematic review was calculated. A score of 0–3 was classified as 'low'; 4–7 as 'moderate'; and 8–11 as 'high'.[21]

Data Synthesis and Analysis

The study characteristics and patient outcomes for all of the systematic reviews that met our inclusion criteria were organized in tabular form. The systematic reviews included were classified into patient safety areas. The classification was adapted from previous reviews on patient safety interventions.[11 12 14] We compiled the pooled effect sizes of meta-analyses reported in the systematic reviews and analyzed the intervention components. Subsequently, we ranked the effective interventions based on their effect size.

RESULTS

Search results

Our initial search identified 11,032 records (**Figure 1**). The title and abstract scan resulted in 172 articles that underwent full-text review. Thirty-six articles met our selection criteria after the full-text review. The exclusion reasons for the 136 articles are given in A**ppendix 5**. Twenty-four additional articles were identified through hand searching, snowballing and an update of our search action. The final set consisted of 60 articles [22-81] that underwent data abstraction and analysis.

Methodological Quality

Four (6.7%) systematic reviews scored low, 30 (50.0%) scored moderate and 26 (43.3%) scored high on methodological quality. Their AMSTAR scores ranged from 2 to 10 (**Appendix 6**), with a mean score of 6.9 (Standard Deviation [SD] ± 2.2). None of the included systematic reviews fulfilled all of the AMSTAR criteria. **Appendix 7** shows the proportion of studies satisfying each of the eleven AMSTAR quality criteria. Most (> 80%) of the included systematic reviews carried out a comprehensive literature search, reported the characteristics of the included studies, assessed the scientific quality of the included studies and used the scientific quality of the included studies appropriately in formulating conclusions. One-third of the systematic reviews referred to a study protocol in which the research questions and inclusion criteria were established before the study was conducted, and provided a list of included and excluded studies. None of the systematic reviews reported the conflicts of interest of the included studies (**Appendix 7**). Six systematic reviews (10.0%) did not include a statement on the presence or absence of potential conflicting sources of support for carrying out the systematic review.[42 45 46 52 68 78]

Characteristics of the Included Systematic Reviews

The characteristics of the included systematic reviews are summarized in **Appendix 8**. More than half (56.7%) of the systematic reviews were published between 2013 and 2015. The total number of included studies ranged from two [67 81] to 138 [65]; the number of relevant studies (i.e. met the inclusion

criteria) ranged from one [67 80 81] to 33 [29]. The number of participants in the relevant studies ranged from 938 [75] to 225,686 [71] and was not reported or unknown in 26 (43.3%) reviews.

The included reviews covered 14 patient safety areas (**Table 1**). Most of the reviews were about preventing adverse drug events (n = 15), followed by infection prevention (n = 8), delirium prevention (n = 7) and adverse events after hospital discharge or clinical handover (n = 7).

There was overlap in the included studies between systematic reviews within specific patient safety areas (**Appendix 9**). For the "delirium prevention" area, the overlap ranges from 25% [45] to 86% [47]; and from 66% [62] to 75% [59 60] for "fall prevention".

Table 1. **Identified systematic reviews (n = 60) classified by Patient-Safety Area (n = 14)**

Patient-Safety Area		Number of systematic reviews (references)	Intervention components relevant to patient safety (effective components are bold)
Adverse drug event	**Sub area**		
	CPOE system	2 (22 23)	Computerized physician order entry (CPOE) system
	Medication review	4 (24-27)	Medication reconciliation
	Computer-assisted decision support/alerts	3 (28-30)	Computerized advice or decision support; computerized drug-lab alerts for clinicians on prescribing or monitoring decisions
	Multicomponent interventions	6 (31-36)	**Multicomponent interventions, including pharmacist involvement and support of care teams or physicians; guideline implementation, including academic detailing, reminders and feedback of data;** multicomponent intervention, including CPOE system, changes in work schedules, education, support systems for clinical decision-making
Infection*	Device-related infections (CAUTI; CLABSI; VAP)	4 (37-40)	**Care bundles and checklists**; empowerment to stop procedure; surveillance; infrastructure and organizational changes; **training on appropriate catheter placement; catheter restriction and removal protocols**; **reminder or stop order to decrease catheter placement;** use of specific technologies
	Sepsis	1 (41)	**Multicomponent program aimed at improving compliance to sepsis care bundles, including education and decision support tools**
	Hand-hygiene compliance	2 (42 43)	Education; audit and feedback; health promotion; variations in availability and type of products used for hand hygiene
	Overall hospital-acquired infection	1 (44)	Education; protocols to remove catheters
Delirium		7 (45-51)	Psychiatric assessment; special care; daily visits by a liaison nurse; interdisciplinary team; supportive psychotherapy; **multicomponent intervention, including cognitive screening, proactive geriatric consultation and psychotherapy; multicomponent intervention, including early mobility, cognition and orientation, sleep-wake- cycle preservation; multicomponent intervention, including physiotherapy, family involvement, and staff/family-member education**
Adverse event after hospital discharge or clinical handover		7 (52-58)	Post-acute intermediate care units; geriatric assessment; liaison nurse; pre-discharge assessment of risks; patient engagement; individualized patient record; multidisciplinary discharge planning team; clinical follow-up; **nurse-led early-discharge planning programs**
Fall		4 (59-62)	**Addressing risk factors by a multidisciplinary team;** care planning; environmental changes; movement alarms; **physiotherapy**; management of urinary incontinence; **multicomponent interventions, including risk alert card, exercise, education, hip protectors and geriatric assessment**
Adverse event in surgery		5 (63-67)	Screening and decolonization of surgical-site infections; sub-specialization; benchmarking; technology or training; **surgical safety checklist**
Cardiopulmonary arrest		4 (68-71)	**Critical-care outreach service**; **rapid-response teams**
Venous thrombo-embolism		2 (72 73)	Alerts and education; real-time audit and feedback; multicomponent interventions to improve appropriate administration of thromboprophylaxis
Staffing		3 (74-76)	**Increasing proportion of support staff**; addition of specialist nursing post to staffing; reducing shift length; protected sleep time; night float; education among residents; **interdisciplinary team interventions**
Pressure ulcer		1 (77)	Standardization of interventions; multidisciplinary teams and leadership; designated skin champions; education; audit and feedback
Mechanical complication and underfeeding		1 (78)	Total parenteral nutrition team: nutrition support for patients who are unable to obtain adequate nutrition either via the oral or enteral route
Clinical pathway		1 (79)	**Clinical pathways**: multidisciplinary care plans with essential steps in care, supporting the translation of clinical guidelines into local protocols and application in practice
Safety culture		1 (80)	Error-prevention training; restructured patient-safety governance; lessons-learned program; cause-analysis program; executive rounds
External inspection		1 (81)	External inspections of compliance with standards (e.g., accreditation)

CAUTI = Catheter-associated urinary tract infection; CLABSI = central-line-associated bloodstream infection; VAP = ventilator-associated pneumonia
*Surgical-site infections were classified as "prevention of adverse events in surgery"

Effects of Patient Safety Interventions

The results of all included systematic reviews are summarized in **Appendix 10.** A meta-analysis was carried out in 30 of the 60 (50.0%) systematic reviews (**Table 2**). The authors addressed the following reasons for not performing a meta-analysis: too few studies identified (n = 5); the heterogeneity of the respective study designs (n = 9), interventions (n = 8), subject groups (n = 5) and reported outcomes (n = 5); and methodological limitations (e.g., lack of available valid data) of the included studies (n = 5).

Seventeen meta-analyses showed a statistically significant effect on adverse drug events,[36] catheter-associated urinary tract infection (CAUTI) rates,[40] central-line-associated bloodstream infection (CLABSI) rates,[39] delirium incidence,[47 50 51] fall rates,[61] surgical site infections (SSIs),[66] incidence of cardiopulmonary arrest,[69 71] complications,[66 79] and mortality rates.[33 41 58 66 71 75 76] Patient safety interventions with statistically significant effect sizes are discussed below.

Table 2 **Effect sizes of Patient-Safety interventions: results from meta-analyses (n = 30) reported in the 60 included systematic reviews**

Patient-Safety area	Reference meta-analysis	Intervention	Patient outcome	Effect size (95% CI) significant effect sizes are bold	p-value	Studies in meta-analysis (n) (relevant* [n])
Adverse drug event Medication review	Holland et al., 2008 [24]	Pharmacist-led medication review	*Mortality*	RR, 0.96 (0.82–1.13)	p = 0.62	22
	Christensen and Lundh, 2013 [26]	Medication review	*Mortality*	RR, 0.98 (0.78–1.23)	p = 0.86	4
	Hohl et al., 2015 [27]	Medication review	*Mortality*	OR, 1.09 (0.69–1.72)	p = 0.71	3
Adverse drug event Computerized advice on drug dosage	Durieux et al., 2008 [28]	Computerized advice on drug dosage	*Mortality*	RR, 0.81 (0.37–1.81)	p = 0.61	6
	Gillaizeau et al., 2013 [29]	Computerized advice on drug dosage	*Mortality*	RR, 1.08 (0.80–1.45)	p = 0.61	10
	Bayoumi et al., 2014 [30]	Computerized drug-lab alerts	*Adverse events (bleeding and thrombosis)*	OR, 0.88 (0.78–1.00)	p = 0.05	4
Adverse drug event Multi component interventions	Davey et al., 2013 [33]	Intervention for antimicrobial therapy	*Mortality*	RR, 0.92 (0.69–1.22)	p = 0.56	3
		Antibiotic guideline for pneumonia	*Mortality*	**RR, 0.89 (0.82–0.97)**	p = 0.01	4
		Decrease excessive prescribing	*Mortality*	RR, 0.92 (0.81–1.06)	p = 0.25	11
	Wang et al., 2015 [36]	Pharmacist interventions	*Preventable adverse drug events*	**OR, 0.23 (0.11–0.48)**	p < 0.01	3 (2)
Infections	Blot et al., 2014 [39]	Care bundle/ checklist interventions	*CLABSI*	**OR, 0.39 (0.33–0.46)**	p < 0.01	41 (5)
			CLABSI rate at 3 months	**OR, 0.30 (0.10–0.88)**	p = 0.03	6 (4)
	Meddings et al., 2014 [40]	Catheter reminder and stop order	*CAUTI episodes per 1000 catheter days*	**RR, 0.47 (0.30–0.64)**	p < 0.01	11 (1)
			CAUTI	**RR, 0.72 (0.52–0.99)**	p = 0.05	8 (2)
	Damiani et al., 2015 [41]	Sepsis bundle	*Mortality*	**OR, 0.66 (0.61–0.72)**	p < 0.01	48 (3)
Delirium	Hempenius et al., 2011 [47]	Multicomponent interventions, including cognitive screening, proactive geriatric consultation and psychotherapy	*Incidence of delirium*	**OR, 0.58 (0.38–0.92)**	NR	5
		One-component interventions	*Incidence of delirium*	OR, 1.05 (0.09–11.57)	NR	2
	Hshieh et al., 2015 [50]	Multicomponent intervention, including early mobility, cognition and orientation	*Incidence of delirium*	**OR, 0.47 (0.38–0.58)**	p < 0.01	11 (7)
	Martinez et al., 2015 [51]	Multicomponent intervention, including physiotherapy, daily reorientation, family involvement and staff/family-member education	*Incidence of delirium*	**RR, 0.73 (0.63–0.85)**	p < 0.01	7
Adverse event after hospital discharge or clinical handover	Griffiths et al., 2005 [52]	Nursing-led inpatients units	*Mortality*	OR, 1.10 (0.56–2.16)	p = 0.64	7
			Mortality 3 or 6 months post- admission	OR, 0.96 (0.63–1.47)	p = 0.62	6
	Conroy et al., 2011 [53]	Comprehensive geriatric assessment	*Mortality*	RR, 0.92 (0.55–1.52)	p = 0.77	5
	Niven et al., 2014 [54]	Critical-care transition programs	*Mortality*	RR, 0.84 (0.66–1.05)	p = 0.1	3 (2)
	Sheppard et al., 2013 [56]	Discharge planning from hospital to home	*Mortality at 6 to 9 months*	RR, 1.00 (0.79–1.26)	p = 0.69	6
			Falls	RR, 0.87 (0.50–1.49)	p = 0.61	1
	Lowthian et al., 2015 [57]	Optimized ED discharge	*Mortality up to 18 months post discharge*	OR, 1.01 (0.70–1.47)	p = 0.94	2
	Zhu et al., 2015 [58]	Nurse-led early-discharge planning	*Mortality*	**RR, 0.70 (0.52–0.95)**	p = 0.02	5
Fall	Oliver et al., 2007 [59]	Multicomponent intervention	*Falls*	RaR, 0.82 (0.68–1.00)	NR	12
			Fallers	RR, 0.95 (0.71–1.27)	NR	12
			Fractures	RaR, 0.59 (0.22–1.58)	NR	12

	Coussement et al., 2008 [60]	Multicomponent intervention	*Falls*	RR, 0.82 (0.65–1.03)	NR	4
			Number of fallers	RR, 0.87 (0.70–1.08)	NR	4
	Cameron et al., 2012 [61]	Multicomponent interventions	*Rate of falls*	**RaR, 0.69 (0.49–0.96)**	p = 0.03	4
			Risk of falling	RR, 0.71 (0.46–1.09)	p = 0.12	3
		Exercises	*Risk of falling*	**RR, 0.36 (0.14–0.93)**	p =0.04	2
Adverse event in surgery	Bergs et al., 2014 [66]	WHO surgical-safety checklist	*Any complication*	**RR, 0.59 (0.47–0.74)**	p < 0.01	5
			Mortality	**RR, 0.77 (0.60–0.98)**	p = 0.04	4 (3)
			Surgical site infections	**RR, 0.57 (0.41–0.79)**	P < 0.01	5
Cardiopulmonary arrest	Chan et al., 2010 [69]	Rapid-response team	*Mortality*	RR, 0.92 (0.82–1.04)	NR	16
			Cardiopulmonary arrest	**RR, 0.65 (0.55–0.77)**	NR	16
	Maharaj et al., 2015 [71]	Rapid-response team	*Mortality*	**RR, 0.91 (0.85–0.97)**	p < 0.01	4
			Cardiopulmonary arrest	**RR, 0.74 (0.56–0.98)**	p = 0.04	2
Venous thromboembolism	Kahn, et al., 2013 [72]	Alerts	*All venous thromboembolism*	RR, 0.85 (0.49–1.46)	NR	3
		Multicomponent interventions	*All venous thromboembolism*	RR, 1.01 (0.51–1.98)	NR	5
			Symptomatic deep vein thromboembolism	RR, 0.59 (0.18–1.98)	NR	3
Staffing	Butler et al., 2011 [75]	Addition of specialist nursing post to staffing	*In-hospital mortality*	RR, 0.96 (0.59–1.56)	p = 0.86	1
			Post-discharge adverse events	RR, 1.03 (0.70–1.53)	p = 0.87	1
		Increasing the proportion of support staff	*Mortality in trauma unit*	RR, 0.41 (0.16–1.01])	p = 0.05	1
			Mortality in hospital	RR, 0.56 (0.29–1.09)	p = 0.09	1
			Mortality at 4 months	**RR, 0.57 (0.34–0.95)**	p = 0.03	1
	Pannick et al., 2015 [76]	Interdisciplinary teams	*Mortality*	wRR, 0.92 (0.82–1.05)	NR	7
		Team practice interventions	*Mortality*	**wRR, 0.67 (0.45–0.99)**	NR	2
Clinical pathway	Rotter et al., 2010 [79]	Clinical pathway	*Mortality*	OR, 0.84 (0.64–1.11)	p = 0.23	3
			Complications up to 3 months	**OR, 0.31 (0.13–0.72)**	p = 0.07	1
			In-hospital complications	**OR, 0.58 (0.36–0.94)**	p = 0.03	5

CAUTI = catheter-associated urinary tract infection; CI = confidence interval; CLABSI = Central-line-associated bloodstream infection; NR = Not Reported; OR= Odds Ratio; RR = Risk/Relative Ratio; RaR = Rate Ratio; wRR = weighted Risk Ratio

*relevant study = study design in accordance with methodological criteria of the Cochrane Effective Practice and Organisation of Care (EPOC) review group and quantitative data on adverse event rates were reported

Adverse drug event

Of the 15 included systematic reviews about adverse drug events, two reported statistically significant results. Davey and colleagues [33] found that interventions aimed at increasing antibiotic guideline compliance for pneumonia were associated with a significant reduction in mortality: risk ratio [RR], 0.89 (95% CI, 0.82 to 0.97; p = 0.01). This found effect was based on four studies. Effective intervention components were formal presentations, academic detailing, letters, frequent reminders by pharmaceutical representatives, preprinted outpatient and admission order sheets and reporting of outcome data to providers.

Wang and colleagues [36] found that participation of a pharmacist in physician rounds and timely information exchange and advice of physicians by the pharmacist (i.e., on drug interactions, appropriate dosages, dose intervals and routes of administration) was associated with a statistically significant reduced adverse-drug-event rate: odds ratio [OR], 0.23 (CI, 0.11 to 0.48; p < 0.01). The found effect was based on three studies, of which two complied with the Cochrane EPOC inclusion criteria for study designs.

Infection

Three systematic reviews reported statistically significant effects on the reduction of infection and mortality rates as a result of implementing interventions and care bundles.[39-41] The meta-analysis performed by Blot and colleagues [39] showed a reduction in the CLABSI rate (OR, 0.39 [CI, 0.33 to 0.46; p < 0.01]) and reduction in the CLABSI rate at three months post intervention (OR, 0.30 [CI, 0.10 to 0.88; p = 0.028]) as a result of care bundles and checklists.[39] These found effects were based on 41 and six studies, respectively, of which five and four studies met our inclusion criteria, respectively.

Meddings and colleagues [40] reported that the use of a reminder and/or stop order to prompt removal of unnecessary urinary catheters led to a 53% reduction of CAUTI episodes per 1,000 catheter days: rate ratio [RaR], 0.47 (CI, 0.30 to 0.64; p < 0.01). This meta-analysis was based on 11 studies, of which only one study complied with the inclusion criteria for study designs.

The implementation of a program to improve compliance to sepsis care bundles led to a statistically significant decreased mortality rate: OR, 0.66 (CI, 0.61 to 0.72; $p < 0.01$). This rate is based on 48 studies, of which three fulfilled the criteria for study designs.[41]

Delirium

Three systematic reviews reported a statistically significant reduction in delirium incidence.[47 50 51] There was a 16% overlap (3 of the 19 studies) between these systematic reviews (**Appendix 9**).

Hempenius and colleagues [47] pooled the effects of five studies and found a statistically significant effect of multicomponent interventions to prevent delirium: OR, 0.58 (CI, 0.38 to 0.92). Components were education, systematic cognitive screening, geriatric consultative services, supportive psychotherapy, and a scheduled pain protocol.

Hshieh and colleagues [50] reviewed studies evaluating non-pharmacological interventions, including the following components: early mobility, cognition and orientation, sleep-wake-cycle preservation, hydration, hearing and vision. They found a statistically significant reduction in delirium incidence: OR, 0.47 (CI, 0.38 to 0.58); $p < 0.01$. This rate was based on 11 studies, of which seven complied with the inclusion criteria for study designs.

Martinez and colleagues [51] found a statistically significant reduction in delirium incidence: RR, 0.73 (CI, 0.63 to 0.85); $p < 0.01$. This rate was based on seven studies using different multicomponent interventions, but a number of specific components were shared: physiotherapy, daily reorientation, family involvement in care, stimulation programs with avoidance of sensorial deprivation and staff/family-member education.

Adverse event after hospital discharge or clinical handover

Six systematic reviews pooled the effect of interventions to improve clinical handover or hospital discharge. One systematic review reported a statistically significant effect size: Nurse-led early-discharge planning programs were associated with a lower mortality rate: RR, 0.70 (CI, 0.52 to 0.95; $p = 0.02$).[58] This found effect was based on five studies. Effective intervention components were an individual discharge plan to address identified transitional care needs, comprehensive discharge plan

and home-based follow-up visits or telephone calls by providers to patients after their hospital discharge.

Fall

One systematic review [61] reported the effectiveness of fall-prevention interventions. Additional physiotherapy reduced the risk of falling: RR, 0.36 (CI, 0.14 to 0.93). Multicomponent interventions reduced the fall rate: RaR, 0.69 (CI, 0.49 to 0.96). These rates were based on two and four studies, respectively. Effective components of the multifactorial interventions were fall-risk alert card and information brochure, exercise program, education program, hip protectors, comprehensive geriatric assessment and treatment of fall risk factors by a multidisciplinary team.

Surgical adverse event

The implementation of a surgical checklist was associated with a reduction of complications, deaths and surgical-site infections: RR, 0.59 (CI, 0.47 to 0.74), 0.77 (CI, 0.60 to 0.98) and 0.57 (CI, 0.41 to 0.79), respectively. These pooled rates were based on five studies.[66] The authors reported that the results were statistically significant but cannot be regarded as definitive in the absence of high-quality studies.[66]

Cardiopulmonary arrest

Two systematic reviews found an association between the implementation of a rapid-response team and improved patient outcomes. There is an 11% overlap (2 of the 19 studies) between these systematic reviews (**Appendix 9**). Chan and colleagues [69] performed a meta-analysis on 16 studies and found a statistically significant reduction of cardiopulmonary arrests outside the intensive care unit (ICU) following the implementation of the rapid-response team: RR, 0.65 (CI, 0.55 to 0.77). The authors of the systematic review raised questions about the effectiveness of rapid-response-team implementation given the lack of an effect of rapid-response teams on mortality.

The systematic review of Maharaj [71] found a statistically significant reduction in cardiopulmonary arrests based on two studies: RR, 0.74 (CI,0.56 to 0.98; p = 0.04) and a statistically significant reduction of deaths based on four studies: RR, 0.91 (CI, 0.85 to 0.97; p < 0.01).

Staffing

Butler and colleagues [75] found 6,202 studies that were potentially relevant to studying the effect of hospital-nurse staffing models on mortality and adverse events. However, one study reported a statistically significant effect: increasing the proportion of support staff (i.e., dietetic assistants) reduced mortality at four months: RR, 0.57 (CI, 0.34 to 0.95; p = 0.03).The authors stated that they were unable to draw conclusions because of the small number of eligible studies.

Pannick and colleagues [76] found that interdisciplinary team interventions reduced mortality rates: RR, 0.67 (CI, 0.45 to 0.99). The finding was based on two studies. Effective intervention components were interdisciplinary rounds, including physician, nurse, pharmacist, nutritionist and social worker; expanded senior clinical nurse roles; incorporating structured detailed assessments of premorbid functional and social patient data and investment in allied health professionals as consistent staff members.

Clinical pathway

Rotter and colleagues [79] found an association between the use of clinical pathways and a reduction of in-hospital complications, based on five studies: OR, 0.58 (CI, 0.36 to 0.94). Examples of reported complications were postoperative confusion, infection, uncontrolled bleeding and deep vein thrombosis, ventilator-associated pneumonia, joint dislocation and decreased post-discharge mobility up to three months post-surgery. The OR for complications up to three months, based on one study, was 0.31 (CI, 0.13 to 0.72).

Ranking Effective Patient Safety Interventions

Patient interventions (n = 17) that result in a significant reduction in adverse event or mortality rates are ranked based on their effect size in **Table 3**.

Pharmacist interventions to reduce adverse drug events, exercises to reduce the risk of falling, care-bundle interventions and checklists to prevent infections and multicomponent interventions to prevent delirium have significantly better results compared to rapid-response teams, changes in staffing and interventions to improve hospital discharge to prevent mortality. Fourteen of the 17 significant effect sizes (82.4%) were based on five or fewer studies that comply with the inclusion criteria for study design. The AMSTAR scores of the systematic reviews of the 17 effective patient-safety interventions ranged from 4 to 10, with a mean score of 7.5 (SD ±1.9).

Three systematic reviews evaluated multicomponent interventions to prevent delirium (all with different compositions of the multicomponent intervention and different effect sizes); two systematic reviews evaluated the effects of rapid response-teams, resulting in 14 unique patient interventions (**Table 4**).

Table 3 **Patient-Safety Interventions (n = 17) ranked by their effect sizes**

Ranking	Patient-Safety Intervention	Patient outcome	Effect size (95%CI)	Relevant* studies in meta-analysis (n)	AMSTAR score
1	Pharmacist interventions [36]	*Adverse drug events*	**OR, 0.23 (0.11–0.48)**	2	7
2	Exercises [61]	*Risk of falling*	**RR, 0.36 (0.14–0.93)**	2	10
3	Care bundle and checklist [39]	*Infections (CLABSI)*	**OR, 0.39 (0.33–0.46)**	5	5
4	Multicomponent interventions, including early mobility, cognition and orientation [50]	*Delirium*	**OR, 0.47 (0.38–0.58)**	7	6
5	Surgical safety checklist [66]	*Surgical-site infections*	**RR, 0.57 (0.41–0.79)**	5	6
6	Increasing the proportion of support staff [75]	*Mortality at 4 months*	**RR, 0.57 (0.34–0.95)**	1	9
7	Multicomponent interventions, including cognitive screening, proactive geriatric consultation and psychotherapy [47]	*Delirium*	**OR, 0.58 (0.38–0.92)**	5	8
8	Clinical pathway [79]	*In-hospital complications*	**OR, 0.58 (0.36–0.94)**	5	10
9	Rapid-response team [69]	*Cardiopulmonary arrest*	**RR, 0.65 (0.55–0.77)**	16	8
10	Sepsis bundle [41]	*Mortality*	**OR, 0.66 (0.61–0.72)**	3	7
11	Interdisciplinary team interventions [76]	*Mortality*	**wRR, 0.67 (0.45–0.99)**	2	4
12	Multicomponent interventions [61]	*Falls*	**RaR, 0.69 (0.49–0.96)**	4	10
13	Nurse-led early-discharge planning programs [58]	*Mortality*	**RR , 0.70 (0.52–0.95)**	5	6
14	Catheter reminder and stop order [40]	*Infections (CAUTI)*	**RR, 0.72 (0.52–0.99)**	2	5
15	Multicomponent interventions, including physiotherapy, daily reorientation, family involvement, and staff/family-member education [51]	*Delirium*	**RR, 0.73 (0.63–0.85)**	7	9
16	Antibiotic guideline for pneumonia [33]	*Mortality*	**RR, 0.89 (0.82–0.97)**	4	9
17	Rapid-response team [71]	*Mortality*	**RR, 0.91 (0.85–0.97)**	4	8

CAUTI = catheter-associated urinary tract infection; CI = confidence interval; CLABSI = Central-line-associated bloodstream infection; OR = Odds Ratio; RR = Risk/Relative Ratio; RaR = Rate Ratio; wRR = weighted Risk Ratio

*Relevant study = study design in accordance with methodological criteria of the Cochrane Effective Practice and Organisation of Care (EPOC) review group and quantitative data on adverse event rates were reported

Table 4 **Evidence-based effective Patient-Safety interventions (n= 14)**
Effective Patient-Safety Interventions; evidence is based on more than 5 valid studies
Multicomponent interventions to prevent delirium
Rapid response team to reduce the risk for cardiopulmonary arrest and reduce mortality rates
Effective Patient-Safety Interventions; evidence is based on 5 or fewer valid studies
Pharmacist interventions to prevent adverse drug events
Exercises to reduce the risk of falling
Multicomponent interventions to reduce the risk of falling
Care bundles and checklists to reduce rates of central line associated blood stream infections
Surgical-safety checklist to reduce the risk for surgical-site infections and reduce mortality rates
Increasing the proportion of support staff to reduce mortality rates
Clinical pathways to avoid complications
Sepsis bundle to reduce mortality rates
Interdisciplinary team interventions to reduce mortality rates
Nurse-led early-discharge planning programs to reduce mortality rates
Catheter reminder and stop order to reduce the risk for developing catheter associated urinary tract infection
Antibiotic guideline for pneumonia to reduce mortality rates

DISCUSSION

We systematically reviewed the literature for effective interventions aimed at reducing adverse event rates and preventable deaths in hospitals. The results showed that there were 14 effective patient-safety interventions (**Table 4**). We found strong evidence, based on effect size and quality of underlying evidence, for the effectiveness of the following two types of interventions: 1) multicomponent interventions to prevent delirium and 2) rapid-response teams to reduce cardiopulmonary arrest and mortality rates. Other effective interventions were pharmacist interventions to reduce adverse drug events, exercises and multicomponent interventions to reduce the risk of falling, care bundles and checklists to reduce infection and mortality rates, changes in staffing and interventions to improve hospital discharge to reduce mortality rates. The evidence base that supports these interventions is moderate because found effect sizes were based on five or fewer primary studies that fulfilled the Cochrane EPOC criteria for study designs.[20]

This review offers a unique overview of effective patient-safety interventions based on data that is synthesized from systematic reviews, thereby producing a stronger evidence-based oversight of effective interventions compared to the outcomes of a systematic review of primary studies.[16] The overlap of primary studies in existing reviews is analyzed to minimize potential effects of "double-counting" primary studies in multiple reviews.[82] Moreover, most of the systematic reviews included in our review were of high methodological quality (mean AMSTAR score of 6.9 for all included reviews and 7.5 for the reviews with positively pooled outcome effects), thereby increasing the credibility and validity of our findings.[18]

Despite the growing number of experimental studies evaluating the effectiveness of patient-safety interventions, our findings show that the evidence base for patient-safety improvement is still not strong. Furthermore, our findings are in contrast to the findings of previous research on this topic. Shekelle and colleagues [83] strongly supported the adoption of 10 patient-safety practices, including hand-hygiene strategies, preoperative checklists, the do-not-use list for hazardous abbreviations and multicomponent interventions to reduce pressure ulcers. We found limited support for the effectiveness of these interventions while finding strong support for delirium-prevention interventions

and rapid-response teams. Our review placed more emphasis on assessing interventions on the basis of patient outcomes (i.e., reduced adverse event and mortality rates) and testing within high-quality designs; this emphasis on the quality of studies produces a very different assessment of which safety interventions are most beneficial for patients and which should be implemented.

Evidence is still lacking for medication reconciliation and several interventions to improve the safety of clinical handover or discharge of hospitalized patients, which are incorporated in national and international patient-safety campaigns and are recommended by the WHO.[84] However, the results of our review showed that by looking strictly at patient outcomes and only including high-quality studies, the evidence that these interventions reduce adverse event or mortality rates remains incomplete.

The lack of evidence for patient-safety interventions does not mean that these interventions do not work; it primarily addresses the lack of valid effect. Policy makers and clinicians show good intentions by implementing ambitious patient-safety programs and investments of resources. However, implementing unproven interventions can lead to the opposite of what is intended with patient-safety improvements: waste of resources, energy and enthusiasm.[85 86] In times of limited resources, we concur with Shekelle and colleagues and underscore previous, urgent calls for more research on the effectiveness of patient-safety interventions.[7 12 83 85 87 88] Patient-safety interventions should be tested on their effectiveness based on the same high-quality standards used for drug studies.[3 89]

This systematic review has several limitations. First, we did not retrieve data from the primary studies; instead, we used the information reported by the authors on aspects such as the description of the interventions and reported outcomes. As a result, the information for some patient-safety interventions and outcomes reported in our systematic review is limited. However, by focusing on the results of the systematic reviews rather than each individual primary study, we were able to obtain a broad overview of the field of patient safety.[90] Second, the found estimates of effectiveness of patient safety interventions might vary across contexts, such as small versus large hospitals, academically affiliated hospitals versus those that are not, and the availability of factors that stimulate successful implementation of interventions, e.g. strong leadership and an electronic patient record.[91] Third, in two-thirds of the included systematic reviews, publication bias was not assessed (**Appendix 7**), meaning that the pooled rates in these reviews may present an overestimation of the effect size.[92]

In conclusion, patient-safety interventions are implemented worldwide, even though evidence for these interventions remains incomplete. A major cause for this problem is the lack of high- quality studies in which interventions are evaluated on their effects. To contribute to evidence-based patient safety, interventions need to be evaluated based on high-quality research standards, including experimental research designs, measured outcomes at the patient level and description of the intervention, implementation process and context in detail. Description of these aspects is necessary to know which factors lead to optimal effects and how to replicate the patient-safety intervention in practice.[93 94] Policy makers and clinicians should stop taking shortcuts but need to spend more time and money conducting high-quality research on the effectiveness of patient-safety interventions to establish progress in patient safety.

CONTRIBUTORS

MZ, GH, CV and HW contributed to the design of the study. MZ, GH and WG did the literature search, reviewed the studies for inclusion, assessed the included studies, extracted and analyzed the data. MZ, GH and WG drafted the manuscript. CV and HW revised the manuscript critically for important intellectual content. All authors read and approved the final manuscript. MZ is the guarantor.

The guarantor affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

COMPETING INTERESTS

All authors declare that they have no competing interests.

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Not needed for this project.

DATA SHARING STATEMENT

No additional data are available.

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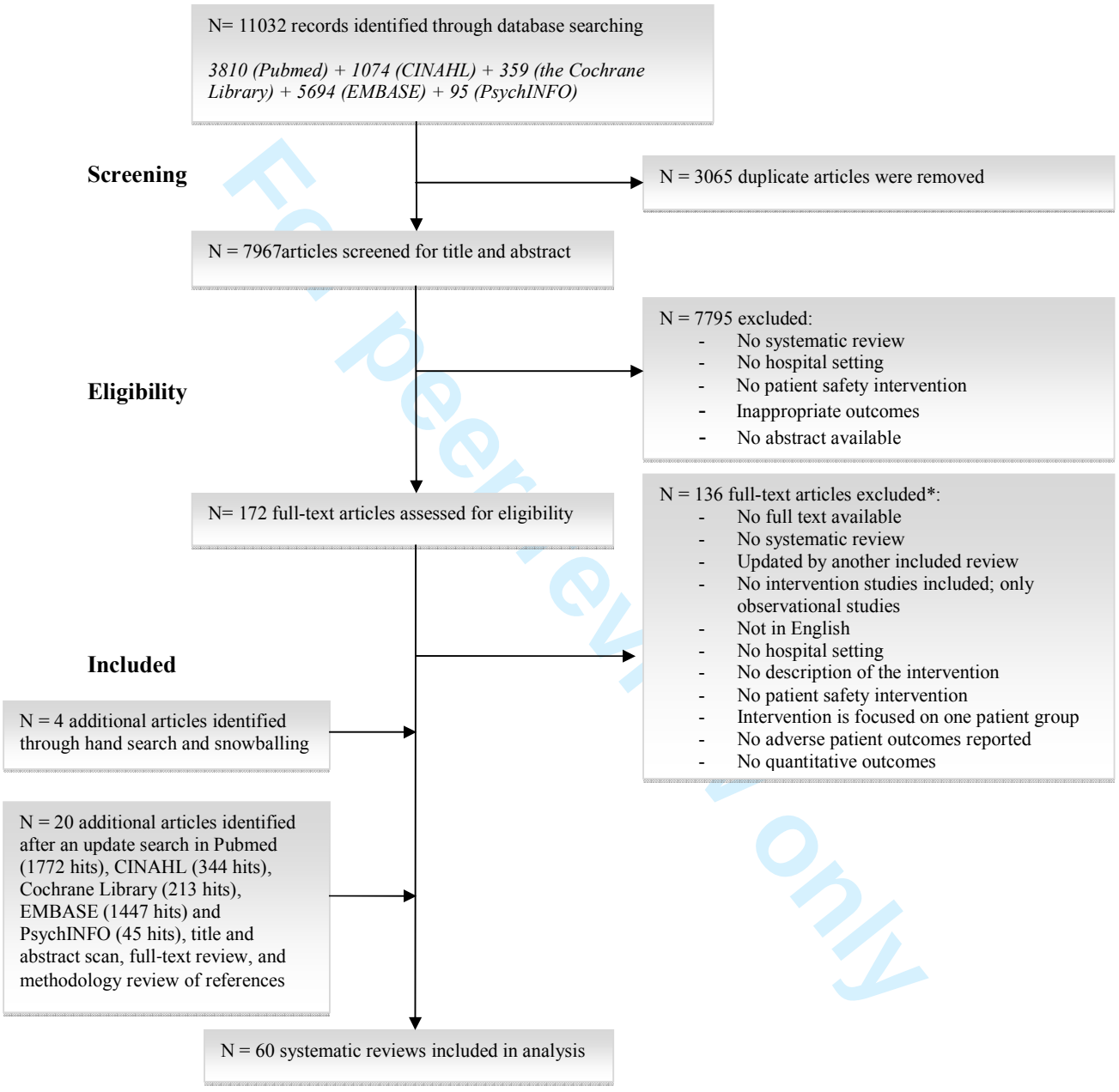
***Figure 1*. Summary of evidence search and selection.**



*See **Appendix 5** for the exclusion reason per systematic review after full text selection

Appendix 1 Protocol Systematic Review Patient-Safety Interventions.

Research question:
What are effective interventions to reduce the rate of adverse events and preventable deaths in hospitals?

Data Sources:
PubMed (including The National library of medicine**,** MEDLINE)
EMBASE
CINAHL
PsycInfo
The Cochrane Library (including the Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts on Reviews and Effectiveness (DARE), Cochrane Controlled Trial Register (CCTR), NHS Economic Evaluation Database (NHS-EED) and Health Technology Assessment Database (HTA))

Selection criteria:
Patients/setting
- Hospitalized patients

Interventions
- Patient-safety interventions are described as interventions, strategies, practices, behavior, actions, procedures, or structures which are aimed to improve patient safety by reducing unintended patient harm as a result of the process of healthcare (adverse events). The interventions should contain 1 or more components (described in the article) that aimed to reduce adverse patient outcomes. The intervention had to compare the effectiveness of a specific patient-safety intervention to other interventions or control.

Control
- Usual hospital care

Outcomes
- At least one or more objectively measured changes in patient-safety outcomes, adverse events, at the patient level (e.g. adverse drug events, mortality, infections, pneumonia, etc) during hospital stay and adverse events that occurred within the first 12 months after hospital stay. Systematic reviews that only report process errors (e.g. diagnostic errors, no hand hygiene, medication/prescribing errors) and errors in structure (e.g. stress and fatigue of health care providers, no safety culture) are not included. Moreover, consequences of adverse events in terms of extra treatment(s), increased length of stay and readmission are not the focus

Type of studies
- Systematic reviews/meta-analysis of primary studies which provide evaluative results of patient safety interventions and comply to the Cochrane Effective Practice and Organisation of Care (EPOC) review group methodological criteria

Languages
- English-language systematic reviews

Data collection and analysis
- See A. Abstract and full text selection form on page 2
- See B. Quality assessment form on page 3 and 4
- See C. Data abstraction form on page 5, 6 and 7

A. FORM FOR ABSTRACT AND FULL TEXT SELECTION

Reviewers	
Name Reviewer 1	
Name Reviewer 2	
Date	

Study	
ID Study	
Authors, year	
Title	

Selection Criteria	
1. ***Study design*** Systematic review, review or meta- analysis ***Yes (include)*** Systematic review of primary research, systematic reviews of systematic reviews, systematic comparative review. Abstract specifies "systematic review" or "meta analysis" as a term. ***No (exclude)*** Primary studies, editorials, letters, comments, expert opinions, unsystematic reviews, narrative reviews (without systematic elements or which don't report methodology), synthesis of non-empirical work, such as guidelines or conceptual articles, reviews of methodology, research protocol articles, critical review.	○ Yes ○ No ○ Unclear
2. ***Setting/Patients*** Intervention is targeted at hospitalized patients and involved health care providers ***Yes (include)*** Acute care, in-hospital care, in both developed as developing countries, systematic reviews including hospital care and other settings, unless effect measures are available for the hospital setting separately ***No (exclude)*** Residential care, nursing homes, dental care, psychiatry, mental care, homecare, primary care, paramedics, tertiary care, public health	○ Yes ○ No ○ Unclear
3. ***Interventions*** Effect evaluation of patient safety interventions, which are aimed to prevent unintended patient harm ***Yes (include)*** A full description of the intervention should be reported. At least the following: title, abstract, aim needs to refer to the patient safety intervention. ***No (exclude)*** No description of the intervention is given. Components of the intervention are unclear. Review of non-interventional studies.	○ Yes ○ No ○ Unclear
4. ***Outcomes*** Effectiveness of a patient safety intervention is measured at patient level ***Yes (include)*** Quantitative outcome(s) on patient level including adverse events, adverse drug events, infections, pneumonia, mortality ***No (exclude)*** Outcome at professional level (performance of professionals; healthcare professional behavior, team climate). Errors in process (diagnostic errors, no hand hygiene, medication/prescribing errors) and errors in structure/ healthcare delivery systems (stress and fatigue of health care providers, no safety culture)	○ Yes ○ No ○ Unclear
5. ***Evidence*** The methodology (including search strategy and design of included studies) is reported ***Yes (include)*** Review contains methodological justification for search strategy and report about the quality of included studies. ***No (exclude)*** No methodological justification for search strategy and the quality of included studies is not reported.	○ Yes ○ No ○ Unclear

CONCLUSION REVIEWER If no to any of the above questions, then **exclude**. If yes or unclear to all, then **include** for full text review.	○ INCLUDE ○ EXCLUDE

B. FORM FOR QUALITY ASSESSMENT OF SYSTEMATIC REVIEWS

1. Reviewers	
a) Name reviewer	
b) Name second reviewer	
c) Date	

2. Study	
a) Title	
b) Authors	
c) Source and year	

3. Quality rating*	
1) Was an ''a priori'' design provided? The research question and inclusion criteria should be established before the conduct of the review. *Note: Need to refer to a protocol, ethics approval, or pre-determined/a priori published research objectives to score a "yes."*	☐ Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
2) Was there duplicate study selection and data extraction? There should be at least two independent data extractors and a consensus procedure for disagreements should be in place. *Note: 2 people do study selection, 2 people do data extraction, consensus process or one person checks the other's work.*	☐ Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
3) Was a comprehensive literature search performed? At least two electronic sources should be searched. The report must include years and databases used. Key words and/or MESH terms must be stated, and where feasible, the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. *Note: If at least 2 sources + one supplementary strategy used, select "yes" (Cochrane register/Central counts as 2 sources; a grey literature search counts as supplementary).*	☐ Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
4) Was the status of publication (i.e., grey literature) used as an inclusion criterion? The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc. *Note: If review indicates that there was a search for "grey literature" or "unpublished literature," indicate "yes." SIGLE database, dissertations, conference proceedings, and trial registries are all considered grey for this purpose. If searching a source that contains both grey and non-grey, must specify that they were searching for grey/unpublished lit.*	☐ Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
5) Was a list of studies (included and excluded) provided? A list of included and excluded studies should be provided. *Note: Acceptable if the excluded studies are referenced. If there is an electronic link*	☐ Yes (1) ☐ No (0)

to the list but the link is dead, select "no."	☐ Can't answer (0) ☐ Not applicable (0)
6) Were the characteristics of the included studies provided? In an aggregated form, such as a table, data from the original studies should be provided on the participants, interventions, and outcomes. The ranges of characteristics in all the studies analyzed, e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. *Note: Acceptable if not in table format as long as they are described as above.*	☐ Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
7) Was the scientific quality of the included studies assessed and documented? ''A priori'' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo-controlled studies, or allocation concealment as inclusion criteria); for other types of studies, alternative items will be relevant. *Note: Can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, etc., or a description of quality items, with some kind of result for EACH study ("low" or "high" is fine, as long as it is clear which studies scored "low" and which scored "high"; a summary score/range for all studies is not acceptable).*	☐ Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
8) Was the scientific quality of the included studies used appropriately in formulating conclusions? The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. *Note: Might say something such as "the results should be interpreted with caution due to poor quality of included studies." Cannot score "yes" for this question if scored "no" for question 7.*	☐ Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
9) Were the methods used to combine the findings of studies appropriate? For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, I2). If heterogeneity exists, a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). *Note: Indicate "yes" if they mention or describe heterogeneity, i.e., if they explain that they cannot pool because of heterogeneity/variability between interventions.*	☐ Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
10) Was the likelihood of publication bias assessed? An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test). *Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.*	☐ Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
11) Was the conflict of interest included? Potential sources of support should be clearly acknowledged in both the systematic review and the included studies. *Note: To get a "yes," must indicate source of funding or support for the systematic review AND for each of the included studies.*	☐ Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
12) Total score	

***** Based on the AMSTAR criteria for Quality assessment of systematic reviews (Shea *et al. BMC Medical Research Methodology* 2007 **7**:10 doi:10.1186/1471-2288-7-10)
Additional notes (in italics) made by Michelle Weir, Julia Worswick, and Carolyn Wayne based on conversations with Bev Shea and/or Jeremy Grimshaw in June and October 2008 and July and September 2010. (http://amstar.ca/docs/AMSTARguideline.pdf)

C. DATA EXTRACTION FORM

1. Reviewers	
a) Name reviewer	
b) Date	
c) Cross-checked	

2. Study	
a) ID study	
b) Title	
c) Authors	
d) Source and year	

3. Objective and methods	
a) Objective/Aim of the review	
b) Number of studies included in the SR	
c) Time range of included studies	From: To:
d) Number of 'relevant' studies included (for the data analysis of this SR)	
e) Target population/participants	
f) Total no. of participants (sum of all 'relevant' included studies)	
g) Design/scientific quality of included studies	No. of Randomized controlled trials (RCTs): No. of non-randomised controlled clinical trials: No. of controlled before-and-after studies:

	No. of interrupted time series: No. of uncontrolled before-after studies and observational studies, including cohort study, case-control studies, cross-sectional studies, case studies:
h) Design/scientific quality of 'relevant' studies included (for the data analysis of this SR)	No. of Randomized controlled trials (RCTs): No. of non-randomised controlled clinical trials: No. of controlled before-and-after studies: No. of interrupted time series: No. of uncontrolled before-after studies and observational studies, including cohort study, case-control studies, cross-sectional studies, case studies:

4. Intervention	
i) Description of intervention (details/ comments)	

5. Outcome measurements	
j) Outcome measure 1	Definition: Qualitative/descriptive data: Quantitative/pooled results/combined ratios (e.g. risk rate):
k) Outcome measure 2	Definition: Qualitative/descriptive data: Quantitative/pooled results/combined ratios (e.g. risk rate):
l) Outcome measure 3	Definition: Qualitative/descriptive data: Quantitative/pooled results/combined ratios (e.g. risk rate):
m) Outcome measure 4	Definition: Qualitative/descriptive data: Quantitative/pooled results/combined ratios (e.g. risk rate):
n) Outcome measure 5	Definition: Qualitative/descriptive data: Quantitative/pooled results/combined ratios (e.g. risk rate):

o) Outcome measure 6	Definition: Qualitative/descriptive data: Quantitative/pooled results/combined ratios (e.g. risk rate):
p) Process evaluation (i.e., barriers and drivers for the implementation of the intervention)	

6. Limitations of the systematic review	
q) Description of limitations	Reported by the authors: Reported by us (researchers/reviewers):

7. Authors' key conclusions	
r) What conclusion did the authors make based on their findings? (e.g. first or last sentence of discussion/conclusion section)	

8. Other	
s) Comments/ remarks	

Appendix 2 PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4 and included as Appendix 1
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4 and Appendix 1
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4 and Appendix 4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix 4
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4, 5 and Appendix 1
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5 and Appendix 1
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	4, 5 and Appendix 1
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5 and assessment form in Appendix 1
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	11-18; Table 2 and 3, Appendix 10

Appendix 2 PRISMA 2009 Checklist

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	Not Applicable

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	5
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Not Applicable
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7 and Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Appendix 8
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	7, Appendix 6, Appendix 7
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	11-18, Appendix 10
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Not Applicable
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	7, Appendix 6, Appendix 7
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Not Applicable
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	20-22 and Table 4
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	21
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	22
FUNDING			

Appendix 2 PRISMA 2009 Checklist

Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	23

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

Appendix 3 Methodological quality systematic review on patient safety interventions.

AMSTAR Quality rating*	
1) Was an ''a priori'' design provided? The research question and inclusion criteria should be established before the conduct of the review. *Note: Need to refer to a protocol, ethics approval, or pre-determined/a priori published research objectives to score a "yes."*	X Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
2) Was there duplicate study selection and data extraction? There should be at least two independent data extractors and a consensus procedure for disagreements should be in place. *Note: 2 people do study selection, 2 people do data extraction, consensus process or one person checks the other's work.*	X Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
3) Was a comprehensive literature search performed? At least two electronic sources should be searched. The report must include years and databases used. Key words and/or MESH terms must be stated, and where feasible, the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. *Note: If at least 2 sources + one supplementary strategy used, select "yes" (Cochrane register/Central counts as 2 sources; a grey literature search counts as supplementary).*	X Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
4) Was the status of publication (i.e., grey literature) used as an inclusion criterion? The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc. *Note: If review indicates that there was a search for "grey literature" or "unpublished literature," indicate "yes." SIGLE database, dissertations, conference proceedings, and trial registries are all considered grey for this purpose. If searching a source that contains both grey and non-grey, must specify that they were searching for grey/unpublished lit.*	X Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
5) Was a list of studies (included and excluded) provided? A list of included and excluded studies should be provided. *Note: Acceptable if the excluded studies are referenced. If there is an electronic link to the list but the link is dead, select "no."*	X Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
6) Were the characteristics of the included studies provided? In an aggregated form, such as a table, data from the original studies should be provided on the participants, interventions, and outcomes. The ranges of characteristics in all the studies analyzed, e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. *Note: Acceptable if not in table format as long as they are described as above.*	X Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
7) Was the scientific quality of the included studies assessed and documented? ''A priori'' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo-controlled studies, or allocation concealment as inclusion criteria); for other types of studies, alternative items will be relevant. *Note: Can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, etc., or a description of quality items, with some kind of result for EACH study ("low" or "high" is fine, as long as it is clear which studies scored "low" and which*	X Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)

scored "high"; a summary score/range for all studies is not acceptable).	
8) Was the scientific quality of the included studies used appropriately in formulating conclusions? The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. *Note: Might say something such as "the results should be interpreted with caution due to poor quality of included studies." Cannot score "yes" for this question if scored "no" for question 7.*	X Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
9) Were the methods used to combine the findings of studies appropriate? For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, I2). If heterogeneity exists, a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). *Note: Indicate "yes" if they mention or describe heterogeneity, i.e., if they explain that they cannot pool because of heterogeneity/variability between interventions.*	☐ Yes (1) ☐ No (0) ☐ Can't answer (0) X Not applicable (0)
10) Was the likelihood of publication bias assessed? An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test). *Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.*	☐ Yes (1) X No (0) ☐ Can't answer (0) ☐ Not applicable (0)
11) Was the conflict of interest included? Potential sources of support should be clearly acknowledged in both the systematic review and the included studies. *Note: To get a "yes," must indicate source of funding or support for the systematic review AND for each of the included studies.*	X Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
12) Total score	9

*Shea *et al. BMC Medical Research Methodology* 2007 **7**:10 doi:10.1186/1471-2288-7-10

Additional notes (in italics) made by Michelle Weir, Julia Worswick, and Carolyn Wayne based on conversations with Bev Shea and/or Jeremy Grimshaw in June and October 2008 and July and September 2010. (http://amstar.ca/docs/AMSTARguideline.pdf)

Appendix 4 Search terms per database

Pubmed (July 22, 2013 / January 13, 2015 / October 6, 2015)

Search strategy

((((((((((((((((((((((Hospitals [Mesh]) OR Inpatients [Mesh]) OR Critical Care [Mesh]) OR Perioperative Care [Mesh]) OR Preoperative Care [Mesh]) OR hospital [tiab]) OR hospitals [tiab]) OR hospitalised [tiab]) OR hospitalized [tiab]) OR inpatient*[tiab]) OR critical care [tiab]) OR intensive care [tiab]) OR perioperative [tiab]) OR preoperative [tiab]) OR postoperative [tiab]) OR peri-operative [tiab]) OR pre-operative [tiab]) OR post-operative [tiab])))) AND ((Attitude of Health Personnel[mesh]) OR ((((((((((((((Patient Safety[mesh]) OR Patient Safety[tiab]) OR Risk Management [Mesh]) OR Risk Management [tiab]) OR Equipment Safety [Mesh]) OR Equipment Safety [tiab]) OR Harm Reduction [Mesh]) OR harm reduc*[tiab]) OR Safety Management[mesh]) OR Safety Management[tiab]) OR (((prevention and control [Subheading])))) OR prevent*[tiab]) OR safe*[tiab])) OR ((Hand Hygiene [Mesh]) OR Hospital Rapid Response Team [Mesh]) OR Hand Hygiene [tiab]) OR Rapid Response Team [tiab]) OR Medication Reconciliation [Mesh]) OR Medication Reconciliation [tiab]) OR Antibiotic Prophylaxis [Mesh]) OR Prophylaxis [tiab]) OR Infection Control [Mesh]) OR Infection Control [tiab]) OR Checklist[mesh]) OR Checklist[tiab]) OR Automatic Data Processing[mesh]) OR Automatic Data Processing[tiab]) OR Pain management[mesh]) OR Pain management[tiab]) OR Leadership[mesh]) OR Leadership[tiab]) OR Patient handoff[mesh]) OR Patient handoff[tiab]) OR Personnel staffing[Mesh term]) OR staff*[tiab]) OR Hospital nursing staff[mesh]) OR Hospital medical staff[mesh]) OR Nurse-Patient Ratio[tiab]) OR Education[mesh]) OR Education[tiab]) OR Patient simulation[mesh]) OR simulation[tiab]) OR Safety rounds[tiab]) OR fall prevent*[tiab]) OR pressure ulcer prevent*[tiab]) OR organizational culture[Mesh]) OR organizational culture[tiab]) OR safety culture[tiab]) OR Team training[tiab]) OR Case management [mesh]) OR Case management [tiab]) OR Continuity of Patient Care [mesh]) OR Quality indicators[mesh]) OR indicators[tiab]) OR Patient Participation[mesh]) OR Patient Participation[tiab])))) AND ((((((((((((((((mortality[mesh]) OR mortality[tiab]) OR adverse effects [Subheading]) OR adverse effect* [tiab]) OR Medical Errors [Mesh]) OR adverse event*[tiab]) OR harm*[tiab]) OR incident*[tiab]) OR Iatrogenic Disease[mesh]) OR complications [Subheading]) OR complication*[tiab]) OR adverse drug event*[tiab]) OR diagnostic err*[tiab]) OR medical err*[tiab]) OR medication err*[tiab]) OR surgical err*[tiab])))) AND (((((((((systematic review [ti]) OR meta-analysis [pt]) OR meta-analysis [ti]) OR systematic literature review [ti]) OR ((review [pt]) AND systematic review [tiab])) OR cochrane database syst rev[ta]) OR metaanal*[tiab]) OR meta-anal*[tiab]))

Hits: 3810 / 1146

CINAHL (July 22, 2013 / January 13, 2015/ October 6, 2015)

Search strategy

S116	S20 AND S102 AND S114 AND S115
S115	S31 OR S71
S114	S103 OR S104 OR S105 OR S106 OR S107 OR S108 OR S109 OR S110 OR S111 OR S112 OR S113
S113	AB systematic review* AND PT review

S112	PT meta analysis
S111	PT systematic review
S110	AB systematic literature review
S109	AB systematic review*
S108	AB Meta-anal*
S107	AB Meta Analysis
S106	(MH "Cochrane Library")
S105	(MH "Meta Analysis")
S104	(MH "Literature Review+")
S103	(MH "Systematic Review")
S102	S73 OR S74 OR S75 OR S76 OR S77 OR S78 OR S79 OR S80 OR S81 OR S82 OR S83 OR S84 OR S85 OR S86 OR S87 OR S88 OR S89 OR S90 OR S91 OR S92 OR S93 OR S94 OR S95 OR S96 OR S97 OR S98 OR S99 OR S100 OR S101
S101	(MH "Postoperative Complications+")
S100	(MH "Intraoperative Complications+")
S99	(MH "Catheter-Related Complications+")
S98	(MH "Blood Transfusion Reaction+")
S97	AB surgical error*
S96	(MH "Wrong Site Surgery")
S95	(MH "Fatal Outcome")
S94	(MH "Treatment Failure")
S93	(MH "Treatment Delay")
S92	AB Medication Error*
S91	(MH "Medication Errors+")
S90	AB Treatment Error*
S89	(MH "Treatment Errors+")
S88	AB Diagnostic Error*
S87	(MH "Diagnostic Errors+")
S86	(MH "Inappropriate Prescribing")
S85	(MH "Sentinel Event")
S84	(MH "Health Care Errors+")
S83	(MH "Iatrogenic Disease")

S82	AB complication*
S81	AB Incident*
S80	AB medical error*
S79	AB adverse event*
S78	AB Adverse Health Care Event*
S77	(MH "Adverse Health Care Event+")
S76	AB Adverse Drug Event*
S75	(MH "Adverse Drug Event+")
S74	AB Mortality
S73	(MH "Mortality+")
S72	S31 OR S71
S71	S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55 OR S56 OR S57 OR S58 OR S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70
S70	(MH "Employee attitudes")
S69	AB patient participation
S68	(MH "Surgical Site Verification")
S67	(MH "Computerized Patient Record")
S66	(MH "Consumer Participation")
S65	AB quality indicator*
S64	(MH "Clinical Indicators")
S63	AB Case Management
S62	(MH "Case Management")
S61	AB team training
S60	(MH "Multidisciplinary Care Team+")
S59	(MH "Communication Skills Training")
S58	AB safety culture
S57	AB Organi* Culture
S56	(MH "Organizational Culture+")
S55	AB Safety round*
S54	AB Simulation*

S53	(MH "Simulations+")
S52	AB Education
S51	(MH "Education+")
S50	AB staffing
S49	(MH "Nurse-Patient Ratio")
S48	(MH "Personnel Staffing and Scheduling+")
S47	AB Handover
S46	(MH "Continuity of Patient Care+")
S45	(MH "SBAR Technique")
S44	(MH "Hand Off (Patient Safety)+")
S43	AB Leadership*
S42	(MH "Leadership")
S41	AB Checklist*
S40	(MH "Checklists")
S39	AB Prophylaxis
S38	(MH "Antibiotic Prophylaxis")
S37	AB Medication Reconciliation*
S36	(MH "Medication Reconciliation")
S35	AB Rapid Response Team*
S34	AB Hand washing
S33	AB infection control*
S32	(MH "Infection Control+")
S31	S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30
S30	AB safe*
S29	AB Prevent*
S28	AB Safety Management
S27	AB harm reduc*
S26	(MH "Harm Reduction")
S25	(MH "Equipment Safety")
S24	AB Risk Management
S23	(MH "Risk Management+")

S22 AB Patient Safety

S21 (MH "Patient Safety+")

S20 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19

S19 AB postoperative care

S18 AB preoperative care

S17 AB perioperative care

S16 AB intensive care

S15 AB critical care

S14 (MH "Postoperative Period")

S13 (MH "Preoperative Period+")

S12 (MH "Preoperative Care+")

S11 (MH "Postoperative Care+")

S10 (MH "Intraoperative Care+")

S9 (MH "Perioperative Care+")

S8 (MH "Intensive Care, Neonatal+")

S7 (MH "Critical Care+")

S6 AB Inpatients*

S5 (MH "Inpatients")

S4 AB hospital*

S3 (MH "Intensive Care Units+")

S2 (MH "Hospital Units+")

S1 (MH "Hospitals+")

Hits: 1074 / 222

Embase (July 22, 2013 / January 13, 2015/ October 6, 2015)

Search strategy

#92 #18 and #63 and #81 and #91

#91 #82 or #83 or #86 or #87 or #90

#90 #88 and #89

#89 #84 or #85

#88 "systematic*".ti,ab.

#87 "meta-anal*".ti,ab.

#86	"meta anal*".ti,ab.
#85	"review"/
#84	exp literature/
#83	meta analysis/
#82	exp "systematic review"/
#81	#64 or #65 or #66 or #67 or #68 or #69 or #70 or #71 or #72 or #73 or #74 or #75 or #76 or #77 or #78 or #79 or #80
#80	"surgical err*".ti,ab.
#79	"medication error*".ti,ab.
#78	"medical err*".ti,ab.
#77	"diagnostic err*".ti,ab.
#76	"medical error*".ti,ab.
#75	"adverse drug event*".ti,ab.
#74	"root complication*".ti,ab.
#73	"root incident*".ti,ab.
#72	"harm*".ti,ab.
#71	"adverse event*".ti,ab.
#70	"adverse effect*".ti,ab.
#69	mortality.ti,ab.
#68	exp complication/
#67	exp iatrogenic disease/
#66	exp medical error/
#65	exp adverse drug reaction/
#64	exp mortality/
#63	19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62
#62	"staff*".ti,ab.
#61	organi?ational culture.ti,ab.
#60	indicators.ti,ab.
#59	patient participation.ti,ab.
#58	case management.ti,ab.
#57	team training.ti,ab.
#56	safety culture.ti,ab.
#55	"fall prevent*".ti,ab.
#54	safety rounds.ti,ab.
#53	patient handoff.ti,ab.

#52	leadership.ti,ab.
#51	pain management.ti,ab.
#50	checklist.ti,ab.
#49	infection control.ti,ab.
#48	prophylaxis.ti,ab.
#47	rapid response team.ti,ab.
#46	hand hygiene.ti,ab.
#45	exp patient participation/
#44	exp case management/
#43	exp teaching/
#42	exp education/
#41	exp nurse patient ratio/
#40	exp medical staff/
#39	exp nursing staff/
#38	exp clinical handover/
#37	exp leadership/
#36	exp checklist/
#35	exp infection control/
#34	exp antibiotic prophylaxis/
#33	exp medication therapy management/
#32	exp rapid response team/
#31	exp hand washing/
#30	exp prevention/
#29	"safe*".ti,ab.
#28	"prevent*".ti,ab.
#27	safety management.ti,ab.
#26	"harm reduc*".ti,ab.
#25	equipment safety.ti,ab.
#24	device safety.ti,ab.
#23	risk management.ti,ab.
#22	exp harm reduction/
#21	exp device safety/
#20	exp risk management/
#19	exp patient safety/
#18	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17

#17 post-operative.ti,ab.
#16 pre-operative.ti,ab.
#15 peri-operative.ti,ab.
#14 postoperative.ti,ab.
#13 preoperative.ti,ab.
#12 perioperative.ti,ab.
#11 intensive care.ti,ab.
#10 critical care.ti,ab.
#9 "inpatient*".ti,ab.
#8 hospitali?ed.ti,ab.
#7 hospitals.ti,ab.
#6 hospital.ti,ab.
#5 exp preoperative care/
#4 exp perioperative period/
#3 exp intensive care/
#2 exp hospital patient/
#1 exp hospital/
Hits: 5694 / 838

Cochrane library (July 22, 2013 / January 13, 2015/ October 6, 2015)

Search strategy
#1 MeSH descriptor: [Hospitals] explode all trees
#2 MeSH descriptor: [Inpatients] explode all trees
#3 MeSH descriptor: [Critical Care] explode all trees
#4 MeSH descriptor: [Perioperative Care] explode all trees
#5 MeSH descriptor: [Preoperative Care] explode all trees
#6 hospital:ti,ab,kw (Word variations have been searched)
#7 critical care:ti,ab,kw (Word variations have been searched)
#8 inpatient:ti,ab,kw (Word variations have been searched)
#9 Preoperative Care:ti,ab,kw (Word variations have been searched)
#10 Perioperative Care:ti,ab,kw (Word variations have been searched)
#11 Postoperative Care:ti,ab,kw (Word variations have been searched)
#12 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #8 or #9 or #10 or #11
#13 MeSH descriptor: [Patient Safety] explode all trees
#14 patient safety:ti,ab,kw (Word variations have been searched)
#15 MeSH descriptor: [Risk Management] explode all trees
#16 risk management:ti,ab,kw (Word variations have been searched)
#17 MeSH descriptor: [Equipment Safety] explode all trees
#18 equipment safety:ti,ab,kw (Word variations have been searched)
#19 MeSH descriptor: [Harm Reduction] explode all trees
#20 harm reduc*:ti,ab,kw (Word variations have been searched)
#21 MeSH descriptor: [Safety Management] explode all trees

#22	safety management:ti,ab,kw (Word variations have been searched)
#23	prevent*:ti,ab,kw (Word variations have been searched)
#24	safe*:ti,ab,kw (Word variations have been searched)
#25	#13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24
#26	MeSH descriptor: [Infection Control] explode all trees
#27	infection control:ti,ab,kw (Word variations have been searched)
#28	MeSH descriptor: [Hand Hygiene] explode all trees
#29	hand hygiene:ti,ab,kw (Word variations have been searched)
#30	MeSH descriptor: [Hospital Rapid Response Team] explode all trees
#31	Rapid Response Team:ti,ab,kw (Word variations have been searched)
#32	MeSH descriptor: [Medication Reconciliation] explode all trees
#33	Medication Reconciliation:ti,ab,kw (Word variations have been searched)
#34	MeSH descriptor: [Antibiotic Prophylaxis] explode all trees
#35	Prophylaxis:ti,ab,kw (Word variations have been searched)
#36	MeSH descriptor: [Checklist] explode all trees
#37	checklist*:ti,ab,kw (Word variations have been searched)
#38	MeSH descriptor: [Automatic Data Processing] explode all trees
#39	MeSH descriptor: [Pain Management] explode all trees
#40	Pain management:ti,ab,kw (Word variations have been searched)
#41	MeSH descriptor: [Leadership] explode all trees
#42	Leadership:ti,ab,kw (Word variations have been searched)
#43	MeSH descriptor: [Patient Handoff] explode all trees
#44	handoff:ti,ab,kw (Word variations have been searched)
#45	handover:ti,ab,kw (Word variations have been searched)
#46	MeSH descriptor: [Continuity of Patient Care] explode all trees
#47	MeSH descriptor: [Personnel Staffing and Scheduling] explode all trees
#48	staff*:ti,ab,kw (Word variations have been searched)
#49	MeSH descriptor: [Nursing Staff, Hospital] explode all trees
#50	MeSH descriptor: [Medical Staff, Hospital] explode all trees
#51	MeSH descriptor: [Education] explode all trees
#52	education:ti,ab,kw (Word variations have been searched)
#53	MeSH descriptor: [Patient Simulation] explode all trees
#54	simulation:ti,ab,kw (Word variations have been searched)
#55	Safety round*:ti,ab,kw (Word variations have been searched)
#56	fall prevention:ti,ab,kw (Word variations have been searched)
#57	pressure ulcer prevention:ti,ab,kw (Word variations have been searched)
#58	MeSH descriptor: [Organizational Culture] explode all trees
#59	organizational culture:ti,ab,kw (Word variations have been searched)
#60	safety culture:ti,ab,kw (Word variations have been searched)
#61	Team training:ti,ab,kw (Word variations have been searched)
#62	MeSH descriptor: [Case Management] explode all trees
#63	Case management:ti,ab,kw (Word variations have been searched)
#64	MeSH descriptor: [Quality Indicators, Health Care] explode all trees
#65	indicator*:ti,ab,kw (Word variations have been searched)
#66	MeSH descriptor: [Patient Participation] explode all trees
#67	Patient Participation:ti,ab,kw (Word variations have been searched)

#68 #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56 or #57 or #58 or #59 or #60 or #61 or #62 or #63 or #64 or #65 or #66 or #67
#69 #25 or #68
#70 MeSH descriptor: [Mortality] explode all trees
#71 mortality:ti,ab,kw (Word variations have been searched)
#72 adverse effect*:ti,ab,kw (Word variations have been searched)
#73 MeSH descriptor: [Medical Errors] explode all trees
#74 medical error*:ti,ab,kw (Word variations have been searched)
#75 adverse event*:ti,ab,kw (Word variations have been searched)
#76 harm*:ti,ab,kw (Word variations have been searched)
#77 incident*:ti,ab,kw (Word variations have been searched)
#78 MeSH descriptor: [Iatrogenic Disease] explode all trees
#79 complication*:ti,ab,kw (Word variations have been searched)
#80 adverse drug event*:ti,ab,kw (Word variations have been searched)
#81 #70 or #71 or #72 or #73 or #74 or #75 or #76 or #77 or #78 or #79 or #80
#82 systematic review:ti,ab,kw (Word variations have been searched)
#83 systematic literature review:ti,ab,kw (Word variations have been searched)
#84 meta-analysis:pt (Word variations have been searched)
#85 review:pt (Word variations have been searched)
#86 meta-anal*:ti,ab,kw (Word variations have been searched)
#87 #82 and #85
#88 #82 or #83 or #84 or #86 or #87
#89 #12 and #69 and #81 and #88: in Cochrane Reviews (Reviews and Protocols) and Other Reviews
Hits: 359 / 134

PsychINFO (July 22, 2013/ January 13, 2015/ October 6, 2015)

Search strategy

#81 #18 and #58 and #75 and #80
#80 #76 or #77 or #78 or #79
#79 "meta-anal*".ab,ti.
#78 "meta anal*".ab,ti.
#77 exp Meta Analysis/
#76 "literature review"/
#75 #59 or #60 or #61 or #62 or #63 or #64 or #65 or #66 or #67 or #68 or #69 or #70 or #71 or #72 or #73 or #74
#74 "surgical err*".ab,ti.
#73 "medical err*".ab,ti.
#72 "diagnostic err*".ab,ti.
#71 '"adverse drug event*"'.ab,ti.
#70 "complication*".ab,ti.
#69 "incident*".ab,ti.

#68	"harm*".ab,ti.
#67	adverse events.ab,ti.
#66	adverse event.ab,ti.
#65	"adverse effect*".ab,ti.
#64	mortality.ab,ti.
#63	exp Postsurgical Complications/
#62	exp "Complications (Disorders)"/
#61	exp Errors/
#60	exp "Side Effects (Drug)"/
#59	exp "Death and Dying"/
#58	#19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56 or #57
#57	" prevent*".ab,ti.
#56	"safe*".ab,ti.
#55	"pressure ulcer prevent*".ab,ti.
#54	'patient participation'.ab,ti.
#53	indicators.ab,ti.
#52	'case management'.ab,ti.
#51	'team training'.ab,ti.
#50	'safety culture'.ab,ti.
#49	'organi?ational culture'.ab,ti.
#48	'safety rounds'.ab,ti.
#47	simulation.ab,ti.
#46	education.ab,ti.
#45	'nurse-patient ratio'.ab,ti.
#44	"staff*".ab,ti.
#43	'patient handoff'.ab,ti.
#42	leadership.ab,ti.
#41	'pain management'.ab,ti.
#40	checklist.ab,ti.
#39	'infection control'.ab,ti.
#38	prophylaxis.ab,ti.
#37	'medication reconciliation'.ab,ti.
#36	'rapid response team'.ab,ti.
#35	'hand hygiene'.ab,ti.

#34	exp "Continuum of Care"/
#33	exp Client Participation/
#32	exp Employee Attitudes/
#31	exp Organizational Climate/
#30	exp Simulation/
#29	exp Education/
#28	exp Medical Personnel/
#27	exp Leadership/
#26	exp Pain Management/
#25	exp Drug Therapy/
#24	exp Emergency Services/
#23	exp Hygiene/
#22	exp Harm Reduction/
#21	exp Safety Devices/
#20	exp Risk Management/
#19	exp Safety/
#18	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17
#17	post-operative.ab,ti.
#16	pre-operative.ab,ti.
#15	peri-operative.ab,ti.
#14	postoperative.ab,ti.
#13	preoperative.ab,ti.
#12	perioperative.ab,ti.
#11	'intensive care'.ab,ti.
#10	'critical care'.ab,ti.
#9	"inpatient*".ab,ti.
#8	hospitalized.ab,ti.
#7	hospitalised.ab,ti.
#6	hospitals.ab,ti.
#5	hospital.ab,ti.
#4	exp Surgery/
#3	exp Intensive Care/
#2	exp Hospitalized Patients/
#1	exp Hospitals/

Hits: 95 / 30

Appendix 5 **Excluded systematic reviews after full text selection (n=136)**

Year	Authors	Title	Reason for exclusion
1997		Collaborative systematic review of the randomised trials of organised inpatient (stroke unit) care after stroke. Stroke Unit Trialists' Collaboration	Intervention is focused on one patient group
1997	Griffith et al.	Internal medicine residency training and outcomes	No adverse patient outcomes reported No patient safety intervention
1998	Saint	Risk reduction in the intensive care unit	Pharmacological studies No patient safety intervention
1999	Meagher	Colorectal cancer: is the surgeon a prognostic factor? A systematic review	Intervention is focused on one patient group
2001	Gillespie et al.	Interventions for preventing falls in elderly people	Updated by another included review
2001	Ioannidis	Evidence on interventions to reduce medical errors: an overview and recommendations for future research	No adverse patient outcomes reported
2001	Rawal	Treating postoperative pain improves outcome	Pharmacological studies
2001	Shojania et al.	Making health care safer: a critical analysis of patient safety practices	Overall review (used for snowballing)
2002	Berenholtz et al.	Qualitative review of intensive care unit quality indicators	No quantitative ouctomes
2002	Harkness	Review: specialised multidisciplinary follow up reduces hospital admissions but not mortality in patients with heart failure	No systematic review
2002	Iregui et al.	Nonpharmacological prevention of hospital-acquired pneumonia	No systematic review
2002	Kehlet	Multimodal strategies to improve surgical outcome	No adverse patient ouctomes reported
2003	Gandjour et al.	Threshold volumes associated with higher survival in health care: a systematic review	No intervention studies included; only observational studies
2003	Kaushal et al.	Effects of computerized physician order entry and clinical decision support systems on medication safety: a systematic review (Structured abstract)	Updated by another included review
2003	McDonnell et al.	Acute pain teams and the management of postoperative pain: a systematic review and meta-analysis	No intervention studies included; only observational studies
2003	Patel et al.	New treatment strategies for severe sepsis and septic shock	No systematic review
2004	Dodek et al.	Evidence-based clinical practice guideline for the prevention of ventilator-associated pneumonia	No adverse patient outcomes reported
2004	Gastmeier	Nosocomial infection surveillance and control policies	No systematic review
2004	Kalant	Volume and outcome of coronary artery bypass graft surgery: are more and less the same?	Intervention is focused on one patient group
2004	Lang et al.	Nurse-patient ratios: a systematic review on the effects of nurse staffing on patient, nurse employee, and hospital outcomes	No quantitative outcomes
2004	Phillips et al.	Comprehensive discharge planning with postdischarge support for older patients with congestive heart failure: a meta-analysis	Intervention is focused on one patient group
2004	Picheansathian	A systematic review on the effectiveness of alcohol-based solutions for hand hygiene	Pharmacological studies
2004	Rideout	Review: comprehensive discharge planning plus post-discharge support reduced total readmissions in older patients with congestive heart failure	No systematic review
2004	Shepperd et al.	Discharge planning from hospital to home	Updated by another included review
2005	Davoli et al.	[Volume and health outcomes: an overview of systematic reviews]	Not in English
2005	Lee	A systematic review for effective management of central venous catheters and catheter sites in acute care paediatric patients	No patient safety intervention
2006	Aneman	Medical emergency teams: a role for expanding intensive care?	Updated by another included review
2006	Gastmeier	Prevention of catheter-related bloodstream infections: analysis of studies published between 2002 and 2005	No patient safety intervention
2006	Lawrence et al.	Clinical guidelines. Strategies to reduce postoperative pulmonary complications after noncardiothoracic surgery: systematic review for the American College of Physicians	Duplicate record
2006	Lawrence et al.	Strategies to reduce postoperative pulmonary complications after noncardiothoracic surgery: systematic review for the American College of Physicians	No patient safety intervention
2006	Numata et al.	Nurse staffing levels and hospital mortality in critical care settings: literature review and meta-analysis	No intervention studies included; only observational studies
2006	Pearson et al.	Systematic review of evidence on the impact of nursing workload and staffing on establishing healthy work environments	No intervention studies included; only observational studies
2006	Rabie	Handwashing and risk of respiratory infections: a quantitative systematic review	No hospital setting
2006	Sanghera et al.	Interventions of hospital pharmacists in improving drug therapy in children: a systematic literature review	No quantitative outcomes
2006	Washer	Infection control strategies for methicillin-resistant staphylococcus aureus and vancomycin-resistant enterococcus: What is the evidence?	No intervention studies included; only observational studies
2007	Aboelela et al.	Effectiveness of bundled behavioural interventions to control healthcare-associated infections: a systematic review of the literature	No intervention studies included; only observational studies
2007	Burgers et al.	[Relationship between volume and quality of care for surgical interventions; results of a literature review]	No intervention studies included; only observational studies Not in English
2007	Chowdhury et al.	A systematic review of the impact of volume of surgery and specialization on patient outcome	No intervention studies included; only observational studies
2007	Foley et al.	Specialized stroke services: a meta-analysis comparing three models of care	Intervention is focused on one patient group No patient safety intervention
2007	Gastmeier	Evidence-based infection control in the ICU (except catheters)	No patient safety intervention

2007	Gastmeier	Prevention of ventilator-associated pneumonia: analysis of studies published since 2004	No patient safety intervention
2007	Kane et al.	The association of registered nurse staffing levels and patient outcomes: Systematic review and meta-analysis	No intervention studies included; only observational studies
2007	Kane et al.	Nurse staffing and quality of patient care	No intervention studies included; only observational studies
2007	McGaughey et al.	Outreach and Early Warning Systems (EWS) for the prevention of Intensive Care admission and death of critically ill adult patients on general hospital wards	Updated by another included review
2007	Pedrosa et al.	Effects of educational programs in post-operative pain [Portuguese]	Not in English
2007	Siddiqi	Interventions for preventing delirium in hospitalised patients (Review)	Updated by another included review
2007	Whitehorn	A review of the use of insulin protocols to maintain normoglycaemia in high dependency patients	No systematic review
2007	Winters et al.	Rapid response systems: a systematic review	Updated by another included review
2007	Wong	The relationship between nursing leadership and patient outcomes: a systematic review (Structured abstract)	No adverse patient ouctomes reported
2008	Allen	How has the impact of 'care pathway technologies' on service integration in stroke care been measured and what is the strength of the evidence to support their effectiveness in this respect?	Intervention is focused on one patient group
2008	Crowe et al.	Systematic review of the effectiveness of nursing interventions in reducing or relieving post-operative pain	Pharmacological studies
2008	Eslami et al.	The impact of computerized physician medication order entry in hospitalized patients--a systematic review	No quantitative ouctomes
2008	Shamliyan et al.	Just what the doctor ordered. Review of the evidence of the impact of computerized physician order entry system on medication errors	No intervention studies included; only observational studies
2008	Yamada et al.	A review of systematic reviews on pain interventions in hospitalized infants	Pharmacological studies and clinical interventions
2009	Arora et al.	Hospitalist handoffs: a systematic review and task force recommendations	No adverse patient outcomes reported
2009	Cohen et al.	Effect of clinical pharmacists on care in the emergency department: a systematic review	No adverse patient outcomes reported
2009	Cozart	Falls aren't us: state of the science	No adverse patient outcomes reported
2009	Dückers et al.	Safety and risk management interventions in hospitals: a systematic review of the literature	Overall review (used for snowballing)
2009	Endacott et al.	An integrative review and meta-synthesis of the scope and impact of intensive care liaison and outreach services	Updated by another included review
2009	Fung-Kee-Fung et al.	Regional collaborations as a tool for quality improvements in surgery: a systematic review of the literature	No quantitative outcomes
2009	Grinstein-Cohen et al.	Improvements and difficulties in postoperative pain management	No adverse patient outcomes reported
2009	Gruen et al.	The effect of provider case volume on cancer mortality: systematic review and meta-analysis	No intervention studies included; only observational studies
2009	Helfand	Assessment and management of acute pain in adult medical inpatients: A systematic review	No adverse patient outcomes reported
2009	Kaur et al.	Interventions that can reduce inappropriate prescribing in the elderly: a systematic review	No adverse patient outcomes reported
2009	Marwick	Care bundles: The holy grail of infectious risk management in hospital?	No systematic review
2009	Reckmann et al.	Does computerized provider order entry reduce prescribing errors for hospital inpatients? A systematic review	No adverse patient ouctomes reported No systematic review
2009	Stern	Interventions to reduce the incidence of falls in older adult patients in acute-care hospitals: a systematic review	Updated by another included review
2009	van Rosse et al.	The effect of computerized physician order entry on medication prescription errors and clinical outcome in pediatric and intensive care: A systematic review	No intervention studies included; only observational studies
2009	West et al.	Nursing resources and patient outcomes in intensive care: a systematic review of the literature	No intervention studies included; only observational studies
2009	Zilberberg et al.	Implementing quality improvements in the intensive care unit: ventilator bundle as an example	No intervention studies included; only observational studies
2010		Nursing staff and patient results: systematic review about the existing relationship [Spanish]	Not in English
2010	Archampong et al.	Impact of surgeon volume on outcomes of rectal cancer surgery: a systematic review and meta-analysis	No intervention studies included; only observational studies
2010	Barocas et al.	Impact of surgeon and hospital volume on outcomes of radical prostatectomy	No intervention studies included; only observational studies
2010	Cameron et al.	Interventions for preventing falls in older people in nursing care facilities and hospitals	Updated by another included review
2010	Chen et al.	Do multi-component hospital-based programs prevent delirium? A systematic review	No full text available
2010	Fanara et al.	Recommendations for the intra-hospital transport of critically ill patients	Designs
2010	Giakoumidakis et al.	The association between the nursing workload and patient mortality [Greek]	Not in English
2010	Hall et al.	Effectiveness of interventions designed to promote patient involvement to enhance safety: a systematic review	No quantitative ouctomes
2010	Karthikesalinga	Volume-outcome relationships in vascular surgery: the current status	No intervention studies included; only

	m et al.		observational studies
2010	Meddings et al.	Systematic review and meta-analysis: reminder systems to reduce catheter-associated urinary tract infections and urinary catheter use in hospitalized patients	Updated by another included review
2010	Muir	A systematic review of the effect of medication reconciliation on medication discrepancies and adverse drug events	No full text available
2010	Rabol et al.	Outcomes of classroom-based team training interventions for multiprofessional hospital staff. A systematic review	No intervention studies included; only observational studies
2010	Seehusen	Clinical pathways: Effects on practice, outcomes, and costs	No systematic review
2010	Subirana Casacuberta et al.	[Nursing staff and patient results: systematic review about the existing relationship]	Not in English
2010	Suri et al.	Post discharge management programs for elderly heart failure patients: A systematic review and meta-analysis of randomized clinical trials	No full text available
2010	Wong et al.	A systematic review of medication safety outcomes related to drug interaction software	No hospital setting
2011	Abbenbroek et al.	Intensive care unit volume - Outcome relationship: Is bigger better?	No full text available
2011	Anderson et al.	Interventions designed to prevent healthcare bed-related injuries in patients	Updated by another included review
2011	Bakker et al.	Perioperative cardiac evaluation, monitoring, and risk reduction strategies in noncardiac surgery patients	No systematic review
2011	Bapoje et al.	Effectiveness of rapid response call criteria: A systematic review and meta-analysis	No full text available
2011	Camp	Efficacy of medication reconciliation in the prevention of adverse events [Spanish]	Not in English
2011	Evans	The effect of surgical training and hospital characteristics on patient outcomes after pediatric surgery: a systematic review	Intervention is focused on one patient group
2011	Fletcher et al.	Patient safety, resident education and resident well-being following implementation of the 2003 ACGME duty hour rules	No intervention studies included; only observational studies
2011	Fry	Literature review of the impact of nurse practitioners in critical care services	No quantitative outcomes
2011	Gomes da et al.	Influence of dimensioning the nursing staff on the quality of care of the critical patient [Portuguese]	Not in English
2011	Hansen et al.	Interventions to reduce 30-day rehospitalization: a systematic review	No patient harm reported
2011	Kaki et al.	Impact of antimicrobial stewardship in critical care: a systematic review	No intervention studies included; only observational studies
2011	Ketelaar et al.	Public release of performance data in changing the behaviour of healthcare consumers, professionals or organisations	No adverse patient outcomes reported Intervention is focused on one patient group
2011	Nikolaidou et al.	Nursing management of postoperative pain in children after cardiac surgery	No full text available
2011	Reddy	Pressure ulcers	Clinical interventions (no specific patient safety interventions)
2011	Rubulotta	Rapid response systems: A re-analysis basedonfrequencyof rrs calls and discovery of methodological issues	No full text available
2011	Wilson	The effect of nurse staffing on clinical outcomes of children in hospital: a systematic review	No intervention studies included; only observational studies
2011	Wulff	Medication administration technologies and patient safety: a mixed-method systematic review	No quantitative outcomes
2012	Anderson et al.	Interventions designed to prevent healthcare bed-related injuries in patients	Updated by another included review
2012	Alsulami et al.	Double checking the administration of medicines: what is the evidence? A systematic review	No adverse patient outcomes reported
2012	Alsulami et al.	A systematic review of the effectiveness of double checking in preventing medication errors	No full text available
2012	de Cordova et al.	Twenty-four/seven: a mixed-method systematic review of the off-shift literature	No intervention studies included; only observational studies
2012	DiBardino et al.	Meta-analysis: multidisciplinary fall prevention strategies in the acute care inpatient population	Updated by another included review
2012	Greig	A review of nosocomial norovirus outbreaks: Infection control interventions found effective	No intervention studies included; only observational studies
2012	Harden	What is best practice to prevent wrong-site surgery?	No full text available
2012	Joram et al.	Healthcare-associated infection prevention in pediatric intensive care units: a review	No systematic review
2012	Kadda et al.	The role of nursing education after a cardiac event	Intervention is focused on one patient group
2012	Kul et al., M.	Effects of care pathways on the in-hospital treatment of heart failure: a systematic review	Intervention is focused on one patient group
2012	Laugaland et al.	Interventions to improve patient safety in transitional care - a review of the evidence	No quantitative outcomes
2012	McGahan et al.	Nurse staffing levels and the incidence of mortality and morbidity in the adult intensive care unit: A literature review	No intervention studies included; only observational studies
2012	Popp	Prevention and treatment options for postoperative delirium in the elderly	No systematic review
2012	Rennke et al.	Interventions to prevent adverse events and readmissions after hospital discharge: A systematic review	No full text available
2012	Rotter et al.	The effects of clinical pathways on professional practice, patient outcomes,	No quantitative outcomes

		length of stay, and hospital costs: Cochrane systematic review and meta-analysis	
2012	Snyder et al.	Effectiveness of barcoding for reducing patient specimen and laboratory testing identification errors: a Laboratory Medicine Best Practices systematic review and meta-analysis	No adverse patient outcomes reported
2013	Aya et al.	Goal-directed therapy in cardiac surgery: a systematic review and meta-analysis	Intervention is focused on one patient group
2013	Benbassat	The effect of clinical interventions on hospital readmissions: a meta-review of published meta-analyses	No patient harm reported
2013	Georgiou et al.	The effect of computerized provider order entry systems on clinical care and work processes in emergency departments: A systematic review of the quantitative literature	No adverse patient outcomes reported
2013	Graabaek	Medication Reviews by Clinical Pharmacists at Hospitals Lead to Improved Patient Outcomes: A Systematic Review	No patient harm reported Mortality data, but no quantitative ouctomes.
2013	Groves	The Relationship Between Safety Culture and Patient Outcomes: Results From Pilot Meta-Analyses	No quantitative outcomes
2013	Holly et al.	Evidence-Based Practices for the Identification, Screening, and Prevention of Acute Delirium in the Hospitalized Elderly: An Overview of Systematic Reviews	No systematic review
2013	Johansson et al.	Effectiveness of non-cardiac preoperative testing in non-cardiac elective surgery: a systematic review	Intervention is focused on one patient group No patient safety intervention
2013	Kwan et al.	Medication reconciliation during transitions of care as a patient safety strategy: a systematic review	Updated by another included review No adverse patient outcomes reported
2013	Li et al.	Oral topical decontamination for preventing ventilator-associated pneumonia: a systematic review and meta-analysis of randomized controlled trials	Intervention is focused on one patient group
2013	Majka et al.	Care Coordination to Enhance Management of Long-Term Enteral Tube Feeding: A Systematic Review and Meta-Analysis	Intervention is focused on one patient group
2013	Ojeleye et al.	The evidence for the effectiveness of safety alerts in electronic patient medication record systems at the point of pharmacy order entry: a systematic review	No adverse patient outcomes reported
2013	Omidvari et al.	Nutritional screening for improving professional practice for patient outcomes in hospital and primary care settings	No quantitative outcomes
2013	Radley et al.	Reduction in medication errors in hospitals due to adoption of computerized provider order entry systems	No adverse patient outcomes reported
2013	Shekelle	Nurse-patient ratios as a patient safety strategy: a systematic review	No intervention studies included; only observational studies
2013	Spinewine et al.	Approaches for improving continuity of care in medication management: a systematic review	No quantitative outcomes
2013	Winters et al.	Rapid-response systems as a patient safety strategy: a systematic review	Updated by another included review No intervention studies included; only observational studies
2013	Wong et al.	The relationship between nursing leadership and patient outcomes: a systematic review update	No intervention studies included; only observational studies

Appendix 6 **Quality assessment: AMSTAR score of included Systematic Reviews* (n=60)**

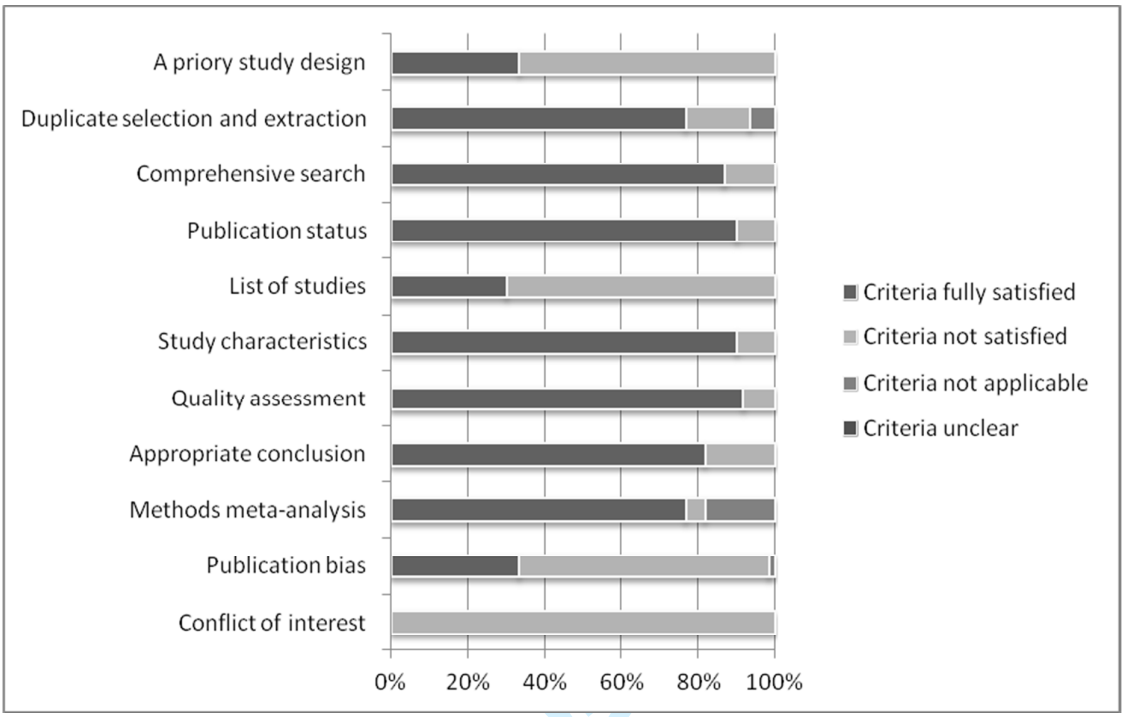
AMSTAR-item	1: priori design provided	2: duplicate study selection and extraction	3: comprehensive literature search performed	4: status publication (grey literature) used as inclusion criteria	5:List of studies (included and excluded) provided	6: characteristics of the included studies provided	7: scientific quality of the included studies assessed and documented	8: scientific quality of the included studies used appropriately in formulating conclusions	9: methods used to combine the findings of studies were appropriate	10: likelihood of publication bias was assessed	11: conflict of interest was included	Total score**
Algie et al., 2015 (67)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9
Bayoumi et al.,2014 (30)	No	No	No	No	No	Yes	Yes	Yes	Yes	No	No	4
Bergs et al., 2014 (66)	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	No	6
Blot et al., 2014 (39)	No	CA	No	Yes	No	No	Yes	Yes	Yes	Yes	No	5
Butler et al., 2011 (75)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9
Cameron et al., 2012 (61)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10
Chan et al., 2010 (69)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	8
Chen et al., 2013 (63)	No	Yes	Yes	No	No	Yes	Yes	No	NA	No	No	4
Christensen and Lundh, 2013 (26)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10
Cole et al., 1998 (45)	No	No	Yes	Yes	No	Yes	Yes	Yes	No	No	No	5
Collinsworth et al., 2014 (49)	No	No	Yes	No	No	No	Yes	Yes	Yes	No	No	4
Conroy et al., 2005 (53)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	8
Coussement et al., 2008 (60)	No	CA	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	6
Damiani et al., 2015 (41)	No	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	7
Davey et al., 2013 (33)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9
Durieux et al.,2008 (28)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9
Ensing et al., 2015 (35)	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	No	No	7
Esmonde et al., 2006 (68)	No	Yes	Yes	Yes	No	No	Yes	Yes	NA	No	No	5
Flodgren et al., 2011 (81)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10
Flodgren et al., 2013 (37)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10
Gillaizeau et al., 2013 (29)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10
Gould et al., 2010 (43)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9
Griffiths et al., 2005 (52)	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	No	6
Hempel et al., 2015 (65)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No	No	7
Hempenius et al., 2011 (47)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	8
Hohl et al., 2015 (27)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	8
Holland et al., 2008 (24)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	8
Howell et al., 2014 (64)	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	7
Hshsieh et al., 2015 (50)	No	No	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	6
Jansson et al., 2013 (38)	No	Yes	No	No	No	No	Yes	Yes	NA	No	No	3
Kaboli et al., 2006 (31)	No	Yes	Yes	Yes	No	Yes	No	No	Yes	No	No	5
Kahn et al., 2013 (72)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10
Lau and Haut., 2014 (73)	No	No	No	Yes	No	Yes	Yes	No	NA	No	No	3
Lowthian et al., 2015 (57)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	8
Maaskant et al., 2015 (23)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	No	9
Maharaj et al., 2015 (71)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	8
Manias et al., 2012 (32)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	7

Martinez et al., 2015 (51)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	9
Massey et al., 2010 (70)	No	No	Yes	Yes	No	Yes	Yes	No	NA	No	No	4
Medding et al., 2014 (40)	No	Yes	Yes	Yes	No	Yes	No	No	Yes	No	No	5
Miake-Lye et al., 2013 (62)	No	No	Yes	No	No	Yes	Yes	Yes	NA	No	No	4
Milisen et al., 2005 (46)	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	7
Mueller et al., 2012 (25)	No	Yes	No	Yes	No	Yes	Yes	Yes	Yes	No	No	6
Naylor et al., 2004 (78)	No	Yes	No	Yes	No	Yes	Yes	Yes	Yes	No	No	6
Niven et al., 2014 (54)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	8
Oliver et al., 2007 (59)	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	8
Pannick et al., 2015 (76)	No	Yes	Yes	Yes	No	Yes	No	No	No	No	No	4
Patterson et al., 2014 (34)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10
Reed et al., 2010 (74)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	8
Rennke et al., 2013 (55)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	7
Reston et al., 2013 (48)	No	No	No	No	No	Yes	Yes	Yes	NA	No	No	3
Rotter et al., 2010 (79)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10
Safdar and Abad, 2008 (44)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	7
Sheppard et al., 2013 (56)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9
Silvestri et al., 2005 (42)	No	CA	No	Yes	No	Yes	No	No	NA	No	No	2
Sullivan and Schoelles, 2013 (77)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	NA	No	No	6
Wang et al., 2015 (36)	No	CA	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	7
Weaver et al., 2013 (80)	No	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	No	6
Wolfstadt et al., 2008 (22)	No	No	Yes	Yes	No	Yes	Yes	Yes	NA	No	No	5
Zhu et al., 2015 (58)	No	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	No	6

*alphabetical order

**Yes = 1; No, Not applicable (NA), Can't Answer (CA) = 0

Appendix 7 **Methodological quality of 60 systematic reviews on patient safety interventions.**



Appendix 8 **Characteristics of relevant studies included in the systematic reviews (n=60)**

Patient-Safety Area	Study, year (reference)	Time range	No. of studies relevant studies (total included studies (n))	Intervention components relevant to patient safety	Studied in-hospital patients	Total no. of participants	Study designs
Prevention of adverse drug events							
CPOE system	Wolfstadt et al., 2008 (22)	Up to 2007	2 (10)	Computerized physician order entry system	Hospital and ICU patients	U	CT = 1; ITS = 1
CPOE system	Maaskant et al., 2015 (23)	Up to 2014	2 (7)	Computerized physician order entry (CPOE)	≥ 18 years	36730	CBA = 1; ITS = 1
Medication reconciliation	Holland et al., 2008 (24)	Up to 2005	22 (32)	Medication review	≥ 60 years	13305	RCT = 22
Medication reconciliation	Mueller et al., 2012 (25)	Up to 2012	5 (26)	Medication reconciliation	Not specified	1819	RCT = 3; non- RCT = 1; CBA = 1
Medication reconciliation	Christensen and Lundh, 2013 (26)	Up to 2011	5 (5)	Medication review	Not specified	1186	RCT = 5
Medication reconciliation	Hohl et al., 2015 (27)	2000-2013	6 (7)	Medication review	≥ 18 years in acute care	1970	RCT = 5; non-RCT = 1
Computer assisted decision support/ alerts	Durieux et al., 2008 (28)	1966 - 2006	10 (23)	Computer-assisted decision support on drug dosage	Patients receiving drug therapy	1210	RCT = 9; non- RCT = 1
Computer assisted decision support/ alerts	Gillaizeau et al., 2013 (29)	1996 - 2013	33 (46)	Computerized advice on drug dosage as a recommendation provided to the healthcare professional	Not specified	30341	RCT = 33
Computer assisted decision support/ alerts	Bayoumi et al., 2014 (30)	1974 - 2013	9 (36)	Computerized drug lab alerts for clinicians on prescribing or monitoring decisions	≥ 18 years	N.R.	RCT = 9
Multi component interventions	Kaboli et al., 2006 (31)	1985 - 2005	13 (36)	Clinical pharmacy activities and responsibilities (patient interview, medication profile and medical record review, presentation of drug regimen, recommendations to care team or physician, participating on rounds with inpatient care team, drug monitoring and recommendation follow-up, drug therapy dosing or management, documentation of clinical interventions or recommendations, patient counseling before discharge and telephone follow-up after discharge)	≥ 18 years	12397	RCT = 7; non- RCT = 1; quasi experimental = 1; CBA = 4
Multi component interventions	Manias et al., 2012 (32)	Up to 2011	10 (24)	Computerized physician order entry; changes in work schedules; intravenous systems; modes of education; medication reconciliation; pharmacist involvement; protocols and guidelines; support systems for clinical decision-making	ICU	U	non- RCT = 2; quasi RCT = 1; CBA = 7

Patient-Safety Area	Study, year (reference)	Time range	No. of studies relevant studies (total included studies (n))	Intervention components relevant to patient safety	Studied in-hospital patients	Total no. of participants	Study designs
Multi component interventions	Davey et al., 2013 (33)	1980 - 2009	23 (89)	Persuasive interventions (e.g. distribution of educational materials, local consensus processes, educational outreach visits and local opinion leaders); restrictive interventions (e.g. selective reporting of laboratory susceptibilities, formulary restriction and requiring prior authorization of prescriptions by infectious diseases physicians, microbiologists, pharmacists etc); structural interventions (e.g. changing from paper to computerized records, rapid laboratory testing and computerized decision support systems)	Acute care	U	RCT = 13; CCT = 2; CBA = 3; ITS = 5
Multi component interventions	Patterson et al., 2014 (34)	Up to 2009	3 (10)	Professional interventions (e.g. educational programs aimed at prescribers); organizational interventions (e.g. skill-mix changes, pharmacist-led medication review services or specialist clinics); information and communication technology (ICT) interventions (e.g. clinical decision support systems or use of risk screening tools); financial interventions (e.g. incentive schemes for changes in prescribing practice); regulatory interventions (e.g. government policy or legislative changes affecting prescribing)	≥ 65 years	1152	RCT = 3
Multi component interventions	Ensing et al., 2015 (35)	Up to 2014	19 (30)	Pharmacist interventions (e.g. different categories: admission, patient counseling, medical team, medication review, discharge reconciliation and provision of adherence aids)	≥ 18 years	7829	RCT = 19
Multi component interventions	Wang et al., 2015 (36)	Up to 2014	2 (4)	Pharmacist interventions (e.g. physician rounds, providing physicians with information and advice on ADE, drug interactions and dose intervals)	(Pediatric) ICU	2794	CBA = 2
Infection prevention							
Prevention of device-related infections (CAUTI; CLABSI; VAP)	Flodgren et al., 2013 (37)	Up to 2012	10 (13)	Interventions to avoid the use, or decrease the length of use of invasive medical devices (i.e. urinary catheters, central line catheters, mechanical ventilators), or interventions to improve adoption of measures to prevent device-related infection, such as: professional interventions (distribution of educational materials, educational meetings, local consensus processes, local opinion leaders, audit and feedback and reminders); organizational interventions (revision of professional roles and clinical multidisciplinary teams); financial interventions; regulatory interventions.	Patients with invasive devices	U	ITS = 10
Prevention of device-related infections (CAUTI;	Jansson et al., 2013 (38)	2003 – 2012	2 (8)	Education: continuing education, ongoing education, clinical education, inter-professional education.	Critically ill patients ICU	N.R.	Quasi experimental = 2

Patient-Safety Area	Study, year (reference)	Time range	No. of studies relevant studies (total included studies (n))	Intervention components relevant to patient safety	Studied in-hospital patients	Total no. of participants	Study designs
CLABSI; VAP)							
Prevention of device-related infections (CAUTI; CLABSI; VAP)	Blot et al., 2014 (39)	1995 – 2012	8 (43)	Education; training; feedback; clinical reminders; bundle; checklist; empowerment to stop procedure; surveillance; leader designation; prepackaging of CVS materials; infrastructure changes; organizational changes	Patients with central line catheters on the ICU	N.R.	CBA = 1; ITS = 7
Prevention of device-related infections (CAUTI; CLABSI; VAP)	Meddings et al., 2014 (40)	2008 – 2012	3 (30)	Education on improving appropriate use in catheter placement and behavior (e.g. catheter restriction and removal protocols); use of specific technologies	Patients with a urinary catheter	U	RCT = 1; non- RCT = 1; CBA =1
Interventions to improve compliance to sepsis bundle interventions	Damiani et al., 2015 (41)	2004-2014	5 (50)	Improving compliance to sepsis bundle interventions, consisting of educational programs (e.g. lectures and training sessions) and decision support tools (e.g. screening tools, checklist or introduction of dedicated staff (e.g. sepsis teams).	≥ 18 years with (severe) sepsis or septic shock	42295	ITS = 5
Interventions to improve hand hygiene compliance	Silvestri et al., 2005 (42)	1976 – 2003	7 (9)	Hand washing	ICU	N.R.	RCT = 2; non- RCT = 5
Interventions to improve hand hygiene compliance	Gould et al., 2010 (43)	Up to 2009	1 (4)	Education; audit with performance feedback; health promotion; and variations in availability and type of products used for hand hygiene.	Not specified	N.R.	ITS = 1
Overall hospital acquired infection prevention	Safdar and Abad, 2008 (44)	Up to 2006	25 (26)	Educational interventions for prevention of healthcare associated infections (lectures or classes, video presentations, posters, questionnaires and fact sheets, practical demonstrations, standardized self-study module, direct feedback and protocols to remove catheters when no longer necessary)	ICU and long-term care	N.R.	RCT = 1; non- RCT = 1; CBA = 23
Delirium prevention							
Delirium prevention	Cole et al., 1998 (45)	Up to 1998	8 (10)	Psychiatric assessment; education of patient and spouse; special (medical, surgical, nursing) care	Cardiac, elderly orthopedic, elderly surgical, elderly medical	N.R.	RCT = 2; non-RCT = 6
Delirium prevention	Milisen et al., 2005 (46)	Up to 2003	7 (7)	Psychiatric assessment; staff education; daily visits by a liaison nurse; screening for early detection of delirium	≥ 60 years	1683	RCT = 3; non-RCT = 3; CBA = 1
Delirium	Hempenius et al.,	1979 – 2009	7 (16)	Non pharmacological interventions to prevention delirium	≥ 18 years	1626	RCT = 1; Non RCT =

Patient-Safety Area	Study, year (reference)	Time range	No. of studies relevant studies (total included studies (n))	Intervention components relevant to patient safety	Studied in-hospital patients	Total no. of participants	Study designs
prevention	2011 (47)			(interdisciplinary team; proactive geriatric consultation; education nursing staff; systematic cognitive screening; scheduled pain protocol; supportive psychotherapy)	(geriatric wards; general medicine service; hip surgery; coronary artery bypass surgery)		3; CBA = 3
Delirium prevention	Reston et al., 2013 (48)	1999 – 2012	17 (19)	Anesthesia protocols; medication review; pain management; staff education	Elderly	U	RCT = 4; non- RCT = 2; CBA = 11
Delirium prevention	Collinsworth et al., 2014 (49)	1988 – 2014	8 (14)	Daily assessment; monitoring; mediating strategies	ICU	2846	RCT = 3; CCT = 5
Delirium prevention	Hshieh et al., 2015 (50)	1999-2013	8 (14)	Multi component non pharmacological delirium interventions (early mobility; cognition and orientation; sleep-wake- cycle preservation; hydration; hearing; vision)	≥ 65 years	3113	RCT = 4; non-RCT = 4
Delirium prevention	Martinez et al., 2015 (51)	Up to 2012	7 (7)	Multi component interventions (e.g. physiotherapy, daily reorientation, family involvement in care, stimulation programmes with avoidance of sensorial deprivation and staff/family member education)	≥ 60 years	1691	RCT = 7
Prevention of adverse event after clinical handover or hospital discharge							
Handover of inpatients	Griffiths et al., 2005 (52)	Up to 2003	8 (9)	Post acute intermediate care	Post acute and ≥ 18 years	N.R.	RCT = 7; quasi RCT = 1
Handover of inpatients	Conroy et al., 2011 (53)	Up to 2009	5 (5)	Geriatric assessment for frail older people being rapidly discharged from acute hospital	≥ 65 years being rapidly discharged (<72 h) from a acute hospital setting	2287	RCT = 5
Handover of inpatients	Niven et al., 2014 (54)	Up to 2012	5 (9)	Critical care transition programs	ICU	16433	CBA = 5
Hospital discharge	Rennke et al., 2013 (55)	1990 – 2012	7 (47)	Intervention to improve transitional care at hospital discharge: pre discharge interventions (assessment of risk for adverse events, patient engagement, creation of individualized patient record, facilitation of communication with outpatient providers, multidisciplinary discharge planning team, dedicated transition provider and medication reconciliation); Postdischarge interventions (Outreach to patients, facilitation of clinical follow-up and medication reconciliation after discharge); Bridging interventions (inclusion of at least 1 predischarge component and at least 1 postdischarge component	≥ 18 years	1943	RCT = 6; non- RCT = 1
Hospital	Sheppard et al.,	Up to 2012	7 (24)	Discharge planning from hospital to home	Elderly medical	U	RCT = 7

Patient-Safety Area	Study, year (reference)	Time range	No. of studies relevant studies (total included studies (n))	Intervention components relevant to patient safety	Studied in-hospital patients	Total no. of participants	Study designs
discharge	2013 (56)				patients, patients recovering from surgery and those with a mix of conditions		
Hospital discharge	Lowthian et al., 2015 (57)	Up to 2013	3 (9)	Comprehensive geriatric nurse assessment; community based service transfer; identifying high risk patients;	≥ 65 years, ED	2668	RCT = 3
Hospital discharge	Zhu et al., 2015 (58)	Up to 2014	5 (10)	Nurse-led early discharge planning programmes (e.g. initial nurse visit within 48 hours of hospital admission; predischarge assessment; structured home visits; telephone follow- ups after discharge)	Older adults	2503	RCT = 5
Fall prevention							
Fall prevention	Oliver et al., 2007 (59)	Up to 2005	12 (43)	Risk assessment; care planning; medical/diagnostic approaches; changes in the physical environment; education; medication review; hip protectors; removal of physical restraints		N.R.	RCT = 5; CBA = 7
Fall prevention	Coussement et al., 2008 (60)	Up to 2006	8 (8)	Unifactorial interventions (vitamin D supplement; identification bracelet; bed alarm system; flooring types) and multifactorial interventions (exercise program; medication review; multidisciplinary teams and meetings; staff awareness; improving patient activities)	≥ 69 years, long stay geriatric care units and geriatric rehabilitation units.	3894	RCT = 6; CT = 2
Fall prevention	Cameron et al., 2012 (61)	Up to 2012	15 (60)	Management of urinary incontinence; fluid or nutritional therapy; environment/ assistive technology (e.g., carpeted floors); social environment; patient education; staff education	≥ 65 years (or mean age > 65 years)	26887	RCT = 15
Fall prevention	Miake-Lye et al., 2013 (62)	2005 - 2012	21 (21)	Patient education; bedside risk sign; staff education; fall alert wristband; footwear; review after fall; toileting schedules; medication review; environment modification; movement alarms; bedrail review; hip protectors; urine screening; vest/ belt or cuff restraint	General population or older adults	U	RCT = 7; non- RCT = 14
Prevention of surgical adverse event							
Preventing surgical site infections	Chen et al., 2013 (63)	Up to 2012	4 (19)	Screening and decolonization of surgical site infections	Orthopedic and trauma	7845	RCT = 2; Systematic review = 2
Interventions to reduce adverse events in surgery	Howell et al., 2014 (64)	Up to 2012	7 (91)	Interventions to reduce adverse events in surgery: staffing factors; subspecialisation; benchmarking; mixed process interventions ; checklist interventions; technology or training; colorectal pathways; care pathways	Surgical patients	88423	RCT = 7

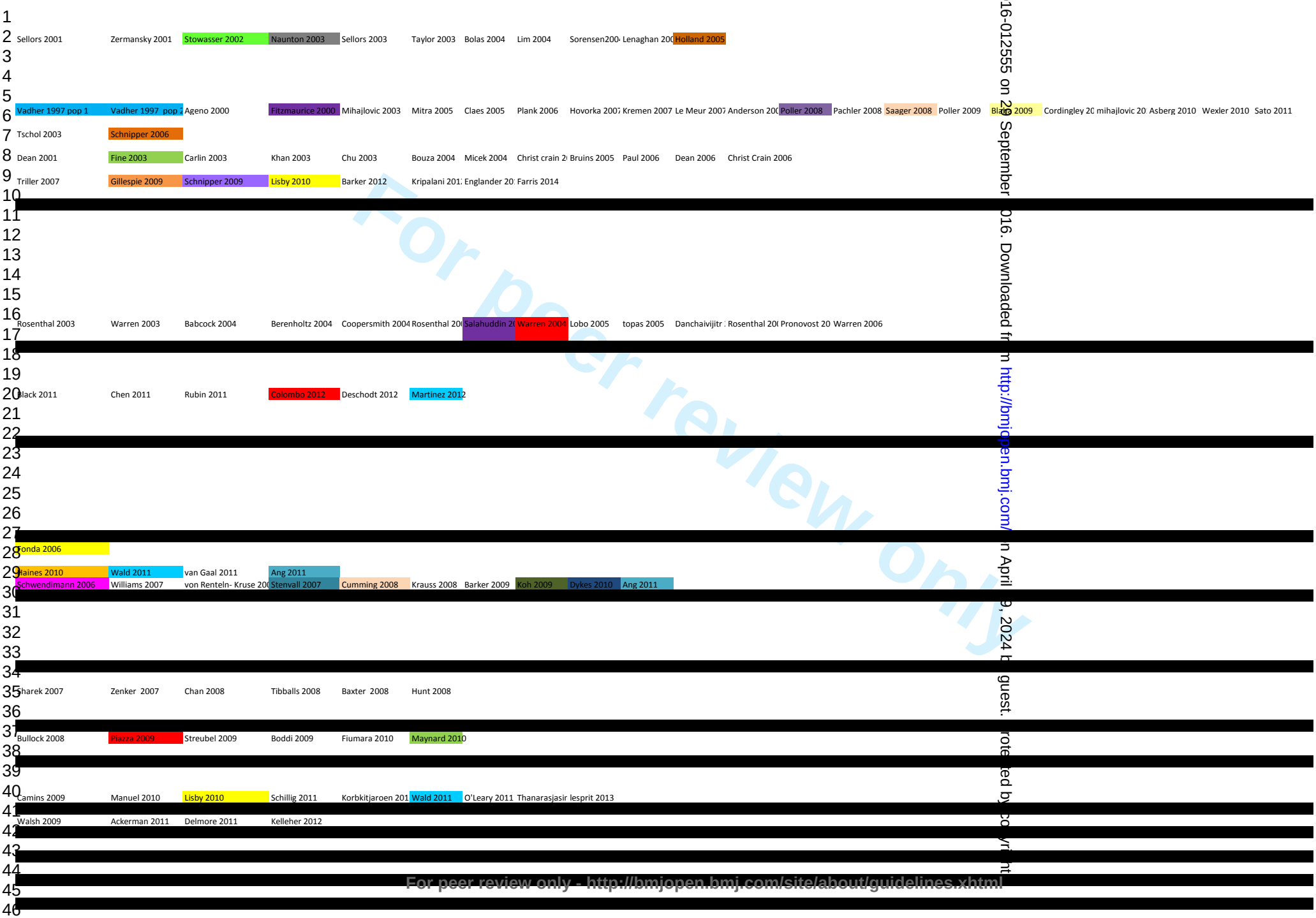
Patient-Safety Area	Study, year (reference)	Time range	No. of studies relevant studies (total included studies (n))	Intervention components relevant to patient safety	Studied in-hospital patients	Total no. of participants	Study designs
Preventing wrong site surgery	Hempel et al., 2015 (65)	2004-2014	4 (138)	Universal protocol; team training and education; retained surgical items	Surgical patients	U	RCT = 1; ITS = 3
Surgical safety checklist	Bergs et al., 2014 (66)	Up to 2013	5 (7)	WHO surgical safety checklist	≥ 18 years, non cardiac surgery; trauma and orthopaedic surgery; elective general surgery; high risk surgical procedures	U	ITS = 5
Surgical safety checklist	Algie et al., 2015 (67)	2011-2014	1 (2)	Preventing wrong site surgery with safety checklist	Surgical patients	22749	ITS = 1
Prevention of hospital mortality and cardiopulmonary arrest with rapid response systems							
Critical care outreach service	Esmonde et al., 2006 (68)	1996-2004	7 (23)	Critical care outreach service	Critically ill patients	N.R.	RCT = 2; quasi experiment = 3; CBA = 2
Rapid response teams	Chan et al., 2010 (69)	Up to 2008	16 (17)	Rapid response teams	Adults and children	N.R.	Non-RCT = 2; CBA = 12; ITS 2
Rapid response systems	Massey et al., 2010 (70)	1995 - 2009	5 (16)	Rapid response systems	Critically ill patients	U	RCT = 2; non- RCT = 2; CBA = 1
Rapid response systems	Maharaj et al., 2015 (71)	1990 - 2013	5 (29)	Rapid response teams	Pediatric and adult patients	225686	RCT = 2; CBA = 1; ITS = 2
Prevention of venous thromboembolism							
Prevention of venous thromboembolism	Kahn et al, 2013 (72)	Up to 2010	17 (55)	Alerts, education and multifaceted interventions for the implementation of appropriate administration of thromboprophylaxis	≥ 18 years, medical or surgical, at risk for venous thromboembolism (VTE)	79021	RCT = 1; quasi RCT =1; non- RCT = 15
Prevention of venous thromboembolism	Lau and Haut 2014 (73)	2001 to 2012	8 (16)	Education; paper based tools; computerized tools; real time audit and feedback or combinations of interventions to improve prescription of VTE prophylaxis	Unknown	U	RCT = 2; CBA = 6
Prevention of adverse events by changes in staffing							
Staffing	Reed et al., 2010 (74)	1989 to 2010	2 (64)	Shift length; protected sleep time; night float; education among residents	Patients and residents	1294	RCT = 1; non- RCT = 1

Patient-Safety Area	Study, year (reference)	Time range	No. of studies relevant studies (total included studies (n))	Intervention components relevant to patient safety	Studied in-hospital patients	Total no. of participants	Study designs
Staffing	Butler et al., 2011 (75)	Up to 2009	2 (15)	Nursing staff models	Not specified	938	RCT = 2
Staffing	Pannick et al., 2015 (76)	1998-2013	20 (30)	Interdisciplinary team care interventions	Geriatrics, infectious disease, pharmacotherapy and stroke	30969	RCT = 14; non-RCT = 5; CBA = 1
Prevention of pressure ulcers							
	Sullivan and Schoelles, 2013 (77)	2000 - 2012	15 (26)	Interventions for preventing pressure ulcers	All inpatient units, including, surgical, ICU, critical care, acute care, rehabilitation, intermediate care medical care, oncology patients	N.R.	ITS = 15
Prevention of mechanical complications and underfeeding							
	Naylor et al., 2004 (78)	Up to 2011	8 (11)	Total parenteral nutrition team	≥ 18 years	U	non- RCT = 8
Prevention of complications and mortality by clinical pathways							
	Rotter et al., 2010 (79)	Up to 2008	10 (27)	Clinical pathways (CPW)	Patients with conditions managed on a CPW	2632	RCT = 9, quasi RCT = 1
Prevention of adverse events by promoting a culture of safety							
	Weaver et al., 2013 (80)	2000 –2012	1 (33)	Intervention to promote a culture of patient safety (error prevention training coaching; family engagement; restructured patient safety governance; lessons learned program; cause analysis program; executive rounds)	≤ 18 years	3752	ITS = 1
Prevention of adverse events by external inspection							
	Flodgren et al., 2011 (81)	Up to 2011	1 (2)	External inspections of compliance with standards	Not reported	U	ITS = 1

CAUTI = catheter associated urinary tract infection; CBA= controlled before after; C(C)T= controlled (clinical) trial; CLABSI = central line associated blood stream infections; IC = intensive care; ICU = intensive care unit; inc = inception of database (start); ITS = Interrupted time series; NR= not reported; RCT = randomized controlled trial; U = unclear; VAP = ventilator-associated pneumonia

Appendix 9 Overlap studies

PATIENT-SAFETY AREA	SUB AREA	AUTHOR AND YEAR	INCLUDED RELEVANT STUDIES										
Adverse drug event	CPOE system	Wolfstadt et al., 2008 (22)	Bates 1999	Colpaert 2006									
		Maaskant et al., 2015 (23)	Kings 2003	Walsh 2008									
	Medication reconciliation	Holland et al., 2008 (24)	Jameson 1995	Hanlon 1996	Begley 1997	Smith 1997	Carter 1998	McMullin 1999	Bond 2000	Mackie 2001	Grymonpre 2001	Krska 2001	Nazareth 2001
		Mueller et al., 2012 (25)	Schnipper 2006	Schnipper 2009	Midlöv 2008	Lisby 2010	Boockvar 2011						
		Christensens & Lundh 2013 (26)	Schnipper 2006	Gillespie 2009	Lisby 2010	Lisby 2011	Gallagher 2011						
		Hohl et al., 2015 (27)	Scullin 2007	Spinewine 2007	Gillespie 2009	Lisby 2010	Lisby	Bladh 2011					
	Computer assisted decision support/ alerts	Durieux et al., 2008 (28)	Rodman 1984	White 1987	Hurley 1989	Begg 1989	Gonzalez 1989	Destache 1990	Burton 1991	Mungall 1994	Vadher 1997	Fitzmaurice 2000	
		Gillaizeau et al., 2013 (29)	Rodman 1984	Hurley 1986	White 1987	Gonzalez 1989	Begg 1989	Destache 1990	Burton 1991	Leehey 1993	Casner 1993	Mungall 1994	Vadher 1997
		Bayoumi et al., 2014 (30)	White 1987	Vadher 1997	Fitzmaurice 2000	Poller 2008	Saager 2008	Blaha 2009	Cavalcanti 2009	Mann 2011	Dumont 2012		
	Multicomponent interventions	Kaboli et al., 2006 (31)	Destache 1989	Burton 1991	Bjornson 1993	Bailey 1997	Fraser 1997	Gums 1999	Dager 2000	Gentry 2000	Leape 2000	Nazareth 2001	Kucukarslan 2003
		Manias et al., 2012 (32)	Leape 1999	Landrigan 2004	Rothschild 2005	Shulman 2005	Bradley 2006	Colpaert 2006	Weant 2007	Nuckols 2008	Klopotowska 2010	Chapuis 2010	
		Davey et al., 2013 (33)	Doern 1994	Pear 1994	McNulty 1997	Bailey 1997	Fraser 1997	Climo 1998	Gums 1999	De Man 2000	Singh 2000	Solomon 2001	Naughton 2001
		Patterson et al., 2014 (34)	Hanlon 1996	Crotty 2004	Schmader 2004								
		Ensing et al., 2015 (35)	Stewart 1998	Stewart 1998	Nazareth 2001	Stowasser 2002	Naunton 2003	Schmader 2004	Holland 2005	Lopez Cabezas 200	Holland 2007	Scullin 2007	Spinewine 2007
		Wang et al., 2015 (26)	Leape 1999	Kaushal 2008									
Infection	Prevention of device-related infections (CAUTI, CLASBI, VAP)	Flodgren et al., 2013 (37)	Kaye 2000	Zack 2002	Coopersmith 2002	Beathard 2003	Salahuddin 2004	Warren 2004	Abbott 2006	Sona 2009	Miller 2010	Parra 2010	
		Jansson et al., 2013 (38)	Abbott 2006	Hawe 2009									
		Blot et al., 2014 (39)	Coopersmith 2002	Warren 2004	Berriel-Cass 2006	Fraher 2009	Lobo 2010	Dixon 2010	Peredo 2010	Parra 2010			
		Meddings et al., 2014 (40)	Cornia 2003	Stephan 2006	Loeb 2008								
		Damiani et al., 2015 (41)	Girardis 2009	Levy 2010	Seoane 2013	van Zanten 2014	Levy 2014						
	Interventions to improve hand-hygiene compliance	Silvestri et al., 2005 (42)	Casewell 1977	Massanari 1984	Maki 1989	Simmons 1990	Doebbeling 1992	Slota 2001	Koss 2001				
		Gould et al., 2010 (43)	Vernaz 2008										
	Overall hospital-acquired infection prevention	Safdar & Abad 2008 (44)	Conly 1989	Kelleghan 1993	Lange 1997	Goetz 1999	Eggimann 2000	Makris 2000	Pittet 2000	Sheretz 2000	Coopersmith 2002	Zack 2002	Mody 2003
Delirium		Cole et al., 1998 (45)	Lazarus 1968	Layne 1971	Owens 1981	Williams 1985	Schindler 1989	Gustafson 1991	Nagley 1986	Wanich 1992			
		Milisen et al., 2005 (46)	Wanich 1992	Cole 1994	Inouye 1999	Marcantonio 2001	Milisen 2001	Cole 2002	Bogardus 2003				
		Hempenius et al., 2011 (47)	Schindler 1989	Wanich 1992	Inouye 1999	Milisen 2001	Wong 2005	Tabet 2005	Caplan 2007				
		Reston et al., 2013 (48)	Marcantonio 2001	Wong 2005	Tabet 2005/2006	Lundström 2005	Lundström 2007	Harari 2007	Vidan 2009	Needham 2010	Björkelund 2010	Inouye 2003/ 1999	Allen 2011
		Collinsworth et al., 2014 (49)	Girard 2008	Schweickert 2009	Needham 2010	Skrobik 2010	Colombo 2012	Mehta 2012	Hager 2013	Balas 2014			
		Hshieh et al., 2015 (50)	Inouye 1999	Lundstrom 2007	Stenvall 2007	Kratz 2008	Vidan 2009	Bo 2009	Martinez 2012	Jeffs 2013			
		Martinez et al., 2015 (51)	Marcantonio 2001	Vidan 2005	Finotto 2006	Lundström 2007	Jeffs 2008	Martinez 2012	Alvarez 2012				
Adverse event after hospital discharge or clinical handover		Griffiths et al., 2005 (52)	Hall 1975	Pearson 1988a	Pearson 1988 b	Griffiths 1995	Walsh 1999	Griffiths 2000	Griffiths 2001	Steiner 2001			
		Conroy et al., 2005 (53)	Close 1999	Mion 2003	McCusker 2003	Caplan 2004	Davidson 2005						
		Niven et al., 2014 (54)	Ball 2003	Leary 2003	Eliott 2008	Pirret 2008	Williams 2010						
		Rennke et al., 2013 (55)	Naylor 1990	Forster 2005	Schnipper 2006	Graumlich 2009	Gallagher 2011	Al ghamdi 2012	Marusic 2012				
		Sheppard et al., 2013 (56)	Rich 1995	Sulch 2000	Nazareth 2001	Pardessus 2002	Laramee 2003	Evans 2003	Legrain 2011				
		Lowthian et al., 2015 (57)	Mion 2001	Caplan 2004	Yim 2011								
		Zhu et al., 2015 (58)	Naylor 1999	Atienza 2004	Jack 2009	Saleh 2012	Altfeld 2013						
Fall		Oliver et al., 2007 (59)	Kilpack 1991	Mayo 1994	Mitchell 1996	Brandis 1999	Savage 2001	Barry 2001	Oliver 2002	Hoffman 2003	Vassallo 2004	Haines 2004	Healey 2004
		Coussement et al., 2008 (60)	Tideiksaar 1993	Mayo 1994	Donald 2000	Haines 2001	Bisschoff 2003	Vassallo 2004	Healey 2004	Schwendimann 2006			
		Cameron et al., 2012 (61)	Mayo 1994	Donald 2000	Mador 2004	Haines 2004	Healey 2004	Stenvall 2007	Jarvis 2007	Burleigh 2007	Cumming 2008	Koh 2009	Dykes 2010
		Miake-lye et al., 2013 (62)	Mitchell 1996	Brandis 1999	Udén 1999	Barry 2001	Oliver 2002	Grenier- Sennelier 2002	Haines 2004	Vassalo 2004	Healey 2004	Fonda 2006	van der helm 2006
Adverse event in surgery		Chen et al., 2013 (63)	Kalmeijer 2001	Kallen 2005	van Rijen 2008	Bode 2010							
		Howell et al., 2014 (64)	Delaney 2003	Gatt 2005	Muehling 2008	Serclova 2009	Brannick 2009	Muller 2009	Ren 2011				
		Hempel et al., 2015 (65)	Mulloy 2008	Greenberg 2008	Neily 2011	James 2012							
		Bergs et al., 2014 (66)	Askarian 2011	Sewell 2011	Kwok 2012	Bliss 2012	van Klei 2012						
		Algie et al., 2015 (67)	Vachhani 2013										
Cardiopulmonary arrest		Esmonde et al., 2006 (68)	Goldhill 1999	Bristow 2000	Salamonson 2001	Priestley 2004	Haji-Michael 2004	MERIT 2005	Ingleby (unpublished)				
		Chan et al., 2010 (69)	Bristow 2000	Buist 2002	Bellomo 2003	Kenward 2004	Priestley 2004	Devita 2004	Jones 2005	Hillman 2005	Brilli 2007	Jones 2007	Dacey 2007
		Massey et al., 2010 (70)	Hodgetts 2002	Bristow 2002	Priestley 2004	Hillman 2005	Dacey 2007						
		Maharaj et al., 2015 (71)	Bristow 2000	Hullman 2004	Priestley 2004	Hanson 2010	Howell 2012						
Venous thromboembolism		Kahn et al., 2013 (72)	Frankel 1999	Peterson 1999	Mosen 2004	Labarere 2004	Kucher 2005	Scaglione 2005	Burns 2005	McMullin 2006	Sellier 2006	Labarere 2007	Lecumberri 2008
		Lau & Haut., 2014 (73)	Scaglione 2005	Kucher 2005	Piazza 2009	Gallagher 2009	Maynard 2010	Liu 2012	Maharaj 2012	Haut 2012			
Staffing		Reed et al., 2010 (74)	Landrigan 2004	Afessa 2005									
		Butler et al., 2011 (75)	Forster 2005	Duncan 2006									
		Pannick et al., 2015 (76)	Soifer 1998	Curley 1998	Webstar 1999	Solomon 2001	Cole 2002	Kucukarslan 2003	Fine 2003	Dey 2005	Mudge 2006	Pitkala 2006	Mannheimer 2006
Pressure ulcer		Sullivan & Schoelles 2013 (77)	Stier 2004	Hiser 2006	Courtney 2006	Gibbons 2006	LeMaster 2007	Ballard 2007	Catania 2007	Dibsie 2008	McInerney 2008	Bales 2009	Chicano 2009
Mechanical complication and underfeeding		Naylor et al., 2004 (78)	Hickey 1979	Dalton 1984	Jacobs 1984	Traeger 1986	Gales 1994	Fisher 1996	Png 1997	Fetter 2000			
Clinical pathway		Rotter et al., 2010 (79)	Kollef 1997	Dowsey 1999	Brook 1999	Choong 2000	Marelich 2000	Cole 2002	Aizawa 2002	Delaney 2003	Kiyama 2003	Smith 2004	
Safety culture		Weaver et al., 2013 (80)	Muething 2012										



Appendix 10 Summary of the results of relevant studies reported in the systematic reviews (n=60)

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of relevant studies)	Conclusion reported by the authors
Prevention of adverse drug events						
Wolfstadt et al., 2008 (22)	CPOE system	Preventable AEs	No (Reason not reported)	N.A.	N.A.	Few studies have measured the effect of CPOE with clinical decision support on the rates of ADEs, and none were randomized controlled trials.
Maaskant et al., 2015 (23)	CPOE system	ADE	No (Heterogeneity of methods of data collection, populations and study designs)	N.A.	N.A.	Current evidence on effective interventions to prevent medication errors and adverse drug events in a pediatric population in hospital is limited.
Holland et al., 2008 (24)	Medication reconciliation	All cause mortality	Yes	Medication review	*Mortality (Relative Risk)* = 0.96, 95% CI [0.82-1.13] p = 0.62 (22 studies; all relevant)	Pharmacist-led medication review interventions do not have any effect on reducing mortality or hospital admission in older people, and cannot be assumed to provide substantial clinical benefit. Such interventions may improve drug knowledge and adherence, but there are insufficient data to know whether quality of life is improved.
Mueller et al., 2012 (25)	Medication reconciliation	ADE; mortality	No (Heterogeneity in methods, interventions, and reported outcomes)	N.A.	N.A.	Rigorously designed studies comparing different inpatient medication reconciliation practices and their effects on clinical outcomes are scarce. Available evidence supports medication reconciliation interventions that heavily use pharmacy staff and focus on patients at high risk for AE.
Christensen and Lundh, 2013 (26)	Medication reconciliation	Mortality; falls; ADE	Yes (for mortality, not for adverse drug events and falls because of the lack of valid data)	Medication review	*Mortality (Risk Ratio)* = 0.98, 95% CI [0.78-1.23] p = 0.86 (4 studies; all relevant)	It is uncertain whether medication review reduces mortality or hospital readmissions, but medication review seems to reduce emergency department contacts. However, the cost-effectiveness of this intervention is not known and due to the uncertainty of the estimates of mortality and readmissions and the short follow-up, important treatment effects may have been overlooked.
Hohl et al., 2015 (27)	Medication reconciliation	Mortality	Yes	Mediation review	*Mortality (Odds Ratio)* = 1.09, 95% CI [0.69-1.72] p = 0.71 (3 studies; all relevant)	This systematic review failed to identify an effect of pharmacist-led medication review on health outcomes.

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of relevant studies)	Conclusion reported by the authors
Durieux et al., 2008 (28)	Computer assisted decision support/ alerts	Deaths; ARs	Yes (for mortality, not for AR due to diversity of drugs and of type of adverse reactions)	Computerized advice on drug dosage	*Deaths (Risk Ratio)* = 0.81, 95% CI [0.37-1.81] p = 0.61(6 studies; all relevant)	This review suggests that computerized advice for drug dosage has some benefits: it increased the initial dose of drug, increased serum drug concentrations and led to a more rapid therapeutic control. It also reduced the risk of toxic drug levels and the length of time spent in the hospital. However, it had no effect on adverse reactions or mortality rates.
Gillaizeau et al., 2013 (29)	Computer assisted decision support/ alerts	Mortality; clinical AE	Yes (for mortality; not for clinical AEs due to diversity in outcomes)	Computerized advice on drug dosage	*Mortality (Risk Ratio)* = 1.08, 95% CI [0.80-1.45] p = 0.61 (10 studies; all relevant)	It tends to decrease unwanted effects for aminoglycoside antibiotics and anti-rejection drugs, and it significantly decreases thromboembolism events for anticoagulants […]. However, there was no evidence that decision support had an effect on mortality or other clinical adverse events for insulin (hypoglycaemia), anaesthetic agents, anti-rejection drugs and antidepressants. […] Taking into account the high risk of bias of, and high heterogeneity between, studies, these results must be interpreted with caution.
Bayoumi et al., 2014 (30)	Computer assisted decision support/ alerts	AE (bleeding and thrombosis)	Yes	Computerized drug- lab alerts	*Adverse events (bleeding and thrombosis) (Odds Ratio)* = 0.88, 95% CI [0.78-1.00] p = 0.05 (4 studies; all relevant)	There is no evidence that computerized drug-lab alerts are associated with important clinical benefits, but there is evidence of improvement in selected clinical surrogate outcomes (time in therapeutic range for vitamin K antagonists), and changes in process outcomes (lab monitoring and prescribing decisions).
Kaboli et al. 2006 (31)	Multi component interventions	(Preventable) ADE; mortality; bleeding complications; VTE	No (Small sample size and methodological limitations of included studies)	N.A.	N.A.	The addition of clinical pharmacist services in the care of inpatients generally resulted in improved care, with no evidence of harm.
Manias et al., 2012 (32)	Multi component interventions	Severity of harm of medication errors; ADE; preventable prescribing AE	No (Heterogeneity for the outcome variable)	N.A.	N.A.	It is not possible to promote any interventions as positive models for reducing medication errors.
Davey et al., 2013 (33)	Multi component interventions	Mortality	Yes	Intervention to increase appropriate antibiotic treatment	*Mortality (Risk Ratio)* = 0.92, 95% CI [0.69-1.22] p = 0.56 (3 studies; all relevant)	The results show that interventions to reduce excessive antibiotic prescribing to hospital inpatients can reduce antimicrobial resistance or hospital-acquired infections, and interventions to increase effective prescribing can improve clinical outcome.

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of relevant studies)	Conclusion reported by the authors
				Antibiotic guideline compliance for pneumonia	*Mortality (Risk Ratio)* = 0.89, 95% CI [0.82-0.97] p = 0.01 (4 studies; all relevant)	
				Interventions to decrease excessive prescribing of antibiotics	*Mortality (Risk Ratio)* = 0.92, 95% CI [0.81-1.06] p = 0.25 (11 studies; all relevant)	
Patterson et al., 2014 (34)	Multi component interventions	ADE	No (Heterogeneity of scales to measure outcome measures and reporting methods)	N.A.	N.A.	It is unclear if interventions to improve appropriate polypharmacy, such as pharmaceutical care, resulted in a clinically significant improvement; however, they appear beneficial in terms of reducing inappropriate prescribing and medication-related problems.
Ensing et al., 2015 (35)	Multi component interventions	Mortality; ADE	No (Heterogeneity among studies)	N.A.	N.A.	In multifaceted intervention programs, performing medication reconciliation alone is insufficient in reducing postdischarge clinical outcomes and should be combined with active patient counseling and a clinical medication review. Furthermore, close collaboration between pharmacists and physicians is beneficial. Finally, it is important to secure continuity of care by integrating pharmacists in these multifaceted programs across health care settings. Ultimately, pharmacists need to know patient clinical background and previous hospital experience.
Wang et al., 2015 (36)	Multi component interventions	Preventable ADE	Yes	Pharmacist interventions	*Preventable ADE (Odds Ratio)* = 0.23, 95% CI [0.11-0.48] p < 0.01 (3 studies, 2 relevant)	Results suggest that pharmacist intervention has no significant contribution to reducing general MEs, although pharmacist intervention may significantly reduce preventable adverse drug events and prescribing errors.

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of relevant studies)	Conclusion reported by the authors
Infection prevention						
Flodgren et al., 2013 (37)	Prevention of device related infections	VAP; CLASBI; mortality	No (Heterogeneity among studies)	N.A.	N.A.	The low to very low quality of the evidence of studies included in this review provides insufficient evidence to determine with certainty which interventions are most effective in changing professional behavior and in what contexts. However, interventions that may be worth further study are educational interventions involving more than one active element and that are repeatedly administered over time, and interventions employing specialized personnel, who are focused on an aspect of care that is supported by evidence e.g. dentists/ dental auxiliaries performing oral care for VAP prevention.
Jansson et al., 2013 (38)	Prevention of device related infections	VAP; mortality	No (Methodological limitations of the included studies)	N.A.	N.A.	Education has significant benefits for improving patient safety, and thus the quality of care. Active implementation strategies involving repeated lectures and regular surveys of VAP occurrence would be beneficial.
Blot et al., 2014 (39)	Prevention of device related infections	CLASBI	Yes	Bundle/ checklist and non bundle/checklist interventions	*Total number of CLASBI (Odds Ratio)* = 0.39, 95% CI [0.33 -0.46] p = <0.01 (41 studies; 5 relevant) *Change in CLASBI rate levels at 3 months post intervention (Odds Ratio)* = 0.30, 95% CI [0.10-0.88] p= 0.03 (6 studies; 4 relevant)	These results suggest that quality improvement interventions contribute to the prevention of central line–associated bloodstream infections. Implementation of care bundles and checklists appears to yield stronger risk reductions.
Meddings et al., 2014 (40)	Prevention of device related infections	CAUTI	Yes	Reminder and stop order	*CAUTI episodes per 1000 catheter days (Risk Ratio)* = 0.47, 95% CI [0.30-0.64] p = < 0.01 (11 studies; 1 relevant) *Percentage of patients who developed CAUTI (Risk Ratio)* = 0.72, 95% CI [0.52-0.99] p = 0.045 (8 studies; 2 relevant)	Urinary Catheter reminders and stop orders appear to reduce CAUTI rates and should be used to improve patient safety.
Damiani et al., 2015 (41)	Interventions to improve compliance to sepsis bundle interventions	Mortality	Yes	Performance improvement program	*Mortality (Odds Ratio)* = 0.66, 95% CI [0.61-0.72] p <0.01 (48 studies, 3 relevant)	Performance improvement programs are associated with increased adherence to resuscitation and management sepsis bundles and with reduced mortality in patients with sepsis, severe sepsis or septic shock.

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of relevant studies)	Conclusion reported by the authors
Silvestri et al., 2005 (42)	Interventions to improve hand hygiene compliance	Infection rates; mortality	No (Reason not reported)	N.A.	N.A.	Hand washing on its own does not abolish but only reduces transmission, as it is dependent upon the bacterial load on the hands of healthcare workers. Hand washing can only influence a subset of long-stay patients on ICUs. Only a randomized trial could support the statement of the Hand washing Liaison Group providing evidence for hand washing being a modest measure with big effects.
Gould et al., 2010 (43)	Interventions to improve hand hygiene compliance	Healthcare associated infections	No (Heterogeneity of interventions and methods)	N.A.	N.A.	The quality of intervention studies intended to increase hand hygiene compliance remains disappointing. Although multifaceted campaigns with social marketing or staff involvement appear to have an effect, there is insufficient evidence to draw a firm conclusion.
Safdar and Abad, 2008 (44)	Overall hospital acquired infection prevention	CRBSI; VAP; CAUTI; overall nosocomial infections	No (Heterogeneity of studies)	N.A.	N.A.	The implementation of educational interventions may reduce healthcare- associated infections considerably.
Delirium prevention						
Cole et al., 1998 (45)	Delirium prevention	ARR of delirium	No (Small number of included studies; mostly nonrandomized designs in which outcomes were not rated blind; heterogeneity of populations and interventions)	N.A.	N.A.	It is difficult to draw firm conclusions because of three methodological problems.
Milisen et al., 2005 (46)	Delirium prevention	Incidence, severity and duration of delirium; mortality	No (Small number of included studies; heterogeneity of populations and interventions; methodological limitations of included studies)	N.A.	N.A.	Multicomponent interventions to prevent delirium are the most effective and should be implemented through synergistic cooperation between the various healthcare disciplines.
Hempenius et al., 2011 (47)	Delirium prevention	Delirium (incidence)	Yes	Multi-component interventions	*Incidence of delirium (Odds Ratio)* = 0.58, 95% CI [0.38- 0.92] p value NR (5 studies; all relevant)	Interventions to prevent delirium are effective. Interventions seem to be more effective when the incidence of delirium in the population under study is above 30%.

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of relevant studies)	Conclusion reported by the authors
				One component interventions	*Incidence of delirium (Odds Ratio)* = 1.05, 95% CI [0.09- 11.57] p value NR (2 studies; all relevant)	
Reston et al., 2013 (48)	Delirium prevention	Incidence of delirium	No (Methodological limitations of included studies, heterogeneity of interventions; small number of studies)	N.A.	N.A.	The evidence from 19 studies that met the inclusion criteria suggests that most multicomponent interventions are effective in preventing onset of delirium in at-risk patients in a hospital setting.
Collinsworth et al., 2014 (49)	Delirium prevention	Incidence and duration of delirium; mortality	No (Heterogeneity of interventions and measured outcomes)	N.A.	N.A.	Although multifaceted care approaches may reduce delirium and improve patient outcomes, greater improvements may be achieved by deploying a comprehensive bundle of care practices including awakening and breathing trials, delirium monitoring and treatment, and early mobility.
Hshieh et al., 2015 (50)	Delirium prevention	Incidence of delirium; falls	Yes	Multi-component interventions	*Incidence delirium (Odds Ratio)* = 0.47, 95% CI [0.38- 0.58] p <0.01 (11 studies; 7 relevant)	Multicomponent nonpharmacological delirium prevention interventions are effective in reducing delirium incidence and preventing falls, with a trend toward decreasing length of stay and avoiding institutionalization.
Martinez et al., 2015 (51)	Delirium prevention	Incidence and duration of delirium; falls	Yes	Multi component interventions	*Prevention of incident delirium (Risk Ratio)* = 0.73, 95% CI [0.63-0.85] p <0.01 (7 studies; all relevant)	Multicomponent interventions are effective in preventing incident delirium among elderly inpatients.
Prevention of mortality or adverse events after discharge						
Griffiths et al., 2005 (52)	Handover of inpatients	Mortality	Yes	NLU (nursing-led inpatients units)	*Inpatient mortality (Odds Ratio)* = 1.10, 95% CI [0.56-2.16] p = 0.64 (7 studies; all relevant) *Mortality to longest follow up 3 or 6 months post- admission (Odds Ratio)* = 0.96, 95% CI [0.63-1.47] p = 0.62 (6 studies; all relevant)	The NLU successfully functions as a form of intermediate care, so far there is no evidence of adverse outcome from the lower level of routine medical care. There is no evidence of benefit over the longer term.
Conroy et al., 2011 (53)	Handover of inpatients	Mortality	Yes	Comprehensive geriatric assessment	*Mortality at final follow up (Risk Ratio)* = 0.92, 95% CI [0.55-1.52] p = 0.77 (5 studies; all relevant)	There is no clear evidence of benefit for comprehensive geriatric assessment interventions in frail older people being discharged from emergency departments or acute medical units.

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of relevant studies)	Conclusion reported by the authors
Niven et al., 2014 (54)	Handover of inpatients	Mortality	Yes		*Mortality (Risk Ratio)* = 0.84, 95% CI [0.66–1.05] p = 0.1 (3 studies; 2 relevant)	Critical care transition programs appear to reduce the risk of ICU readmission in patients discharged from ICU to a general hospital ward.
Rennke et al., 2013 (55)	Hospital discharge	Postdischarge AE; ADE; ADR; falls	No (Heterogeneity of interventions, study settings, and patient populations)	N.A.	N.A.	Because of scant evidence, no conclusions could be reached on methods to prevent postdischarge AEs. Most studies did not report intervention context, implementation, or cost. The strategies hospitals should implement to improve patient safety at hospital discharge remain unclear.
Sheppard et al., 2013 (56)	Hospital discharge	Mortality; falls	Yes	Discharge planning from hospital to home	*Mortality at 6 to 9 months (Risk Ratio)* = 1.00, 95% CI [0.79-1.26] p = 0.69 (6 studies; all relevant) *Number of falls at follow up (Risk Ratio)* = 0.87, 95% CI [0.50-1.49] p = 0.61 (1 study)	The evidence suggests that a discharge plan tailored to the individual patient probably brings about reductions in hospital length of stay and readmission rates for older people admitted to hospital with a medical condition. The impact of discharge planning on mortality, health outcomes and cost remains uncertain.
Lowthian et al., 2015 (57)	Hospital discharge	Mortality	Yes	Optimized ED discharge	*Mortality up to 18 months post discharge (Odds Ratio)* = 1.01, 95% CI [0.70-1.47] p = 0.94 (2 studies; all relevant)	There is limited high-quality data to guide confident recommendations about optimal ED community transition strategies, highlighting a need to encourage better integration of researchers and clinicians in the design and evaluation process, and increased reporting, including appropriate robust evaluation of efficacy and effectiveness of these innovative models of care.
Zhu et al., 2015 (58)	Hospital discharge	Mortality	Yes	Nurse-led early discharge planning programmes	*Mortality (all cause) (Risk Ratio)* = 0.70, 95% CI [0.52-0.95] p = 0.02 (5 studies; all relevant)	Compared to standard care, nurse-led early discharge planning programmes have a positive impact on several aspects of care for inpatients with chronic disease and rehabilitation requirements, including reducing readmission, readmission length of stay and mortality and improving quality of life.
Fall prevention						
Oliver et al., 2007 (59)	Fall prevention	Falls; fallers; fractures	Yes	Multifaceted interventions	*Falls (Rate Ratio)* = 0.82, 95% CI [0.68-1.00)] p value NR (12 studies; all relevant) *Fallers (Relative Risk)* = 0.95, 95% CI [0.71-1.27] p value NR (12 studies; all relevant)	There is some evidence that multifaceted interventions in hospital reduce the number of falls. There is insufficient evidence, however, for the effectiveness of other single interventions in hospitals.

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of relevant studies)	Conclusion reported by the authors
					Fractures (Rate Ratio) = 0.59, 95% CI [0.22-1.58] p value NR (12 studies; all relevant)	
Coussement et al., 2008 (60)	Fall prevention	Falls; fallers; physical injuries	Yes (for falls and fallers, not for physical injuries)	Multifactorial intervention	*Fall (Risk Ratio)* = 0.82, 95% CI [0.65-1.03] p value NR (4 studies; all relevant) *Number of fallers (Risk Ratio)* = 0.87, 95% CI [0.70-1.08] p value NR (4 studies; all relevant)	This meta-analysis found no conclusive evidence that hospital fall prevention programs can reduce the number of falls or fallers, although more studies are needed to confirm the tendency observed in the analysis of individual studies that targeting a patient's most important risk factors for falls actively helps in reducing the number of falls. These interventions seem to be useful only on longstay care units.
Cameron et al., 2012 (61)	Fall prevention	Rate of falls; risk of fallings; number of people sustaining a fracture	Yes	Multifactorial interventions	*Rate of falls (Rate Ratio)* = 0.69, 95% CI [0.49-0.96] p = 0.03 (4 studies; all relevant) *Risk of fallings (Risk ratio)* = 0.71, 95% CI [0.46-1.09] p = 0.12 (3 studies; all relevant) *Number of people sustaining a fracture (Risk Ratio)* = 0.43, 95% CI [0.10-1.78] p = 0.24 (3 studies; all relevant)	Exercise in subacute hospital settings appears effective. There is evidence that multifactorial interventions reduce falls in hospitals but the evidence for risk of falling was inconclusive.
				Exercises	*Risk of falling (Rate Ratio)* = 0.36, 95% CI [0.14-0.93] p = 0.04 (2 studies; all relevant)	
Miake-Lye et al., 2013 (62)	Fall prevention	Reduction in fall rate; incidence of falls; injuries per fall; injury rate per fall	No (Reason not reported)	N.A.	N.A.	For multicomponent inpatient fall programs, our review provides both evidence that such programs reduce falls and insight into how facilities can successfully implement them.
Interventions to reduce adverse events in surgery						
Chen et al., 2013 (63)	Preventing surgical site infections	Overal SSI; infections of S aureus; MRSA; wound complications	No (Heterogeneity of studies)	N.A.	N.A.	Preoperative screening and decolonization of S. aureus in orthopaedic patients is a cost-effective means to reduce SSIs.
Howell et al., 2014 (64)	Interventions to reduce adverse events in surgery	Adverse events	No (Heterogeneity of subject groups, end points, and specialties)	N.A.	N.A.	Only a small cohort of medium- to high-quality interventions effectively reduce surgical harm and are feasible to implement.

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of relevant studies)	Conclusion reported by the authors
Hempel et al., 2015 (65)	Preventing wrong site surgery	Incidence of wrong site surgery	No (Heterogeneity of publications)	N.A.	N.A.	Despite promising approaches and global Universal Protocol evaluations, empirical evidence for interventions is limited.
Bergs et al., 2014 (66)	Surgical safety checklist	Any complication; mortality; surgical site infections	Yes	WHO surgical safety checklist	*Any complication (Risk Ratio)* = 0.59, 95% CI [0.47-0.74] p = <0.01 (5 studies; all relevant) *Mortality (Risk Ratio)* = 0.77, 95% CI [0.60-0.98] p = 0.04 (4 studies, 3 relevant) *Surgical site infections (Risk Ratio)* = 0.57, 95% CI p = <0.01 [0.41-0.79] (5 studies; all relevant)	The evidence is highly suggestive of a reduction in postoperative complications and mortality following implementation of the WHO SSC, but cannot be regarded as definitive in the absence of higher-quality studies.
Algie et al., 2015 (67)	Surgical safety checklist	Incidence of wrong site neurological events	No (Small number of studies)	N.A.	N.A.	The data suggested a strong downward trend in the incidence of wrong-site surgery prior to the intervention with the incidence rate approaching zero. The effect of the intervention in these studies however remains unclear, as data reflect only two small low-quality studies in very specific population groups.
Prevention of hospital mortality and cardiopulmonary arrest with rapid response systems						
Esmonde et al., 2006 (68)	Critical care outreach service	Mortality; cardiac arrest	No (Reason not reported)	N.A.	N.A.	Although improvements in patient outcomes were found, the evidence in this review is insufficient to demonstrate this conclusively.
Chan et al., 2010 (69)	Rapid response teams	Mortality; cardiopulmonary arrest	Yes	Rapid response team	*Hospital mortality (Relative Risk)* = 0.92, 95% CI [0.82-1.04] p value NR (16 studies; all relevant) *Cardiopulmonary arrest (Relative Risk)* = 0.65, 95% CI [0.55-0.77] p value NR (16 studies; all relevant)	Although rapid response teams have broad appeal, robust evidence to support their effectiveness in reducing hospital mortality is lacking.

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of relevant studies)	Conclusion reported by the authors
Massey et al., 2013 (70)	Rapid response systems	Mortality; cardiac arrest	No (Reason not reported)	N.A.	N.A.	The paper illustrates two important gaps in the literature. First, 'ramp-up' systems have not been subjected to formal evaluation. Second, rapid response systems are under-activated and underused by nursing staff. There is an urgent need to explore the reasons for this and to identify interventions to improve the activation of these systems in an effort to promote safe and effective care to the deteriorating ward patient.
Maharaj et al., 2015 (71)	Rapid response teams	Mortality; cardiopulmonary arrest	Yes	Rapid response team	*Hospital mortality adults (Risk Ratio)* = 0.91, 95% CI [0.85-0.97] p < 0.01 (4 studies; all relevant) *Hospital mortality pediatric patients (Risk Ratio)* = 0.76, 95% CI [0.53-1.09] p = 0.14 (1 study; all relevant) *Cardiopulmonary arrest adults (Risk Ratio)* = 0.74, 95% CI [0.56-0.98] p = 0.04 (2 studies; all relevant) *Cardiopulmonary arrest pediatric patients (Risk Ratio)* = 0.35, 95% CI [0.08-1.59] p = 0.17 (1 study; all relevant)	Rapid response systems were associated with a reduction in hospital mortality and cardiopulmonary arrest. Meta-regression did not identify the presence of a physician in the rapid response system to be significantly associated with a mortality reduction.
Prevention of venous thromboembolism						
Kahn, et al., 2013 (72)	Prevention of venous thromboembolism	All VTE; DVT; PE; bleeding; mortality	Yes	Alerts	*All VTE (Risk Ratio)* = 0.85, 95% CI [0.49-1.46] p value NR (3 studies; all relevant)	We found statistically significant improvements in prescription of prophylaxis associated with alerts (RCTs) and multifaceted interventions (RCTs and NRS), and improvements in prescription of appropriate prophylaxis in NRS with the use of education, alerts and multifaceted interventions. Multifaceted interventions with an alert component may be the most effective.
				Multifaceted	*All VTE (Risk Ratio)* = 1.01, 95% CI [0.51-1.98] p value NR (5 studies; all relevant) *Symptomatic DVT (Risk Ratio)* = 0.59, 95% CI [0.18-1.98] p value NR (3 studies; all relevant)	

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of relevant studies)	Conclusion reported by the authors
Lau and Haut 2014 (73)	Prevention of venous thromboembolism	(Preventable) VTE	No (Reason not reported)	N.A.	N.A.	Many intervention types have proven effective to different degrees in improving VTE prevention. Provider education is likely a required additional component and should be combined with other intervention types. Active mandatory tools are likely more effective than passive ones. Information technology tools that are well integrated into provider workflow, such as alerts and computerized clinical decision support, can improve best practice prophylaxis use and prevent patient harm resulting from VTE.
Prevention of adverse events by changes in staffing						
Reed et al., 2010 (74)	Staffing	Preventable AE; mortality	No (Heterogeneity of outcomes)	N.A.	N.A.	For the limited outcomes measured, most studies supported reducing shift length but did not adequately address the optimal shift duration.
Butler et al., 2011 (75)	Staffing	Mortality; post discharge adverse events	Yes	Addition of specialist nursing post to staffing	*In-hospital mortality (Risk Ratio)* = 0.96, 95% CI [0.59-1.56] p = 0.86 (1 study)	The findings suggest interventions relating to hospital nurse staffing models may improve some patient outcomes, particularly the addition of specialist nursing and specialist support roles to the nursing workforce. Interventions relating to hospital nurse staffing models may also improve staff-related outcomes, particularly the introduction of primary nursing and self-scheduling. However, these findings should be treated with extreme caution due to the limited evidence available from the research conducted to date.
					Post discharge adverse events (Risk Ratio) = 1.03, 95% CI [0.70-1.53] p = 0.87 (1 study)	
				Increasing the proportion of support staff	*Death in trauma unit (Risk Ratio)* = 0.41, 95% CI [0.16-1.01] p = 0.05 (1 study)	
					Death in hospital (Risk Ratio) = 0.56, 95% CI [0.29-1.09] p = 0.09 (1 study)	
					Death at 4 months (Risk Ratio) = 0.57, 95% CI [0.34-0.95] p = 0.03 (1 study)	
Pannick et al., 2015 (76)	Staffing	Mortality; delirium episode; ADE; bleeding; falls; AE	Yes (for mortality, not for the other outcomes)	Interdisciplinary team composition interventions	*Mortality (weighted risk ratio)* = 0.92, 95% CI [0.816-1.049] p value NR (7 studies; all relevant)	Current evidence suggests that interdisciplinary team care interventions on general medical wards have little effect on traditional measures of health care quality. Complications of care or preventable adverse events may merit inclusion as quality indicators for general medical wards.
				Team practice interventions	*Mortality (weighted risk ratio)* = 0.665, 95% CI [0.449-0.986] p value NR (2 studies, all relevant)	

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of relevant studies)	Conclusion reported by the authors
Prevention of pressure ulcers						
Sullivan and Schoelles, 2013 (77)	Prevention of pressure ulcers	Pressure ulcer prevalence	No (Reason not reported)	N.A.	N.A.	Moderate-strength evidence from 26 implementation studies suggests that the integration of a common set of components in pressure ulcer prevention programs could lead to reductions in pressure ulcer rates. Key issues were the simplification and standardization of pressure-ulcer specific interventions and documentation, involvement of multidisciplinary teams and leadership, designated skin champions, ongoing staff education, and sustained audit and feedback for promoting.
Prevention of mechanical complications and underfeeding						
Naylor et al., 2004 (78)	Prevention of mechanical complications and underfeeding	Mechanical complication, underfeeding	No (Heterogeneity of studies)	N.A.	N.A.	The general effectiveness of the total parenteral nutrition team has not been conclusively demonstrated. There is evidence that patients managed by TPN teams have a reduced incidence of total mechanical complications; however, it is unclear if there is a reduction in catheter-related sepsis and metabolic and electrolyte complications.
Prevention of complications and mortality by clinical pathways						
Rotter et al., 2010 (79)	Prevention of complications and mortality by clinical pathways	Mortality rate; (in hospital) complications	Yes	Clinical pathway	*Mortality rate (Odds Ratio)* = 0.84, 95%CI [0.64-1.11] p = 0.23 (3 studies; all relevant) *Complications up to three months (Odds Ratio)* = 0.31, 95% CI [0.13-0.72] p = 0.07 (1 study; all relevant) *In- hospital complications (Odds Ratio)* = 0.58, 95% CI [0.36-0.94] p = 0.03 (5 studies; all relevant)	Clinical pathways are associated with reduced in-hospital complications and improved documentation without negatively impacting on length of stay and hospital costs.

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of relevant studies)	Conclusion reported by the authors
Prevention of adverse events by promoting a culture of safety						
Weaver et al., 2013 (80)	Prevention of adverse events by promoting a culture of safety	AE	No (Heterogeneity of interventions and survey instruments and outcomes)	N.A.	N.A.	Twenty-nine studies reported some improvement in safety culture or patient outcomes, but measured outcomes were highly heterogeneous. Strength of evidence was low, and most studies were pre–post evaluations of low to moderate quality. Within these limits, evidence suggests that interventions can improve perceptions of safety culture and potentially reduce patient harm.
Prevention of adverse events by external inspection						
Flodgren, et al., 2011 (81)	Prevention of adverse events by external inspection	MRSA rates	No (Too few studies identified)	N.A.	N.A.	No firm conclusions could therefore be drawn about the effectiveness of external inspection on compliance with standards.

ADE: Adverse Drug Events; ADR: Adverse Drug Reaction; AE: Adverse events; AR: Adverse reactions; ARR: Absolute risk reduction; CAUTI: Catheter associated urinary tract infection; CI: Confidence interval; CLASBI: Central line associated blood stream infections; CRBSI: Catheter Related Blood Stream Infections; DVT: Deep vein thrombosis; N.A: Not applicable; PE: Pulmonary embolism; SSI: Surgical site infections; VAP: Ventilator associated pneumonia; VTE: Venous thromboembolism

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Evidence-Based Interventions to Reduce Adverse Events in Hospitals: A Systematic Review of Systematic Reviews

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ABSTRACT

Objective: To provide an overview of effective interventions aimed at reducing rates of adverse events in hospitals.

Design: Systematic review of systematic reviews.

Data sources: PubMed, CINAHL, PsycINFO, the Cochrane Library and EMBASE were searched for systematic reviews published up until October 2015.

Study selection: English-language systematic reviews of interventions aimed at reducing adverse events in hospitals, including studies with an experimental design and reporting adverse event rates were included. Two reviewers independently assessed each study's quality and extracted data on the study population, study design, intervention characteristics and adverse patient outcomes.

Results: Sixty systematic reviews with moderate to high quality were included. Statistically significant pooled effect sizes were found for 14 types of interventions, including: 1) multicomponent interventions to prevent delirium; 2) rapid response teams to reduce cardiopulmonary arrest and mortality rates; 3) pharmacist interventions to reduce adverse drug events; 4) exercises and multicomponent interventions to prevent falls; and 5) care bundle interventions, checklists and reminders to reduce infections. Most (82%) of the significant effect sizes were based on five or fewer primary studies with an experimental study design.

Conclusion: The evidence for patient safety interventions implemented in hospitals worldwide is weak. The findings address the need to invest in high-quality research standards in order to identify interventions that have a real impact on patient safety. Interventions to prevent delirium, cardiopulmonary arrest and mortality, adverse drug events, infections and falls are most effective and should therefore be prioritized by clinicians.

Strengths and limitations of this study

- This review offers a unique overview of effective patient-safety interventions based on data from systematic reviews, thereby producing a stronger evidence-based oversight of effective interventions compared to the outcomes of a systematic review of primary studies.

- For several patient-safety interventions that are implemented worldwide, there is a lack of high- quality studies in which these interventions are evaluated.

- The found estimates of effectiveness of patient safety interventions might vary across contexts, such as small versus large hospitals, academically affiliated hospitals versus those that are not, and the availability of factors that stimulate successful implementation of interventions.

INTRODUCTION

Improving patient safety is an ongoing concern for healthcare providers, managers and policy makers. Worldwide, the prevalence of patient harm and death as a result of adverse events is about 10% among hospitalized patients. Half of these adverse events are considered avoidable.[1] Despite the widespread implementation of interventions to reduce patient harm, patient safety is not improving.[2-4]

Substantial effort has been invested into developing and implementing safety improvements.[5-7] Patient safety improvement interventions have been defined as: practices, strategies, structures, procedures, behavior or actions to prevent or mitigate unintended patient harm resulting from the healthcare process across a range of diseases and procedures.[8-11] Several reviews have studied the nature and effectiveness of a broad range of these patient safety interventions.[5 12-15] However, the findings of these reviews need to be seen in the light of several limitations. The reviews included studies with weak designs, lacking a systematic approach or were conducted more than one decade ago. Most importantly, none of the reviews reviewed or prioritized patient safety interventions based on their effects on adverse event and mortality rates. So far, patient safety interventions have not been reviewed or prioritized based on effect measures.

Better insight into the effectiveness of interventions aimed to reduce adverse events and preventable deaths within hospitals is needed to assist managers and healthcare providers with deliberately selecting patient safety interventions based on available evidence [16] and to disseminate effective patient safety improvement interventions into routine practice.[3] Therefore, the aim of this study is to systematically review systematic reviews of interventions aimed at improving patient safety in hospitals by evaluating interventions, the studies they were tested in and the effect sizes found.

METHODS

We conducted this systematic review with a pre-specified protocol (**Appendix 1**), in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) and the AMSTAR checklist for systematic reviews (**Appendices 2 and 3**).[17 18]

Data Sources and Searches

We searched for systematic reviews from inception to 22 July 2013, using the following scientific databases: PubMed (including MEDLINE), CINAHL, PsycINFO, the Cochrane Library, and EMBASE. We used the filters for searching papers on patient safety developed by Tanon and colleagues [19] to maximize the sensitivity of our literature search. The search terms used are described in detail in **Appendix 4**. We updated the search until 6 October 2015 (see Flow Chart in **Figure 1**).

Additional hand searches were conducted in high-impact journals and online databases in the field of patient safety, from April 2010 to May 2015, including: *Systematic Reviews Journal*, *Annals of Internal Medicine*, *BMJ*, *BMJ Quality and Safety in Healthcare* and *the International Journal of Quality in Healthcare*. Finally, references from the included systematic reviews and bibliographies of published and unpublished reviews related to our study objective were scanned to identify eligible systematic reviews.

Systematic Review Selection

Two researchers (MZ, GH) independently assessed the inclusion eligibility of the retrieved systematic reviews according to a standardized format (**Appendix 1**). The initial selection for inclusion was based on the title and abstract of the systematic reviews. A full-text copy of the article was retrieved and reviewed, in case the title and abstract provided insufficient information to determine its relevance. For the final selection, a full-text copy of the systematic reviews was examined to determine whether it fulfilled the inclusion criteria. Disagreement about inclusion was solved by discussion. When no consensus could be achieved, a third reviewer (HW) made the final decision.

Each systematic review had to meet the following criteria (**Appendix 1**):

1) English-language, full-text published and unpublished systematic reviews;

2) including any study matching the Cochrane Effective Practice and Organisation of Care (EPOC)criteria for study designs, including: randomized controlled trials (RCTs), non-randomized controlled trials (NRCTs), controlled before-after (CBA) studies and interrupted time series (ITS).[20]

3) focusing on population of hospitalized patients across a range of diseases and procedures;

4) regarding patient safety interventions (aimed at changing healthcare processes, structures, strategies, behavior or actions) targeted at reducing adverse events; and

5) reporting quantitative effect measures.

Systematic reviews that met any of the flowing criteria were excluded from the review:

1) only obtaining observational studies;

2) only obtaining pharmacological studies;

3) only obtaining psychiatric, obstetric patients or neonates as the study population/sample; and

4) only including process errors or consequences of adverse events (e.g., readmission and length of stay).

Systematic reviews were included if they included both observational studies and studies that met the EPOC criteria. Of these systematic reviews, only the studies that met the EPOC criteria for study designs were studied and were called 'eligible studies'.

Data Extraction and Quality Assessment

One researcher (WG) extracted the data from the included systematic reviews using a standardized form (**Appendix 1**). The extracted data were checked by a second researcher (GH). Disagreement was resolved through discussion, and a third person (MZ) was consulted if needed. We limited the data extraction to the pre-specified elements, including the intervention components, design and number of included studies, study sample (nature and size) and effect measures. Of all of the studies in a systematic review, only data from studies that met our selection criteria (called 'eligible studies') were extracted and analyzed.

Three reviewers (MZ, GH, WG) independently assessed the extent to which the systematic review was conducted to the highest possible standards, using a quality assessment form (**Appendix 1**)

that included the eleven AMSTAR quality criteria (A MeaSurement Tool to Assess systematic Reviews).[18] Systematic reviews scored 1 point for each fulfilled criterion, and a total score for each systematic review was calculated. A score of 0–3 was classified as 'low'; 4–7 as 'moderate'; and 8–11 as 'high'.[21]

Data Synthesis and Analysis

The study characteristics and patient outcomes for all of the systematic reviews that met our inclusion criteria were organized in tabular form. The systematic reviews included were classified into patient safety areas. The classification was adapted from previous reviews on patient safety interventions.[11 12 14]

The overlap in primary studies between systematic reviews was studied. Systematic reviews of which all included studies were included in a more recent systematic review (100% overlap) were excluded. We reported the proportion (%) overlap between included systematic reviews per patient safety area.

We compiled the pooled effect sizes of meta-analyses reported in the systematic reviews and analyzed the intervention components. Subsequently, we ranked the effective interventions based on their effect size.

RESULTS

Search results

Our initial search identified 11,032 records (**Figure 1**). The title and abstract scan resulted in 172 articles that underwent full-text review. Thirty-six articles met our selection criteria after the full-text review. The exclusion reasons for the 136 articles are given in A**ppendix 5**. Four additional articles were identified through hand searching and snowballing and twenty additional articles were identified through an update of our search action. The final set consisted of 60 articles [22-81] that underwent data abstraction and analysis.

Methodological Quality

Four (6.7%) systematic reviews scored low, 30 (50.0%) scored moderate and 26 (43.3%) scored high on methodological quality. Their AMSTAR scores ranged from 2 to 10 (**Appendix 6**), with a mean score of 6.9 (Standard Deviation [SD] ± 2.2). None of the included systematic reviews fulfilled all of the AMSTAR criteria. **Appendix 7** shows the proportion of studies satisfying each of the eleven AMSTAR quality criteria. Most (> 80%) of the included systematic reviews carried out a comprehensive literature search, reported the characteristics of the included studies, assessed the scientific quality of the included studies and used the scientific quality of the included studies appropriately in formulating conclusions. One-third of the systematic reviews referred to a study protocol in which the research questions and inclusion criteria were established before the study was conducted, and provided a list of included and excluded studies. None of the systematic reviews reported the conflicts of interest of the included studies (**Appendix 7**). Six systematic reviews (10.0%) did not include a statement on the presence or absence of potential conflicting sources of support for carrying out the systematic review.[42 45 46 52 68 78]

Characteristics of the Included Systematic Reviews

The characteristics of the included systematic reviews are summarized in **Appendix 8**. More than half (56.7%) of the systematic reviews were published between 2013 and 2015. The total number of

included studies ranged from two [67 81] to 138 [65]; the number of eligible studies (i.e. met the inclusion criteria) ranged from one [67 80 81] to 33 [29]. The number of participants in the eligible studies ranged from 938 [75] to 225,686 [71] and was not reported or unknown in 26 (43.3%) reviews.

The included reviews covered 14 patient safety areas (**Table 1**). Most of the reviews were about preventing adverse drug events (n = 15), followed by infection prevention (n = 8), delirium prevention (n = 7) and adverse events after hospital discharge or clinical handover (n = 7).

There was overlap in the included studies between systematic reviews within specific patient safety areas (**Appendix 9**). For the "delirium prevention" area, the overlap ranges from 25% [45] to 86% [47]; and from 66% [62] to 75% [59 60] for "fall prevention".

Table 1. **Identified systematic reviews (n = 60) classified by Patient-Safety Area (n = 14)**

Patient-Safety Area		Number of systematic reviews (references)	Intervention components relevant to patient safety (effective components are bold)
Adverse drug event	**Sub area**		
	CPOE system	2 (22 23)	Computerized physician order entry (CPOE) system
	Medication review	4 (24-27)	Medication reconciliation
	Computer-assisted decision support/alerts	3 (28-30)	Computerized advice or decision support; computerized drug-lab alerts for clinicians on prescribing or monitoring decisions
	Multicomponent interventions	6 (31-36)	**Multicomponent interventions, including pharmacist involvement and support of care teams or physicians; guideline implementation, including academic detailing, reminders and feedback of data;** multicomponent intervention, including CPOE system, changes in work schedules, education, support systems for clinical decision-making
Infection*	Device-related infections (CAUTI; CLABSI; VAP)	4 (37-40)	**Care bundles and checklists**; empowerment to stop procedure; surveillance; infrastructure and organizational changes; **training on appropriate catheter placement; catheter restriction and removal protocols**; **reminder or stop order to decrease catheter placement;** use of specific technologies
	Sepsis	1 (41)	**Multicomponent program aimed at improving compliance to sepsis care bundles, including education and decision support tools**
	Hand-hygiene compliance	2 (42 43)	Education; audit and feedback; health promotion; variations in availability and type of products used for hand hygiene
	Overall hospital-acquired infection	1 (44)	Education; protocols to remove catheters
Delirium		7 (45-51)	Psychiatric assessment; special care; daily visits by a liaison nurse; interdisciplinary team; supportive psychotherapy; **multicomponent intervention, including cognitive screening, proactive geriatric consultation and psychotherapy; multicomponent intervention, including early mobility, cognition and orientation, sleep-wake- cycle preservation; multicomponent intervention, including physiotherapy, family involvement, and staff/family-member education**
Adverse event after hospital discharge or clinical handover		7 (52-58)	Post-acute intermediate care units; geriatric assessment; liaison nurse; pre-discharge assessment of risks; patient engagement; individualized patient record; multidisciplinary discharge planning team; clinical follow-up; **nurse-led early-discharge planning programs**
Fall		4 (59-62)	**Addressing risk factors by a multidisciplinary team;** care planning; environmental changes; movement alarms; **physiotherapy**; management of urinary incontinence; **multicomponent interventions, including risk alert card, exercise, education, hip protectors and geriatric assessment**
Adverse event in surgery		5 (63-67)	Screening and decolonization of surgical-site infections; sub-specialization; benchmarking; technology or training; **surgical safety checklist**
Cardiopulmonary arrest		4 (68-71)	**Critical-care outreach service**; **rapid-response teams**
Venous thrombo-embolism		2 (72 73)	Alerts and education; real-time audit and feedback; multicomponent interventions to improve appropriate administration of thromboprophylaxis
Staffing		3 (74-76)	**Increasing proportion of support staff**; addition of specialist nursing post to staffing; reducing shift length; protected sleep time; night float; education among residents; **interdisciplinary team interventions**
Pressure ulcer		1 (77)	Standardization of interventions; multidisciplinary teams and leadership; designated skin champions; education; audit and feedback
Mechanical complication and underfeeding		1 (78)	Total parenteral nutrition team: nutrition support for patients who are unable to obtain adequate nutrition either via the oral or enteral route
Clinical pathway		1 (79)	**Clinical pathways**: multidisciplinary care plans with essential steps in care, supporting the translation of clinical guidelines into local protocols and application in practice
Safety culture		1 (80)	Error-prevention training; restructured patient-safety governance; lessons-learned program; cause-analysis program; executive rounds
External inspection		1 (81)	External inspections of compliance with standards (e.g., accreditation)

CAUTI = Catheter-associated urinary tract infection; CLABSI = central-line-associated bloodstream infection; VAP = ventilator-associated pneumonia
*Surgical-site infections were classified as "prevention of adverse events in surgery"

Effects of Patient Safety Interventions

The results of all included systematic reviews are summarized in **Appendix 10.** A meta-analysis was carried out in 30 of the 60 (50.0%) systematic reviews (**Table 2**). The authors addressed the following reasons for not performing a meta-analysis: too few studies identified (n = 5); the heterogeneity of the respective study designs (n = 9), interventions (n = 8), subject groups (n = 5) and reported outcomes (n = 5); and methodological limitations (e.g., lack of available valid data) of the included studies (n = 5).

Seventeen meta-analyses showed a statistically significant effect on adverse drug events,[36] catheter-associated urinary tract infection (CAUTI) rates,[40] central-line-associated bloodstream infection (CLABSI) rates,[39] delirium incidence,[47 50 51] fall rates,[61] surgical site infections (SSIs),[66] incidence of cardiopulmonary arrest,[69 71] complications,[66 79] and mortality rates.[33 41 58 66 71 75 76] Patient safety interventions with statistically significant effect sizes are discussed below.

Table 2 **Effect sizes of Patient-Safety interventions: results from meta-analyses (n = 30) reported in the 60 included systematic reviews**

Patient-Safety area	Reference meta-analysis	Intervention	Patient outcome	Effect size (95% CI) significant effect sizes are bold	p-value	Studies in meta-analysis (n) (eligible studies* [n])
Adverse drug event Medication review	Holland et al., 2008 [24]	Pharmacist-led medication review	*Mortality*	RR, 0.96 (0.82–1.13)	p = 0.62	22
	Christensen and Lundh, 2013 [26]	Medication review	*Mortality*	RR, 0.98 (0.78–1.23)	p = 0.86	4
	Hohl et al., 2015 [27]	Medication review	*Mortality*	OR, 1.09 (0.69–1.72)	p = 0.71	3
Adverse drug event Computerized advice on drug dosage	Durieux et al., 2008 [28]	Computerized advice on drug dosage	*Mortality*	RR, 0.81 (0.37–1.81)	p = 0.61	6
	Gillaizeau et al., 2013 [29]	Computerized advice on drug dosage	*Mortality*	RR, 1.08 (0.80–1.45)	p = 0.61	10
	Bayoumi et al., 2014 [30]	Computerized drug-lab alerts	*Adverse events (bleeding and thrombosis)*	OR, 0.88 (0.78–1.00)	p = 0.05	4
Adverse drug event Multi component interventions	Davey et al., 2013 [33]	Intervention for antimicrobial therapy	*Mortality*	RR, 0.92 (0.69–1.22)	p = 0.56	3
		Antibiotic guideline for pneumonia	*Mortality*	**RR, 0.89 (0.82–0.97)**	p = 0.01	4
		Decrease excessive prescribing	*Mortality*	RR, 0.92 (0.81–1.06)	p = 0.25	11
	Wang et al., 2015 [36]	Pharmacist interventions	*Preventable adverse drug events*	**OR, 0.23 (0.11–0.48)**	p < 0.01	3 (2)
Infections	Blot et al., 2014 [39]	Care bundle/ checklist interventions	*CLABSI*	**OR, 0.39 (0.33–0.46)**	p < 0.01	41 (5)
			CLABSI rate at 3 months	**OR, 0.30 (0.10–0.88)**	p = 0.03	6 (4)
	Meddings et al., 2014 [40]	Catheter reminder and stop order	*CAUTI episodes per 1000 catheter days*	**RR, 0.47 (0.30–0.64)**	p < 0.01	11 (1)
			CAUTI	**RR, 0.72 (0.52–0.99)**	p = 0.05	8 (2)
	Damiani et al., 2015 [41]	Sepsis bundle	*Mortality*	**OR, 0.66 (0.61–0.72)**	p < 0.01	48 (3)
Delirium	Hempenius et al., 2011 [47]	Multicomponent interventions, including cognitive screening, proactive geriatric consultation and psychotherapy	*Incidence of delirium*	**OR, 0.58 (0.38–0.92)**	NR	5
		One-component interventions	*Incidence of delirium*	OR, 1.05 (0.09–11.57)	NR	2
	Hshieh et al., 2015 [50]	Multicomponent intervention, including early mobility, cognition and orientation	*Incidence of delirium*	**OR, 0.47 (0.38–0.58)**	p < 0.01	11 (7)
	Martinez et al., 2015 [51]	Multicomponent intervention, including physiotherapy, daily reorientation, family involvement and staff/family-member education	*Incidence of delirium*	**RR, 0.73 (0.63–0.85)**	p < 0.01	7
Adverse event after hospital discharge or clinical handover	Griffiths et al., 2005 [52]	Nursing-led inpatients units	*Mortality*	OR, 1.10 (0.56–2.16)	p = 0.64	7
			Mortality 3 or 6 months post-admission	OR, 0.96 (0.63–1.47)	p = 0.62	6
	Conroy et al., 2011 [53]	Comprehensive geriatric assessment	*Mortality*	RR, 0.92 (0.55–1.52)	p = 0.77	5
	Niven et al., 2014 [54]	Critical-care transition programs	*Mortality*	RR, 0.84 (0.66–1.05)	p = 0.1	3 (2)
	Sheppard et al., 2013 [56]	Discharge planning from hospital to home	*Mortality at 6 to 9 months*	RR, 1.00 (0.79–1.26)	p = 0.69	6
			Falls	RR, 0.87 (0.50–1.49)	p = 0.61	1
	Lowthian et al., 2015 [57]	Optimized ED discharge	*Mortality up to 18 months post discharge*	OR, 1.01 (0.70–1.47)	p = 0.94	2

	Zhu et al., 2015 [58]	Nurse-led early-discharge planning	*Mortality*	**RR, 0.70 (0.52–0.95)**	p = 0.02	5
Fall	Oliver et al., 2007 [59]	Multicomponent intervention	*Falls*	RaR, 0.82 (0.68–1.00)	NR	12
			Fallers	RR, 0.95 (0.71–1.27)	NR	12
			Fractures	RaR, 0.59 (0.22–1.58)	NR	12
	Coussement et al., 2008 [60]	Multicomponent intervention	*Falls*	RR, 0.82 (0.65–1.03)	NR	4
			Number of fallers	RR, 0.87 (0.70–1.08)	NR	4
	Cameron et al., 2012 [61]	Multicomponent interventions	*Rate of falls*	**RaR, 0.69 (0.49–0.96)**	p = 0.03	4
			Risk of falling	RR, 0.71 (0.46–1.09)	p = 0.12	3
		Exercises	*Risk of falling*	**RR, 0.36 (0.14–0.93)**	p =0.04	2
Adverse event in surgery	Bergs et al., 2014 [66]	WHO surgical-safety checklist	*Any complication*	**RR, 0.59 (0.47–0.74)**	p < 0.01	5
			Mortality	**RR, 0.77 (0.60–0.98)**	p = 0.04	4 (3)
			Surgical site infections	**RR, 0.57 (0.41–0.79)**	P < 0.01	5
Cardiopulmonary arrest	Chan et al., 2010 [69]	Rapid-response team	*Mortality*	RR, 0.92 (0.82–1.04)	NR	16
			Cardiopulmonary arrest	**RR, 0.65 (0.55–0.77)**	NR	16
	Maharaj et al., 2015 [71]	Rapid-response team	*Mortality*	**RR, 0.91 (0.85–0.97)**	p < 0.01	4
			Cardiopulmonary arrest	**RR, 0.74 (0.56–0.98)**	p = 0.04	2
Venous thromboembolism	Kahn, et al., 2013 [72]	Alerts	*All venous thromboembolism*	RR, 0.85 (0.49–1.46)	NR	3
		Multicomponent interventions	*All venous thromboembolism*	RR, 1.01 (0.51–1.98)	NR	5
			Symptomatic deep vein thromboembolism	RR, 0.59 (0.18–1.98)	NR	3
Staffing	Butler et al., 2011 [75]	Addition of specialist nursing post to staffing	*In-hospital mortality*	RR, 0.96 (0.59–1.56)	p = 0.86	1
			Post-discharge adverse events	RR, 1.03 (0.70–1.53)	p = 0.87	1
		Increasing the proportion of support staff	*Mortality in trauma unit*	RR, 0.41 (0.16–1.01])	p = 0.05	1
			Mortality in hospital	RR, 0.56 (0.29–1.09)	p = 0.09	1
			Mortality at 4 months	**RR, 0.57 (0.34–0.95)**	p = 0.03	1
	Pannick et al., 2015 [76]	Interdisciplinary teams	*Mortality*	wRR, 0.92 (0.82–1.05)	NR	7
		Team practice interventions	*Mortality*	**wRR, 0.67 (0.45–0.99)**	NR	2
Clinical pathway	Rotter et al., 2010 [79]	Clinical pathway	*Mortality*	OR, 0.84 (0.64–1.11)	p = 0.23	3
			Complications up to 3 months	**OR, 0.31 (0.13–0.72)**	p = 0.07	1
			In-hospital complications	**OR, 0.58 (0.36–0.94)**	p = 0.03	5

CAUTI = catheter-associated urinary tract infection; CI = confidence interval; CLABSI = Central-line-associated bloodstream infection; NR = Not Reported; OR= Odds Ratio; RR = Risk/Relative Ratio; RaR = Rate Ratio; wRR = weighted Risk Ratio

* study design in accordance with methodological criteria of the Cochrane Effective Practice and Organisation of Care (EPOC) review group and quantitative data on adverse event rates were reported

Adverse drug event

Of the 15 included systematic reviews about adverse drug events, two reported statistically significant results. Davey and colleagues [33] found that interventions aimed at increasing antibiotic guideline compliance for pneumonia were associated with a significant reduction in mortality: risk ratio [RR], 0.89 (95% CI, 0.82 to 0.97; p = 0.01). This found effect was based on four studies. Effective intervention components were formal presentations, academic detailing, letters, frequent reminders by pharmaceutical representatives, preprinted outpatient and admission order sheets and reporting of outcome data to providers.

Wang and colleagues [36] found that participation of a pharmacist in physician rounds and timely information exchange and advice of physicians by the pharmacist (i.e., on drug interactions, appropriate dosages, dose intervals and routes of administration) was associated with a statistically significant reduced adverse-drug-event rate: odds ratio [OR], 0.23 (CI, 0.11 to 0.48; p < 0.01). The found effect was based on three studies, of which two complied with the Cochrane EPOC inclusion criteria for study designs.

Infection

Three systematic reviews reported statistically significant effects on the reduction of infection and mortality rates as a result of implementing interventions and care bundles.[39-41] The meta-analysis performed by Blot and colleagues [39] showed a reduction in the CLABSI rate (OR, 0.39 [CI, 0.33 to 0.46; p < 0.01]) and reduction in the CLABSI rate at three months post intervention (OR, 0.30 [CI, 0.10 to 0.88; p = 0.028]) as a result of care bundles and checklists.[39] These found effects were based on 41 and six studies, respectively, of which five and four studies met our inclusion criteria, respectively.

Meddings and colleagues [40] reported that the use of a reminder and/or stop order to prompt removal of unnecessary urinary catheters led to a 53% reduction of CAUTI episodes per 1,000 catheter days: rate ratio [RaR], 0.47 (CI, 0.30 to 0.64; p < 0.01). This meta-analysis was based on 11 studies, of which only one study complied with the inclusion criteria for study designs.

The implementation of a program to improve compliance to sepsis care bundles led to a statistically significant decreased mortality rate: OR, 0.66 (CI, 0.61 to 0.72; $p < 0.01$). This rate is based on 48 studies, of which three fulfilled the criteria for study designs.[41]

Delirium

Three systematic reviews reported a statistically significant reduction in delirium incidence.[47 50 51] There was a 16% overlap (3 of the 19 studies) between these systematic reviews (**Appendix 9**).

Hempenius and colleagues [47] pooled the effects of five studies and found a statistically significant effect of multicomponent interventions to prevent delirium: OR, 0.58 (CI, 0.38 to 0.92). Components were education, systematic cognitive screening, geriatric consultative services, supportive psychotherapy, and a scheduled pain protocol.

Hshieh and colleagues [50] reviewed studies evaluating non-pharmacological interventions, including the following components: early mobility, cognition and orientation, sleep-wake-cycle preservation, hydration, hearing and vision. They found a statistically significant reduction in delirium incidence: OR, 0.47 (CI, 0.38 to 0.58); $p < 0.01$. This rate was based on 11 studies, of which seven complied with the inclusion criteria for study designs.

Martinez and colleagues [51] found a statistically significant reduction in delirium incidence: RR, 0.73 (CI, 0.63 to 0.85); $p < 0.01$. This rate was based on seven studies using different multicomponent interventions, but a number of specific components were shared: physiotherapy, daily reorientation, family involvement in care, stimulation programs with avoidance of sensorial deprivation and staff/family-member education.

Adverse event after hospital discharge or clinical handover

Six systematic reviews pooled the effect of interventions to improve clinical handover or hospital discharge. One systematic review reported a statistically significant effect size: Nurse-led early-discharge planning programs were associated with a lower mortality rate: RR, 0.70 (CI, 0.52 to 0.95; $p = 0.02$).[58] This found effect was based on five studies. Effective intervention components were an individual discharge plan to address identified transitional care needs, comprehensive discharge plan

and home-based follow-up visits or telephone calls by providers to patients after their hospital discharge.

Fall

One systematic review [61] reported the effectiveness of fall-prevention interventions. Additional physiotherapy reduced the risk of falling: RR, 0.36 (CI, 0.14 to 0.93). Multicomponent interventions reduced the fall rate: RaR, 0.69 (CI, 0.49 to 0.96). These rates were based on two and four studies, respectively. Effective components of the multifactorial interventions were fall-risk alert card and information brochure, exercise program, education program, hip protectors, comprehensive geriatric assessment and treatment of fall risk factors by a multidisciplinary team.

Surgical adverse event

The implementation of a surgical checklist was associated with a reduction of complications, deaths and surgical-site infections: RR, 0.59 (CI, 0.47 to 0.74), 0.77 (CI, 0.60 to 0.98) and 0.57 (CI, 0.41 to 0.79), respectively. These pooled rates were based on five studies.[66] The authors reported that the results were statistically significant but cannot be regarded as definitive in the absence of high-quality studies.[66]

Cardiopulmonary arrest

Two systematic reviews found an association between the implementation of a rapid-response team and improved patient outcomes. There is an 11% overlap (2 of the 19 studies) between these systematic reviews (**Appendix 9**). Chan and colleagues [69] performed a meta-analysis on 16 studies and found a statistically significant reduction of cardiopulmonary arrests outside the intensive care unit (ICU) following the implementation of the rapid-response team: RR, 0.65 (CI, 0.55 to 0.77). The authors of the systematic review raised questions about the effectiveness of rapid-response-team implementation given the lack of an effect of rapid-response teams on mortality.

The systematic review of Maharaj [71] found a statistically significant reduction in cardiopulmonary arrests based on two studies: RR, 0.74 (CI,0.56 to 0.98; p = 0.04) and a statistically significant reduction of deaths based on four studies: RR, 0.91 (CI, 0.85 to 0.97; p < 0.01).

Staffing

Butler and colleagues [75] found 6,202 studies that were potentially relevant to studying the effect of hospital-nurse staffing models on mortality and adverse events. However, one study reported a statistically significant effect: increasing the proportion of support staff (i.e., dietetic assistants) reduced mortality at four months: RR, 0.57 (CI, 0.34 to 0.95; p = 0.03).The authors stated that they were unable to draw conclusions because of the small number of eligible studies.

Pannick and colleagues [76] found that interdisciplinary team interventions reduced mortality rates: RR, 0.67 (CI, 0.45 to 0.99). The finding was based on two studies. Effective intervention components were interdisciplinary rounds, including physician, nurse, pharmacist, nutritionist and social worker; expanded senior clinical nurse roles; incorporating structured detailed assessments of premorbid functional and social patient data and investment in allied health professionals as consistent staff members.

Clinical pathway

Rotter and colleagues [79] found an association between the use of clinical pathways and a reduction of in-hospital complications, based on five studies: OR, 0.58 (CI, 0.36 to 0.94). Examples of reported complications were postoperative confusion, infection, uncontrolled bleeding and deep vein thrombosis, ventilator-associated pneumonia, joint dislocation and decreased post-discharge mobility up to three months post-surgery. The OR for complications up to three months, based on one study, was 0.31 (CI, 0.13 to 0.72).

Summary of Effective Patient Safety Interventions

Patient safety interventions that result in a significant reduction in adverse event or mortality rates are presented in **Table 3**.

Exercises to reduce the risk of falling, surgical safety checklist to reduce the rate of surgical-site infection, rapid-response team to prevent cardiopulmonary arrest and multicomponent interventions to prevent delirium have significantly better results compared to changes in staffing and interventions to improve hospital discharge to prevent mortality. Pharmacist interventions and care-bundle interventions and checklists were significantly associated with, respectively, reduced rates of adverse drug events and infection rates. These effect measures are, however, partly based on experimental studies (**Table 3**).

Fourteen of the 17 significant effect sizes (82.4%) were based on five or fewer studies that comply with the inclusion criteria for study design. The effect measures were based on sample sizes varying from 83 to 1143495 patients, for exercises to reduce the risk of falling and raped response-team to reduce the rate of cardiopulmonary arrest respectively (**Table 3**). The AMSTAR scores of the systematic reviews of the 17 effective patient-safety interventions ranged from 4 to 10, with a mean score of 7.5 (SD ±1.9).

Three systematic reviews evaluated multicomponent interventions to prevent delirium (all with different compositions of the multicomponent intervention and different effect measures); two systematic reviews evaluated the effects of rapid response-teams, resulting in 14 unique patient interventions (**Table 4**).

Table 3 **Effective Patient-Safety Interventions (n = 14*)**

Intervention effect estimates based on meta-analysis with only eligible studies	**Patient outcome**	**Effect size (95%CI)**	**Sample size (n patients)**	**Study size (n studies)**	**Designs of studies (n)**
Exercises [61]	*Risk of falling*	RR, 0.36 (0.14–0.93)	83	2	RCT (2)
Surgical safety checklist [66]	*Surgical-site infections*	RR, 0.57 (0.41–0.79)	15198	5	ITS (5)
Increasing the proportion of support staff [75]	*Mortality at 4 months*	RR, 0.57 (0.34–0.95)	302	1	RCT (1)
Rapid-response team [69]	*Cardiopulmonary arrest*	RR, 0.65 (0.55–0.77)	1143495	16	Non-RCT (2); CBA (12); ITS (2)
Nurse-led early-discharge planning programs [58]	*Mortality*	RR, 0.70 (0.52–0.95)	2503	5	RCT (5)
Multicomponent interventions, including physiotherapy, daily reorientation, family involvement, and staff/family-member education [51]	*Delirium*	RR, 0.73 (0.63–0.85)	1691	7	RCT (7)
Antibiotic guideline for pneumonia [33]	*Mortality*	RR, 0.89 (0.82–0.97)	22526	4	RCT (1); CBA (3)
Rapid-response team [71]	*Mortality*	RR, 0.91 (0.85–0.97)	209639	4	RCT (2); CBA (1); ITS (1)
Interdisciplinary team interventions [76]	*Mortality*	wRR, 0.67 (0.45–0.99)	2640	2	Non-RCT (2)
Multicomponent interventions [61]	*Falls*	RaR, 0.69 (0.49–0.96)	6478	4	RCT (4)
Multicomponent interventions, including cognitive screening, proactive geriatric consultation and psychotherapy [47]	*Delirium*	OR, 0.58 (0.38–0.92)	1343	5	Non-RCT (3); CBA (2)
Clinical pathway [79]	*In-hospital complications*	OR, 0.58 (0.36–0.94)	664	5	RCT (4); CCT (1)
Intervention effect estimates based on meta-analysis with both eligible and non –eligible studies	**Patient outcome**	**Effect size (95%CI)**	**Sample size (n eligible patients) and proportion eligible patients of all patients (%)**	**Study size (n) and proportion of eligible studies (n;%)**	**Designs of eligible studies (n)**
Catheter reminder and stop order [40]	*Infections (CAUTI)*	RR, 0.72 (0.52–0.99)	U	8 (2;25)	RCT (1); non-RCT (1)
Pharmacist interventions [36]	*Adverse drug events*	OR, 0.23 (0.11–0.48)	2794 (30.4)	3 (2; 66.7)	CBA (2)
Care bundle and checklist [39]	*Infections (CLABSI)*	OR, 0.39 (0.33–0.46)	70358 (2.8)	41 (5; 12.2)	BA (36); ITS (5)
Multicomponent interventions, including early mobility, cognition and orientation [50]	*Delirium*	OR, 0.47 (0.38–0.58)	2914 (68.3)	11 (7; 63.6)	RCT (3); Non-RCT (4)
Sepsis bundle [41]	*Mortality*	OR, 0.66 (0.61–0.72)	11720 (2.7)	48 (3; 6.3)	ITS (3)

CAUTI = catheter-associated urinary tract infection; CBA= controlled before after; C(C)T= controlled (clinical) trial; CI = confidence interval; CLABSI = Central-line-associated bloodstream infection; ITS = Interrupted time series; NR= not reported; OR = Odds Ratio; RCT = randomized controlled trial; RR = Risk/Relative Ratio; RaR = Rate Ratio; U = unclear; wRR = weighted Risk Ratio

*17 systematic reviews reported about 14 types of interventions.

**Studies with a design in accordance with methodological criteria of the Cochrane Effective Practice and Organisation of Care (EPOC) review group.

Table 4 **Evidence-based effective Patient-Safety interventions (n= 14)**
Antibiotic guideline for pneumonia to reduce mortality rates
Catheter reminder and stop order to reduce the risk for developing catheter associated urinary tract infection
Care bundles and checklists to reduce rates of central line associated blood stream infections
Clinical pathways to avoid complications
Exercises to reduce the risk of falling
Increasing the proportion of support staff to reduce mortality rates
Interdisciplinary team interventions to reduce mortality rates
Multicomponent interventions to reduce the risk of falling
Multicomponent interventions to prevent delirium
Nurse-led early-discharge planning programs to reduce mortality rates
Pharmacist interventions to prevent adverse drug events
Rapid response team to reduce the risk for cardiopulmonary arrest and reduce mortality rates
Sepsis bundle to reduce mortality rates
Surgical-safety checklist to reduce the risk for surgical-site infections and reduce mortality rates

DISCUSSION

We systematically reviewed the literature for effective interventions aimed at reducing adverse event rates and preventable deaths in hospitals. The results showed that there were 14 effective patient-safety interventions (**Table 4**), including: multicomponent interventions to prevent delirium; rapid-response teams to reduce cardiopulmonary arrest and mortality rates; exercises and multicomponent interventions to reduce the risk of falling and surgical safety checklist to reduce the rate of surgical-site infection. Other effective interventions were pharmacist interventions to reduce adverse drug events, , care bundles and checklists to reduce infection and mortality rates, changes in staffing and interventions to improve hospital discharge to reduce mortality rates. The evidence base that supports the interventions is moderate because 82% of the found effect measures were based on five or fewer primary studies that fulfilled the Cochrane EPOC criteria for study designs.[20]

This review offers a unique overview of effective patient-safety interventions based on data that is synthesized from systematic reviews, thereby producing a stronger evidence-based oversight of effective interventions compared to the outcomes of a systematic review of primary studies.[16] The overlap of primary studies in existing reviews is analyzed to minimize potential effects of "double-counting" primary studies in multiple reviews.[82] Moreover, most of the systematic reviews included in our review were of high methodological quality (mean AMSTAR score of 6.9 for all included reviews and 7.5 for the reviews with positively pooled outcome effects), thereby increasing the credibility and validity of our findings.[18]

Despite the growing number of experimental studies evaluating the effectiveness of patient-safety interventions, our findings show that the evidence base for patient-safety improvement is still not strong. Furthermore, our findings are in contrast to the findings of previous research on this topic. Shekelle and colleagues [83] strongly supported the adoption of 10 patient-safety practices, including hand-hygiene strategies, the do-not-use list for hazardous abbreviations and multicomponent interventions to reduce pressure ulcers. We found limited support for the effectiveness of these interventions while finding strong support for delirium-prevention interventions and rapid-response teams. Our review placed more emphasis on assessing interventions on the basis of patient outcomes

(i.e., reduced adverse event and mortality rates) and testing within high-quality designs; this emphasis on the quality of studies produces a very different assessment of which safety interventions are most beneficial for patients and which should be implemented.

Evidence is still lacking for medication reconciliation and several interventions to improve the safety of clinical handover or discharge of hospitalized patients, which are incorporated in national and international patient-safety campaigns and are recommended by the WHO.[84] However, the results of our review showed that by looking strictly at patient outcomes and only including high-quality studies, the evidence that these interventions reduce adverse event or mortality rates remains incomplete.

The lack of evidence for patient-safety interventions does not mean that these interventions do not work; it primarily addresses the lack of valid effect. Policy makers and clinicians show good intentions by implementing ambitious patient-safety programs and investments of resources. However, implementing unproven interventions can lead to the opposite of what is intended with patient-safety improvements: waste of resources, energy and enthusiasm.[85 86] In times of limited resources, we concur with Shekelle and colleagues and underscore previous, urgent calls for more research on the effectiveness of patient-safety interventions.[7 12 83 85 87 88] Patient-safety interventions should be tested on their effectiveness based on the same high-quality standards used for drug studies.[3 89]

This systematic review has several limitations. First, we did not retrieve data from the primary studies; instead, we used the information reported by the authors on aspects such as the description of the interventions and reported outcomes. As a result, the information for some patient-safety interventions and outcomes reported in our systematic review is limited. However, by focusing on the results of the systematic reviews rather than each individual primary study, we were able to obtain a broad overview of the field of patient safety.[90] Second, the found estimates of effectiveness of patient safety interventions might vary across contexts, such as small versus large hospitals, academically affiliated hospitals versus those that are not, and the availability of factors that stimulate successful implementation of interventions, e.g. strong leadership and an electronic patient record.[91] Third, in two-thirds of the included systematic reviews, publication bias was not assessed (**Appendix 7**), meaning that the pooled rates in these reviews may present an overestimation of the effect size.[92] Fourth, in this study valuable narrative syntheses from systematic reviews may have been

underreported, because we focused on the quantitative evidence of safety interventions. The large amount of eligible systematic reviews and subsequent data from primary studies restricted us to focus on the results from meta-analyses, which are widely considered as the highest level of evidence for the effectiveness of interventions (Oxford Centre for Evidence-Based Medicine - Levels of Evidence). Fifth, the focus of our systematic review was to summarize quantitative evidence for existing patient safety interventions. A limitation of this approach is that the found statistically significant effect measures may not be clinically significant and, vice versa, effects that are clinical relevant may not be statistically significant and were not captured in our systematic review.

In conclusion, patient-safety interventions are implemented worldwide, even though evidence for these interventions remains incomplete. A major cause for this problem is the lack of high- quality studies in which interventions are evaluated on their effects. To contribute to evidence-based patient safety, interventions need to be evaluated based on high-quality research standards, including experimental research designs, measured outcomes at the patient level and description of the intervention, implementation process and context in detail. Description of these aspects is necessary to know which factors lead to optimal effects and how to replicate the patient-safety intervention in practice.[93 94] Policy makers and clinicians should stop taking shortcuts but need to spend more time and money conducting high-quality research on the effectiveness of patient-safety interventions to establish progress in patient safety.

CONTRIBUTORSHIP

MZ, GH, CV and HW contributed to the design of the study. MZ, GH and WG did the literature search, reviewed the studies for inclusion, assessed the included studies, extracted and analyzed the data. MZ, GH and WG drafted the manuscript. CV and HW revised the manuscript critically for important intellectual content. All authors read and approved the final manuscript. MZ is the guarantor.

The guarantor affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if eligible, registered) have been explained.

COMPETING INTERESTS

All authors declare that they have no competing interests.

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ETHICAL APPROVAL

Not needed for this project.

DATA SHARING STATEMENT

No additional data are available.

FIGURE LEGEND

Figure 1. Summary of evidence search and selection.

*See **Appendix 5** for the exclusion reason per systematic review after full text selection

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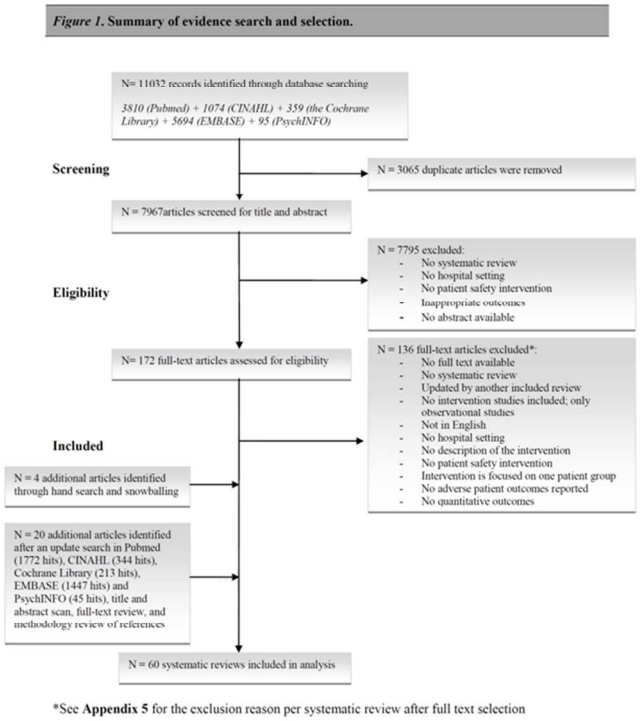


Figure 1. Summary of evidence search and selection.
*See Appendix 5 for the exclusion reason per systematic review after full text selection

81x60mm (300 x 300 DPI)

Appendix 1 Protocol Systematic Review Patient-Safety Interventions.

Research question:
What are effective interventions to reduce the rate of adverse events and preventable deaths in hospitals?

Data Sources:
PubMed (including The National library of medicine**,** MEDLINE)
EMBASE
CINAHL
PsycInfo
The Cochrane Library (including the Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts on Reviews and Effectiveness (DARE), Cochrane Controlled Trial Register (CCTR), NHS Economic Evaluation Database (NHS-EED) and Health Technology Assessment Database (HTA))

Selection criteria:
Patients/setting
- Hospitalized patients

Interventions
- Patient-safety interventions are described as interventions, strategies, practices, behavior, actions, procedures, or structures which are aimed to improve patient safety by reducing unintended patient harm as a result of the process of healthcare (adverse events). The interventions should contain 1 or more components (described in the article) that aimed to reduce adverse patient outcomes. The intervention had to compare the effectiveness of a specific patient-safety intervention to other interventions or control.

Control
- Usual hospital care

Outcomes
- At least one or more objectively measured changes in patient-safety outcomes, adverse events, at the patient level (e.g. adverse drug events, mortality, infections, pneumonia, etc) during hospital stay and adverse events that occurred within the first 12 months after hospital stay. Systematic reviews that only report process errors (e.g. diagnostic errors, no hand hygiene, medication/prescribing errors) and errors in structure (e.g. stress and fatigue of health care providers, no safety culture) are not included. Moreover, consequences of adverse events in terms of extra treatment(s), increased length of stay and readmission are not the focus

Type of studies
- Systematic reviews/meta-analysis of primary studies which provide evaluative results of patient safety interventions and comply to the Cochrane Effective Practice and Organisation of Care (EPOC) review group methodological criteria

Languages
- English-language systematic reviews

Data collection and analysis
- See A. Abstract and full text selection form on page 2
- See B. Quality assessment form on page 3 and 4
- See C. Data abstraction form on page 5, 6 and 7

A. FORM FOR ABSTRACT AND FULL TEXT SELECTION

Reviewers	
Name Reviewer 1	
Name Reviewer 2	
Date	

Study	
ID Study	
Authors, year	
Title	

Selection Criteria	
1. ***Study design*** Systematic review, review or meta- analysis ***Yes (include)*** Systematic review of primary research, systematic reviews of systematic reviews, systematic comparative review. Abstract specifies "systematic review" or "meta analysis" as a term. ***No (exclude)*** Primary studies, editorials, letters, comments, expert opinions, unsystematic reviews, narrative reviews (without systematic elements or which don't report methodology), synthesis of non-empirical work, such as guidelines or conceptual articles, reviews of methodology, research protocol articles, critical review.	○ Yes ○ No ○ Unclear
2. ***Setting/Patients*** Intervention is targeted at hospitalized patients and involved health care providers ***Yes (include)*** Acute care, in-hospital care, in both developed as developing countries, systematic reviews including hospital care and other settings, unless effect measures are available for the hospital setting separately ***No (exclude)*** Residential care, nursing homes, dental care, psychiatry, mental care, homecare, primary care, paramedics, tertiary care, public health	○ Yes ○ No ○ Unclear
3. ***Interventions*** Effect evaluation of patient safety interventions, which are aimed to prevent unintended patient harm ***Yes (include)*** A full description of the intervention should be reported. At least the following: title, abstract, aim needs to refer to the patient safety intervention. ***No (exclude)*** No description of the intervention is given. Components of the intervention are unclear. Review of non-interventional studies.	○ Yes ○ No ○ Unclear
4. ***Outcomes*** Effectiveness of a patient safety intervention is measured at patient level ***Yes (include)*** Quantitative outcome(s) on patient level including adverse events, adverse drug events, infections, pneumonia, mortality ***No (exclude)*** Outcome at professional level (performance of professionals; healthcare professional behavior, team climate). Errors in process (diagnostic errors, no hand hygiene, medication/prescribing errors) and errors in structure/ healthcare delivery systems (stress and fatigue of health care providers, no safety culture)	○ Yes ○ No ○ Unclear
5. ***Evidence*** The methodology (including search strategy and design of included studies) is reported ***Yes (include)*** Review contains methodological justification for search strategy and report about the quality of included studies. ***No (exclude)*** No methodological justification for search strategy and the quality of included studies is not reported.	○ Yes ○ No ○ Unclear

CONCLUSION REVIEWER If no to any of the above questions, then **exclude**. If yes or unclear to all, then **include** for full text review.	○ INCLUDE ○ EXCLUDE

B. FORM FOR QUALITY ASSESSMENT OF SYSTEMATIC REVIEWS

1. Reviewers	
a) Name reviewer	
b) Name second reviewer	
c) Date	

2. Study	
a) Title	
b) Authors	
c) Source and year	

3. Quality rating*	
1) Was an ''a priori'' design provided? The research question and inclusion criteria should be established before the conduct of the review. *Note: Need to refer to a protocol, ethics approval, or pre-determined/a priori published research objectives to score a "yes."*	☐ Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
2) Was there duplicate study selection and data extraction? There should be at least two independent data extractors and a consensus procedure for disagreements should be in place. *Note: 2 people do study selection, 2 people do data extraction, consensus process or one person checks the other's work.*	☐ Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
3) Was a comprehensive literature search performed? At least two electronic sources should be searched. The report must include years and databases used. Key words and/or MESH terms must be stated, and where feasible, the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. *Note: If at least 2 sources + one supplementary strategy used, select "yes" (Cochrane register/Central counts as 2 sources; a grey literature search counts as supplementary).*	☐ Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
4) Was the status of publication (i.e., grey literature) used as an inclusion criterion? The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc. *Note: If review indicates that there was a search for "grey literature" or "unpublished literature," indicate "yes." SIGLE database, dissertations, conference proceedings, and trial registries are all considered grey for this purpose. If searching a source that contains both grey and non-grey, must specify that they were searching for grey/unpublished lit.*	☐ Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
5) Was a list of studies (included and excluded) provided? A list of included and excluded studies should be provided. *Note: Acceptable if the excluded studies are referenced. If there is an electronic link*	☐ Yes (1) ☐ No (0)

to the list but the link is dead, select "no."	☐ Can't answer (0) ☐ Not applicable (0)
6) Were the characteristics of the included studies provided? In an aggregated form, such as a table, data from the original studies should be provided on the participants, interventions, and outcomes. The ranges of characteristics in all the studies analyzed, e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. *Note: Acceptable if not in table format as long as they are described as above.*	☐ Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
7) Was the scientific quality of the included studies assessed and documented? ''A priori'' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo-controlled studies, or allocation concealment as inclusion criteria); for other types of studies, alternative items will be relevant. *Note: Can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, etc., or a description of quality items, with some kind of result for EACH study ("low" or "high" is fine, as long as it is clear which studies scored "low" and which scored "high"; a summary score/range for all studies is not acceptable).*	☐ Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
8) Was the scientific quality of the included studies used appropriately in formulating conclusions? The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. *Note: Might say something such as "the results should be interpreted with caution due to poor quality of included studies." Cannot score "yes" for this question if scored "no" for question 7.*	☐ Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
9) Were the methods used to combine the findings of studies appropriate? For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, I2). If heterogeneity exists, a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). *Note: Indicate "yes" if they mention or describe heterogeneity, i.e., if they explain that they cannot pool because of heterogeneity/variability between interventions.*	☐ Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
10) Was the likelihood of publication bias assessed? An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test). *Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.*	☐ Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
11) Was the conflict of interest included? Potential sources of support should be clearly acknowledged in both the systematic review and the included studies. *Note: To get a "yes," must indicate source of funding or support for the systematic review AND for each of the included studies.*	☐ Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
12) Total score	

* Based on the AMSTAR criteria for Quality assessment of systematic reviews (Shea *et al. BMC Medical Research Methodology* 2007 **7**:10 doi:10.1186/1471-2288-7-10)
Additional notes (in italics) made by Michelle Weir, Julia Worswick, and Carolyn Wayne based on conversations with Bev Shea and/or Jeremy Grimshaw in June and October 2008 and July and September 2010. (http://amstar.ca/docs/AMSTARguideline.pdf)

C. DATA EXTRACTION FORM

1. Reviewers	
a) Name reviewer	
b) Date	
c) Cross-checked	

2. Study	
a) ID study	
b) Title	
c) Authors	
d) Source and year	

3. Objective and methods	
a) Objective/Aim of the review	
b) Number of studies included in the SR	
c) Time range of included studies	From: To:
d) Number of 'relevant' studies included (for the data analysis of this SR)	
e) Target population/participants	
f) Total no. of participants (sum of all 'relevant' included studies)	
g) Design/scientific quality of included studies	No. of Randomized controlled trials (RCTs): No. of non-randomised controlled clinical trials: No. of controlled before-and-after studies:

	No. of interrupted time series: No. of uncontrolled before-after studies and observational studies, including cohort study, case-control studies, cross-sectional studies, case studies:
h) Design/scientific quality of 'relevant' studies included (for the data analysis of this SR)	No. of Randomized controlled trials (RCTs): No. of non-randomised controlled clinical trials: No. of controlled before-and-after studies: No. of interrupted time series: No. of uncontrolled before-after studies and observational studies, including cohort study, case-control studies, cross-sectional studies, case studies:

4. Intervention	
i) Description of intervention (details/ comments)	

5. Outcome measurements	
j) Outcome measure 1	Definition: Qualitative/descriptive data: Quantitative/pooled results/combined ratios (e.g. risk rate):
k) Outcome measure 2	Definition: Qualitative/descriptive data: Quantitative/pooled results/combined ratios (e.g. risk rate):
l) Outcome measure 3	Definition: Qualitative/descriptive data: Quantitative/pooled results/combined ratios (e.g. risk rate):
m) Outcome measure 4	Definition: Qualitative/descriptive data: Quantitative/pooled results/combined ratios (e.g. risk rate):
n) Outcome measure 5	Definition: Qualitative/descriptive data: Quantitative/pooled results/combined ratios (e.g. risk rate):

o) Outcome measure 6	Definition: Qualitative/descriptive data: Quantitative/pooled results/combined ratios (e.g. risk rate):
p) Process evaluation (i.e., barriers and drivers for the implementation of the intervention)	

6. Limitations of the systematic review	
q) Description of limitations	Reported by the authors: Reported by us (researchers/reviewers):

7. Authors' key conclusions	
r) What conclusion did the authors make based on their findings? (e.g. first or last sentence of discussion/conclusion section)	

8. Other	
s) Comments/ remarks	

Appendix 2 PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4 and included as Appendix 1
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4 and Appendix 1
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4 and Appendix 4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix 4
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4, 5 and Appendix 1
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5 and Appendix 1
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	4, 5 and Appendix 1
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5 and assessment form in Appendix 1
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	11-18; Table 2 and 3, Appendix 10

Appendix 2 PRISMA 2009 Checklist

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	Not Applicable

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	5
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Not Applicable
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7 and Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Appendix 8
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	7, Appendix 6, Appendix 7
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	11-18, Appendix 10
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Not Applicable
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	7, Appendix 6, Appendix 7
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Not Applicable
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	20-22 and Table 4
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	21
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	22
FUNDING			

Appendix 2 PRISMA 2009 Checklist

Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	23

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

Appendix 3 Methodological quality systematic review on patient safety interventions.

AMSTAR Quality rating*	
1) Was an ''a priori'' design provided? The research question and inclusion criteria should be established before the conduct of the review. *Note: Need to refer to a protocol, ethics approval, or pre-determined/a priori published research objectives to score a "yes."*	X Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
2) Was there duplicate study selection and data extraction? There should be at least two independent data extractors and a consensus procedure for disagreements should be in place. *Note: 2 people do study selection, 2 people do data extraction, consensus process or one person checks the other's work.*	X Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
3) Was a comprehensive literature search performed? At least two electronic sources should be searched. The report must include years and databases used. Key words and/or MESH terms must be stated, and where feasible, the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. *Note: If at least 2 sources + one supplementary strategy used, select "yes" (Cochrane register/Central counts as 2 sources; a grey literature search counts as supplementary).*	X Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
4) Was the status of publication (i.e., grey literature) used as an inclusion criterion? The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc. *Note: If review indicates that there was a search for "grey literature" or "unpublished literature," indicate "yes." SIGLE database, dissertations, conference proceedings, and trial registries are all considered grey for this purpose. If searching a source that contains both grey and non-grey, must specify that they were searching for grey/unpublished lit.*	X Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
5) Was a list of studies (included and excluded) provided? A list of included and excluded studies should be provided. *Note: Acceptable if the excluded studies are referenced. If there is an electronic link to the list but the link is dead, select "no."*	X Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
6) Were the characteristics of the included studies provided? In an aggregated form, such as a table, data from the original studies should be provided on the participants, interventions, and outcomes. The ranges of characteristics in all the studies analyzed, e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. *Note: Acceptable if not in table format as long as they are described as above.*	X Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
7) Was the scientific quality of the included studies assessed and documented? ''A priori'' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo-controlled studies, or allocation concealment as inclusion criteria); for other types of studies, alternative items will be relevant. *Note: Can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, etc., or a description of quality items, with some kind of result for EACH study ("low" or "high" is fine, as long as it is clear which studies scored "low" and which*	X Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)

scored "high"; a summary score/range for all studies is not acceptable).	
8) Was the scientific quality of the included studies used appropriately in formulating conclusions? The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. *Note: Might say something such as "the results should be interpreted with caution due to poor quality of included studies." Cannot score "yes" for this question if scored "no" for question 7.*	X Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
9) Were the methods used to combine the findings of studies appropriate? For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, I2). If heterogeneity exists, a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). *Note: Indicate "yes" if they mention or describe heterogeneity, i.e., if they explain that they cannot pool because of heterogeneity/variability between interventions.*	☐ Yes (1) ☐ No (0) ☐ Can't answer (0) X Not applicable (0)
10) Was the likelihood of publication bias assessed? An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test). *Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.*	☐ Yes (1) X No (0) ☐ Can't answer (0) ☐ Not applicable (0)
11) Was the conflict of interest included? Potential sources of support should be clearly acknowledged in both the systematic review and the included studies. *Note: To get a "yes," must indicate source of funding or support for the systematic review AND for each of the included studies.*	X Yes (1) ☐ No (0) ☐ Can't answer (0) ☐ Not applicable (0)
12) Total score	9

*Shea *et al. BMC Medical Research Methodology* 2007 **7**:10 doi:10.1186/1471-2288-7-10

Additional notes (in italics) made by Michelle Weir, Julia Worswick, and Carolyn Wayne based on conversations with Bev Shea and/or Jeremy Grimshaw in June and October 2008 and July and September 2010. (http://amstar.ca/docs/AMSTARguideline.pdf)

Appendix 4 Search terms per database

Pubmed (July 22, 2013 / January 13, 2015 / October 6, 2015)

Search strategy

((((((((((((((((((((Hospitals [Mesh]) OR Inpatients [Mesh]) OR Critical Care [Mesh]) OR Perioperative Care [Mesh]) OR Preoperative Care [Mesh]) OR hospital [tiab]) OR hospitals [tiab]) OR hospitalised [tiab]) OR hospitalized [tiab]) OR inpatient*[tiab]) OR critical care [tiab]) OR intensive care [tiab]) OR perioperative [tiab]) OR preoperative [tiab]) OR postoperative [tiab]) OR peri-operative [tiab]) OR pre-operative [tiab]) OR post-operative [tiab]))) AND ((Attitude of Health Personnel[mesh]) OR ((((((((((((Patient Safety[mesh]) OR Patient Safety[tiab]) OR Risk Management [Mesh]) OR Risk Management [tiab]) OR Equipment Safety [Mesh]) OR Equipment Safety [tiab]) OR Harm Reduction [Mesh]) OR harm reduc*[tiab]) OR Safety Management[mesh]) OR Safety Management[tiab]) OR (((prevention and control [Subheading])))) OR prevent*[tiab]) OR safe*[tiab])) OR ((((((((((((((((((((((((((((((((((((Hand Hygiene [Mesh]) OR Hospital Rapid Response Team [Mesh]) OR Hand Hygiene [tiab]) OR Rapid Response Team [tiab]) OR Medication Reconciliation [Mesh]) OR Medication Reconciliation [tiab]) OR Antibiotic Prophylaxis [Mesh]) OR Prophylaxis [tiab]) OR Infection Control [Mesh]) OR Infection Control [tiab]) OR Checklist[mesh]) OR Checklist[tiab]) OR Automatic Data Processing[mesh]) OR Automatic Data Processing[tiab]) OR Pain management[mesh]) OR Pain management[tiab]) OR Leadership[mesh]) OR Leadership[tiab]) OR Patient handoff[mesh]) OR Patient handoff[tiab]) OR Personnel staffing[Mesh term]) OR staff*[tiab]) OR Hospital nursing staff[mesh]) OR Hospital medical staff[mesh]) OR Nurse-Patient Ratio[tiab]) OR Education[mesh]) OR Education[tiab]) OR Patient simulation[mesh]) OR simulation[tiab]) OR Safety rounds[tiab]) OR fall prevent*[tiab]) OR pressure ulcer prevent*[tiab]) OR organizational culture[Mesh]) OR organizational culture[tiab]) OR safety culture[tiab]) OR Team training[tiab]) OR Case management [mesh]) OR Case management [tiab]) OR Continuity of Patient Care [mesh]) OR Quality indicators[mesh]) OR indicators[tiab]) OR Patient Participation[mesh]) OR Patient Participation[tiab])))) AND ((((((((((((((((mortality[mesh]) OR mortality[tiab]) OR adverse effects [Subheading]) OR adverse effect* [tiab]) OR Medical Errors [Mesh]) OR adverse event*[tiab]) OR harm*[tiab]) OR incident*[tiab]) OR Iatrogenic Disease[mesh]) OR complications [Subheading]) OR complication*[tiab]) OR adverse drug event*[tiab]) OR diagnostic err*[tiab]) OR medical err*[tiab]) OR medication err*[tiab]) OR surgical err*[tiab]))) AND (((((((((systematic review [ti]) OR meta-analysis [pt]) OR meta-analysis [ti]) OR systematic literature review [ti]) OR ((review [pt]) AND systematic review [tiab])) OR cochrane database syst rev[ta]) OR metaanal*[tiab]) OR meta-anal*[tiab]))

Hits: 3810 / 1146

CINAHL (July 22, 2013 / January 13, 2015/ October 6, 2015)

Search strategy

S116	S20 AND S102 AND S114 AND S115
S115	S31 OR S71
S114	S103 OR S104 OR S105 OR S106 OR S107 OR S108 OR S109 OR S110 OR S111 OR S112 OR S113
S113	AB systematic review* AND PT review

S112	PT meta analysis
S111	PT systematic review
S110	AB systematic literature review
S109	AB systematic review*
S108	AB Meta-anal*
S107	AB Meta Analysis
S106	(MH "Cochrane Library")
S105	(MH "Meta Analysis")
S104	(MH "Literature Review+")
S103	(MH "Systematic Review")
S102	S73 OR S74 OR S75 OR S76 OR S77 OR S78 OR S79 OR S80 OR S81 OR S82 OR S83 OR S84 OR S85 OR S86 OR S87 OR S88 OR S89 OR S90 OR S91 OR S92 OR S93 OR S94 OR S95 OR S96 OR S97 OR S98 OR S99 OR S100 OR S101
S101	(MH "Postoperative Complications+")
S100	(MH "Intraoperative Complications+")
S99	(MH "Catheter-Related Complications+")
S98	(MH "Blood Transfusion Reaction+")
S97	AB surgical error*
S96	(MH "Wrong Site Surgery")
S95	(MH "Fatal Outcome")
S94	(MH "Treatment Failure")
S93	(MH "Treatment Delay")
S92	AB Medication Error*
S91	(MH "Medication Errors+")
S90	AB Treatment Error*
S89	(MH "Treatment Errors+")
S88	AB Diagnostic Error*
S87	(MH "Diagnostic Errors+")
S86	(MH "Inappropriate Prescribing")
S85	(MH "Sentinel Event")
S84	(MH "Health Care Errors+")
S83	(MH "Iatrogenic Disease")

S82	AB complication*
S81	AB Incident*
S80	AB medical error*
S79	AB adverse event*
S78	AB Adverse Health Care Event*
S77	(MH "Adverse Health Care Event+")
S76	AB Adverse Drug Event*
S75	(MH "Adverse Drug Event+")
S74	AB Mortality
S73	(MH "Mortality+")
S72	S31 OR S71
S71	S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55 OR S56 OR S57 OR S58 OR S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70
S70	(MH "Employee attitudes")
S69	AB patient participation
S68	(MH "Surgical Site Verification")
S67	(MH "Computerized Patient Record")
S66	(MH "Consumer Participation")
S65	AB quality indicator*
S64	(MH "Clinical Indicators")
S63	AB Case Management
S62	(MH "Case Management")
S61	AB team training
S60	(MH "Multidisciplinary Care Team+")
S59	(MH "Communication Skills Training")
S58	AB safety culture
S57	AB Organi* Culture
S56	(MH "Organizational Culture+")
S55	AB Safety round*
S54	AB Simulation*

S53	(MH "Simulations+")
S52	AB Education
S51	(MH "Education+")
S50	AB staffing
S49	(MH "Nurse-Patient Ratio")
S48	(MH "Personnel Staffing and Scheduling+")
S47	AB Handover
S46	(MH "Continuity of Patient Care+")
S45	(MH "SBAR Technique")
S44	(MH "Hand Off (Patient Safety)+")
S43	AB Leadership*
S42	(MH "Leadership")
S41	AB Checklist*
S40	(MH "Checklists")
S39	AB Prophylaxis
S38	(MH "Antibiotic Prophylaxis")
S37	AB Medication Reconciliation*
S36	(MH "Medication Reconciliation")
S35	AB Rapid Response Team*
S34	AB Hand washing
S33	AB infection control*
S32	(MH "Infection Control+")
S31	S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30
S30	AB safe*
S29	AB Prevent*
S28	AB Safety Management
S27	AB harm reduc*
S26	(MH "Harm Reduction")
S25	(MH "Equipment Safety")
S24	AB Risk Management
S23	(MH "Risk Management+")

S22 AB Patient Safety

S21 (MH "Patient Safety+")

S20 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19

S19 AB postoperative care

S18 AB preoperative care

S17 AB perioperative care

S16 AB intensive care

S15 AB critical care

S14 (MH "Postoperative Period")

S13 (MH "Preoperative Period+")

S12 (MH "Preoperative Care+")

S11 (MH "Postoperative Care+")

S10 (MH "Intraoperative Care+")

S9 (MH "Perioperative Care+")

S8 (MH "Intensive Care, Neonatal+")

S7 (MH "Critical Care+")

S6 AB Inpatients*

S5 (MH "Inpatients")

S4 AB hospital*

S3 (MH "Intensive Care Units+")

S2 (MH "Hospital Units+")

S1 (MH "Hospitals+")

Hits: 1074 / 222

Embase (July 22, 2013 / January 13, 2015/ October 6, 2015)

Search strategy

#92 #18 and #63 and #81 and #91

#91 #82 or #83 or #86 or #87 or #90

#90 #88 and #89

#89 #84 or #85

#88 "systematic*".ti,ab.

#87 "meta-anal*".ti,ab.

#86	"meta anal*".ti,ab.
#85	"review"/
#84	exp literature/
#83	meta analysis/
#82	exp "systematic review"/
#81	#64 or #65 or #66 or #67 or #68 or #69 or #70 or #71 or #72 or #73 or #74 or #75 or #76 or #77 or #78 or #79 or #80
#80	"surgical err*".ti,ab.
#79	"medication error*".ti,ab.
#78	"medical err*".ti,ab.
#77	"diagnostic err*".ti,ab.
#76	"medical error*".ti,ab.
#75	"adverse drug event*".ti,ab.
#74	"root complication*".ti,ab.
#73	"root incident*".ti,ab.
#72	"harm*".ti,ab.
#71	"adverse event*".ti,ab.
#70	"adverse effect*".ti,ab.
#69	mortality.ti,ab.
#68	exp complication/
#67	exp iatrogenic disease/
#66	exp medical error/
#65	exp adverse drug reaction/
#64	exp mortality/
#63	19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62
#62	"staff*".ti,ab.
#61	organi?ational culture.ti,ab.
#60	indicators.ti,ab.
#59	patient participation.ti,ab.
#58	case management.ti,ab.
#57	team training.ti,ab.
#56	safety culture.ti,ab.
#55	"fall prevent*".ti,ab.
#54	safety rounds.ti,ab.
#53	patient handoff.ti,ab.

#52	leadership.ti,ab.
#51	pain management.ti,ab.
#50	checklist.ti,ab.
#49	infection control.ti,ab.
#48	prophylaxis.ti,ab.
#47	rapid response team.ti,ab.
#46	hand hygiene.ti,ab.
#45	exp patient participation/
#44	exp case management/
#43	exp teaching/
#42	exp education/
#41	exp nurse patient ratio/
#40	exp medical staff/
#39	exp nursing staff/
#38	exp clinical handover/
#37	exp leadership/
#36	exp checklist/
#35	exp infection control/
#34	exp antibiotic prophylaxis/
#33	exp medication therapy management/
#32	exp rapid response team/
#31	exp hand washing/
#30	exp prevention/
#29	"safe*".ti,ab.
#28	"prevent*".ti,ab.
#27	safety management.ti,ab.
#26	"harm reduc*".ti,ab.
#25	equipment safety.ti,ab.
#24	device safety.ti,ab.
#23	risk management.ti,ab.
#22	exp harm reduction/
#21	exp device safety/
#20	exp risk management/
#19	exp patient safety/
#18	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17

#17 post-operative.ti,ab.
#16 pre-operative.ti,ab.
#15 peri-operative.ti,ab.
#14 postoperative.ti,ab.
#13 preoperative.ti,ab.
#12 perioperative.ti,ab.
#11 intensive care.ti,ab.
#10 critical care.ti,ab.
#9 "inpatient*".ti,ab.
#8 hospitali?ed.ti,ab.
#7 hospitals.ti,ab.
#6 hospital.ti,ab.
#5 exp preoperative care/
#4 exp perioperative period/
#3 exp intensive care/
#2 exp hospital patient/
#1 exp hospital/
Hits: 5694 / 838

Cochrane library (July 22, 2013 / January 13, 2015/ October 6, 2015)

Search strategy
#1 MeSH descriptor: [Hospitals] explode all trees
#2 MeSH descriptor: [Inpatients] explode all trees
#3 MeSH descriptor: [Critical Care] explode all trees
#4 MeSH descriptor: [Perioperative Care] explode all trees
#5 MeSH descriptor: [Preoperative Care] explode all trees
#6 hospital:ti,ab,kw (Word variations have been searched)
#7 critical care:ti,ab,kw (Word variations have been searched)
#8 inpatient:ti,ab,kw (Word variations have been searched)
#9 Preoperative Care:ti,ab,kw (Word variations have been searched)
#10 Perioperative Care:ti,ab,kw (Word variations have been searched)
#11 Postoperative Care:ti,ab,kw (Word variations have been searched)
#12 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #8 or #9 or #10 or #11
#13 MeSH descriptor: [Patient Safety] explode all trees
#14 patient safety:ti,ab,kw (Word variations have been searched)
#15 MeSH descriptor: [Risk Management] explode all trees
#16 risk management:ti,ab,kw (Word variations have been searched)
#17 MeSH descriptor: [Equipment Safety] explode all trees
#18 equipment safety:ti,ab,kw (Word variations have been searched)
#19 MeSH descriptor: [Harm Reduction] explode all trees
#20 harm reduc*:ti,ab,kw (Word variations have been searched)
#21 MeSH descriptor: [Safety Management] explode all trees

#22	safety management:ti,ab,kw (Word variations have been searched)
#23	prevent*:ti,ab,kw (Word variations have been searched)
#24	safe*:ti,ab,kw (Word variations have been searched)
#25	#13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24
#26	MeSH descriptor: [Infection Control] explode all trees
#27	infection control:ti,ab,kw (Word variations have been searched)
#28	MeSH descriptor: [Hand Hygiene] explode all trees
#29	hand hygiene:ti,ab,kw (Word variations have been searched)
#30	MeSH descriptor: [Hospital Rapid Response Team] explode all trees
#31	Rapid Response Team:ti,ab,kw (Word variations have been searched)
#32	MeSH descriptor: [Medication Reconciliation] explode all trees
#33	Medication Reconciliation:ti,ab,kw (Word variations have been searched)
#34	MeSH descriptor: [Antibiotic Prophylaxis] explode all trees
#35	Prophylaxis:ti,ab,kw (Word variations have been searched)
#36	MeSH descriptor: [Checklist] explode all trees
#37	checklist*:ti,ab,kw (Word variations have been searched)
#38	MeSH descriptor: [Automatic Data Processing] explode all trees
#39	MeSH descriptor: [Pain Management] explode all trees
#40	Pain management:ti,ab,kw (Word variations have been searched)
#41	MeSH descriptor: [Leadership] explode all trees
#42	Leadership:ti,ab,kw (Word variations have been searched)
#43	MeSH descriptor: [Patient Handoff] explode all trees
#44	handoff:ti,ab,kw (Word variations have been searched)
#45	handover:ti,ab,kw (Word variations have been searched)
#46	MeSH descriptor: [Continuity of Patient Care] explode all trees
#47	MeSH descriptor: [Personnel Staffing and Scheduling] explode all trees
#48	staff*:ti,ab,kw (Word variations have been searched)
#49	MeSH descriptor: [Nursing Staff, Hospital] explode all trees
#50	MeSH descriptor: [Medical Staff, Hospital] explode all trees
#51	MeSH descriptor: [Education] explode all trees
#52	education:ti,ab,kw (Word variations have been searched)
#53	MeSH descriptor: [Patient Simulation] explode all trees
#54	simulation:ti,ab,kw (Word variations have been searched)
#55	Safety round*:ti,ab,kw (Word variations have been searched)
#56	fall prevention:ti,ab,kw (Word variations have been searched)
#57	pressure ulcer prevention:ti,ab,kw (Word variations have been searched)
#58	MeSH descriptor: [Organizational Culture] explode all trees
#59	organizational culture:ti,ab,kw (Word variations have been searched)
#60	safety culture:ti,ab,kw (Word variations have been searched)
#61	Team training:ti,ab,kw (Word variations have been searched)
#62	MeSH descriptor: [Case Management] explode all trees
#63	Case management:ti,ab,kw (Word variations have been searched)
#64	MeSH descriptor: [Quality Indicators, Health Care] explode all trees
#65	indicator*:ti,ab,kw (Word variations have been searched)
#66	MeSH descriptor: [Patient Participation] explode all trees
#67	Patient Participation:ti,ab,kw (Word variations have been searched)

#68 #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56 or #57 or #58 or #59 or #60 or #61 or #62 or #63 or #64 or #65 or #66 or #67
#69 #25 or #68
#70 MeSH descriptor: [Mortality] explode all trees
#71 mortality:ti,ab,kw (Word variations have been searched)
#72 adverse effect*:ti,ab,kw (Word variations have been searched)
#73 MeSH descriptor: [Medical Errors] explode all trees
#74 medical error*:ti,ab,kw (Word variations have been searched)
#75 adverse event*:ti,ab,kw (Word variations have been searched)
#76 harm*:ti,ab,kw (Word variations have been searched)
#77 incident*:ti,ab,kw (Word variations have been searched)
#78 MeSH descriptor: [Iatrogenic Disease] explode all trees
#79 complication*:ti,ab,kw (Word variations have been searched)
#80 adverse drug event*:ti,ab,kw (Word variations have been searched)
#81 #70 or #71 or #72 or #73 or #74 or #75 or #76 or #77 or #78 or #79 or #80
#82 systematic review:ti,ab,kw (Word variations have been searched)
#83 systematic literature review:ti,ab,kw (Word variations have been searched)
#84 meta-analysis:pt (Word variations have been searched)
#85 review:pt (Word variations have been searched)
#86 meta-anal*:ti,ab,kw (Word variations have been searched)
#87 #82 and #85
#88 #82 or #83 or #84 or #86 or #87
#89 #12 and #69 and #81 and #88: in Cochrane Reviews (Reviews and Protocols) and Other Reviews
Hits: 359 / 134

PsychINFO (July 22, 2013/ January 13, 2015/ October 6, 2015)

Search strategy

#81 #18 and #58 and #75 and #80
#80 #76 or #77 or #78 or #79
#79 "meta-anal*".ab,ti.
#78 "meta anal*".ab,ti.
#77 exp Meta Analysis/
#76 "literature review"/
#75 #59 or #60 or #61 or #62 or #63 or #64 or #65 or #66 or #67 or #68 or #69 or #70 or #71 or #72 or #73 or #74
#74 "surgical err*".ab,ti.
#73 "medical err*".ab,ti.
#72 "diagnostic err*".ab,ti.
#71 "'adverse drug event*'".ab,ti.
#70 "complication*".ab,ti.
#69 "incident*".ab,ti.

#68	"harm*".ab,ti.
#67	adverse events.ab,ti.
#66	adverse event.ab,ti.
#65	"adverse effect*".ab,ti.
#64	mortality.ab,ti.
#63	exp Postsurgical Complications/
#62	exp "Complications (Disorders)"/
#61	exp Errors/
#60	exp "Side Effects (Drug)"/
#59	exp "Death and Dying"/
#58	#19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56 or #57
#57	" prevent*".ab,ti.
#56	"safe*".ab,ti.
#55	"pressure ulcer prevent*".ab,ti.
#54	'patient participation'.ab,ti.
#53	indicators.ab,ti.
#52	'case management'.ab,ti.
#51	'team training'.ab,ti.
#50	'safety culture'.ab,ti.
#49	'organi?ational culture'.ab,ti.
#48	'safety rounds'.ab,ti.
#47	simulation.ab,ti.
#46	education.ab,ti.
#45	'nurse-patient ratio'.ab,ti.
#44	"staff*".ab,ti.
#43	'patient handoff'.ab,ti.
#42	leadership.ab,ti.
#41	'pain management'.ab,ti.
#40	checklist.ab,ti.
#39	'infection control'.ab,ti.
#38	prophylaxis.ab,ti.
#37	'medication reconciliation'.ab,ti.
#36	'rapid response team'.ab,ti.
#35	'hand hygiene'.ab,ti.

#34	exp "Continuum of Care"/
#33	exp Client Participation/
#32	exp Employee Attitudes/
#31	exp Organizational Climate/
#30	exp Simulation/
#29	exp Education/
#28	exp Medical Personnel/
#27	exp Leadership/
#26	exp Pain Management/
#25	exp Drug Therapy/
#24	exp Emergency Services/
#23	exp Hygiene/
#22	exp Harm Reduction/
#21	exp Safety Devices/
#20	exp Risk Management/
#19	exp Safety/
#18	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17
#17	post-operative.ab,ti.
#16	pre-operative.ab,ti.
#15	peri-operative.ab,ti.
#14	postoperative.ab,ti.
#13	preoperative.ab,ti.
#12	perioperative.ab,ti.
#11	'intensive care'.ab,ti.
#10	'critical care'.ab,ti.
#9	"inpatient*".ab,ti.
#8	hospitalized.ab,ti.
#7	hospitalised.ab,ti.
#6	hospitals.ab,ti.
#5	hospital.ab,ti.
#4	exp Surgery/
#3	exp Intensive Care/
#2	exp Hospitalized Patients/
#1	exp Hospitals/

Hits: 95 / 30

Appendix 5 Excluded systematic reviews after full text selection (n=136)			
Year	**Authors**	**Title**	**Reason for exclusion**
1997		Collaborative systematic review of the randomised trials of organised inpatient (stroke unit) care after stroke. Stroke Unit Trialists' Collaboration	Intervention is focused on one patient group
1997	Griffith et al.	Internal medicine residency training and outcomes	No adverse patient outcomes reported No patient safety intervention
1998	Saint	Risk reduction in the intensive care unit	Pharmacological studies No patient safety intervention
1999	Meagher	Colorectal cancer: is the surgeon a prognostic factor? A systematic review	Intervention is focused on one patient group
2001	Gillespie et al.	Interventions for preventing falls in elderly people	Updated by another included review
2001	Ioannidis	Evidence on interventions to reduce medical errors: an overview and recommendations for future research	No adverse patient outcomes reported
2001	Rawal	Treating postoperative pain improves outcome	Pharmacological studies
2001	Shojania et al.	Making health care safer: a critical analysis of patient safety practices	Overall review (used for snowballing)
2002	Berenholtz et al.	Qualitative review of intensive care unit quality indicators	No quantitative ouctomes
2002	Harkness	Review: specialised multidisciplinary follow up reduces hospital admissions but not mortality in patients with heart failure	No systematic review
2002	Iregui et al.	Nonpharmacological prevention of hospital-acquired pneumonia	No systematic review
2002	Kehlet	Multimodal strategies to improve surgical outcome	No adverse patient ouctomes reported
2003	Gandjour et al.	Threshold volumes associated with higher survival in health care: a systematic review	No intervention studies included; only observational studies
2003	Kaushal et al.	Effects of computerized physician order entry and clinical decision support systems on medication safety: a systematic review (Structured abstract)	Updated by another included review
2003	McDonnell et al.	Acute pain teams and the management of postoperative pain: a systematic review and meta-analysis	No intervention studies included; only observational studies
2003	Patel et al.	New treatment strategies for severe sepsis and septic shock	No systematic review
2004	Dodek et al.	Evidence-based clinical practice guideline for the prevention of ventilator-associated pneumonia	No adverse patient outcomes reported
2004	Gastmeier	Nosocomial infection surveillance and control policies	No systematic review
2004	Kalant	Volume and outcome of coronary artery bypass graft surgery: are more and less the same?	Intervention is focused on one patient group
2004	Lang et al.	Nurse-patient ratios: a systematic review on the effects of nurse staffing on patient, nurse employee, and hospital outcomes	No quantitative outcomes
2004	Phillips et al.	Comprehensive discharge planning with postdischarge support for older patients with congestive heart failure: a meta-analysis	Intervention is focused on one patient group
2004	Picheansathian	A systematic review on the effectiveness of alcohol-based solutions for hand hygiene	Pharmacological studies
2004	Rideout	Review: comprehensive discharge planning plus post-discharge support reduced total readmissions in older patients with congestive heart failure	No systematic review
2004	Shepperd et al.	Discharge planning from hospital to home	Updated by another included review
2005	Davoli et al.	[Volume and health outcomes: an overview of systematic reviews]	Not in English
2005	Lee	A systematic review for effective management of central venous catheters and catheter sites in acute care paediatric patients	No patient safety intervention
2006	Aneman	Medical emergency teams: a role for expanding intensive care?	Updated by another included review
2006	Gastmeier	Prevention of catheter-related bloodstream infections: analysis of studies published between 2002 and 2005	No patient safety intervention
2006	Lawrence et al.	Clinical guidelines. Strategies to reduce postoperative pulmonary complications after noncardiothoracic surgery: systematic review for the American College of Physicians	Duplicate record
2006	Lawrence et al.	Strategies to reduce postoperative pulmonary complications after noncardiothoracic surgery: systematic review for the American College of Physicians	No patient safety intervention
2006	Numata et al.	Nurse staffing levels and hospital mortality in critical care settings: literature review and meta-analysis	No intervention studies included; only observational studies
2006	Pearson et al.	Systematic review of evidence on the impact of nursing workload and staffing on establishing healthy work environments	No intervention studies included; only observational studies
2006	Rabie	Handwashing and risk of respiratory infections: a quantitative systematic review	No hospital setting
2006	Sanghera et al.	Interventions of hospital pharmacists in improving drug therapy in children: a systematic literature review	No quantitative outcomes
2006	Washer	Infection control strategies for methicillin-resistant staphylococcus aureus and vancomycin-resistant enterococcus: What is the evidence?	No intervention studies included; only observational studies
2007	Aboelela et al.	Effectiveness of bundled behavioural interventions to control healthcare-associated infections: a systematic review of the literature	No intervention studies included; only observational studies
2007	Burgers et al.	[Relationship between volume and quality of care for surgical interventions; results of a literature review]	No intervention studies included; only observational studies Not in English
2007	Chowdhury et al.	A systematic review of the impact of volume of surgery and specialization on patient outcome	No intervention studies included; only observational studies
2007	Foley et al.	Specialized stroke services: a meta-analysis comparing three models of care	Intervention is focused on one patient group No patient safety intervention
2007	Gastmeier	Evidence-based infection control in the ICU (except catheters)	No patient safety intervention

2007	Gastmeier	Prevention of ventilator-associated pneumonia: analysis of studies published since 2004	No patient safety intervention
2007	Kane et al.	The association of registered nurse staffing levels and patient outcomes: Systematic review and meta-analysis	No intervention studies included; only observational studies
2007	Kane et al.	Nurse staffing and quality of patient care	No intervention studies included; only observational studies
2007	McGaughey et al.	Outreach and Early Warning Systems (EWS) for the prevention of Intensive Care admission and death of critically ill adult patients on general hospital wards	Updated by another included review
2007	Pedrosa et al.	Effects of educational programs in post-operative pain [Portuguese]	Not in English
2007	Siddiqi	Interventions for preventing delirium in hospitalised patients (Review)	Updated by another included review
2007	Whitehorn	A review of the use of insulin protocols to maintain normoglycaemia in high dependency patients	No systematic review
2007	Winters et al.	Rapid response systems: a systematic review	Updated by another included review
2007	Wong	The relationship between nursing leadership and patient outcomes: a systematic review (Structured abstract)	No adverse patient ouctomes reported
2008	Allen	How has the impact of 'care pathway technologies' on service integration in stroke care been measured and what is the strength of the evidence to support their effectiveness in this respect?	Intervention is focused on one patient group
2008	Crowe et al.	Systematic review of the effectiveness of nursing interventions in reducing or relieving post-operative pain	Pharmacological studies
2008	Eslami et al.	The impact of computerized physician medication order entry in hospitalized patients--a systematic review	No quantitative ouctomes
2008	Shamliyan et al.	Just what the doctor ordered. Review of the evidence of the impact of computerized physician order entry system on medication errors	No intervention studies included; only observational studies
2008	Yamada et al.	A review of systematic reviews on pain interventions in hospitalized infants	Pharmacological studies and clinical interventions
2009	Arora et al.	Hospitalist handoffs: a systematic review and task force recommendations	No adverse patient outcomes reported
2009	Cohen et al.	Effect of clinical pharmacists on care in the emergency department: a systematic review	No adverse patient outcomes reported
2009	Cozart	Falls aren't us: state of the science	No adverse patient outcomes reported
2009	Dückers et al.	Safety and risk management interventions in hospitals: a systematic review of the literature	Overall review (used for snowballing)
2009	Endacott et al.	An integrative review and meta-synthesis of the scope and impact of intensive care liaison and outreach services	Updated by another included review
2009	Fung-Kee-Fung et al.	Regional collaborations as a tool for quality improvements in surgery: a systematic review of the literature	No quantitative outcomes
2009	Grinstein-Cohen et al.	Improvements and difficulties in postoperative pain management	No adverse patient outcomes reported
2009	Gruen et al.	The effect of provider case volume on cancer mortality: systematic review and meta-analysis	No intervention studies included; only observational studies
2009	Helfand	Assessment and management of acute pain in adult medical inpatients: A systematic review	No adverse patient outcomes reported
2009	Kaur et al.	Interventions that can reduce inappropriate prescribing in the elderly: a systematic review	No adverse patient outcomes reported
2009	Marwick	Care bundles: The holy grail of infectious risk management in hospital?	No systematic review
2009	Reckmann et al.	Does computerized provider order entry reduce prescribing errors for hospital inpatients? A systematic review	No adverse patient ouctomes reported No systematic review
2009	Stern	Interventions to reduce the incidence of falls in older adult patients in acute-care hospitals: a systematic review	Updated by another included review
2009	van Rosse et al.	The effect of computerized physician order entry on medication prescription errors and clinical outcome in pediatric and intensive care: A systematic review	No intervention studies included; only observational studies
2009	West et al.	Nursing resources and patient outcomes in intensive care: a systematic review of the literature	No intervention studies included; only observational studies
2009	Zilberberg et al.	Implementing quality improvements in the intensive care unit: ventilator bundle as an example	No intervention studies included; only observational studies
2010		Nursing staff and patient results: systematic review about the existing relationship [Spanish]	Not in English
2010	Archampong et al.	Impact of surgeon volume on outcomes of rectal cancer surgery: a systematic review and meta-analysis	No intervention studies included; only observational studies
2010	Barocas et al.	Impact of surgeon and hospital volume on outcomes of radical prostatectomy	No intervention studies included; only observational studies
2010	Cameron et al.	Interventions for preventing falls in older people in nursing care facilities and hospitals	Updated by another included review
2010	Chen et al.	Do multi-component hospital-based programs prevent delirium? A systematic review	No full text available
2010	Fanara et al.	Recommendations for the intra-hospital transport of critically ill patients	Designs
2010	Giakoumidakis et al.	The association between the nursing workload and patient mortality [Greek]	Not in English
2010	Hall et al.	Effectiveness of interventions designed to promote patient involvement to enhance safety: a systematic review	No quantitative ouctomes
2010	Karthikesalinga	Volume-outcome relationships in vascular surgery: the current status	No intervention studies included; only

	m et al.		observational studies
2010	Meddings et al.	Systematic review and meta-analysis: reminder systems to reduce catheter-associated urinary tract infections and urinary catheter use in hospitalized patients	Updated by another included review
2010	Muir	A systematic review of the effect of medication reconciliation on medication discrepancies and adverse drug events	No full text available
2010	Rabol et al.	Outcomes of classroom-based team training interventions for multiprofessional hospital staff. A systematic review	No intervention studies included; only observational studies
2010	Seehusen	Clinical pathways: Effects on practice, outcomes, and costs	No systematic review
2010	Subirana Casacuberta et al.	[Nursing staff and patient results: systematic review about the existing relationship]	Not in English
2010	Suri et al.	Post discharge management programs for elderly heart failure patients: A systematic review and meta-analysis of randomized clinical trials	No full text available
2010	Wong et al.	A systematic review of medication safety outcomes related to drug interaction software	No hospital setting
2011	Abbenbroek et al.	Intensive care unit volume - Outcome relationship: Is bigger better?	No full text available
2011	Anderson et al.	Interventions designed to prevent healthcare bed-related injuries in patients	Updated by another included review
2011	Bakker et al.	Perioperative cardiac evaluation, monitoring, and risk reduction strategies in noncardiac surgery patients	No systematic review
2011	Bapoje et al.	Effectiveness of rapid response call criteria: A systematic review and meta-analysis	No full text available
2011	Camp	Efficacy of medication reconciliation in the prevention of adverse events [Spanish]	Not in English
2011	Evans	The effect of surgical training and hospital characteristics on patient outcomes after pediatric surgery: a systematic review	Intervention is focused on one patient group
2011	Fletcher et al.	Patient safety, resident education and resident well-being following implementation of the 2003 ACGME duty hour rules	No intervention studies included; only observational studies
2011	Fry	Literature review of the impact of nurse practitioners in critical care services	No quantitative outcomes
2011	Gomes da et al.	Influence of dimensioning the nursing staff on the quality of care of the critical patient [Portuguese]	Not in English
2011	Hansen et al.	Interventions to reduce 30-day rehospitalization: a systematic review	No patient harm reported
2011	Kaki et al.	Impact of antimicrobial stewardship in critical care: a systematic review	No intervention studies included; only observational studies
2011	Ketelaar et al.	Public release of performance data in changing the behaviour of healthcare consumers, professionals or organisations	No adverse patient outcomes reported Intervention is focused on one patient group
2011	Nikolaidou et al.	Nursing management of postoperative pain in children after cardiac surgery	No full text available
2011	Reddy	Pressure ulcers	Clinical interventions (no specific patient safety interventions)
2011	Rubulotta	Rapid response systems: A re-analysis basedonfrequencyof rrs calls and discovery of methodological issues	No full text available
2011	Wilson	The effect of nurse staffing on clinical outcomes of children in hospital: a systematic review	No intervention studies included; only observational studies
2011	Wulff	Medication administration technologies and patient safety: a mixed-method systematic review	No quantitative outcomes
2012	Anderson et al.	Interventions designed to prevent healthcare bed-related injuries in patients	Updated by another included review
2012	Alsulami et al.	Double checking the administration of medicines: what is the evidence? A systematic review	No adverse patient outcomes reported
2012	Alsulami et al.	A systematic review of the effectiveness of double checking in preventing medication errors	No full text available
2012	de Cordova et al.	Twenty-four/seven: a mixed-method systematic review of the off-shift literature	No intervention studies included; only observational studies
2012	DiBardino et al.	Meta-analysis: multidisciplinary fall prevention strategies in the acute care inpatient population	Updated by another included review
2012	Greig	A review of nosocomial norovirus outbreaks: Infection control interventions found effective	No intervention studies included; only observational studies
2012	Harden	What is best practice to prevent wrong-site surgery?	No full text available
2012	Joram et al.	Healthcare-associated infection prevention in pediatric intensive care units: a review	No systematic review
2012	Kadda et al.	The role of nursing education after a cardiac event	Intervention is focused on one patient group
2012	Kul et al., M.	Effects of care pathways on the in-hospital treatment of heart failure: a systematic review	Intervention is focused on one patient group
2012	Laugaland et al.	Interventions to improve patient safety in transitional care - a review of the evidence	No quantitative outcomes
2012	McGahan et al.	Nurse staffing levels and the incidence of mortality and morbidity in the adult intensive care unit: A literature review	No intervention studies included; only observational studies
2012	Popp	Prevention and treatment options for postoperative delirium in the elderly	No systematic review
2012	Rennke et al.	Interventions to prevent adverse events and readmissions after hospital discharge: A systematic review	No full text available
2012	Rotter et al.	The effects of clinical pathways on professional practice, patient outcomes,	No quantitative outcomes

		length of stay, and hospital costs: Cochrane systematic review and meta-analysis	
2012	Snyder et al.	Effectiveness of barcoding for reducing patient specimen and laboratory testing identification errors: a Laboratory Medicine Best Practices systematic review and meta-analysis	No adverse patient outcomes reported
2013	Aya et al.	Goal-directed therapy in cardiac surgery: a systematic review and meta-analysis	Intervention is focused on one patient group
2013	Benbassat	The effect of clinical interventions on hospital readmissions: a meta-review of published meta-analyses	No patient harm reported
2013	Georgiou et al.	The effect of computerized provider order entry systems on clinical care and work processes in emergency departments: A systematic review of the quantitative literature	No adverse patient outcomes reported
2013	Graabaek	Medication Reviews by Clinical Pharmacists at Hospitals Lead to Improved Patient Outcomes: A Systematic Review	No patient harm reported Mortality data, but no quantitative ouctomes.
2013	Groves	The Relationship Between Safety Culture and Patient Outcomes: Results From Pilot Meta-Analyses	No quantitative outcomes
2013	Holly et al.	Evidence-Based Practices for the Identification, Screening, and Prevention of Acute Delirium in the Hospitalized Elderly: An Overview of Systematic Reviews	No systematic review
2013	Johansson et al.	Effectiveness of non-cardiac preoperative testing in non-cardiac elective surgery: a systematic review	Intervention is focused on one patient group No patient safety intervention
2013	Kwan et al.	Medication reconciliation during transitions of care as a patient safety strategy: a systematic review	Updated by another included review No adverse patient outcomes reported
2013	Li et al.	Oral topical decontamination for preventing ventilator-associated pneumonia: a systematic review and meta-analysis of randomized controlled trials	Intervention is focused on one patient group
2013	Majka et al.	Care Coordination to Enhance Management of Long-Term Enteral Tube Feeding: A Systematic Review and Meta-Analysis	Intervention is focused on one patient group
2013	Ojeleye et al.	The evidence for the effectiveness of safety alerts in electronic patient medication record systems at the point of pharmacy order entry: a systematic review	No adverse patient outcomes reported
2013	Omidvari et al.	Nutritional screening for improving professional practice for patient outcomes in hospital and primary care settings	No quantitative outcomes
2013	Radley et al.	Reduction in medication errors in hospitals due to adoption of computerized provider order entry systems	No adverse patient outcomes reported
2013	Shekelle	Nurse-patient ratios as a patient safety strategy: a systematic review	No intervention studies included; only observational studies
2013	Spinewine et al.	Approaches for improving continuity of care in medication management: a systematic review	No quantitative outcomes
2013	Winters et al.	Rapid-response systems as a patient safety strategy: a systematic review	Updated by another included review No intervention studies included; only observational studies
2013	Wong et al.	The relationship between nursing leadership and patient outcomes: a systematic review update	No intervention studies included; only observational studies

Appendix 6 **Quality assessment: AMSTAR score of included Systematic Reviews* (n=60)**

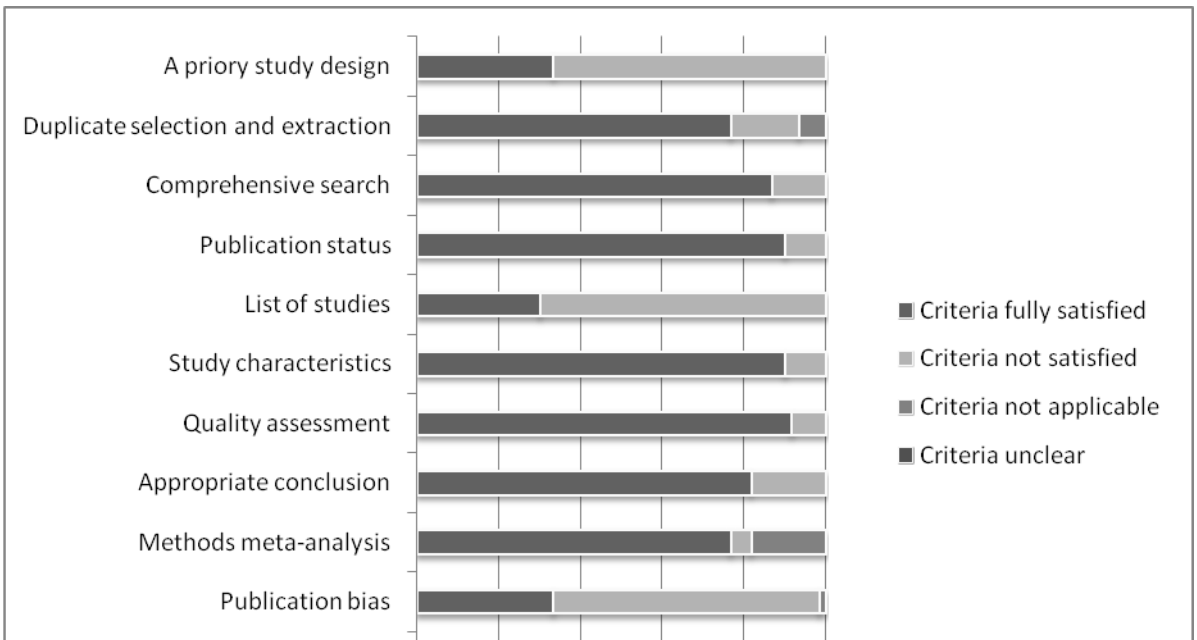
AMSTAR-item	1: priori design provided	2: duplicate study selection and extraction	3: comprehensive literature search performed	4: status publication (grey literature) used as inclusion criteria	5:List of studies (included and excluded) provided	6: characteristics of the included studies provided	7: scientific quality of the included studies assessed and documented	8: scientific quality of the included studies used appropriately in formulating conclusions	9: methods used to combine the findings of studies were appropriate	10: likelihood of publication bias was assessed	11: conflict of interest was included	Total score**
Algie et al., 2015 (67)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9
Bayoumi et al.,2014 (30)	No	No	No	No	No	Yes	Yes	Yes	Yes	No	No	4
Bergs et al., 2014 (66)	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	No	6
Blot et al., 2014 (39)	No	CA	No	Yes	No	No	Yes	Yes	Yes	Yes	No	5
Butler et al., 2011 (75)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9
Cameron et al., 2012 (61)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10
Chan et al., 2010 (69)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	8
Chen et al., 2013 (63)	No	Yes	Yes	No	No	Yes	Yes	No	NA	No	No	4
Christensen and Lundh, 2013 (26)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10
Cole et al., 1998 (45)	No	No	Yes	Yes	No	Yes	Yes	Yes	No	No	No	5
Collinsworth et al., 2014 (49)	No	No	Yes	No	No	No	Yes	Yes	Yes	No	No	4
Conroy et al., 2005 (53)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	8
Coussement et al., 2008 (60)	No	CA	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	6
Damiani et al., 2015 (41)	No	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	7
Davey et al., 2013 (33)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9
Durieux et al.,2008 (28)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9
Ensing et al., 2015 (35)	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	No	No	7
Esmonde et al., 2006 (68)	No	Yes	Yes	Yes	No	No	Yes	Yes	NA	No	No	5
Flodgren et al., 2011 (81)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10
Flodgren et al., 2013 (37)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10
Gillaizeau et al., 2013 (29)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10
Gould et al., 2010 (43)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9
Griffiths et al., 2005 (52)	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	No	6
Hempel et al., 2015 (65)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No	No	7
Hempenius et al., 2011 (47)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	8
Hohl et al., 2015 (27)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	8
Holland et al., 2008 (24)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	8
Howell et al., 2014 (64)	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	7
Hshsieh et al., 2015 (50)	No	No	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	6
Jansson et al., 2013 (38)	No	Yes	No	No	No	No	Yes	Yes	NA	No	No	3
Kaboli et al., 2006 (31)	No	Yes	Yes	Yes	No	Yes	No	No	Yes	No	No	5
Kahn et al., 2013 (72)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10
Lau and Haut., 2014 (73)	No	No	No	Yes	No	Yes	Yes	No	NA	No	No	3
Lowthian et al., 2015 (57)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	8
Maaskant et al., 2015 (23)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	No	9
Maharaj et al., 2015 (71)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	8
Manias et al., 2012 (32)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	7

Martinez et al., 2015 (51)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	9
Massey et al., 2010 (70)	No	No	Yes	Yes	No	Yes	Yes	No	NA	No	No	4
Medding et al., 2014 (40)	No	Yes	Yes	Yes	No	Yes	No	No	Yes	No	No	5
Miake-Lye et al., 2013 (62)	No	No	Yes	No	No	Yes	Yes	Yes	NA	No	No	4
Milisen et al., 2005 (46)	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	7
Mueller et al., 2012 (25)	No	Yes	No	Yes	No	Yes	Yes	Yes	Yes	No	No	6
Naylor et al., 2004 (78)	No	Yes	No	Yes	No	Yes	Yes	Yes	Yes	No	No	6
Niven et al., 2014 (54)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	8
Oliver et al., 2007 (59)	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	8
Pannick et al., 2015 (76)	No	Yes	Yes	Yes	No	Yes	No	No	No	No	No	4
Patterson et al., 2014 (34)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10
Reed et al., 2010 (74)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	8
Rennke et al., 2013 (55)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	7
Reston et al., 2013 (48)	No	No	No	No	No	No	Yes	Yes	NA	No	No	3
Rotter et al., 2010 (79)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10
Safdar and Abad, 2008 (44)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	7
Sheppard et al., 2013 (56)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9
Silvestri et al., 2005 (42)	No	CA	No	Yes	No	Yes	No	No	NA	No	No	2
Sullivan and Schoelles, 2013 (77)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	NA	No	No	6
Wang et al., 2015 (36)	No	CA	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	7
Weaver et al., 2013 (80)	No	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	No	6
Wolfstadt et al., 2008 (22)	No	No	Yes	Yes	No	Yes	Yes	Yes	NA	No	No	5
Zhu et al., 2015 (58)	No	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	No	6

*alphabetical order

**Yes = 1; No, Not applicable (NA), Can't Answer (CA) = 0

Appendix 7 **Methodological quality of 60 systematic reviews on patient safety interventions.**



Appendix 8 Characteristics of eligible studies included in the systematic reviews (n=60)

Patient-Safety Area	Study, year (reference)	Time range	No. of studies eligible studies (total included studies (n))	Intervention components eligible to patient safety	Studied in hospital patients	Total no. of participants	Study designs
Prevention of adverse drug events							
CPOE system	Wolfstadt et al., 2008 (22)	Up to 2007	2 (10)	Computerized physician order entry system	Hospital and ICU patients	U	CT = 1; ITS = 1
CPOE system	Maaskant et al., 2015 (23)	Up to 2014	2 (7)	Computerized physician order entry (CPOE)	≥ 18 years	36730	CBA = 1; ITS = 1
Medication reconciliation	Holland et al., 2008 (24)	Up to 2005	22 (32)	Medication review	≥ 60 years	13305	RCT = 22
Medication reconciliation	Mueller et al., 2012 (25)	Up to 2012	5 (26)	Medication reconciliation	Not specified	1819	RCT = 3; non- RCT = 1; CBA = 1
Medication reconciliation	Christensen and Lundh, 2013 (26)	Up to 2011	5 (5)	Medication review	Not specified	1186	RCT = 5
Medication reconciliation	Hohl et al., 2015 (27)	2000-2013	6 (7)	Medication review	≥ 18 years in acute care	1970	RCT = 5; non-RCT = 1
Computer assisted decision support/ alerts	Durieux et al., 2008 (28)	1966 - 2006	10 (23)	Computer-assisted decision support on drug dosage	Patients receiving drug therapy	1210	RCT = 9; non- RCT = 1
Computer assisted decision support/ alerts	Gillaizeau et al., 2013 (29)	1996 - 2013	33 (46)	Computerized advice on drug dosage as a recommendation provided to the healthcare professional	Not specified	30341	RCT = 33
Computer assisted decision support/ alerts	Bayoumi et al., 2014 (30)	1974 - 2013	9 (36)	Computerized drug lab alerts for clinicians on prescribing or monitoring decisions	≥ 18 years	N.R.	RCT = 9
Multi component interventions	Kaboli et al., 2006 (31)	1985 - 2005	13 (36)	Clinical pharmacy activities and responsibilities (patient interview, medication profile and medical record review, presentation of drug regimen, recommendations to care team or physician, participating on rounds with inpatient care team, drug monitoring and recommendation follow-up, drug therapy dosing or management, documentation of clinical interventions or recommendations, patient counseling before discharge and telephone follow-up after discharge)	≥ 18 years	12397	RCT = 7; non- RCT = 1; quasi experimental = 1; CBA = 4
Multi component interventions	Manias et al., 2012 (32)	Up to 2011	10 (24)	Computerized physician order entry; changes in work schedules; intravenous systems; modes of education; medication reconciliation; pharmacist involvement; protocols and guidelines; support systems for clinical decision-making	ICU	U	non- RCT = 2; quasi RCT = 1; CBA = 7

Patient-Safety Area	Study, year (reference)	Time range	No. of studies eligible studies (total included studies (n))	Intervention components eligible to patient safety	Studied in hospital patients	Total no. of participants	Study designs
Multi component interventions	Davey et al., 2013 (33)	1980 - 2009	23 (89)	Persuasive interventions (e.g. distribution of educational materials, local consensus processes, educational outreach visits and local opinion leaders); restrictive interventions (e.g. selective reporting of laboratory susceptibilities, formulary restriction and requiring prior authorization of prescriptions by infectious diseases physicians, microbiologists, pharmacists etc); structural interventions (e.g. changing from paper to computerized records, rapid laboratory testing and computerized decision support systems)	Acute care	U	RCT = 13; CCT = 2; CBA = 3; ITS = 5
Multi component interventions	Patterson et al., 2014 (34)	Up to 2009	3 (10)	Professional interventions (e.g. educational programs aimed at prescribers); organizational interventions (e.g. skill-mix changes, pharmacist-led medication review services or specialist clinics); information and communication technology (ICT) interventions (e.g. clinical decision support systems or use of risk screening tools); financial interventions (e.g. incentive schemes for changes in prescribing practice); regulatory interventions (e.g. government policy or legislative changes affecting prescribing)	≥ 65 years	1152	RCT = 3
Multi component interventions	Ensing et al., 2015 (35)	Up to 2014	19 (30)	Pharmacist interventions (e.g. different categories: admission, patient counseling, medical team, medication review, discharge reconciliation and provision of adherence aids)	≥ 18 years	7829	RCT = 19
Multi component interventions	Wang et al., 2015 (36)	Up to 2014	2 (4)	Pharmacist interventions (e.g. physician rounds, providing physicians with information and advice on ADE, drug interactions and dose intervals)	(Pediatric) ICU	2794	CBA = 2
Infection prevention							
Prevention of device-related infections (CAUTI; CLABSI; VAP)	Flodgren et al., 2013 (37)	Up to 2012	10 (13)	Interventions to avoid the use, or decrease the length of use of invasive medical devices (i.e. urinary catheters, central line catheters, mechanical ventilators), or interventions to improve adoption of measures to prevent device-related infection, such as: professional interventions (distribution of educational materials, educational meetings, local consensus processes, local opinion leaders, audit and feedback and reminders); organizational interventions (revision of professional roles and clinical multidisciplinary teams); financial interventions; regulatory interventions.	Patients with invasive devices	U	ITS = 10
Prevention of device-related infections (CAUTI;	Jansson et al., 2013 (38)	2003 – 2012	2 (8)	Education: continuing education, ongoing education, clinical education, inter-professional education.	Critically ill patients ICU	N.R.	Quasi experimental = 2

Patient-Safety Area	Study, year (reference)	Time range	No. of studies eligible studies (total included studies (n))	Intervention components eligible to patient safety	Studied in hospital patients	Total no. of participants	Study designs
CLABSI; VAP)							
Prevention of device-related infections (CAUTI; CLABSI; VAP)	Blot et al., 2014 (39)	1995 – 2012	8 (43)	Education; training; feedback; clinical reminders; bundle; checklist; empowerment to stop procedure; surveillance; leader designation; prepackaging of CVS materials; infrastructure changes; organizational changes	Patients with central lines, catheters at the ICU	N.R.	CBA = 1; ITS = 7
Prevention of device-related infections (CAUTI; CLABSI; VAP)	Meddings et al., 2014 (40)	2008 – 2012	3 (30)	Education on improving appropriate use in catheter placement and behavior (e.g. catheter restriction and removal protocols); use of specific technologies	Patients with a urinary catheter	U	RCT = 1; non- RCT = 1; CBA =1
Interventions to improve compliance to sepsis bundle interventions	Damiani et al., 2015 (41)	2004-2014	5 (50)	Improving compliance to sepsis bundle interventions, consisting of educational programs (e.g. lectures and training sessions) and decision support tools (e.g. screening tools, checklist or introduction of dedicated staff (e.g. sepsis teams).	≥ 18 years with (severe) sepsis or septic shock	42295	ITS = 5
Interventions to improve hand hygiene compliance	Silvestri et al., 2005 (42)	1976 – 2003	7 (9)	Hand washing	ICU	N.R.	RCT = 2; non- RCT = 5
Interventions to improve hand hygiene compliance	Gould et al., 2010 (43)	Up to 2009	1 (4)	Education; audit with performance feedback; health promotion; and variations in availability and type of products used for hand hygiene.	Not specified	N.R.	ITS = 1
Overall hospital acquired infection prevention	Safdar and Abad, 2008 (44)	Up to 2006	25 (26)	Educational interventions for prevention of healthcare associated infections (lectures or classes, video presentations, posters, questionnaires and fact sheets, practical demonstrations, standardized self-study module, direct feedback and protocols to remove catheters when no longer necessary)	ICU and long-term care	N.R.	RCT = 1; non- RCT = 1; CBA = 23
Delirium prevention							
Delirium prevention	Cole et al., 1998 (45)	Up to 1998	8 (10)	Psychiatric assessment; education of patient and spouse; special (medical, surgical, nursing) care	Cardiac, elderly orthopedic, elderly surgical, elderly medical	N.R.	RCT = 2; non-RCT = 6
Delirium prevention	Milisen et al., 2005 (46)	Up to 2003	7 (7)	Psychiatric assessment; staff education; daily visits by a liaison nurse; screening for early detection of delirium	≥ 60 years	1683	RCT = 3; non-RCT = 3; CBA = 1
Delirium	Hempenius et al.,	1979 – 2009	7 (16)	Non pharmacological interventions to prevention delirium	≥ 18 years	1626	RCT = 1; Non RCT =

Patient-Safety Area	Study, year (reference)	Time range	No. of studies eligible studies (total included studies (n))	Intervention components eligible to patient safety	Studied in hospital patients	Total no. of participants	Study designs
prevention	2011 (47)			(interdisciplinary team; proactive geriatric consultation; education nursing staff; systematic cognitive screening; scheduled pain protocol; supportive psychotherapy)	(geriatric wards; general medicine service; hip surgery; coronary artery bypass surgery)		3; CBA = 3
Delirium prevention	Reston et al., 2013 (48)	1999 – 2012	17 (19)	Anesthesia protocols; medication review; pain management; staff education	Elderly	U	RCT = 4; non- RCT = 2; CBA = 11
Delirium prevention	Collinsworth et al., 2014 (49)	1988 – 2014	8 (14)	Daily assessment; monitoring; mediating strategies	ICU	2846	RCT = 3; CCT = 5
Delirium prevention	Hshieh et al., 2015 (50)	1999-2013	8 (14)	Multi component non pharmacological delirium interventions (early mobility; cognition and orientation; sleep-wake- cycle preservation; hydration; hearing; vision)	≥ 65 years	3113	RCT = 4; non-RCT = 4
Delirium prevention	Martinez et al., 2015 (51)	Up to 2012	7 (7)	Multi component interventions (e.g. physiotherapy, daily reorientation, family involvement in care, stimulation programmes with avoidance of sensorial deprivation and staff/family member education)	≥ 60 years	1691	RCT = 7
Prevention of adverse event after clinical handover or hospital discharge							
Handover of inpatients	Griffiths et al., 2005 (52)	Up to 2003	8 (9)	Post acute intermediate care	Post acute and ≥ 18 years	N.R.	RCT = 7; quasi RCT = 1
Handover of inpatients	Conroy et al., 2011 (53)	Up to 2009	5 (5)	Geriatric assessment for frail older people being rapidly discharged from acute hospital	≥ 65 years being rapidly discharged (<72 h) from a acute hospital setting	2287	RCT = 5
Handover of inpatients	Niven et al., 2014 (54)	Up to 2012	5 (9)	Critical care transition programs	ICU	16433	CBA = 5
Hospital discharge	Rennke et al., 2013 (55)	1990 – 2012	7 (47)	Intervention to improve transitional care at hospital discharge: pre discharge interventions (assessment of risk for adverse events, patient engagement, creation of individualized patient record, facilitation of communication with outpatient providers, multidisciplinary discharge planning team, dedicated transition provider and medication reconciliation); Postdischarge interventions (Outreach to patients, facilitation of clinical follow-up and medication reconciliation after discharge); Bridging interventions (inclusion of at least 1 predischarge component and at least 1 postdischarge component	≥ 18 years	1943	RCT = 6; non- RCT = 1
Hospital	Sheppard et al.,	Up to 2012	7 (24)	Discharge planning from hospital to home	Elderly medical	U	RCT = 7

Patient-Safety Area	Study, year (reference)	Time range	No. of studies eligible studies (total included studies (n))	Intervention components eligible to patient safety	Studied in hospital patients	Total no. of participants	Study designs
discharge	2013 (56)				patients, patients recovering from surgery and those with a mix of conditions		
Hospital discharge	Lowthian et al., 2015 (57)	Up to 2013	3 (9)	Comprehensive geriatric nurse assessment; community based service transfer; identifying high risk patients;	≥ 65 years, ED	2668	RCT = 3
Hospital discharge	Zhu et al., 2015 (58)	Up to 2014	5 (10)	Nurse-led early discharge planning programmes (e.g. initial nurse visit within 48 hours of hospital admission; predischarge assessment; structured home visits; telephone follow- ups after discharge)	Older adults	2503	RCT = 5
Fall prevention							
Fall prevention	Oliver et al., 2007 (59)	Up to 2005	12 (43)	Risk assessment; care planning; medical/diagnostic approaches; changes in the physical environment; education; medication review; hip protectors; removal of physical restraints		N.R.	RCT = 5; CBA = 7
Fall prevention	Coussement et al., 2008 (60)	Up to 2006	8 (8)	Unifactorial interventions (vitamin D supplement; identification bracelet; bed alarm system; flooring types) and multifactorial interventions (exercise program; medication review; multidisciplinary teams and meetings; staff awareness; improving patient activities)	≥ 69 years, long stay geriatric care units and geriatric rehabilitation units.	3894	RCT = 6; CT = 2
Fall prevention	Cameron et al., 2012 (61)	Up to 2012	15 (60)	Management of urinary incontinence; fluid or nutritional therapy; environment/ assistive technology (e.g., carpeted floors); social environment; patient education; staff education	≥ 65 years (or mean age ≥ 65 years)	26887	RCT = 15
Fall prevention	Miake-Lye et al., 2013 (62)	2005 - 2012	21 (21)	Patient education; bedside risk sign; staff education; fall alert wristband; footwear; review after fall; toileting schedules; medication review; environment modification; movement alarms; bedrail review; hip protectors; urine screening; vest/ belt or cuff restraint	General population or older adults	U	RCT = 7; non- RCT = 14
Prevention of surgical adverse event							
Preventing surgical site infections	Chen et al., 2013 (63)	Up to 2012	4 (19)	Screening and decolonization of surgical site infections	Orthopedic and trauma	7845	RCT = 2; Systematic review = 2
Interventions to reduce adverse events in surgery	Howell et al., 2014 (64)	Up to 2012	7 (91)	Interventions to reduce adverse events in surgery: staffing factors; subspecialisation; benchmarking; mixed process interventions ; checklist interventions; technology or training; colorectal pathways; care pathways	Surgical patients	88423	RCT = 7

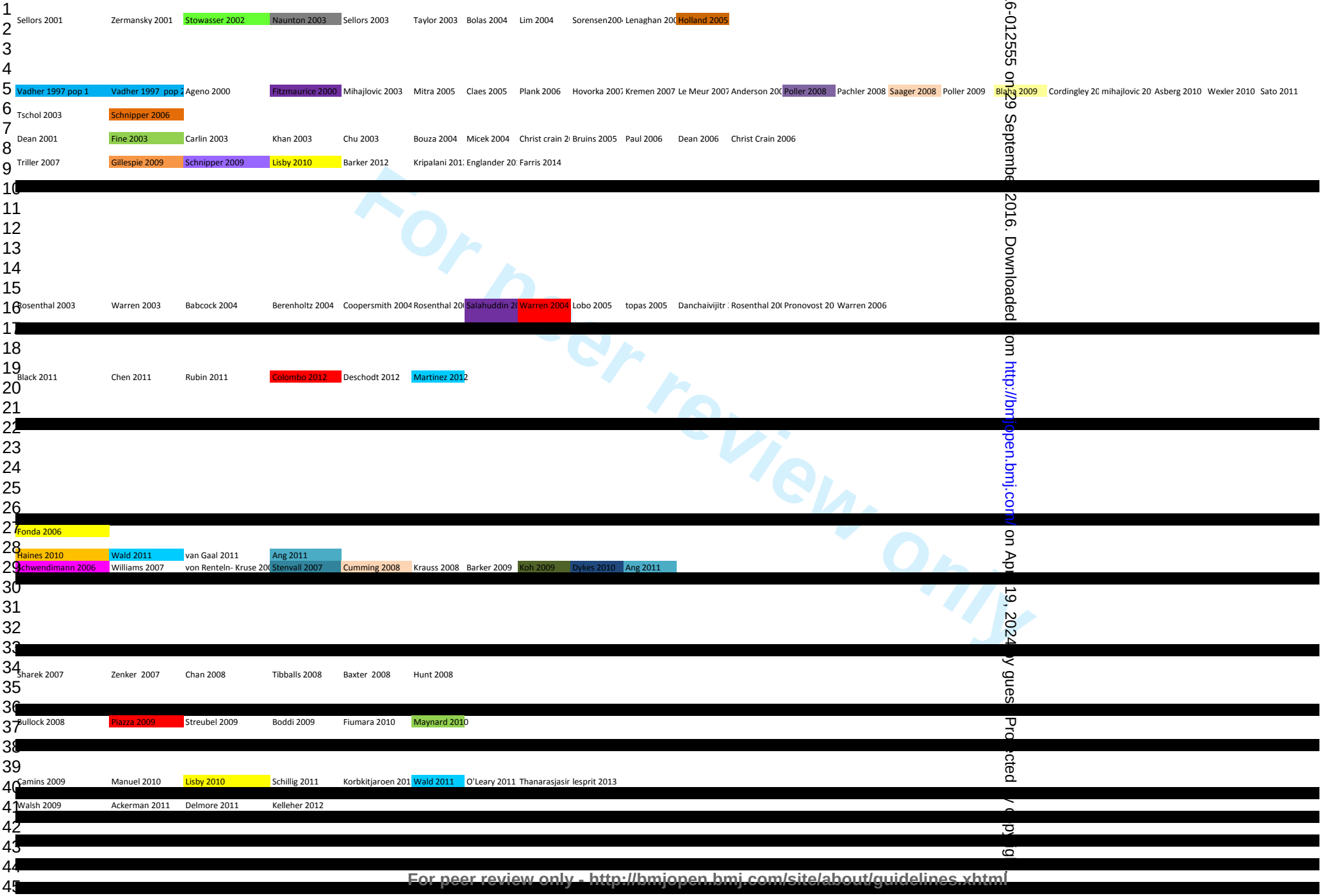
Patient-Safety Area	Study, year (reference)	Time range	No. of studies eligible studies (total included studies (n))	Intervention components eligible to patient safety	Studied in hospital patients	Total no. of participants	Study designs
Preventing wrong site surgery	Hempel et al., 2015 (65)	2004-2014	4 (138)	Universal protocol; team training and education; retained surgical items	Surgical patients	U	RCT = 1; ITS = 3
Surgical safety checklist	Bergs et al., 2014 (66)	Up to 2013	5 (7)	WHO surgical safety checklist	≥ 18 years; non cardiac surgery; trauma and orthopaedic surgery; elective general surgery; high risk surgical procedures	U	ITS = 5
Surgical safety checklist	Algie et al., 2015 (67)	2011-2014	1 (2)	Preventing wrong site surgery with safety checklist	Surgical patients	22749	ITS = 1
Prevention of hospital mortality and cardiopulmonary arrest with rapid response systems							
Critical care outreach service	Esmonde et al., 2006 (68)	1996-2004	7 (23)	Critical care outreach service	Critically ill patients	N.R.	RCT = 2; quasi experiment = 3; CBA = 2
Rapid response teams	Chan et al., 2010 (69)	Up to 2008	16 (17)	Rapid response teams	Adults and children	N.R.	Non-RCT = 2; CBA = 12; ITS 2
Rapid response systems	Massey et al., 2010 (70)	1995 - 2009	5 (16)	Rapid response systems	Critically ill patients	U	RCT = 2; non- RCT = 2; CBA = 1
Rapid response systems	Maharaj et al., 2015 (71)	1990 - 2013	5 (29)	Rapid response teams	Pediatric and adult patients	225686	RCT = 2; CBA = 1; ITS = 2
Prevention of venous thromboembolism							
Prevention of venous thromboembolism	Kahn et al, 2013 (72)	Up to 2010	17 (55)	Alerts, education and multifaceted interventions for the implementation of appropriate administration of thromboprophylaxis	≥ 18 years; medical or surgical, at risk for venous thromboembolism (VTE)	79021	RCT = 1; quasi RCT =1; non- RCT = 15
Prevention of venous thromboembolism	Lau and Haut 2014 (73)	2001 to 2012	8 (16)	Education; paper based tools; computerized tools; real time audit and feedback or combinations of interventions to improve prescription of VTE prophylaxis	Unknown	U	RCT = 2; CBA = 6
Prevention of adverse events by changes in staffing							
Staffing	Reed et al., 2010 (74)	1989 to 2010	2 (64)	Shift length; protected sleep time; night float; education among residents	Patients and residents	1294	RCT = 1; non- RCT = 1

Patient-Safety Area	Study, year (reference)	Time range	No. of studies eligible studies (total included studies (n))	Intervention components eligible to patient safety	Studied in hospital patients	Total no. of participants	Study designs
Staffing	Butler et al., 2011 (75)	Up to 2009	2 (15)	Nursing staff models	Not specified	938	RCT = 2
Staffing	Pannick et al., 2015 (76)	1998-2013	20 (30)	Interdisciplinary team care interventions	Geriatrics, infectious disease, pharmacotherapy and stroke	30969	RCT = 14; non-RCT = 5; CBA = 1
Prevention of pressure ulcers							
	Sullivan and Schoelles, 2013 (77)	2000 - 2012	15 (26)	Interventions for preventing pressure ulcers	All inpatient units, including, surgical, ICU, critical care, acute care, rehabilitation, intermediate care medical care, oncology patients	N.R.	ITS = 15
Prevention of mechanical complications and underfeeding							
	Naylor et al., 2004 (78)	Up to 2011	8 (11)	Total parenteral nutrition team	≥ 18 years	U	non- RCT = 8
Prevention of complications and mortality by clinical pathways							
	Rotter et al., 2010 (79)	Up to 2008	10 (27)	Clinical pathways (CPW)	Patients with conditions managed in a CPW	2632	RCT = 9, quasi RCT = 1
Prevention of adverse events by promoting a culture of safety							
	Weaver et al., 2013 (80)	2000 –2012	1 (33)	Intervention to promote a culture of patient safety (error prevention training coaching; family engagement; restructured patient safety governance; lessons learned program; cause analysis program; executive rounds)	≤ 18 years	3752	ITS = 1
Prevention of adverse events by external inspection							
	Flodgren et al., 2011 (81)	Up to 2011	1 (2)	External inspections of compliance with standards	Not reported	U	ITS = 1

CAUTI = catheter associated urinary tract infection; CBA= controlled before after; C(C)T= controlled (clinical) trial; CLABSI = central line associated blood stream infections; IC = intensive care; ICU = intensive care unit; inc = inception of database (start); ITS = Interrupted time series; NR= not reported; RCT = randomized controlled trial; U = unclear; VAP = ventilator-associated pneumonia

Appendix 9 Overlap studies

PATIENT-SAFETY AREA	SUB AREA	AUTHOR AND YEAR	INCLUDED ELIGIBLE STUDIES										
Adverse drug event	CPOE system	Wolfstadt et al., 2008 (22)	Bates 1999	Colpaert 2006									
		Maaskant et al., 2015 (23)	Kings 2003	Walsh 2008									
	Medication reconciliation	Holland et al., 2008 (24)	Jameson 1995	Hanlon 1996	Begley 1997	Smith 1997	Carter 1998	McMullin 1999	Bond 2000	Mackie 2001	Grymonpre 2001	Krska 2001	Nazareth 2001
		Mueller et al., 2012 (25)	Schnipper 2006	Schnipper 2009	Midlöv 2008	Lisby 2010	Boockvar 2011						
		Christensens & Lundh 2013 (26)	Schnipper 2006	Gillespie 2009	Lisby 2010	Lisby 2011	Gallagher 2011						
		Hohl et al., 2015 (27)	Scullin 2007	Spinewine 2007	Gillespie 2009	Lisby 2010	Lisby	Bladh 2011					
	Computer assisted decision support/ alerts	Durieux et al., 2008 (28)	Rodman 1984	White 1987	Hurley 1989	Begg 1989	Gonzalez 1989	Destache 1990	Burton 1991	Mungall 1994	Vadher 1997	Fitzmaurice 2000	
		Gillaizeau et al., 2013 (29)	Rodman 1984	Hurley 1986	White 1987	Gonzalez 1989	Begg 1989	Destache 1990	Burton 1991	Leehey 1993	Casner 1993	Mungall 1994	Vadher 1997
		Bayoumi et al., 2014 (30)	White 1987	Vadher 1997	Fitzmaurice 2000	Poller 2008	Saager 2008	Blaha 2009	Cavalcanti 2009	Mann 2011	Dumont 2012		
	Multicomponent interventions	Kaboli et al., 2006 (31)	Destache 1989	Burton 1991	Bjornson 1993	Bailey 1997	Fraser 1997	Gums 1999	Dager 2000	Gentry 2000	Leape 2000	Nazareth 2001	Kucukarslan 2003
		Manias et al., 2012 (32)	Leape 1999	Landrigan 2004	Rothschild 2005	Shulman 2005	Bradley 2006	Colpaert 2006	Weant 2007	Nuckols 2008	Klopotowska 2010	Chapuis 2010	
		Davey et al., 2013 (33)	Doern 1994	Pear 1994	McNulty 1997	Bailey 1997	Fraser 1997	Climo 1998	Gums 1999	De Man 2000	Singh 2000	Solomon 2001	Naughton 2001
		Patterson et al., 2014 (34)	Hanlon 1996	Crotty 2004	Schmader 2004								
		Ensing et al., 2015 (35)	Stewart 1998	Stewart 1998	Nazareth 2001	Stowasser 2002	Naunton 2003	Schmader 2004	Holland 2005	Lopez Cabezas 200	Holland 2007	Scullin 2007	Spinewine 2007
		Wang et al., 2015 (26)	Leape 1999	Kaushal 2008									
Infection	Prevention of device-related infections (CAUTI, CLASBI, VAP)	Flodgren et al., 2013 (37)	Kaye 2000	Zack 2002	Coopersmith 2002	Beathard 2003	Salahuddin 2004	Warren 2004	Abbott 2006	Sona 2009	Miller 2010	Parra 2010	
		Jansson et al., 2013 (38)	Abbott 2006	Hawe 2009									
		Blot et al., 2014 (39)	Coopersmith 2002	Warren 2004	Berriel-Cass 2006	Fraher 2009	Lobo 2010	Dixon 2010	Peredo 2010	Parra 2010			
		Meddings et al., 2014 (40)	Cornia 2003	Stephan 2006	Loeb 2008								
		Damiani et al., 2015 (41)	Girardis 2009	Levy 2010	Seoane 2013	van Zanten 2014	Levy 2014						
	Interventions to improve hand-hygiene compliance	Silvestri et al., 2005 (42)	Casewell 1977	Massanari 1984	Maki 1989	Simmons 1990	Doebbeling 1992	Slota 2001	Koss 2001				
		Gould et al., 2010 (43)	Vernaz 2008										
	Overall hospital-acquired infection prevention	Safdar & Abad 2008 (44)	Conly 1989	Kelleghan 1993	Lange 1997	Goetz 1999	Eggimann 2000	Makris 2000	Pittet 2000	Sheretz 2000	Coopersmith 2002	Zack 2002	Mody 2003
Delirium		Cole et al., 1998 (45)	Lazarus 1968	Layne 1971	Owens 1981	Williams 1985	Schindler 1989	Gustafson 1991	Nagley 1986	Wanich 1992			
		Milisen et al., 2005 (46)	Wanich 1992	Cole 1994	Inouye 1999	Marcantonio 2001	Milisen 2001	Cole 2002	Bogaards 2003				
		Hempenius et al., 2011 (47)	Schindler 1989	Wanich 1992	Inouye 1999	Milisen 2001	Wong 2005	Tabet 2005	Caplan 2007				
		Reston et al., 2013 (48)	Marcantonio 2001	Wong 2005	Tabet 2005/2006	Lundström 2005	Lundström 2007	Harari 2007	Vidán 2009	Needham 2010	Björkelund 2010	Inouye 2003/ 1999	Allen 2011
		Collinsworth et al., 2014 (49)	Girard 2008	Schweickert 2009	Needham 2010	Skrobik 2010	Colombo 2012	Mehta 2012	Hager 2013	Balas 2014			
		Hshieh et al., 2015 (50)	Inouye 1999	Lundstrom 2007	Stenvall 2007	Kratz 2008	Vidan 2009	Bo 2009	Martinez 2012	Jeffs 2013			
		Martinez et al., 2015 (51)	Marcantonio 2001	Vidan 2005	Finotto 2006	Lundström 2007	Jeffs 2008	Martinez 2012	Alvarez 2012				
Adverse event after hospital discharge or clinical handover		Griffiths et al., 2005 (52)	Hall 1975	Pearson 1988a	Pearson 1988 b	Griffiths 1995	Walsh 1999	Griffiths 2000	Griffiths 2001	Steiner 2001			
		Conroy et al., 2005 (53)	Close 1999	Mion 2003	McCusker 2003	Caplan 2004	Davidson 2005						
		Niven et al., 2014 (54)	Ball 2003	Leary 2003	Eliott 2008	Pirret 2008	Williams 2010						
		Rennke et al., 2013 (55)	Naylor 1990	Forster 2005	Schnipper 2006	Graumlich 2009	Gallagher 2011	Al ghamdi 2012	Marusic 2012				
		Sheppard et al., 2013 (56)	Rich 1995	Sulch 2000	Nazareth 2001	Pardessus 2002	Laramee 2003	Evans 2003	Legrain 2011				
		Lowthian et al., 2015 (57)	Mion 2001	Caplan 2004	Yim 2011								
		Zhu et al., 2015 (58)	Naylor 1999	Atienza 2004	Jack 2009	Saleh 2012	Altfeld 2013						
Fall		Oliver et al., 2007 (59)	Kilpack 1991	Mayo 1994	Mitchell 1996	Brandis 1999	Savage 2001	Barry 2001	Oliver 2002	Hoffman 2003	Vassallo 2004	Haines 2004	Healey 2004
		Coussement et al., 2008 (60)	Tideiksaar 1993	Mayo 1994	Donald 2000	Haines 2001	Bisschoff 2003	Vassallo 2004	Healey 2004	Schwendimann 2006			
		Cameron et al., 2012 (61)	Mayo 1994	Donald 2000	Mador 2004	Haines 2004	Healey 2004	Stenvall 2007	Jarvis 2007	Burleigh 2007	Cumming 2008	Koh 2009	Dykes 2010
		Miake-lye et al., 2013 (62)	Mitchell 1996	Brandis 1999	Udén 1999	Barry 2001	Oliver 2002	Grenier- Sennelier 2002	Haines 2004	Vassalo 2004	Healey 2004	Fonda 2006	van der helm 2006
Adverse event in surgery		Chen et al., 2013 (63)	Kalmeijer 2001	Kallen 2005	van Rijen 2008	Bode 2010							
		Howell et al., 2014 (64)	Delaney 2003	Gatt 2005	Muehling 2008	Serclova 2009	Brannick 2009	Muller 2009	Ren 2012				
		Hempel et al., 2015 (65)	Mulloy 2008	Greenberg 2008	Neily 2011	James 2012							
		Bergs et al., 2014 (66)	Askarian 2011	Sewell 2011	Kwok 2012	Bliss 2012	van Klei 2012						
		Algie et al., 2015 (67)	Vachhani 2013										
Cardiopulmonary arrest		Esmonde et al., 2006 (68)	Goldhill 1999	Bristow 2000	Salamonson 2001	Priestley 2004	Haji-Michael 2004	MERIT 2005	Ingleby (unpublished)				
		Chan et al., 2010 (69)	Bristow 2000	Buist 2002	Bellomo 2003	Kenward 2004	Priestley 2004	Devita 2004	Jones 2005	Hillman 2005	Brilli 2007	Jones 2007	Dacey 2007
		Massey et al., 2010 (70)	Hodgetts 2002	Bristow 2002	Priestley 2004	Hillman 2005	Dacey 2007						
		Maharaj et al., 2015 (71)	Bristow 2000	Hullman 2004	Priestley 2004	Hanson 2010	Howell 2012						
Venous thromboembolism		Kahn et al., 2013 (72)	Frankel 1999	Peterson 1999	Mosen 2004	Labarere 2004	Kucher 2005	Scaglione 2005	Burns 2005	McMullin 2006	Sellier 2006	Labarere 2007	Lecumberri 2008
		Lau & Haut., 2014 (73)	Scaglione 2005	Kucher 2005	Piazza 2009	Gallagher 2009	Maynard 2010	Liu 2012	Maharaj 2012	Haut 2012			
Staffing		Reed et al., 2010 (74)	Landrigan 2004	Afessa 2005									
		Butler et al., 2011 (75)	Forster 2005	Duncan 2006									
		Pannick et al., 2015 (76)	Soifer 1998	Curley 1998	Webstar 1999	Solomon 2001	Cole 2002	Kucukarslan 2003	Fine 2005	Dey 2005	Mudge 2006	Pitkala 2006	Mannheimer 2006
Pressure ulcer		Sullivan & Schoelles 2013 (77)	Stier 2004	Hiser 2006	Courtney 2006	Gibbons 2006	LeMaster 2007	Ballard 2007	Catania 2007	Dibsie 2008	McInerney 2008	Bales 2009	Chicano 2009
Mechanical complication and underfeeding		Naylor et al., 2004 (78)	Hickey 1979	Dalton 1984	Jacobs 1984	Traeger 1986	Gales 1994	Fisher 1996	Png 1997	Fetter 2000			
Clinical pathway		Rotter et al., 2010 (79)	Kollef 1997	Dowsey 1999	Brook 1999	Choong 2000	Marelich 2000	Cole 2002	Aizawa 2002	Delaney 2003	Kiyama 2003	Smith 2004	
Safety culture		Weaver et al., 2013 (80)	Meething 2012										
External inspection		Flodgren et al., 2011 (81)	OPM 2009										



Appendix 10 Summary of the results of eligible studies reported in the systematic reviews (n=60)

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of eligible studies)	Conclusion reported by the authors
Prevention of adverse drug events						
Wolfstadt et al., 2008 (22)	CPOE system	Preventable AEs	No (Reason not reported)	N.A.	N.A.	Few studies have measured the effect of CPOE with clinical decision support on the rates of ADEs, and none were randomized controlled trials.
Maaskant et al., 2015 (23)	CPOE system	ADE	No (Heterogeneity of methods of data collection, populations and study designs)	N.A.	N.A.	Current evidence on effective interventions to prevent medication errors and adverse drug events in a pediatric population in hospital is limited.
Holland et al., 2008 (24)	Medication reconciliation	All cause mortality	Yes	Medication review	*Mortality (Relative Risk)* = 0.96, 95% CI [0.82-1.13] p = 0.62 (22 studies; all eligible)	Pharmacist-led medication review interventions do not have any effect on reducing mortality or hospital admission in older people, and cannot be assumed to provide substantial clinical benefit. Such interventions may improve drug knowledge and adherence, but there are insufficient data to know whether quality of life is improved.
Mueller et al., 2012 (25)	Medication reconciliation	ADE; mortality	No (Heterogeneity in methods, interventions, and reported outcomes)	N.A.	N.A.	Rigorously designed studies comparing different inpatient medication reconciliation practices and their effects on clinical outcomes are scarce. Available evidence supports medication reconciliation interventions that heavily use pharmacy staff and focus on patients at high risk for AE.
Christensen and Lundh, 2013 (26)	Medication reconciliation	Mortality; falls; ADE	Yes (for mortality, not for adverse drug events and falls because of the lack of valid data)	Medication review	*Mortality (Risk Ratio)* = 0.98, 95% CI [0.78-1.23] p = 0.86 (4 studies; all eligible)	It is uncertain whether medication review reduces mortality or hospital readmissions, but medication review seems to reduce emergency department contacts. However, the cost-effectiveness of this intervention is not known and due to the uncertainty of the estimates of mortality and readmissions and the short follow-up, important treatment effects may have been overlooked.
Hohl et al., 2015 (27)	Medication reconciliation	Mortality	Yes	Mediation review	*Mortality (Odds Ratio)* = 1.09, 95% CI [0.69-1.72] p = 0.71 (3 studies; all eligible)	This systematic review failed to identify an effect of pharmacist-led medication review on health outcomes.

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of eligible studies)	Conclusion reported by the authors
Durieux et al., 2008 (28)	Computer assisted decision support/ alerts	Deaths; ARs	Yes (for mortality, not for AR due to diversity of drugs and of type of adverse reactions)	Computerized advice on drug dosage	*Deaths (Risk Ratio)* = 0.81, 95% CI [0.37-1.81] p = 0.61(6 studies; all eligible)	This review suggests that computerized advice for drug dosage has some benefits: it increased the initial dose of drug, increased serum drug concentrations and led to a more rapid therapeutic control. It also reduced the risk of toxic drug levels and the length of time spent in the hospital. However, it had no effect on adverse reactions or mortality rates.
Gillaizeau et al., 2013 (29)	Computer assisted decision support/ alerts	Mortality; clinical AE	Yes (for mortality; not for clinical AEs due to diversity in outcomes)	Computerized advice on drug dosage	*Mortality (Risk Ratio)* = 1.08, 95% CI [0.80-1.45] p = 0.61 (10 studies; all eligible)	It tends to decrease unwanted effects for aminoglycoside antibiotics and anti-rejection drugs, and significantly decreases thromboembolism events for anticoagulants […]. However, there was no evidence that decision support had an effect on mortality or other clinical adverse events for insulin (hypoglycaemia), anaesthetic agents, anti-rejection drugs and antidepressants. […] Taking into account the high risk of bias of, and high heterogeneity between, studies, these results must be interpreted with caution.
Bayoumi et al., 2014 (30)	Computer assisted decision support/ alerts	AE (bleeding and thrombosis)	Yes	Computerized drug- lab alerts	*Adverse events (bleeding and thrombosis) (Odds Ratio)* = 0.88, 95% CI [0.78-1.00] p = 0.05 (4 studies; all eligible)	There is no evidence that computerized drug-lab alerts are associated with important clinical benefits, but there is evidence of improvement in selected clinical surrogate outcomes (time in therapeutic range for vitamin K antagonists), and changes in process outcomes (lab monitoring and prescribing decisions).
Kaboli et al. 2006 (31)	Multi component interventions	(Preventable) ADE; mortality; bleeding complications; VTE	No (Small sample size and methodological limitations of included studies)	N.A.	N.A.	The addition of clinical pharmacist services in the care of inpatients generally resulted in improved care, with no evidence of harm.
Manias et al., 2012 (32)	Multi component interventions	Severity of harm of medication errors; ADE; preventable prescribing AE	No (Heterogeneity for the outcome variable)	N.A.	N.A.	It is not possible to promote any interventions as positive models for reducing medication errors.
Davey et al., 2013 (33)	Multi component interventions	Mortality	Yes	Intervention to increase appropriate antibiotic treatment	*Mortality (Risk Ratio)* = 0.92, 95% CI [0.69-1.22] p = 0.56 (3 studies; all eligible)	The results show that interventions to reduce excessive antibiotic prescribing to hospital inpatients can reduce antimicrobial resistance or hospital-acquired infections, and interventions to increase effective prescribing can improve clinical outcome.

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of eligible studies)	Conclusion reported by the authors
				Antibiotic guideline compliance for pneumonia	*Mortality (Risk Ratio)* = 0.89, 95% CI [0.82-0.97] p = 0.01 (4 studies; all eligible)	
				Interventions to decrease excessive prescribing of antibiotics	*Mortality (Risk Ratio)* = 0.92, 95% CI [0.81-1.06] p = 0.25 (11 studies; all eligible)	
Patterson et al., 2014 (34)	Multi component interventions	ADE	No (Heterogeneity of scales to measure outcome measures and reporting methods)	N.A.	N.A.	It is unclear if interventions to improve appropriate polypharmacy, such as pharmaceutical care, resulted in a clinically significant improvement; however, they appear beneficial in terms of reducing inappropriate prescribing and medication-related problems.
Ensing et al., 2015 (35)	Multi component interventions	Mortality; ADE	No (Heterogeneity among studies)	N.A.	N.A.	In multifaceted intervention programs, performing medication reconciliation alone is insufficient in reducing postdischarge clinical outcomes and should be combined with active patient counseling and a clinical medication review. Furthermore, close collaboration between pharmacists and physicians is beneficial. Finally, it is important to secure continuity of care by integrating pharmacists in these multifaceted programs across health care settings. Ultimately, pharmacists need to know patient clinical background and previous hospital experience.
Wang et al., 2015 (36)	Multi component interventions	Preventable ADE	Yes	Pharmacist interventions	*Preventable ADE (Odds Ratio)* = 0.23, 95% CI [0.11-0.48] p < 0.01 (3 studies, 2 eligible)	Results suggest that pharmacist intervention has no significant contribution to reducing general MEs, although pharmacist intervention may significantly reduce preventable adverse drug events and prescribing errors.

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of eligible studies)	Conclusion reported by the authors
Infection prevention						
Flodgren et al., 2013 (37)	Prevention of device related infections	VAP; CLASBI; mortality	No (Heterogeneity among studies)	N.A.	N.A.	The low to very low quality of the evidence of studies included in this review provides insufficient evidence to determine with certainty which interventions are most effective in changing professional behavior and in what contexts. However, interventions that may be worth further study are educational interventions involving more than one active element and that are repeatedly administered over time, and interventions employing specialized personnel, who are focused on an aspect of care that is supported by evidence e.g. dentists/ dental auxiliaries performing oral care for VAP prevention.
Jansson et al., 2013 (38)	Prevention of device related infections	VAP; mortality	No (Methodological limitations of the included studies)	N.A.	N.A.	Education has significant benefits for improving patient safety, and thus the quality of care. Active implementation strategies involving repeated lectures and regular surveys of VAP occurrence would be beneficial.
Blot et al., 2014 (39)	Prevention of device related infections	CLASBI	Yes	Bundle/ checklist and non bundle/checklist interventions	*Total number of CLASBI (Odds Ratio)* = 0.39, 95% CI [0.33 -0.46] p = <0.01 (41 studies; 5 eligible) *Change in CLASBI rate levels at 3 months post intervention (Odds Ratio)* = 0.30, 95% CI [0.10-0.88] p= 0.03 (6 studies; 4 eligible)	These results suggest that quality improvement interventions contribute to the prevention of central line-associated bloodstream infections. Implementation of care bundles and checklists appears to yield stronger risk reductions.
Meddings et al., 2014 (40)	Prevention of device related infections	CAUTI	Yes	Reminder and stop order	*CAUTI episodes per 1000 catheter days (Risk Ratio)* = 0.47, 95% CI [0.30-0.64] p = < 0.01 (11 studies; 1 eligible) *Percentage of patients who developed CAUTI (Risk Ratio)* = 0.72, 95% CI [0.52-0.99] p = 0.045 (8 studies; 2 eligible)	Urinary Catheter reminders and stop orders appear to reduce CAUTI rates and should be used to improve patient safety.
Damiani et al., 2015 (41)	Interventions to improve compliance to sepsis bundle interventions	Mortality	Yes	Performance improvement program	*Mortality (Odds Ratio)* = 0.66, 95% CI [0.61-0.72] p <0.01 (48 studies, 3 eligible)	Performance improvement programs are associated with increased adherence to resuscitation and management sepsis bundles and with reduced mortality in patients with sepsis, severe sepsis or septic shock.

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of eligible studies)	Conclusion reported by the authors
Silvestri et al., 2005 (42)	Interventions to improve hand hygiene compliance	Infection rates; mortality	No (Reason not reported)	N.A.	N.A.	Hand washing on its own does not abolish but only reduces transmission, as it is dependent upon the bacterial load on the hands of healthcare workers. Hand washing can only influence a subset of long-stay patients on ICUs. Only a randomized trial could support the statement of the Hand washing Liaison Group providing evidence for hand washing being a modest measure with big effects.
Gould et al., 2010 (43)	Interventions to improve hand hygiene compliance	Healthcare associated infections	No (Heterogeneity of interventions and methods)	N.A.	N.A.	The quality of intervention studies intended to increase hand hygiene compliance remains disappointing. Although multifaceted campaigns with social marketing or staff involvement appear to have an effect, there is insufficient evidence to draw a firm conclusion.
Safdar and Abad, 2008 (44)	Overall hospital acquired infection prevention	CRBSI; VAP; CAUTI; overall nosocomial infections	No (Heterogeneity of studies)	N.A.	N.A.	The implementation of educational interventions may reduce healthcare- associated infections considerably.
Delirium prevention						
Cole et al., 1998 (45)	Delirium prevention	ARR of delirium	No (Small number of included studies; mostly nonrandomized designs in which outcomes were not rated blind; heterogeneity of populations and interventions)	N.A.	N.A.	It is difficult to draw firm conclusions because of three methodological problems.
Milisen et al., 2005 (46)	Delirium prevention	Incidence, severity and duration of delirium; mortality	No (Small number of included studies; heterogeneity of populations and interventions; methodological limitations of included studies)	N.A.	N.A.	Multicomponent interventions to prevent delirium are the most effective and should be implemented through synergistic cooperation between the various healthcare disciplines.
Hempenius et al., 2011 (47)	Delirium prevention	Delirium (incidence)	Yes	Multi-component interventions	*Incidence of delirium (Odds Ratio)* = 0.58, 95% CI [0.38- 0.92] p value NR (5 studies; all eligible)	Interventions to prevent delirium are effective. Interventions seem to be more effective when the incidence of delirium in the population under study is above 30%.

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of eligible studies)	Conclusion reported by the authors
				One component interventions	*Incidence of delirium (Odds Ratio)* = 1.05, 95% CI [0.09- 11.57] p value NR (2 studies; all eligible)	
Reston et al., 2013 (48)	Delirium prevention	Incidence of delirium	No (Methodological limitations of included studies, heterogeneity of interventions; small number of studies)	N.A.	N.A.	The evidence from 19 studies that met the inclusion criteria suggests that most multicomponent interventions are effective in preventing onset of delirium in at-risk patients in a hospital setting.
Collinsworth et al., 2014 (49)	Delirium prevention	Incidence and duration of delirium; mortality	No (Heterogeneity of interventions and measured outcomes)	N.A.	N.A.	Although multifaceted care approaches may reduce delirium and improve patient outcomes, greater improvements may be achieved by deploying a comprehensive bundle of care practices including awakening and breathing trials, delirium monitoring and treatment, and early mobility.
Hshieh et al., 2015 (50)	Delirium prevention	Incidence of delirium; falls	Yes	Multi-component interventions	*Incidence delirium (Odds Ratio)* = 0.47, 95% CI [0.38- 0.58] p <0.01 (11 studies; 7 eligible)	Multicomponent nonpharmacological delirium prevention interventions are effective in reducing delirium incidence and preventing falls, with a trend toward decreasing length of stay and avoiding institutionalization.
Martinez et al., 2015 (51)	Delirium prevention	Incidence and duration of delirium; falls	Yes	Multi component interventions	*Prevention of incident delirium (Risk Ratio)* = 0.73, 95% CI [0.63-0.85] p <0.01 (7 studies; all eligible)	Multicomponent interventions are effective in preventing incident delirium among elderly inpatients.
Prevention of mortality or adverse events after discharge						
Griffiths et al., 2005 (52)	Handover of inpatients	Mortality	Yes	NLU (nursing-led inpatients units)	*Inpatient mortality (Odds Ratio)* = 1.10, 95% CI [0.56-2.16] p = 0.64 (7 studies; all eligible) *Mortality to longest follow up 3 or 6 months post- admission (Odds Ratio)* = 0.96, 95% CI [0.63-1.47] p = 0.62 (6 studies; all eligible)	The NLU successfully functions as a form of intermediate care, so far there is no evidence of adverse outcome from the lower level of routine medical care. There is no evidence of benefit over the longer term.
Conroy et al., 2011 (53)	Handover of inpatients	Mortality	Yes	Comprehensive geriatric assessment	*Mortality at final follow up (Risk Ratio)* = 0.92, 95% CI [0.55-1.52] p = 0.77 (5 studies; all eligible)	There is no clear evidence of benefit for comprehensive geriatric assessment interventions in frail older people being discharged from emergency departments or acute medical units.

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of eligible studies)	Conclusion reported by the authors
Niven et al., 2014 (54)	Handover of inpatients	Mortality	Yes		*Mortality (Risk Ratio)* = 0.84, 95% CI [0.66–1.05] p = 0.1 (3 studies; 2 eligible)	Critical care transition programs appear to reduce the risk of ICU readmission in patients discharged from ICU to a general hospital ward.
Rennke et al., 2013 (55)	Hospital discharge	Postdischarge AE; ADE; ADR; falls	No (Heterogeneity of interventions, study settings, and patient populations)	N.A.	N.A.	Because of scant evidence, no conclusions could be reached on methods to prevent postdischarge AEs. Most studies did not report intervention context, implementation, or cost. The strategies hospitals should implement to improve patient safety at hospital discharge remain unclear.
Sheppard et al., 2013 (56)	Hospital discharge	Mortality; falls	Yes	Discharge planning from hospital to home	*Mortality at 6 to 9 months (Risk Ratio)* = 1.00, 95% CI [0.79-1.26] p = 0.69 (6 studies; all eligible) *Number of falls at follow up (Risk Ratio)* = 0.87, 95% CI [0.50-1.49] p = 0.61 (1 study)	The evidence suggests that a discharge plan tailored to the individual patient probably brings about reductions in hospital length of stay and readmission rates for older people admitted to hospital with a medical condition. The impact of discharge planning on mortality, health outcomes and cost remains uncertain.
Lowthian et al., 2015 (57)	Hospital discharge	Mortality	Yes	Optimized ED discharge	*Mortality up to 18 months post discharge (Odds Ratio)* = 1.01, 95% CI [0.70-1.47] p = 0.94 (2 studies; all eligible)	There is limited high-quality data to guide confident recommendations about optimal ED community transition strategies, highlighting a need to encourage better integration of researchers and clinicians in the design and evaluation process, and increased reporting, including appropriate robust evaluation of efficacy and effectiveness of these innovative models of care.
Zhu et al., 2015 (58)	Hospital discharge	Mortality	Yes	Nurse-led early discharge planning programmes	*Mortality (all cause) (Risk Ratio)* = 0.70, 95% CI [0.52-0.95] p = 0.02 (5 studies; all eligible)	Compared to standard care, nurse-led early discharge planning programmes have a positive impact on several aspects of care for inpatients with chronic disease and rehabilitation requirements, including reducing readmission, readmission length of stay and mortality and improving quality of life.
Fall prevention						
Oliver et al., 2007 (59)	Fall prevention	Falls; fallers; fractures	Yes	Multifaceted interventions	*Falls (Rate Ratio)* = 0.82, 95% CI [0.68-1.00)] p value NR (12 studies; all eligible) *Fallers (Relative Risk)* = 0.95, 95% CI [0.71-1.27] p value NR (12 studies; all eligible)	There is some evidence that multifaceted interventions in hospital reduce the number of falls. There is insufficient evidence, however, for the effectiveness of other single interventions in hospitals.

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of eligible studies)	Conclusion reported by the authors
					Fractures (Rate Ratio) = 0.59, 95% CI [0.22-1.58] p value NR (12 studies; all eligible)	
Coussement et al., 2008 (60)	Fall prevention	Falls; fallers; physical injuries	Yes (for falls and fallers, not for physical injuries)	Multifactorial intervention	*Fall (Risk Ratio)* = 0.82, 95% CI [0.65-1.03] p value NR (4 studies; all eligible) *Number of fallers (Risk Ratio)* = 0.87, 95% CI [0.70-1.08] p value NR (4 studies; all eligible)	This meta-analysis found no conclusive evidence that hospital fall prevention programs can reduce the number of falls or fallers, although more studies are needed to confirm the tendency observed in the analysis of individual studies that targeting a patient's most important risk factors for falls actively helps in reducing the number of falls. These interventions seem to be useful only on longstay care units.
Cameron et al., 2012 (61)	Fall prevention	Rate of falls; risk of fallings; number of people sustaining a fracture	Yes	Multifactorial interventions	*Rate of falls (Rate Ratio)* = 0.69, 95% CI [0.49-0.96] p = 0.03 (4 studies; all eligible) *Risk of fallings (Risk ratio)* = 0.71, 95% CI [0.46-1.09] p = 0.12 (3 studies; all eligible) *Number of people sustaining a fracture (Risk Ratio)* = 0.43, 95% CI [0.10-1.78] p = 0.24 (3 studies; all eligible)	Exercise in subacute hospital settings appears effective. There is evidence that multifactorial interventions reduce falls in hospitals but the evidence for risk of falling was inconclusive.
				Exercises	*Risk of falling (Rate Ratio)* = 0.36, 95% CI [0.14-0.93] p = 0.04 (2 studies; all eligible)	
Miake-Lye et al., 2013 (62)	Fall prevention	Reduction in fall rate; incidence of falls; injuries per fall; injury rate per fall	No (Reason not reported)	N.A.	N.A.	For multicomponent inpatient fall programs, our review provides both evidence that such programs reduce falls and insight into how facilities can successfully implement them.
Interventions to reduce adverse events in surgery						
Chen et al., 2013 (63)	Preventing surgical site infections	Overal SSI; infections of S aureus; MRSA; wound complications	No (Heterogeneity of studies)	N.A.	N.A.	Preoperative screening and decolonization of S. aureus in orthopaedic patients is a cost-effective means to reduce SSIs.
Howell et al., 2014 (64)	Interventions to reduce adverse events in surgery	Adverse events	No (Heterogeneity of subject groups, end points, and specialties)	N.A.	N.A.	Only a small cohort of medium- to high-quality interventions effectively reduce surgical harm and are feasible to implement.

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of eligible studies)	Conclusion reported by the authors
Hempel et al., 2015 (65)	Preventing wrong site surgery	Incidence of wrong site surgery	No (Heterogeneity of publications)	N.A.	N.A.	Despite promising approaches and global Universal Protocol evaluations, empirical evidence for interventions is limited.
Bergs et al., 2014 (66)	Surgical safety checklist	Any complication; mortality; surgical site infections	Yes	WHO surgical safety checklist	*Any complication (Risk Ratio)* = 0.59, 95% CI [0.47-0.74] p = <0.01 (5 studies; all eligible) *Mortality (Risk Ratio)* = 0.77, 95% CI [0.60-0.98] p = 0.04 (4 studies, 3 eligible) *Surgical site infections (Risk Ratio)* = 0.57, 95% CI p = <0.01 [0.41-0.79] (5 studies; all eligible)	The evidence is highly suggestive of a reduction in postoperative complications and mortality following implementation of the WHO SSC, but cannot be regarded as definitive in the absence of higher-quality studies.
Algie et al., 2015 (67)	Surgical safety checklist	Incidence of wrong site neurological events	No (Small number of studies)	N.A.	N.A.	The data suggested a strong downward trend in the incidence of wrong-site surgery prior to the intervention with the incidence rate approaching zero. The effect of the intervention in these studies however remains unclear, as data reflect only two small low-quality studies in very specific population groups.
Prevention of hospital mortality and cardiopulmonary arrest with rapid response systems						
Esmonde et al., 2006 (68)	Critical care outreach service	Mortality; cardiac arrest	No (Reason not reported)	N.A.	N.A.	Although improvements in patient outcomes were found, the evidence in this review is insufficient to demonstrate this conclusively.
Chan et al., 2010 (69)	Rapid response teams	Mortality; cardiopulmonary arrest	Yes	Rapid response team	*Hospital mortality (Relative Risk)* = 0.92, 95% CI [0.82-1.04] p value NR (16 studies; all eligible) *Cardiopulmonary arrest (Relative Risk)* = 0.65, 95% CI [0.55-0.77] p value NR (16 studies; all eligible)	Although rapid response teams have broad appeal, robust evidence to support their effectiveness in reducing hospital mortality is lacking.

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of eligible studies)	Conclusion reported by the authors
Massey et al., 2013 (70)	Rapid response systems	Mortality; cardiac arrest	No (Reason not reported)	N.A.	N.A.	The paper illustrates two important gaps in the literature. First, 'ramp-up' systems have not been subjected to formal evaluation. Second, rapid response systems are under-activated and underused by nursing staff. There is an urgent need to explore the reasons for this and to identify interventions to improve the activation of these systems in an effort to promote safe and effective care to the deteriorating ward patient.
Maharaj et al., 2015 (71)	Rapid response teams	Mortality; cardiopulmonary arrest	Yes	Rapid response team	*Hospital mortality adults (Risk Ratio)* = 0.91, 95% CI [0.85-0.97] p < 0.01 (4 studies; all eligible) *Hospital mortality pediatric patients (Risk Ratio)* = 0.76, 95% CI [0.53-1.09] p = 0.14 (1 study; all eligible) *Cardiopulmonary arrest adults (Risk Ratio)* = 0.74, 95% CI [0.56-0.98] p = 0.04 (2 studies; all eligible) *Cardiopulmonary arrest pediatric patients (Risk Ratio)* = 0.35, 95% CI [0.08-1.59] p = 0.17 (1 study; all eligible)	Rapid response systems were associated with a reduction in hospital mortality and cardiopulmonary arrest. Meta-regression did not identify the presence of a physician in the rapid response system to be significantly associated with a mortality reduction.
Prevention of venous thromboembolism						
Kahn, et al., 2013 (72)	Prevention of venous thromboembolism	All VTE; DVT; PE; bleeding; mortality	Yes	Alerts	*All VTE (Risk Ratio)* = 0.85, 95% CI [0.49-1.46] p value NR (3 studies; all eligible)	We found statistically significant improvements in prescription of prophylaxis associated with alerts (RCTs) and multifaceted interventions (RCTs and NRS), and improvements in prescription of appropriate prophylaxis in NRS with the use of education, alerts and multifaceted interventions. Multifaceted interventions with an alert component may be the most effective.
				Multifaceted	*All VTE (Risk Ratio)* = 1.01, 95% CI [0.51-1.98] p value NR (5 studies; all eligible) *Symptomatic DVT (Risk Ratio)* = 0.59, 95% CI [0.18-1.98] p value NR (3 studies; all eligible)	

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of eligible studies)	Conclusion reported by the authors
Lau and Haut 2014 (73)	Prevention of venous thromboembolism	(Preventable) VTE	No (Reason not reported)	N.A.	N.A.	Many intervention types have proven effective to different degrees in improving VTE prevention. Provider education is likely a required additional component and should be combined with other intervention types. Active mandatory tools are likely more effective than passive ones. Information technology tools that are well integrated into provider workflow, such as alerts and computerized clinical decision support, can improve best practice prophylaxis use and prevent patient harm resulting from VTE.
Prevention of adverse events by changes in staffing						
Reed et al., 2010 (74)	Staffing	Preventable AE; mortality	No (Heterogeneity of outcomes)	N.A.	N.A.	For the limited outcomes measured, most studies supported reducing shift length but did not adequately address the optimal shift duration.
Butler et al., 2011 (75)	Staffing	Mortality; post discharge adverse events	Yes	Addition of specialist nursing post to staffing	*In-hospital mortality (Risk Ratio)* = 0.96, 95% CI [0.59-1.56] p = 0.86 (1 study)	The findings suggest interventions relating to hospital nurse staffing models may improve some patient outcomes, particularly the addition of specialist nursing and specialist support roles to the nursing workforce. Interventions relating to hospital nurse staffing models may also improve staff-related outcomes, particularly the introduction of primary nursing and self-scheduling. However, these findings should be treated with extreme caution due to the limited evidence available from the research conducted to date.
					Post discharge adverse events (Risk Ratio) = 1.03, 95% CI [0.70-1.53] p = 0.87 (1 study)	
				Increasing the proportion of support staff	*Death in trauma unit (Risk Ratio)* = 0.41, 95% CI [0.16-1.01] p = 0.05 (1 study)	
					Death in hospital (Risk Ratio) = 0.56, 95% CI [0.29-1.09] p = 0.09 (1 study)	
					Death at 4 months (Risk Ratio) = 0.57, 95% CI [0.34-0.95] p = 0.03 (1 study)	
Pannick et al., 2015 (76)	Staffing	Mortality; delirium episode; ADE; bleeding; falls; AE	Yes (for mortality, not for the other outcomes)	Interdisciplinary team composition interventions	*Mortality (weighted risk ratio)* = 0.92, 95% CI [0.816-1.049] p value NR (7 studies; all eligible)	Current evidence suggests that interdisciplinary team care interventions on general medical wards have little effect on traditional measures of health care quality. Complications of care or preventable adverse events may merit inclusion as quality indicators for general medical wards.
				Team practice interventions	*Mortality (weighted risk ratio)* = 0.665, 95% CI [0.449-0.986] p value NR (2 studies, all eligible)	

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of eligible studies)	Conclusion reported by the authors
Prevention of pressure ulcers						
Sullivan and Schoelles, 2013 (77)	Prevention of pressure ulcers	Pressure ulcer prevalence	No (Reason not reported)	N.A.	N.A.	Moderate-strength evidence from 26 implementation studies suggests that the integration of a common set of components in pressure ulcer prevention programs could lead to reductions in pressure ulcer rates. Key issues were the simplification and standardization of pressure-ulcer specific interventions and documentation, involvement of multidisciplinary teams and leadership, designated skin champions, ongoing staff education, and sustained audit and feedback for promoting.
Prevention of mechanical complications and underfeeding						
Naylor et al., 2004 (78)	Prevention of mechanical complications and underfeeding	Mechanical complication, underfeeding	No (Heterogeneity of studies)	N.A.	N.A.	The general effectiveness of the total parenteral nutrition team has not been conclusively demonstrated. There is evidence that patients managed by TPN teams have a reduced incidence of total mechanical complications; however, it is unclear if there is a reduction in catheter-related sepsis and metabolic and electrolyte complications.
Prevention of complications and mortality by clinical pathways						
Rotter et al., 2010 (79)	Prevention of complications and mortality by clinical pathways	Mortality rate; (in hospital) complications	Yes	Clinical pathway	*Mortality rate (Odds Ratio)* = 0.84, 95%CI [0.64-1.11] p = 0.23 (3 studies; all eligible) *Complications up to three months (Odds Ratio)* = 0.31, 95% CI [0.13-0.72] p = 0.07 (1 study; all eligible) *In- hospital complications (Odds Ratio)* = 0.58, 95% CI [0.36-0.94] p = 0.03 (5 studies; all eligible)	Clinical pathways are associated with reduced in-hospital complications and improved documentation without negatively impacting on length of stay and hospital costs.

Study, year (reference)	Patient-Safety Area	Patient outcome	Meta analysis	Intervention component	Outcome (n = studies included in meta analysis; number of eligible studies)	Conclusion reported by the authors
Prevention of adverse events by promoting a culture of safety						
Weaver et al., 2013 (80)	Prevention of adverse events by promoting a culture of safety	AE	No (Heterogeneity of interventions and survey instruments and outcomes)	N.A.	N.A.	Twenty-nine studies reported some improvement in safety culture or patient outcomes, but measured outcomes were highly heterogeneous. Strength of evidence was low, and most studies were pre–post evaluations of low to moderate quality. Within these limits, evidence suggests that interventions can improve perceptions of safety culture and potentially reduce patient harm.
Prevention of adverse events by external inspection						
Flodgren, et al., 2011 (81)	Prevention of adverse events by external inspection	MRSA rates	No (Too few studies identified)	N.A.	N.A.	No firm conclusions could therefore be drawn about the effectiveness of external inspection on compliance with standards.

ADE: Adverse Drug Events; ADR: Adverse Drug Reaction; AE: Adverse events; AR: Adverse reactions; ARR: Absolute risk reduction; CAUTI: Catheter associated urinary tract infection; CI: Confidence interval; CLASBI: Central line associated blood stream infections; CRBSI: Catheter Related Blood Stream Infections; DVT: Deep vein thrombosis; N.A: Not applicable; PE: Pulmonary embolism; SSI: Surgical site infections; VAP: Ventilator associated pneumonia; VTE: Venous thromboembolism