

# **WHO Guidelines on Core Components of Infection Prevention and Control Programmes at the National and Health Care Facility Level**

## **Web Appendix I**

**Core elements of effective infection prevention and control programmes in acute health care facilities: a systematic review  
(update of the SIGHT review)**

## CONTENTS

<b>1. INTRODUCTION</b> .....	<b>3</b>
<b>2. METHODOLOGY</b> .....	<b>5</b>
2.1 RESEARCH QUESTION .....	5
2.2 LITERATURE SEARCH .....	5
2.3 ELIGIBILITY CRITERIA .....	6
2.4 STUDY SELECTION .....	6
2.5 DATA EXTRACTION .....	6
2.6 QUALITY ASSESSMENT .....	7
<b>3. RESULTS</b> .....	<b>8</b>
3.1 SUMMARY .....	8
3.2 KEY COMPONENTS IDENTIFIED .....	10
3.3 HAND HYGIENE IMPROVEMENT .....	11
3.4 PREVENTION OF VENTILATOR-ASSOCIATED PNEUMONIA .....	13
3.5 PREVENTION OF CENTRAL LINE-ASSOCIATED BLOODSTREAM INFECTION .....	13
3.6 PREVENTION OF MULTIDRUG-RESISTANT ORGANISM TRANSMISSION AND HEALTH CARE-ASSOCIATED INFECTION .....	14
3.7 RISK OF BIAS .....	15
<b>4. SUMMARY RESULTS FOR NON-EPOC STUDIES</b> .....	<b>17</b>
<b>5. DISCUSSION</b> .....	<b>22</b>
<b>APPENDIX 1: SEARCH TERMS OF THE SYSTEMATIC REVIEW AND EVIDENCE-BASED GUIDANCE ON THE ORGANIZATION OF HOSPITAL INFECTION CONTROL PROGRAMMES (SIGHT)</b> .....	<b>23</b>
<b>APPENDIX 2: INCLUSION CRITERIA</b> .....	<b>33</b>
<b>APPENDIX 3: SUGGESTED RISK OF BIAS CRITERIA FOR EPOC REVIEWS</b> .....	<b>37</b>
<b>APPENDIX 4: DETAILS OF THE STUDIES ANALYSED AND SYNTHESIZED IN THE SYSTEMATIC REVIEW</b> .....	<b>40</b>
<b>APPENDIX 5: RISK OF BIAS FOR CLUSTER RANDOMIZED TRIALS, NON- RANDOMISED CLUSTER TRIALS AND CONTROLLED BEFORE-AND-AFTER STUDIES</b> .....	<b>53</b>
<b>APPENDIX 6: RISK OF BIAS FOR INTERRUPTED TIME SERIES STUDIES</b> .....	<b>55</b>
<b>REFERENCES</b> .....	<b>57</b>

## 1. Introduction

Health care-associated infection (HAI) is one of the most frequently occurring adverse events and a major public health problem. HAI impacts on morbidity and mortality, quality of life and presents an economic burden at the societal level. A large percentage of the various types of HAI are thought to be preventable. There is now a growing body of work on the global burden of harm caused by HAI (1, 2), as well as the strategies necessary for its reduction and prevention (3).

In 2011, the World Health Organization (WHO) reported that 7% of patients in developed and 10% in developing countries will acquire at least one HAI at any given time. In Europe, more than 4 million patients are affected by approximately 4.5 million episodes of HAIs annually, leading to 16 million extra-days of hospital stay, 37 000 attributable deaths and contributing to an additional 110 000. In the United States of America (USA), around 1.7 million patients are affected by HAIs annually with a prevalence of 4.5% and accounting for 99 000 deaths. Limited data are available from low- and middle-income countries (LMICs), but the prevalence of HAI is estimated to be between 5.7% and 19.1%. In developing countries, the increased length of hospital stay associated with HAIs ranges between 5 and 29.5 days. In adult patients in Latin America, Asia and Africa, excess mortality due to these infections were 18.5%, 23.6% and 29.3%, for catheter-associated urinary tract infections (CAUTI), central line-associated bloodstream infections (CLABSI) and ventilator-associated pneumonia (VAP), respectively. Limited data exist on the economic burden of HAI, particularly in developing countries. However, available evidence from the USA and Europe suggests a multi-billion dollar impact.

Risks of developing a HAI are common across developed and developing countries and relate to multiple factors including the health care system and its organization, health care interventions and patient status. Significant progress has been made to reduce or eliminate HAI in many parts of the world, but no country has successfully eliminated the entire risk of acquisition. An additional concern is the underlying threat to all populations in all countries from antimicrobial resistance (AMR), given that antimicrobials are the treatment of choice for infections. However, the international call to action against AMR includes more than the prevention and management of HAI. This increasing global challenge has highlighted the importance of fundamental infection prevention and control (IPC) measures when providing health care where acquired infections may not be treatable (4-6). A recent WHO report, produced in collaboration with Member States and other partners, outlines the magnitude of AMR and the current state of surveillance worldwide (7).

The International Health Regulations (IHR) give further weight to IPC as a central strategy for dealing with public health threats of international concern (8). These strategies have been tested recently based on infectious diseases such as the Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS).

In summary, HAI can be described as a systems problem in that it is both influenced by and impacts on the six building blocks of health systems (9), particularly those related to service delivery. Strategies to prevent HAI exist in complex health care systems and, as such, they must embrace issues of structure, governance, accountability and human factors. Health care workers need to function within a

system that supports the implementation of the right interventions at the right time to maintain patient safety and, at the same time, they must be accountable for the performance of their own safe and competent practices.

In 2009, WHO published the report of the expert group of the IPC Informal Network that outlined eight core components of national and facility level IPC programmes (10). The report and associated work was the product of a collaborative effort across WHO and led by the Biorisk Reduction for Dangerous Pathogens Unit from the Department of Epidemic and Pandemic Alert and Response. The original aim of the 2009 work was to develop the meeting report into a more formal WHO publication and to issue it as a “best practice principle” or a similar type of document.

In 2013, the systematic review and evidence-based guidance on organization of hospital infection control programmes (SIGHT) group, including WHO, published a systematic review and expert consensus on the organization of effective IPC programmes in hospitals. A total of 92 studies published from 1996 to 2012 were assessed and 10 key (core) components were identified as the main elements for IPC programmes designed to reduce HAIs and improve patient safety (11).

The objective of this project undertaken by the WHO IPC Global Unit (IPC-GU) is to use the WHO guideline development process to formulate evidence- and consensus-based recommendations to identify the core elements for effective IPC programmes at the national and facility level, supported by the previous list of essential core components and by the research published in the scientific literature. The ultimate aim is to support Member States in their efforts to develop and strengthen IPC programmes at national and facility level, both in their strategic approach and field implementation, within the context of implementing the AMR global action plan and health security agenda. This systematic review was conducted by the IPC-GU team to evaluate the results and the quality of research targeting effective IPC programmes and interventions aimed at reducing HAIs and improving practices at health facility level, with a particular focus on acute care hospitals. In agreement with the WHO Guidelines Review Committee, the WHO IPC-GU team has undertaken an update of the review published by the SIGHT group in 2015 using the same methodology.

## 2. Methodology

### 2.1 Research question

The main research question was: “What are the core elements for an effective IPC programme aimed at reducing HAIs, including those due to antimicrobial-resistant pathogens, and improving practices in acute care health facilities?” Specifications of this question were articulated based on the nine dimensions (Table 1) identified by Zingg and colleagues for the SIGHT project (11).

### 2.2 Literature search

We searched Medline, the Cochrane Controlled Trials Register, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), the Excerpta Medica Database (Embase), the Outbreak Database and the WHO Institutional Repository for Information Sharing (IRIS) for reports published from January 1, 2013 to November 23, 2015. The search was stratified by nine dimensions that were addressed separately (Table 1). A comprehensive list of search terms was used, including Medical Subject Headings (MeSH) (Appendix 1).

**Table 2.1: Dimensions and corresponding thematic areas**

Dimension N°	Thematic area	Description
1	Organization and structure	Organizational and structural arrangements to implement infection control programmes, including access to qualified infection control professionals and management roles.
2	Surveillance	Targets and methods of HAI surveillance, outbreak management and the role of feedback.
3	Education and training	Methods and effectiveness of educating and training health care workers.
4	Behaviour change strategies	Effectiveness of interventions on behavioural change and quality of care (that is, multimodal strategies).
5	Standard and transmission-based precautions	Overview and effectiveness of local policies and resources for standard and transmission-based isolation precautions.
6	Auditing	The process of auditing and its impact on HAI.
7	Patient participation	Patient empowerment and involvement in the prevention of HAI.
8	Target setting	Setting targets or goals and the impact on HAI

		prevention.
9	Knowledge management	A range of strategies to identify, create and distribute information and data within and outside an institution.
HAIs: health care-associated infections		

### 2.3 Eligibility criteria

Studies were eligible for inclusion if they were performed in an acute care institution setting and described an IPC intervention fitting into one of the nine identified dimensions with a target population of health care workers or patients in the context of infection control. A broad range of study design types was considered, including both quantitative (randomized controlled trials [RCTs], non-randomized controlled clinical trials [NRCTs], case-control studies, controlled before-and-after studies [CBAs], interrupted time series [ITT], non-controlled cohort studies and non-CBAs) and qualitative (in-depth interviews, questionnaires, surveys, focus groups and direct observations) or a combination of quantitative and qualitative investigations. Appendix 2 provides details of inclusion criteria used. Reviews, letters, notes, theses, conference proceedings and opinion articles that did not report primary data were excluded. Interventions related to non-acute care (such as community care, primary care, antibiotic prescribing or some combination thereof) and long-term care settings were excluded. Antibiotic stewardship, cost-effectiveness and occupational health were not addressed.

### 2.4 Study selection

We began with an initial assessment comprising the screening of titles and abstracts against the inclusion/exclusion criteria by six primary reviewers assigned to the nine dimensions. All reports that had relevant titles, but no abstracts were read in full. One third (30%) of titles and abstracts in each dimension were screened by a secondary reviewer and disagreements resolved by consensus or by a third reviewer if no agreement could be achieved. Studies in English, French, Portuguese and Spanish were included if a title and/or abstract were available in English for review.

The full text was obtained for studies that met the inclusion/exclusion criteria or when there was insufficient information to make an informed judgement on relevance. If the full text could not be retrieved, the study was excluded from further review. A final decision for inclusion was made after full text review by the same six primary reviewers. All studies were retained for data extraction. However, only those of an appropriate study design type according to the Cochrane Effective Practice and Organization of Care (EPOC) risk of bias criteria (12) underwent quality assessment.

### 2.5 Data extraction

The six reviewers extracted data in a predefined evidence table as previously used by Zingg and colleagues and critically appraised the retrieved studies. Any disagreements were resolved through discussion or after consultation with the senior project lead when no agreement could be met.

## **2.6 Quality assessment**

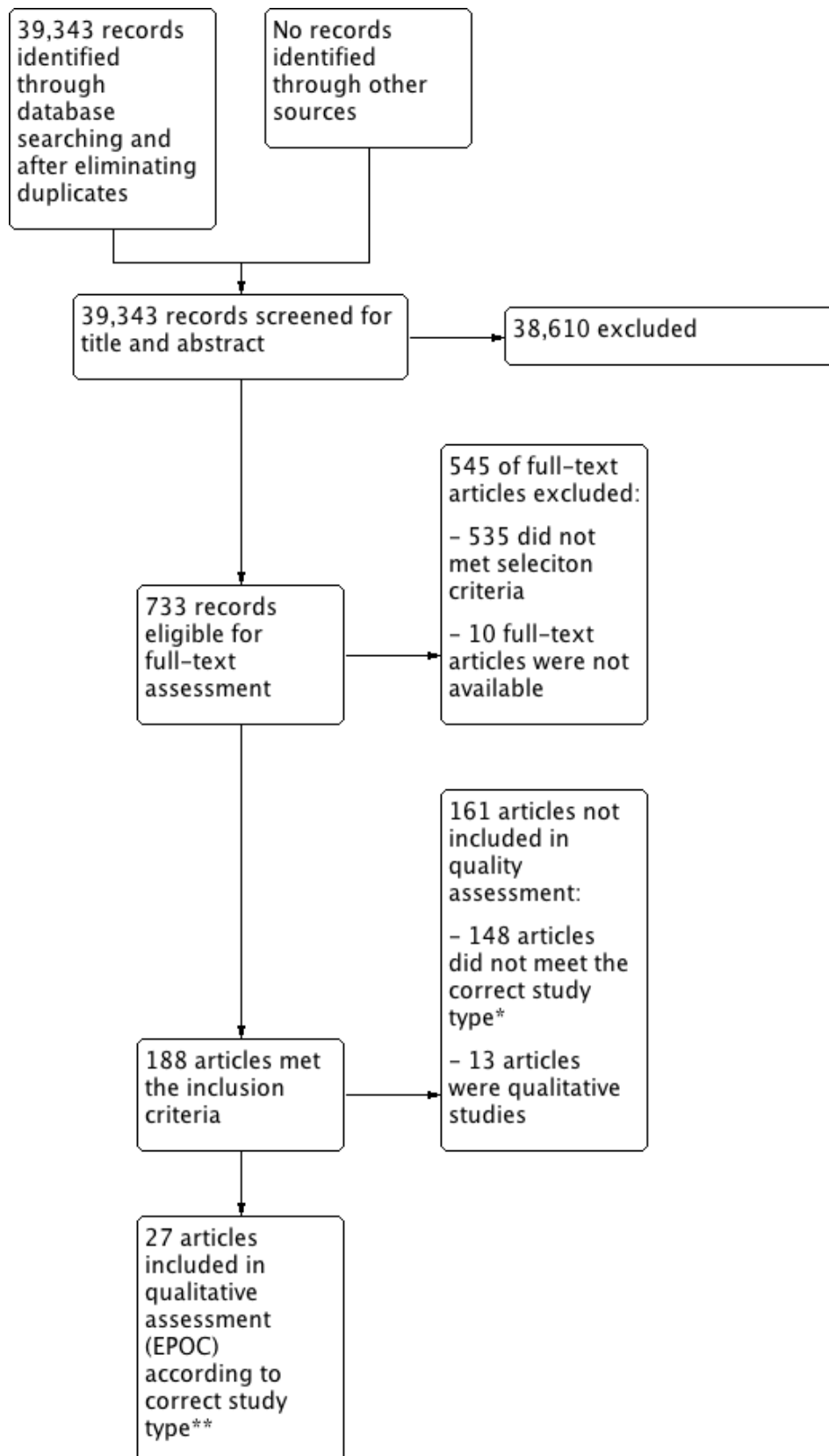
Individual studies were assessed for risk of bias according to the EPOC quality assessment framework using the standard EPOC (12) criteria (Appendix 3). The quality of evidence is judged to be high, low or with an unclear risk of bias across the respective criteria corresponding to the study design type. As defined by EPOC, only RCTs, NRCTs, CBAs or ITS were included in the quality assessment. Two reviewers performed the quality assessment for all studies. Disagreements were resolved by consensus or consultation with the project methodologist if no agreement could be reached.

### **3. Results**

#### **3.1 Summary**

Our search combining all nine dimensions identified a total of 39 343 titles and abstracts. After completing our initial screening, 733 studies were retrieved for full text review; 188 met the outlined inclusion criteria. Of these, only 27 studies were eligible for quality assessment according to the EPOC criteria (Figure 1) (13-39). Data extraction was completed for all 188 studies and studies not included in the EPOC evaluation were considered separately. A summary of the studies included in the EPOC evaluation is provided in Appendix 4.

**Figure 3.1: Flow chart of the study selection process**



\*Before-and-after studies; cohort studies.

\*\*Randomized controlled trials; non-randomized controlled trials; controlled before-and-after studies; interrupted time series.

Of the 27 studies included for quality assessment and analysis, four broad categories were apparent, based on the focus of the interventions and the primary outcomes: hand hygiene improvement (10 studies) (14, 20, 22, 23, 25, 26, 31, 32, 37, 38); prevention of multidrug-resistant organism (MDRO) transmission and HAI (9 studies) (13, 16, 17, 19, 21, 24, 25, 33, 34); prevention of CLABSI (4 studies) (15, 18, 30, 36); and prevention of VAP (4 studies) (27, 28, 35, 39).

In addition to these 27 studies, a further 148 studies were identified that met the inclusion criteria, but not the EPOC criteria based on study design. Although these 148 studies were ineligible for the main analysis, it was felt that they could still provide valuable information relevant to the broader framework and discussion for the development of recommendations on the core elements of IPC programmes. An overall analysis of this report is provided in Section 4 (Summary results for non-EPOC studies).

**Table 3.1: Types of study design contributing to the evidence**

Study design	EPOC studies	non-EPOC studies	Qualitative
RCT	11 (41%)		
ITS	14 (52%)		
CBA	2 (7%)		
Before-and-after/cohort		148 (100%)	
Qualitative			13 (100%)
Total	27	148	13

EPOC: Effective Practice and Organization of Care; RCT: randomized controlled trial; ITS: interrupted time series; CBA: controlled before-and-after.

### 3.2 Key components identified

As this report was conducted as an update to the original SIGHT report by Zingg and colleagues, the components identified from their work were maintained as the same core components for this systematic review. Of the identified 27 studies, most (13 studies) (14, 15, 17, 20, 22, 23, 26, 29, 32, 36-39) were in support of core component eight as they were behavioural change interventions based on the use of multimodal strategies or bundles. However, 12 studies did not fit the original core component structure because they were based on a single intervention, which could not be categorized in any of the SIGHT components. Therefore, they were included to form a new category named “single intervention” (13, 16, 19, 21, 24, 27, 28, 30, 31, 33-35). Table 3 provides a complete breakdown of studies classified by core components.

**Table 3.2: EPOC studies categorized by core component according to study design and intervention studied**

Core component	RCT	ITS	CBA	Total
CC1: Infection control programme		1		1
CC2: Ward occupancy and workload				
CC3: Materials, equipment and ergonomics		1		1
CC4: Use of guidelines in combination with education and training				
CC5: Team- and task-oriented training and education		5		6
CC6: Standardization of audits		1		2
CC7: Surveillance and feedback		1		1
CC8: Multimodal strategies and tools	2	10	1	13
CC9: Champions			1	1
CC10: Organizational culture	1	2		3
Other: Single intervention	8	3	1	12

CC: core component; RCT: randomized controlled trial; ITS: interrupted time series; CBA: controlled before-and-after.

Given the limited evidence identified during this updated systematic review, we summarize the newly identified studies according to the four key categories as mentioned above.

### 3.3 Hand hygiene improvement

#### 3.3.1 Identified studies

The systematic review revealed a total of 10 studies (14, 20, 22, 23, 25, 26, 31, 32, 37, 38) retrieved from dimensions 1 (organization and structure), 2 (surveillance) and 4 (behaviour change strategies) that met both the inclusion and EPOC criteria, that is, three RCTs (22, 31, 37), one CBA (26), five ITS (14, 20, 23, 25, 38) and one stepped wedge trial (32). Eight of the 10 studies included a multimodal strategy (14, 20, 22, 23, 26, 32, 37, 38), while only two were single intervention studies (25, 31). All included studies had the same intervention population (health care workers) and primary outcome (improving hand hygiene compliance). All studies were performed in high-income countries and conducted in both single (six studies) (14, 20, 23, 25, 26, 38) and multicentre facilities (four studies) (22, 31, 32, 37).

#### 3.3.2 Summary of the findings

The first RCT by Huis and colleagues reported a significant increase in hand hygiene compliance by increasing social influence and enhanced leadership when developing hand hygiene strategies (21) (odds ratio [OR]: 1.64; 95% confidence interval [CI]:1.33–2.02;  $P < 0.001$ ). In a RCT by Reisinger and colleagues, they failed to show any hand hygiene improvement between groups that had point-of-use reminder signs (using theoretically grounded messages) vs. those that did not (31). In the third RCT by Stevenson and colleagues, a significant change in absolute “complete hand hygiene compliance” was observed in the intervention hospitals (20.1%) compared to

control hospitals (−3.1%;  $P=0.001$ ). This occurred following implementation of individualized multimodal strategies for hand hygiene improvement in resource-limited US hospitals, most notably by offering incentives to staff by providing rewards based on participation and performance (35).

In a CBA study by Lieber and colleagues, a multimodal strategy was used and achieved significant change in hand hygiene compliance (36.6% to 71%, respectively;  $P<0.001$ ). However, this study also demonstrated the influence of hand hygiene champions as the retirement of a senior physician known to be a powerful hand hygiene champion led to a significant decrease in hand hygiene compliance across disciplines (nurses: 50.8% to 7.5%;  $P<0.001$ ; physicians: 50.7% to 2.6%;  $P<0.001$ ) (26).

In the stepped wedge trial by Rodriguez and colleagues, the five thematic areas of a multimodal strategy were tested. They observed an increase in hand hygiene compliance among staff, but also an association between the intervention and hand hygiene compliance (OR 1.17; 95% CI: 1.13–1.22) (32).

All five ITS studies implemented a multimodal strategy using similar strategic elements, but there were variations in the exact approach to implementing these interventions (14, 20, 23, 25, 38). These elements included a system change approach, educational interventions, evaluation and feedback tools, reminders in the workplace and promotion of a patient safety culture.

A study by Kwok and colleagues did not report any significant change in hand hygiene compliance despite using a multimodal approach that emphasized an automated training system for self-directed learning (25). Conversely, Higgins and colleagues noted a significant change in the overall technique and adherence to compliance (42% to 84%) with an added emphasis on the incorporation of automated teaching technology and an accompanying audit tool into a broader hand hygiene programme (19).

In a study by Johnson and colleagues, there was an overall increased hand hygiene adherence rate (58% to 98%), as well as an overall decrease in CLABSI rates during the same time period (4.08 per 1000 device-days to 0.42 per 1000 device-days), following the implementation of a hand hygiene action plan feeding into the overall multimodal implementation strategy (22).

Al-Tawfiq and colleagues achieved a significant change in overall hand hygiene compliance (38% to 85%;  $P<0.001$ ) and overall decreases in device-associated infections (VAP: 6.12 to 0.78/1000 device days;  $P<0.001$ ; CLABSI: 8.23 to 4.8/1000 device days;  $P<0.04$ ; CAUTI: 7.08 to 3.5/1000 device days;  $P<0.01$ ) and methicillin-resistant *Staphylococcus aureus* (MRSA) infections (0.42 to 0.08/1000 patient days;  $P<0.001$ ) by implementing a multimodal strategy over 5 years with a strong emphasis on feedback and communication and visible engagement by senior leadership (14).

Talbot and colleagues achieved similar significant changes, again in overall hand hygiene compliance rates ( $P<0.0001$ ), as well as inversely-correlated device-associated standardized infection ratios ( $R^2 = 0.70$ ). A key difference in their implementation strategy included the added value of financial incentives linked to a unit or department's performance in relation to hand hygiene compliance (36) and reinvested by the unit in further improvement actions.

### **3.4 Prevention of VAP**

#### ***3.4.1 Identified studies***

The systematic review identified a total of four studies (27, 28, 35, 39) that met both the inclusion and EPOC criteria: 3 RCTs (27, 28, 35) and one ITS (39). All RCTs were retrieved from dimension 1 (organization and structure) and the ITS from dimension 3 (education and training). All studies involved the use of a single intervention and were conducted in one high-income country (35) and three upper-middle-income countries (27, 28, 39). Each study shared the same intervention population (patients) with the same outcome measure (prevention of VAP), but there was a slight variation in the patient age groups, that is, three adult groups (27, 35, 39) and one paediatric group (28).

#### ***3.4.2 Summary of the findings***

In the two RCTs by Seguin and colleagues and Lin and colleagues, the impact of oral care on the reduction and prevention of VAP was investigated (27, 35). Seguin and colleagues tested the use of povidone-iodine preventive oral care and found no evidence of effectiveness in severely brain injured or cerebral haemorrhage patients (35). By contrast, Lin and colleagues used preoperative chlorhexidine 0.2% oral rinse vs. saline rinse and observed a significant reduction in the incidence of postoperative VAP ( $P < 0.049$ ) (27).

In a study by Liu and colleagues, paediatric patients were randomized into three groups to investigate the impact of mechanical cleaning (three vs. two times daily vs. control) of endotracheal tubes with sterile urethral catheters to reduce biofilm formation on VAP rates. A significant reduction in the occurrence of VAP was observed ( $P < 0.005$ ) (28).

In an ITS study by Viana and colleagues, a decrease was found in mean VAP rates (18.6 to 11.4/1000 ventilator days) following the implementation of a VAP educational module together with a bundle checklist and standardization of oral care in all patients (39).

### **3.5 Prevention of CLABSI**

#### ***3.5.1 Identified studies***

The systematic review revealed a total of four studies (15, 18, 30, 36) from dimensions 1 (organization and structure), 3 (education and training) and 4 (behaviour change strategies) that met both the inclusion and EPOC criteria, that is, one RCT (30) and three ITS (15, 18, 36). All four studies were from the USA and ranged in intervention scope from two single (19, 30) to two multimodal (15, 36) strategies implemented in intensive care units (ICUs) with a mixed target population of patients (15, 18, 30) and health care workers (36).

#### ***3.5.2 Summary of findings***

Milstone and colleagues conducted a RCT to investigate the benefits of daily chlorhexidine bathing with impregnated cloths vs. standard bathing in critically ill children across 10 paediatric ICUs at five hospitals in the USA. Although a lower incidence was recorded in CLABSI rates in the intervention group, the reduction was not statistically significant (30).

A single intervention ITS study was performed by Gerolemou and colleagues to evaluate the effectiveness of a simulation-based training module for nurses on sterile techniques for central vein catheterization. During a 12-month follow-up period after completion of the simulation-based training, the mean CLABSI rate in the unit decreased by 85% from 2.61 to 0.4 infections per 1000 catheter-days ( $P=0.02$ ) (18).

The remaining two ITS studies conducted a multimodal strategy with some common elements: educational interventions; evaluation and feedback; infrastructure or system change; promotion of patient safety culture; and providing additional resources/materials to frontline health care (15,36). By incorporating simulation training and providing already assembled catheter kits, Allen and colleagues were able to observe a reduction in CLABSI in one of two ICUs (2.72 per 1000 catheter-days to 0.40 per 1000 catheter-days;  $P<0.01$ ) (15). Shepherd and colleagues used a quality initiative attempting to achieve a complete system change, including leveraging leadership support for the reduction and prevention of CLABSI rates (36). This study observed an overall decrease in CLABSI rates when comparing baseline to intervention periods (6.0 to 1.43 per 1000 catheter-days) (36).

### **3.6 Prevention of MDRO transmission and HAI**

#### **3.6.1 Identified studies**

The systematic review revealed a total of nine studies (13, 16, 17, 19, 21, 24, 29, 33, 34) from dimensions 1 (organization and structure), 2 (surveillance), 4 (behaviour change strategies) and 5 (standard and transmission-based precautions) that met both the inclusion and EPOC criteria, that is, four RCTs (13, 19, 21, 33), one CBA (24) and four ITS (16, 17, 29, 34). Eight studies were from high-income (13, 16, 17, 19, 21, 29, 33, 34) countries and one study was from a LMIC (24). All involved mixed populations across multicentre hospitals. Outcomes varied across studies, including reductions in MRSA infections (17, 21, 34), MDRO transmission (19, 33) and general HAI prevention (that is, *Clostridium difficile* and vancomycin-resistant enterococci [VRE])(13, 16, 24, 29). Seven studies were based on single interventions (13, 16, 19, 21, 33, 34) and two on multimodal strategies (17, 29).

#### **3.6.2 Summary of findings**

In the four RCTs, all studies examined a single intervention strategy investigating universal vs. targeted decolonization (21), rapid vs. culture-based screening (33), universal gown and glove use (19) and daily chlorhexidine bathing (13). Huang and colleagues observed that universal decolonization was more effective than targeted decolonization or screening and isolation in reducing rates of MRSA clinical isolates and bloodstream infection from any pathogen ( $P<0.001$ ) (21). Conversely, the three remaining studies were unable to determine any effect due to a low observance of the

incidence of nosocomial MRSA (19, 33) infection or no statistically significant changes in HAI between groups (13).

Kampiatu and colleagues investigated the use of an antiseptic hand hygiene product with a sustained antibacterial effect and its impact on HAI acquisition rates in three wards during a three-month trial (the first and third months served as controls) (24). The results indicated a statistically significant reduction in all HAIs ( $P < 0.0005$ ) when comparing the pre-intervention standardized rate across all wards (23.1%) with the intervention period infection rate (0%) (24).

Derde and colleagues conducted an ITS and a RCT in 13 ICUs in eight countries to investigate the benefit of universal chlorhexidine body washing combined with hand hygiene improvement and to compare conventional vs. rapid screening for antimicrobial-resistant bacteria (16). An overall mean increase in hand hygiene compliance was observed, but no changes were observed in infection rates due to MRSA, VRE or highly-resistant *Enterobacteriaceae*, regardless of the type of screening (16).

Sarma and colleagues investigated the impact of universal screening on MRSA bacteraemia, improving the blood culture technique and re-issuing the blood culture policy indicating new requirements for authorization. The approach was shown to be effective based on a sharp fall in MRSA bacteraemia from 15 cases (2nd quarter, 2007) to six cases (3rd quarter, 2007) (beta-2: -0.577;  $P < 0.001$ ), particularly MRSA bacteraemia occurring  $\geq 48$  hours after hospitalization (34). The declining trend continued and reached zero in the 2nd quarter of 2009 and the 4th quarter of 2010 for those with  $\geq 48$  hours of hospitalization, but it was not statistically significant (beta-2: -0.216;  $P = 0.298$ ) (34).

Fisher and colleagues implemented a bundle strategy to reduce MRSA infections, which incorporated screening and isolation, evaluation and feedback, promotion of a patient safety culture and financial incentives based on performance. They observed a decline in MRSA bacteraemia from 0.26/1000 inpatient days (95% CI: 0.18-0.34) to 0.11/1000 inpatient-days (95% CI: 0.07-0.19), respectively, between the 1st quarter of 2004 and 2012 (17). Moreover, hand hygiene compliance rose significantly from 47% (95% CI: 44-49) to 69% (95% CI: 68-71), respectively, between the 1<sup>st</sup> quarter of 2009 and 2012 (17).

Mermel and colleagues implemented a hospital-wide, multidisciplinary six-pronged approach to combat endemic *C. difficile* infection rates. The most notable interventions were the development of an IPC action plan, improved monitoring and surveillance, improved sensitivity of *C. difficile* toxin testing, enhanced cleaning and an appropriate treatment protocol (29). An overall decrease in *C. difficile* incidence was observed from 2.2/1000 discharges during the 2nd quarter of 2006 to 3.6/1000 discharges during the 3rd quarter of 2012 ( $P < 0.005$ ) (29).

### 3.7 Risk of bias

A summary of the individual study assessments for quality is documented in

Appendices 5 and 6. No overall assessments were made, but rather each domain was assessed individually for each study.

Among the RCTs, several were scored as “unclear” for baseline outcome measurements as none were reported within the studies. Moreover, it remained unclear as to whether or not incomplete outcome data were appropriately addressed and if there was adequate protection against contamination.

In many ITS studies, it was unclear whether the intervention was independent from other actions, whether the primary outcomes were assessed blindly, and whether or not incomplete outcome data were adequately addressed.

Given the low quality of evidence retrieved in this review, it is not surprising that the quality assessment displays similar results or remains unclear. This highlights further the need for quality improvement in future IPC research.

#### **4. Summary results for non-EPOC studies**

A total of 148 studies could not be assessed by EPOC because they were non-CBA studies (120/148; 81%), cohort studies (27/148; 18%), or case-control studies (1/148; 0.7%). Most studies were published in 2013 (71/148; 48%), followed by 2014 (38/148; 26%), 2015 (36/148; 24%), 2016 (2/148; 1.4%), and 2012 (1/148; 0.7%). The vast majority of papers were published in English (142/148; 96%), followed by Spanish (5/148; 3.4%) and Portuguese (1/148; 0.7%) and conducted in high-income countries (100/148; 68%), followed by upper-middle (22/148; 14.8%), lower-middle (20/148; 13.6%) and low-income countries (4/148; 2.7%). Most non-EPOC studies were from the Region of the Americas/Pan American Health Organization (66/148; 45%) and the European Region (33/148; 22.4%). Three studies were from the African Region (2.0%), 12 from the Eastern Mediterranean Region (8.2%), 11 from the South-East Asia Region (7.5%), 22 from the Western Pacific Region (15%) and one cross-regional (0.7%).

**Table 4.1: Study characteristics of non-EPOC studies**

<b>Study characteristics</b>	<b>No. (%)</b>
<i>Study design</i>	
Non-controlled before-and-after	120 (81.08)
Cohort	27 (18.24)
Case-control	1 (0.68)
<i>Language</i>	
English	142 (95.95)
Portuguese	1 (0.68)
Spanish	5 (3.38)
<i>Year of publication</i>	
2012	1 (0.68)
2013	71 (46.97)
2014	38 (25.68)
2015	36 (24.32)
2016	2 (1.35)
<i>Income level</i>	
Low	4 (2.70)
Lower-middle	20 (13.51)
Upper-middle	22 (14.86)
High	100 (67.57)
Mixed income	2 (1.35)
<i>WHO region</i>	
African Region	3 (2.03)
Region of the Americas/Pan American Health Organization	66 (44.59)
Eastern Mediterranean Region	12 (8.11)
European Region	33 (22.30)
South-East Asia Region	11 (7.43)
Western Pacific Region	22 (14.86)
Multiple regions	1 (0.68)

Hand hygiene compliance was the primary outcome of most non-EPOC studies (36/148; 24.3%), followed by CLABSI (33/148; 22.3%). Other primary outcomes include VAP (18/148; 12.2%), CAUTI (11/148; 7.4%), MDRO-MRSA (11/148; 7.4%), bloodstream infection (BSI) (7/148; 4.7%), bundle compliance (7/148; 4.7%), HAI (7/148; 4.7%), surgical site infection (SSI) (7/148; 4.7%) and catheter-related bloodstream infection (CRBSI) (5/148; 3.4%). There were fewer than five non-EPOC studies with *C. difficile* infection (1/148; 0.7%), health care-associated pneumonia (HAP) (1/148; 0.7%), late-onset sepsis (LOS) (2/148; 1.3%), unspecified MDRO (1/148; 0.7%), ventilator-associated tracheobronchitis (VAT) (1/148; 0.7%) or VRE (1/148; 0.7%) as the primary outcome.

**Table 4.2: Primary outcomes for non-EPOC studies**

Primary outcome	N (%)
BSI	7 (4.73)
Bundle	7 (4.73)
CAUTI	11 (7.43)
CDI	1 (0.68)
CLABSI	33 (22.30)
CRBSI	5 (3.38)
HAI	7 (4.73)
HAP	1 (0.68)
HH	36 (24.32)
LOS	2 (1.35)
MDRO-MRSA	11 (7.43)
MDRO-UNSP	1 (0.68)
SSI	7 (4.73)
VAP	18 (12.24)
VAT	1 (0.68)
VRE	1 (0.68)

BSI: bloodstream infection; Bundle: bundle compliance; CAUTI: catheter-associated urinary tract infection; CDI: *C. difficile* infection; CLABSI: central line-associated bloodstream infection; CRBSI: catheter-related bloodstream infection; HAI: health care-associated infection; HAP: health care-associated pneumonia; HH: hand hygiene; LOS: late-onset sepsis (neonates only); MDRO-MRSA: transmission of methicillin-resistant *Staphylococcus aureus*; MDRO-UNSP: transmission of any multidrug-resistant organism; MRSA: infection with methicillin-resistant *Staphylococcus aureus*; SSI: surgical site infection; VAP: ventilator-associated pneumonia; VAT: ventilator-associated tracheobronchitis; VRE: vancomycin-resistant enterococci.

The vast majority of non-EPOC studies were categorized within core component 8 (multimodal strategies and tools; 91/151; 60.3%) followed by core component 5 team- and task-oriented training and education; 23/151; 15.2%). The complete breakdown of non-EPOC studies by core component and study design are shown in Table 6.

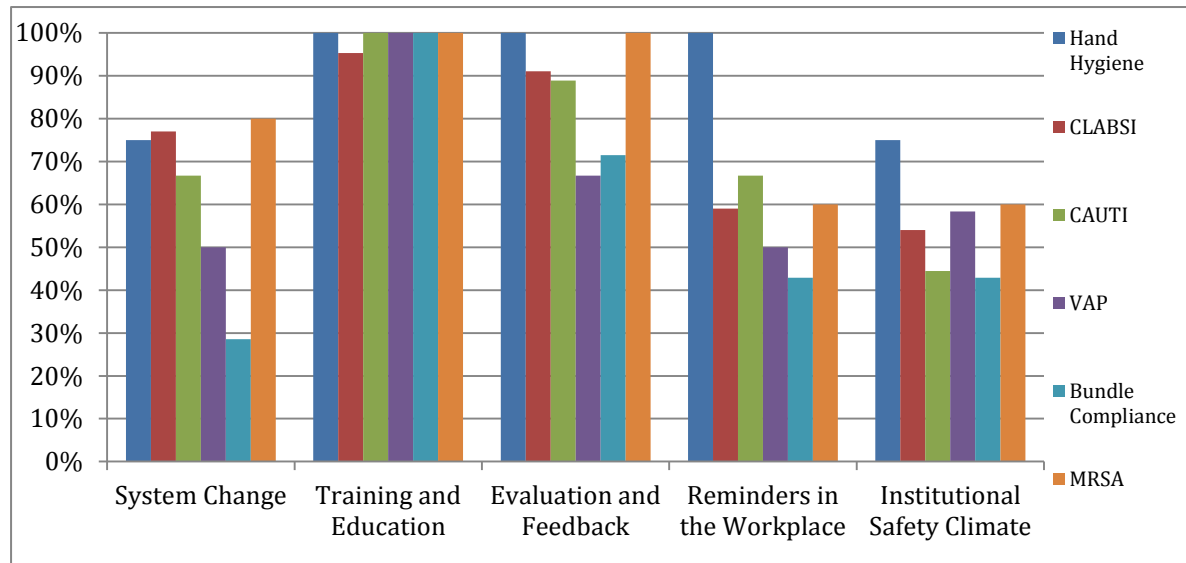
**Table 4.3: Non-EPOC studies categorized by core component according to study design and intervention studied**

<b>Core component</b>	<b>Before-after</b>	<b>Cohort</b>	<b>Case-control</b>	<b>Total</b>
CC1: Infection control programme	1	0	0	1
CC2: Ward occupancy and workload	0	0	0	0
CC3: Materials, equipment and ergonomics	1	0	0	1
CC4: Use of guidelines in combination with education and training	1	0	0	1
CC5: Team- and task-oriented training and education	22	1	0	22
CC6: Standardization of audits	3	1	0	3
CC7: Surveillance and feedback	4	4	0	8
CC8: Multimodal strategies and tools	72	18	1	91
CC9: Champions	0	1	0	1
CC10: Organizational culture	1	1	0	2
CC Other	18	1	0	19

CC: core component

The inclusion of implementation strategy components in the 91 non-EPOC studies categorized within core component 8 (multimodal strategies and tools) was documented and categorized by primary outcome. Primary outcomes of five or more non-EPOC studies are shown in Figure 2. The implementation strategy components are as follows: 1) system change; 2) training and education; 3) evaluation and feedback; 4) reminders in the workplace; and 5) institutional safety climate. Almost all studies included training and education as an implementation strategy component, while system change, reminders in the workplace and institutional safety climate were the least included components across all studies. All studies with hand hygiene or MRSA as the primary outcome included training and education and evaluation and feedback as implementation strategy components. System change was the most neglected implementation strategy component in non-EPOC studies with bundle compliance as the primary outcome.

**Figure 4.1: Implementation strategy components included in non-EPOC studies categorized within core component 8: multimodal strategies and tools**



CLABSI: central line-associated bloodstream infection; CAUTI: catheter-associated urinary tract infection; VAP: ventilator-associated pneumonia; MRSA: methicillin-resistant *S. aureus*.

## 5. Discussion

This review is intended to provide an update to the SIGHT report published by Zingg and colleagues (11) and to form background evidence for the development of recommendations on effective core elements of IPC programmes at the health care facility level (10). A 20-year period of scientific publications in the field of IPC is covered by the SIGHT report and this review. Using a slightly different, but rigorous system to include studies in the final selection based on quality, the SIGHT report identified 92 studies between 1996 and 2012.

This update of the SIGHT systematic review identified an additional 28 studies contributing towards the predefined core components using EPOC selection criteria. While scrutinizing these studies according to the core components identified by Zingg and colleagues (11), new contributions were included in all components, apart from components 2 (ward occupancy and workload) and 4 (use of guidelines in combination with education and training). However, the great majority were in support of core component 8 (behavioural change interventions) and based on the use of multimodal strategies or bundles. The main targeted outcomes were MDRO transmission and infection, HAIs in general, CLABSI and VAP. In a large number of studies (10/28), the intervention consisted of hand hygiene improvement strategies aimed at HAI reduction and an increase in hand hygiene compliance. Most studies using interventions that can be categorized according to the SIGHT core components for effective IPC programmes in hospitals showed a significant positive impact on the primary outcome measured and were mainly multimodal. Twelve studies could not be matched to any SIGHT core component and mainly included specific single interventions. Only four studies were conducted in developing countries and only one was a low-income country.

It must be acknowledged that according to the EPOC approach, the overall evidence of these 27 studies is of low quality. In addition, the updated review identified 148 studies (cohort or non-CBA), which could not be included in the evidence background for recommendation development due to exclusion criteria for EPOC quality evaluation. Similar to the EPOC selected studies, most interventions used in these investigations were multimodal. Despite the very low quality, we believe that this body of evidence should still be taken into consideration, especially when deliberating on the practical implementation of IPC, aspects of feasibility and learning new creative approaches.

In the field of IPC, there remains an overall abundance of low quality evidence, despite the vast amounts of published literature and the experts' evaluation of the results of this work will help to develop a strong research agenda. However, there is a general high-level recognition and increasing understanding of the critical importance of IPC, especially in support of the AMR agenda.

## Appendix 1: Search terms of the systematic review and evidence-based guidance on the organization of hospital infection control programmes (SIGHT)

### DIMENSION 1

#### Medline (via OVID)

- #1 cross infection.mp. or exp cross infection/
- #2 infection control.mp. or exp infection nontrol/
- #3 nosocomial infection.mp.
- #4 healthcare-associated Infection?.mp.
- #5 HAI.mp.
- #6 HCAI.mp.
- #7 catheter-related infection?.mp. or exp catheter-related infections/
- #8 exp catheterization, central venous/
- #9 CRBSI.mp.
- #10 catheter-associated infection?.mp.
- #11 methicillin-resistant *Staphylococcus aureus*.mp. or exp methicillin-resistant *Staphylococcus aureus*/
- #12 MRSA.mp.
- #13 *Clostridium difficile*.mp. or exp *Clostridium difficile*/
- #14 CDI.mp.
- #15 bacteremia.mp. or exp bacteremia/
- #16 pneumonia, ventilator-associated.mp. or exp pneumonia, ventilator-associated/
- #17 VAP.mp.
- #18 handwashing.mp. or exp handwashing/
- #19 exp decision making, organizational/
- #20 exp efficiency, organizational/
- #21 exp health facility administration/
- #22 exp hospital administration/
- #23 exp institutional management teams/
- #24 exp management audit/
- #25 exp management information systems/
- #26 exp models, organizational/
- #27 exp organizational culture/
- #28 exp organizational innovation/
- #29 exp personnel management/
- #30 exp program development/
- #31 exp total quality management/
- #32 leadership.mp.
- #33 exp infection control practitioners/
- #34 exp administrative personnel/

#35 \*"organization and administration"/

#36 exp infection control/or [organization & administration]

#37 exp organizational case studies/

#38 1or2or3or4or5or6or7or8or9or10or11or12or13or14or15or16or17or18

#39 exp knowledge management/

#40 exp organizational affiliation/

#41 exp career mobility/

#42 exp career mobility/

#43 exp employee discipline/

#44 exp employee grievances/

#45 exp employee incentive plans/

#46 exp employee performance appraisal/

#47 exp management quality circles/

#48 exp negotiating/

#49 exp ersonnel administration, hospital/

#50 exp personnel downsizing/ or exp personnel selection/

#51 exp personnel loyalty/

#52 exp "personnel staffing and scheduling"/

#53 exp personnel turnover/

#54 exp "salaries and fringe benefits"/

#55 exp staff development/

#56 exp workload/

#57 exp workplace/

#58 41or42or43or44or45or46or47or48or49or50or51or52or53or54or55or56 or57

#59 19or20or21or22or23or24or25or26or27or28or29or30or31or32or33or34or35or36  
or 37 or 39 or 40 or 58

#60 exp hospital-physician relations/

#61 exp professional practice/

#62 risk management/

#63 safety management/

#64 59or60or61or62or63

#65 38 and 64

#66 limit 65 to (humans and yr="1996 -current" and (English or French or German or Italian or Portuguese or Spanish))

## **EMBASE**

('organization and management'/mj OR 'hospital management'/exp OR 'organizational development'/exp OR 'organizational structure'/exp OR 'organizational efficiency'/exp OR 'leadership'/exp OR 'personnel management'/exp OR 'program development'/exp OR 'management audit' OR 'hospital administration' OR 'organizational efficiency' OR 'staff development' OR 'risk management'/exp) AND ('hospital infection'/exp OR 'cross infection'/exp OR 'infection control'/exp OR 'nosocomial infection'/exp OR 'healthcare-associated infection' OR 'hai' OR 'hcai' OR 'catheter-related infection'/exp

OR 'catheter infection'/exp OR 'central venous catheterization'/exp OR 'crbsi' OR 'catheter-associated infection'/exp OR 'methicillin resistant staphylococcus aureus'/exp OR 'mrsa'/exp OR 'clostridium difficile'/exp OR 'cdi' OR 'bacteremia'/exp OR 'ventilator associated pneumonia'/exp OR 'vap' OR 'handwashing'/exp OR 'hand washing'/exp) AND ([english]/lim OR [french]/lim OR [german]/lim OR [italian]/lim OR [portuguese]/lim OR [spanish]/lim) AND [humans]/lim NOT [medline]/lim AND [embase]/lim AND [1996-2011]/py

## **DIMENSION 2**

### **Medline (via OVID)**

- #3 Search infection prevention [TIAB] OR infection control [TIAB]
- #4 Search "infection control"[Mesh:NoExp]
- #5 Search nosocomial infection\* [TIAB]
- #7 Search "cross Infection"[Mesh]
- #8 Search (hospital acquired [TIAB] OR healthcare acquired [TIAB] OR health care acquired [TIAB] OR healthcare associated [TIAB] OR health care associated [TIAB]) AND (infection [TIAB] OR infections [TIAB])
- #9 Search HAI [TIAB] OR HCAI [TIAB]
- #10 Search bacteremia [TIAB] OR bacteraemia [TIAB]
- #13 Search "bacteremia"[Mesh]
- #14 Search (catheter associated [TIAB] OR catheter related [TIAB]) AND (infection [TIAB] OR infections [TIAB])
- #15 Search CRBSI [TIAB]
- #18 Search "catheter-related infections"[Mesh] #20 Search device associated infection\* [TIAB] #19 Search central line associated bloodstream infection\* [TIAB]
- #21 Search ventilator associated pneumonia [TIAB] OR VAP [TIAB] #24 Search "pneumonia, ventilator-associated"[Mesh]
- #25 Search surgical site infection\* [TIAB] OR SSI [TIAB]
- #27 Search "surgical wound infection"[Mesh]
- #28 Search (methicillin resistant *Staphylococcus aureus* [TIAB] OR methicillin resistant *Staphylococcus aureus* [TIAB] OR MRSA [TIAB]) AND (infection [TIAB] OR infections [TIAB])
- #32 Search *Clostridium difficile* infection\* [TIAB] OR CDI [TIAB] OR *Clostridium difficile* associated diarrhoea [TIAB] OR CDAD [TIAB] OR *Clostridium difficile* associated disease\* [TIAB]
- #33 Search (vancomycin resistant enterococcus [TIAB] OR vancomycin resistant enterococci [TIAB] OR VRE [TIAB]) AND (infection [TIAB] or infections [TIAB])
  
- #34 Search surveillance [TIAB]
- #38 Search ("population surveillance"[Majr:NoExp]) OR "sentinel"

surveillance"[Majr]

#39 Search (#3) OR #4

#40 Search (((((((((((((#5) OR #7) OR #8) OR #9) OR #10) OR #13) OR #14) OR #15) OR #18) OR #19) OR #20) OR #21) OR #24) OR #25) OR #27

#41 Search ((#28) OR #32) OR #33

#42 Search ((#39) OR #40) OR #41

#43 Search (#34) OR #38

#44 Search (#42) AND #43

#45 Search (#42) AND #43 Limits: English, French, German, Italian, Spanish, Portuguese, publication date from 1996/01/01 to 2010/12/31

### **DIMENSION 3**

#### **Medline (via PubMed)**

("education"[MeSH Terms] OR Educat\$[Text Word] OR Training[Text Word]) AND ("infection control"[MeSH Terms] OR "cross infection"[MeSH Terms] OR "cross infection"[Text Word] OR "infection control"[Text Word] OR "nosocomial infection"[Text Word] OR "healthcare-Associated Infection"[Text Word] OR "healthcare-related infection"[Text Word] OR HAI[Text Word] OR HCAI[Text Word] OR "catheter-related infections"[MeSH Terms] OR "catheter-related infection?"[Text Word] OR "catheter- associated infection?"[Text Word] OR "catheterization, central venous"[MeSH Terms] OR CRBSI[Text Word] OR "methicillin-resistant *Staphylococcus aureus*"[MeSH Terms] OR MRSA[Text Word] OR "methicillin-resistant *Staphylococcus aureus*"[Text Word] OR "*Clostridium difficile*"[MeSH Terms] OR "*Clostridium difficile*"[Text Word] OR CDI[Text Word] OR "bacteremia"[MeSH Terms] OR bacteremia[Text Word] OR "pneumonia, ventilator-associated"[MeSH Terms] OR VAP[Text Word] OR "ventilator associated pneumonia"[Text Word] OR "handwashing"[MeSH Terms] OR "handwashing"[Text Word]) AND ("humans"[MeSH Terms] AND (English[lang] OR French[lang] OR German[lang] OR Italian[lang] OR Spanish[lang] OR Portuguese[lang])) AND ("1996"[PDAT] : "3000"[PDAT]))

#### **EMBASE**

('training'/exp OR 'education'/exp) AND ('hospital infection'/exp OR 'cross infection'/exp OR 'infection control'/exp OR 'nosocomial infection'/exp OR 'healthcare-associated infection' OR 'hai' OR 'hcai' OR 'catheter-related infection'/exp OR 'catheter infection'/exp OR 'central venous catheterization'/exp OR 'crbsi' OR 'catheter-associated infection'/exp OR 'methicillin resistant staphylococcus aureus'/exp OR 'mrsa'/exp OR 'clostridium difficile'/exp OR 'cdi' OR 'bacteremia'/exp OR 'ventilator associated pneumonia'/exp OR 'vap' OR 'handwashing'/exp OR 'hand washing'/exp) AND ([english]/lim OR [french]/lim OR [german]/lim OR [italian]/lim

OR [portuguese]/lim OR [spanish]/lim) AND [humans]/lim AND [embase]/lim NOT [medline]/lim AND [1996- 2011]/py

#### **DIMENSION 4**

##### **Medline (via OVID)**

- #1 infection control.mp. or exp infection control/
- #2 ((infection adj control) or (infection adj3 prevention) or (infection adj3 management)).mp.
- #3 nosocomial infection?.mp. or exp Cross Infection/
- #4 (hospital acquired infection? or healthcare associated infection? or health care associated infection? or healthcare-associated infection? or health care-associated infection? or HAI or HCAI).mp.
- #5 methicillin resistant *Staphylococcus aureus*.mp. or meticillin resistant *Staphylococcus aureus*.mp. or exp methicillin-resistant *Staphylococcus aureus*/
- #6 MRSA.mp.
- #7 methicillin-sensitive *Staphylococcus aureus*.mp. or meticillin-sensitive *Staphylococcus aureus*.mp.
- #8 MSSA.mp.
- #9 *Clostridium difficile*.mp. or exp *Clostridium difficile*/
- #10 C-diff.mp. or CDI.mp. or CDAD.mp. or *Clostridium difficile* infection.mp. or *Clostridium difficile* associated disease?.mp.
- #11 catheter-related infections.mp.
- #12 bacter?emia.mp. or exp bacteremia/
- #13 (ventilator associated pneumonia or VAP).mp.
- #14 (device associated infection? or device-associated infection?).mp.
- #15 surgical site infection.mp.
- #16 \*disease outbreaks/pc [prevention & control]
- #17 handwashing/
- #18 (control or prevention or management or guideline\*).mp.
- #19 (hand? hygiene or hand washing or isolation or screening or precaution).mp.
- #20 decontamination.mp.
- #21 care bundle?.mp. or bundle?.mp. or high impact intervention?.mp. or multimodal.mp. or checklist?.mp. or care pathway?.mp.
- #22 behavio?r\* change.mp. or planned behavio?r\*.mp.
- #23 (decision making or intention? or attitude? or practic\* or routine? or procedure? or work\*).mp.
- #24 exp decision making/ or intention/ or exp health personnel attitudes/ or health personnel attitude?.mp.
- #25 (learning or training or education or knowledge).mp or exp education/ or exp staff development/ or professional development.mp.

#26 exp learning/ or organizational learning.mp.

#27 (workload or ((patient? adj1 staff) adj1 contact?) or practice improvement? or professional competence? or human factor).mp.

#28 (use? adj2 medical device?).mp.

#29 motivation.mp. or exp motivation/

#30 (organizational culture or organisational culture).mp.

#31 exp organizational innovation/ or organizational innovation.mp. or organisational innovation.mp.

#32 (organisational change or organizational change).mp.

#33 critical pathway?.mp.

#34 nurs\* practice pattern?.mp.

#35 interven\*.mp.

#36 (guideline? adj3 implement\*).mp.

#37 exp clinical competence/

#38 clinical governance.mp. or exp clinical governance/

#39 treatment guideline?.mp. or best practice?.mp.

#40 exp guideline adherence/ or ((guideline? adj adherence) or (guideline? adj compliance)).mp.

#41 exp clinical audit/ or audit.mp. or feedback?.mp.

#42 exp guidelines as topic/

#43 quality improvement/ or quality improvement?.mp.

#44 (service improvement or improvement methodolog\*).mp.

#45 exp health personnel/ or (health personnel or healthcare professional? or healthcare worker?).mp.

#46 (clinical staff or medical personnel or clinical personnel).mp.

#47 infection control practitioners/ or infection control practitioner?.mp. or infection control nurse?.mp. or infection control team?.mp.

#48 exp medical staff, hospital/ or (hospital staff or hospital personnel or hospital worker?).mp.

#49 exp nurses/ or (nurse? or nursing staff or nursing student?).mp.

#50 exp personnel, hospital/

#51 exp physicians/ or (physician? or doctor? or clinician? or surgeon? or resident? or medical student?).mp.

#52 community healthcare.mp. or community service?.mp. or exp community health services/ or community health care.mp. or community care.mp.

#53 exp primary health care/ or exp family practice/ or exp community health centers/ or health centre.mp. or GP practice.mp. or general practice.mp. or family practice.mp. or primary care.mp. or primary healthcare.mp. or primary health care.mp.

#54 family physicians/ or general practitioners/ or primary care physicians/ or hospitalists/ or (general practitioner? or family practitioner? or family doctor? or primary care doctor?.mp. or primary care physician?.mp.).mp.

#55 52or53or54

- #56 3or4or5or6or7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17
- #57 18or19or20or21
- #58 56 and 57
- #59 1or2or 58
- #60 22or23 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35
- #61 36or37 or 38 or 40 or 41 or 42 or 43 or 44
- #62 60or61
- #63 45or46 or 47 or 48 or 49 or 50 or 51
- #64 59and62and63
- #65 64 not 55
- #66 limit 65 to (yr="1996 - 2010" and (english or french or german or italian or portuguese or spanish))
- #67 remove duplicates form 66

## **DIMENSION 5**

### **Medline (via PubMed)**

- #1 Search "resource" OR "resources"
- #5 Search ("health resources"[Mesh] OR "resource allocation"[Mesh] OR "health manpower"[Mesh]) OR "organization and administration" [Subheading]
- #6 Search "requirement" OR "requirements"
- #7 Search "policy" OR "policies"
- #9 Search "policy making"[Mesh] OR "health policy"[Mesh] OR "economics"[Mesh]
  
- #10 Search "strategy" OR "strategies"
- #11 Search (((((#1) OR #5) OR #6) OR #7) OR #9) OR #10
- #12 Search standard precaution\*
- #13 Search "universal precaution"
- #14 Search "universal precautions"
- #16 Search "universal precautions"[Mesh]
- #17 Search "hand hygiene"
- #18 Search hand disinfection
- #19 Search "transmission based precautions"
- #20 Search "transmission based" AND "precautions"
- #21 Search "droplet precautions"
- #22 Search contact precaution\*
- #24 Search airborne precaution
- #25 Search airborne precautions
- #26 Search "isolation precaution"
- #27 Search "isolation precautions"
- #29 Search "patient isolation"[Mesh]

#30 Search ((((((((((((((#12) OR #13) OR #14) OR #16) OR #17) OR #18) OR #19) OR 20) OR #21) OR #22) OR #24) OR #25) OR #26) OR #27) OR #29

#31 Search hospital acquired infection\*

#32 Search healthcare associated infection\*

#33 Search nosocomial

#35 Search "cross infection"[Mesh]

#36 Search "infection control" OR "infection prevention"

#39 Search "prevention and control" [Subheading]

#40 Search *Clostridium difficile*

#41 Search MRSA

#42 Search VRE

#43 Search "vancomycin resistant enterococcus" OR "vancomycin resistant enterococci"

#44 Search ((((((((((#31) OR #32) OR #33) OR #35) OR #36) OR #39) OR #40) OR #41) OR #42) OR #43

#45 Search (#11) AND #30

#46 Search (#45) AND #44

#47 Search (#45) AND #44 limits: English, French, German, Italian, Spanish, Portuguese, publication date from 1996/01/01 to 2010/12/31

## **DIMENSION 6**

### **Medline (via PubMed)**

("clinical audit" [MeSH Terms] OR "management audit" [MeSH Terms] OR "audit\*" [Text Word] OR "auditing" [Text Word]) AND ("infection control"[MeSH Terms] OR "cross infection"[MeSH Terms] OR "cross infection"[Text Word] OR "infection control"[Text Word] OR "nosocomial infection"[Text Word] OR "healthcare-associated infection"[Text Word] OR "healthcare-related infection"[Text Word] OR HAI[Text Word] OR HCAI[Text Word] OR "catheter-related infections"[MeSH Terms] OR "catheter-related infection?"[Text Word] OR "catheter-associated infection?"[Text Word] OR "catheterization, central venous"[MeSH Terms] OR CRBSI[Text Word] OR "methicillin-resistant *Staphylococcus aureus*"[MeSH Terms] OR MRSA[Text Word] OR "methicillin-resistant *Staphylococcus aureus*"[Text Word] OR "*clostridium difficile*"[MeSH Terms] OR "Clostridium difficile"[Text Word] OR CDI[Text Word] OR "bacteremia"[MeSH Terms] OR bacteremia[Text Word] OR "pneumonia, ventilator-associated"[MeSH Terms] OR VAP[Text Word] OR "ventilator associated pneumonia"[Text Word] OR "handwashing"[MeSH Terms] OR "handwashing"[Text Word] OR "hand hygiene"[Text Word] OR "handrub\*" [Text Word] OR "hand rub"[Text Word] OR "handrub" [Text Word])

## **DIMENSION 7**

### **Medline (via PubMed)**

("patient participation"[MeSH Terms] OR "patient empowerment"[Text Word] OR "patient empowering"[Text Word] OR "empowering patients"[Text Word]) AND ("infection control"[MeSH Terms] OR "cross infection"[MeSH Terms] OR "cross infection"[Text Word] OR "infection control"[Text Word] OR "nosocomial infection"[Text Word] OR "healthcare-associated infection"[Text Word] OR "healthcare-related infection"[Text Word] OR HAI[Text Word] OR HCAI[Text Word] OR "catheter-related infections"[MeSH Terms] OR "catheter-related infection?"[Text Word] OR "catheter-associated infection?"[Text Word] OR "catheterization, central venous"[MeSH Terms] OR CRBSI[Text Word] OR "methicillin-resistant *Staphylococcus aureus*"[MeSH Terms] OR MRSA[Text Word] OR "methicillin-resistant *Staphylococcus aureus*"[Text Word] OR "clostridium difficile"[MeSH Terms] OR "Clostridium difficile"[Text Word] OR CDI[Text Word] OR "bacteremia"[MeSH Terms] OR bacteremia[Text Word] OR "pneumonia, ventilator-associated"[MeSH Terms] OR VAP[Text Word] OR "ventilator associated pneumonia"[Text Word] OR "handwashing"[MeSH Terms] OR "handwashing"[Text Word] OR "hand hygiene"[Text Word] OR "handrub\*" [Text Word] OR "hand rub"[Text Word])

## **DIMENSION 8**

### **Medline (via PubMed)**

("target\*" [Text Word] OR "target setting" [Text Word] OR "goal setting" [Text Word] OR goals [MeSH Terms] OR "organizational objectives" [MeSH Terms]) AND ("infection control"[MeSH Terms] OR "cross infection"[MeSH Terms] OR "cross infection"[Text Word] OR "infection control"[Text Word] OR "nosocomial infection"[Text Word] OR "healthcare-associated infection"[Text Word] OR "healthcare-related infection"[Text Word] OR HAI[Text Word] OR HCAI[Text Word] OR "catheter-related infections"[MeSH Terms] OR "catheter-related infection?"[Text Word] OR "catheter-associated infection?"[Text Word] OR "catheterization, central venous"[MeSH Terms] OR CRBSI[Text Word] OR "methicillin-resistant *Staphylococcus aureus*"[MeSH Terms] OR MRSA[Text Word] OR "methicillin-resistant *Staphylococcus aureus*"[Text Word] OR "clostridium difficile"[MeSH Terms] OR "Clostridium difficile"[Text Word] OR CDI[Text Word] OR "bacteremia"[MeSH Terms] OR bacteremia[Text Word] OR "pneumonia, ventilator-associated"[MeSH Terms] OR VAP[Text Word] OR "ventilator associated pneumonia"[Text Word] OR "handwashing"[MeSH Terms] OR "handwashing"[Text Word] OR "hand hygiene"[Text Word] OR "handrub\*" [Text Word] OR "hand rub"[Text Word])

## **DIMENSION 9**

### **Medline (via PubMed)**

'knowledge management'/exp OR 'knowledge management':ti,ab OR 'information management'/exp OR 'knowledge'/exp OR 'EVIDENCE BASED MEDICINE'/exp OR 'MEDICAL RECORDS SYSTEMS, COMPUTERIZED'/exp OR 'INFORMATION STORAGE AND RETRIEVAL'/exp OR 'INFORMATION DISSEMINATION'/exp OR 'USER COMPUTER INTERFACE'/exp OR 'DIFFUSION OF INNOVATION'/exp OR 'DECISION SUPPORT SYSTEMS, CLINICAL'/exp OR 'MEDICAL INFORMATICS'/exp OR 'INFORMATION SYSTEMS'/exp OR 'ORGANIZATIONAL INNOVATION'/exp OR 'SYSTEMS INTEGRATION'/exp OR 'KNOWLEDGE BASES'/exp

TIAB; title – abstract; MeSH: Medical Subject Headings.

## Appendix 2: Inclusion criteria

	<b>Inclusion criteria</b>	<b>Outcome measures</b>
Dimension 1	<ol style="list-style-type: none"> <li>1. Studies evaluating interventions to change or improve the organization or structure of IPC.</li> <li>2. Studies evaluating the role of hospital management and leadership.</li> <li>3. Studies evaluating the role of staffing, workload or work experience.</li> <li>4. Studies providing information about work processes in the context of patient safety and, specifically, HAI prevention.</li> <li>5. Studies evaluating infrastructure, ergonomics and work organization.</li> <li>6. Studies evaluating the role of organizational culture.</li> <li>7. Studies reporting qualitative research about perceptions, attitudes, and beliefs about the above-mentioned criteria.</li> </ol>	<ol style="list-style-type: none"> <li>1. Changes in HAI, such as HAI in general, or specific HAIs, for example, SSI, CLABSI/CRBSI, VAP, CDI, and CAUTI.</li> <li>2. Adherence to device management (including appropriate placement and use) and perioperative management.</li> <li>3. Shifts in the incidence of MDRO.</li> <li>4. Compliance with hand hygiene.</li> <li>5. Change (or establishment) in surveillance and feedback of HAIs, and hand hygiene compliance</li> <li>6. Perception of the above-mentioned outcomes by health care professionals.</li> </ol>
Dimension 2	<ol style="list-style-type: none"> <li>1. Studies evaluating the effect of surveillance and feedback of HAI (for example, SSI, CLABSI/CRBSI, VAP, CDI, and CAUTI) and hand hygiene compliance.</li> </ol>	

Dimension 3	<ol style="list-style-type: none"> <li>1. Studies evaluating education or training of healthcare professionals (yes/no; quantitative).</li> <li>2. Studies evaluating the effectiveness of specific training methodologies: <ul style="list-style-type: none"> <li>- Ex cathedra teaching</li> <li>- Written information</li> <li>- Visual cues</li> <li>- Bedside teaching</li> <li>- Focus groups</li> <li>- Workshops</li> <li>- Interactive teaching</li> <li>- (Knowledge) questionnaires</li> <li>- Simulation-based learning</li> <li>- Audiovisual learning</li> <li>- Guidelines.</li> </ul> </li> <li>3. Studies evaluating the role of health care workers in IPC training (peer-to-peer; train-the-trainer; external trainers; formal leaders).</li> <li>4. Studies reporting qualitative research about perceptions, attitudes and beliefs about the above-mentioned criteria.</li> </ol>	
Dimension 4	<ol style="list-style-type: none"> <li>1. Studies evaluating combined strategies for the prevention of HAI and improvement of hand hygiene compliance: <ul style="list-style-type: none"> <li>- Bundles</li> <li>- Multimodal strategies</li> <li>- Multidisciplinary strategies.</li> </ul> </li> <li>2. Studies evaluating barriers and/or facilitators for the prevention of HAI and improvement of hand hygiene compliance.</li> <li>3. Studies evaluating the effect of professional roles in the prevention of HAIs and improvement of hand hygiene compliance.</li> <li>4. Studies evaluating the effect of (personal) perceptions, attitudes, culture, views and (professional) experience for the prevention of HAI and improvement of hand hygiene compliance.</li> </ol>	

Dimension 5	<ol style="list-style-type: none"> <li>1. Studies evaluating the role of resources for standard and transmission-based isolation precautions and the consequences of resource modification.</li> <li>2. Studies evaluating the role of resources of established policies in relation to their effectiveness in IPC.</li> </ol>	
Dimension 6	<ol style="list-style-type: none"> <li>1. Studies evaluating the auditing process with feedback (peer evaluation or anonymous) in relation to IPC.</li> <li>2. Studies evaluating audits as a means to increase awareness of IPC efforts.</li> </ol>	
Dimension 7	<ol style="list-style-type: none"> <li>1. Studies evaluating the impact of patient participation through educational initiatives, in particular, patient willingness to remind health care workers to perform hand hygiene.</li> <li>2. Studies evaluating the empowerment of patients and promoting patients to take responsibility (or a more active role) in their own care.</li> </ol>	

Dimension 8	1. Studies evaluating the effectiveness of target setting or goals for the successful management of IPC programmes.	
Dimension 9	1. Studies evaluating the dissemination of knowledge within, into and out of an institution in relation to IPC.	

IPC: infection prevention and control; HAI: health care-associated infection; SSI: surgical site infection; CLABSI: central line-associated bloodstream infection; CRBSI: catheter-related bloodstream infection; VAP: ventilator-associated infection; CDI: *Clostridium difficile* infection; CAUTI: catheter-associated urinary tract infection; MDRO: multidrug-resistant organism/s.

### **Appendix 3: Risk of bias criteria for EPOC reviews (12)**

#### **Risk of bias for studies with a separate control group**

- Randomized controlled trials (RCTs)
- Non-randomized controlled trials (NRCTs)
- Controlled before-and-after (CBA) studies

Nine standard criteria are suggested for all RCTs, NRCTs and CBA studies. Further information can be obtained from the Cochrane handbook section on risk of bias.

1. Was the allocation sequence adequately generated?  
Score “low risk” if a random component in the sequence generation process is described (for example, referring to a random number table). Score “high risk” when a non-random method is used (for example, performed by date of admission). NRCTs and CBA studies should be scored “high risk”. Score “unclear risk” if not specified in the paper.
2. Was the allocation adequately concealed?  
Score “low risk” if the unit of allocation was by institution, team or professional and allocation was performed on all units at the start of the study, or if the unit of allocation was by patient or episode of care and there was some form of centralized randomization scheme, such as an on-site computer system or the use of sealed opaque envelopes. CBA studies should be scored “high risk”. Score “unclear risk” if not specified in the paper.
3. Were baseline outcome measurements similar?  
Score “low risk” if performance or patient outcomes were measured prior to the intervention and no important differences were present across study groups. In RCTs, score “low risk” if imbalanced, but an appropriate adjusted analysis was performed (for example, analysis of covariance). Score “high risk” if important differences were present and not adjusted for in analysis. If RCTs have no baseline measure of outcome, score “unclear risk”.
4. Were baseline characteristics similar?  
Score “low risk” if baseline characteristics of the study and control providers are reported and similar. Score “unclear risk” if it is not clear in the paper (for example, characteristics are mentioned in the text, but no data were presented). Score “high risk” if there is no report of characteristics in the text or tables or if there are differences between control and intervention providers. Note that in some cases an imbalance in patient characteristics may be due to recruitment bias whereby the provider was responsible for recruiting patients into the trial.
5. Were incomplete outcome data adequately addressed?  
Score “low risk” if missing outcome measures were unlikely to bias the results (for example, the proportion of missing data was similar in the intervention and control groups or the proportion of missing data was less than the effect size, that is, unlikely to overturn the study result). Score “high risk” if missing

outcome data was likely to bias the results. Score “unclear risk” if not specified in the paper. (Do not assume 100% follow-up unless stated explicitly.)

6. Was knowledge of the allocated interventions adequately prevented during the study?  
Score “low risk” if the authors state explicitly that the primary outcome variables were assessed blindly or the outcomes are objective, for example, length of hospital stay. Primary outcomes are those variables that correspond to the primary hypothesis or question defined by the authors. Score “high risk” if the outcomes were not assessed blindly. Score “unclear risk” if not specified in the paper.
7. Was the study adequately protected against contamination?  
Score “low risk” if allocation was by community, institution or practice and it is unlikely that the control group received the intervention. Score “high risk” if it is likely that the control group received the intervention (for example, if patients rather than professionals were randomized). Score “unclear risk” if professionals were allocated within a clinic or practice and it is possible that communication between intervention and control professionals could have occurred (for example, physicians within practices were allocated to intervention or control).
8. Was the study free from selective outcome reporting?  
Score “low risk” if there is no evidence that outcomes were selectively reported (for example, all relevant outcomes in the methods section are reported in the results section). Score “high risk” if some important outcomes are subsequently omitted from the results. Score “unclear risk” if not specified in the paper.
9. Was the study free from other risks of bias?  
Score “low risk” if there is no evidence of other risk of biases

### **Risk of bias for interrupted time series (ITS) studies**

Seven standard criteria are used for all ITS studies. Further information can be obtained from the Cochrane handbook section on risk of bias and from the draft methods paper on risk of bias under specific resources section of the EPOC website.

Note: If the ITS study has ignored secular (trend) changes and performed a simple t-test of the pre- versus post-intervention periods without further justification, the study should not be included in the review unless re-analysis is possible.

1. Was the intervention independent of other changes?  
Score “low risk” if there are compelling arguments that the intervention occurred independently of other changes over time and the outcome was not influenced by other confounding variables/historic events during the study period. If events/variables are identified, note what they are. Score “high risk”

if it is reported that the intervention was not independent of other changes in time.

2. Was the shape of the intervention effect pre-specified?  
Score “low risk” if the point of analysis is the point of intervention or if a rational explanation for the shape of the intervention effect was given by the author(s). Where appropriate, this should include an explanation if the point of analysis is not the point of intervention. Score “high risk” if it is clear that the condition above is not met.
3. Was the intervention unlikely to affect data collection?  
Score “low risk” if reported that the intervention itself was unlikely to affect data collection (for example, sources and methods of data collection were the same before and after the intervention). Score “high risk” if the intervention itself was likely to affect data collection (for example, any change in source or method of data collection reported).
4. Was knowledge of the allocated interventions adequately prevented during the study?  
Score “low risk” if the authors state explicitly that the primary outcome variables were assessed blindly or if the outcomes are objective, for example, length of hospital stay. Primary outcomes are those variables that correspond to the primary hypothesis or question defined by the authors. Score “high risk” if the outcomes were not assessed blindly. Score “unclear risk” if not specified in the paper.
5. Were incomplete outcome data adequately addressed?  
Score “low risk” if missing outcome measures were unlikely to bias the results (for example, the proportion of missing data was similar in the pre- and post-intervention periods or the proportion of missing data was less than the effect size, that is, unlikely to overturn the study result). Score “high risk” if missing outcome data were likely to bias the results. Score “unclear risk” if not specified in the paper. (Do not assume 100% follow-up unless stated explicitly.)
6. Was the study free from selective outcome reporting?  
Score “low risk” if there is no evidence that outcomes were selectively reported (for example, all relevant outcomes in the methods section are reported in the results section). Score “high risk” if some important outcomes are subsequently omitted from the results. Score “unclear risk” if not specified in the paper.
7. Was the study free from other risks of bias?  
Score “low risk” if there is no evidence of other risk of biases, for example, it should be considered if seasonality is an issue. For example, if January to June comprises the pre-intervention period and July to December the post-intervention, could the “seasons” have caused a spurious effect?

**Appendix 4: Details of the studies analysed and synthesized in the systematic review**

<b>Study</b>	<b>Design</b>	<b>Intervention</b>	<b>Sample size</b>	<b>Outcome</b>	<b>Impact</b>	<b>Risk of bias</b>	<b>SIGHT key components</b>
<b>Mermel et al, 2013, USA</b>	ITS	Multimodal C. difficile strategy - C. difficile infection plan - Morbidity and mortality of C. difficile - Improve C. difficile toxin testing using PCR - Enhanced cleaning - C. difficile treatment plan - Other occurring interventions	719-bed, tertiary care hospital	HAI (C. difficile)	The incidence of C. difficile infection decreased from 12.2 to 3.6/1000 discharges (adjusted P=0.005).	High risk: Intervention effect pre-specified plus intervention affects data collection. Unclear: Intervention independent plus blinding primary outcome plus incomplete primary outcome data.  High risk of bias	1/8
<b>Allen et al, 2014, USA</b>	ITS	Multimodal CLABSI programme - Simulation training - EMR-based documentation - Standardized CLABSI kits	2 ICUs, 1 facility MICU: 21 infections, 16 331 catheter- days SICU: 16 infections, 14 222 catheter- days	CLABSI	MICU: Decrease from 2.72 to 0.40/1000 catheter-days; P<0.01. SICU: No change, 1.09 to 1.14/1000 catheter-days; P<0.86.	Unclear: Intervention independent plus blinding primary outcome plus incomplete primary outcome data.  High risk of bias	3/5/8

<b>Gerolemou et al, 2014, USA</b>	ITS	Simulation-based training (CVC insertion)	46 nurses, CCU 7 infections, 4811 catheter-days	CRBSI	Decrease from 2.61 to 0.4/1000 catheter-days; P = 0.02	Unclear: Incomplete primary outcome data.  Medium risk of bias	5
<b>Johnson et al, 2014, USA</b>	ITS	Multimodal (quality improvement) hand hygiene project - Hand hygiene action plan to inform strategy - Hand sanitizer product selection and accessibility - Hand hygiene education for medical students prior to clerkship - Patient improvement approach (supplying information on hand hygiene “moments”) and speaking up - Compliance and	1 health centre 63 375 hand hygiene opportunities	Primary: Hand hygiene compliance Secondary: CLABSI	Primary: Increase from 58% to 98% (P <0 .001). Secondary: Significant decrease from 4.08 to 0.42/1000 device-days (P not available).	High risk: Intervention independent plus intervention affects data collection plus blinding primary outcome. Unclear: Incomplete primary outcome data.  High risk of bias	5/8/10

		accountability (hand hygiene monitoring) - Organizational culture, promotion of safety					
<b>Kwok et al, 2015, Australia</b>	ITS	Volunteer self-directed automated training system	1 hospital, 789 health care workers	Hand hygiene compliance	There was no significant change in compliance rates.	High risk: Intervention independent. Unclear: Intervention effect pre-specified plus blinding primary outcome plus incomplete primary outcome data.	5
<b>Viana et al, 2013, Brazil</b>	ITS	Educational module for VAP prevention	1 hospital, 1 ICU N=224 ventilated patients	VAP	Mean rate decreases from $18.6 \pm 7.8/1000$ ventilator-days to $11.8 \pm 7.8/1000$ ventilator-days (95% CI 15.5–21.7); P=0.002.	High risk: Blinding primary outcome. Unclear: Incomplete primary outcome data.	5/8
<b>Fisher et al., 2013, Singapore</b>	ITS	MRSA bundle - Active surveillance - Promotion of hand hygiene	Single facility	Primary: HAI (MRSA) Secondary: hand	Primary: Decrease from 0.26/1000 inpatient-days (95% CI: 0.18-0.34) to 0.11/1000 inpatient-days (95% CI: 0.07-0.19).	Unclear: Intervention independent plus blinding primary outcome plus incomplete primary	6/7/8

		(education and sociobehavioural measures) - Auditing hand hygiene compliance - Isolation or cohorting of MRSA patients - Public feedback - Financial rewards		hygiene compliance	Secondary: Increase from 47% (95% CI: 44-49) to 69% (95% CI: 68-71).	outcome data. High risk of bias	
<b>Huis et al, 2013, Netherlands</b>	RCT	Social influence and team leaders directed strategy for hand hygiene improvement in addition to: - Education - Reminders - Feedback - Targeting adequate supplies	3 hospitals, 67 wards/units 2733 nurses 10 785 hand hygiene opportunities	Hand hygiene compliance	The difference between both strategies showed an OR of 1.64 (95% CI:1.33–2.02) in favour of the team and leader-directed strategy.	Unclear: Baseline characteristics plus incomplete outcome primary data plus contamination. High risk of bias	8/10

<b>Talbot et al, 2013, USA</b>	ITS	Multimodal hand hygiene programme - Direct observation - Accountability structure and process - Financial incentives	Tertiary medical centre 109 988 hand hygiene opportunities	Hand hygiene compliance	Sustained increase in hand hygiene adherence ( $P<0.0001$ ).	Unclear: Intervention independent plus blinding primary outcome plus incomplete primary outcome data.  High risk of bias	8/10
<b>Lieber et al, 2014, Italy</b>	CBA	Multimodal hand hygiene programme (1) looking at sustainability;(2) loss in leadership - Education - Leadership engagement - Distribution of personal hand rub bottles - Advertising campaign for hand hygiene	1 hospital, 2 wards 1044 hand hygiene opportunities	Hand hygiene compliance	(1) Adherence for all health care workers was higher 4 years' post-intervention (71.0% compared to 36.6%; $P<0.001$ ). (2) Adherence dropped among physicians (50.7% - 2.6%) and nurses (50.8% - 7.5%) after a hand hygiene leader stepped down. ( $P<0.001$ ).	High risk: Allocation (sequence generation) plus allocation concealment plus baseline characteristics Unclear: Blinding primary outcome data plus contamination.  High risk of bias	<b>8/9</b>

<b>Al-Tawfiq et al, 2013, Kingdom of Saudi Arabia</b>	ITS	Multimodal hand hygiene programme - Hand hygiene compliance monitoring - Setting compliance goals - Feedback (posting data shared with health care workers) - Hand rub placement - Promotion (pins, education, banners) - Leadership commitment (organizational dashboard)	Community hospital 76 873 hand hygiene observations	<b>Primary:</b> hand hygiene compliance <b>Secondary:</b> HAI (MRSA); CLABSI; VAP; CAUTI	<b>Primary:</b> 38% (baseline) to 85% in 2011 (post-intervention) ( $P < 0.001$ ). <b>Secondary:</b> HAI: decrease from 0.42 to 0.08/1000 patient days; $P < .001$ CLABSI: decrease from 8.23 to 4.8/1000 device-days; $P < 0.04$ VAP: Decrease from 6.12 to 0.78/1000 device-days; $P < 0.001$ CAUTI: Decrease from 7.08 to 3.5/1000 device-days; $P < 0.01$ .	High risk: Intervention effect pre-specified. Unclear: Intervention independent plus blinding primary outcome plus incomplete primary outcome data.  High risk of bias	<b>8</b>
<b>Higgins et al, 2013, Ireland</b>	ITS	Multimodal hand hygiene programme - Hand hygiene compliance monitoring and posters	Single facility 1840 hand hygiene opportunities	Hand hygiene compliance	Hand hygiene technique and compliance improved significantly (20% to 86%) over the study period ( $P < 0.0001$ ).	High risk: Intervention independent plus intervention affects data collection. Unclear: Blinding primary outcome data	<b>8</b>

		<ul style="list-style-type: none"> <li>- increased supplies</li> <li>- ATP audits of hands</li> <li>- Automated training (SureWash)</li> </ul>				<p>plus incomplete primary outcome data.</p> <p>High risk of bias</p>	
<b>Rodriguez et al, 2015, Argentina</b>	Stepped wedge	<p>Multimodal hand hygiene programme</p> <ul style="list-style-type: none"> <li>- Leadership commitment</li> <li>- Surveillance of hand hygiene supplies</li> <li>- Utilization of reminders</li> <li>- Storyboard of the project</li> <li>- Feedback (hand hygiene compliance)</li> </ul>	10 429 hand hygiene opportunities 705 health care workers	Hand hygiene compliance	<p><b>Hand hygiene compliance:</b> Control 66% vs. intervention 75.6%.</p> <p>Univariate analysis showed an association between intervention and hand hygiene compliance (OR: 1.17; 95% CI: 1.13–1.22).</p>	<p>Unclear: Blinding primary outcome plus incomplete primary outcome data.</p> <p>Medium risk of bias</p>	<b>8</b>
<b>Shepherd et al, 2015, USA</b>	ITS	<p>Multimodal (quality improvement) CLABSI strategy</p> <ul style="list-style-type: none"> <li>- Strong executive support</li> </ul>	8 NICUs	CLABSI	<p>Significant decrease from 6.0 to 0.68/1000 catheter days (<math>P&lt;0.001</math>).</p>	<p>Unclear: Intervention independent plus intervention affects data collection plus blinding primary outcome plus</p>	<b>8</b>

						<ul style="list-style-type: none"> <li>- Monthly meetings</li> <li>- Bundles made and revised based on efficacy and compliance</li> <li>- CLABSI bundle team review within 72 hours of positive blood culture</li> <li>- Sharing of lessons learned from case reviews</li> <li>- Chlorhexidine-ethanol skin antiseptics (and impregnated discs)</li> <li>- Alcohol-based port protectors and neutral displacement connectors</li> </ul>	<p>Incomplete primary outcome data.</p> <p>High risk of bias</p>	
<b>Stevenson et al, 2014, USA</b>	RCT	Multimodal hand hygiene programme in rural hospitals	10 rural hospitals	Hand hygiene compliance	Significant change in absolute “complete hand hygiene compliance” in intervention hospitals	Unclear: Baseline characteristics. Medium risk of bias	<b>8</b>	

		(feasibility): - Individualized hand hygiene campaigns - Education - Availability of alcohol - Personal protective equipment at patient care areas - Recognition and rewards programme - Availability of written materials			(20.1%) when compared to control hospitals (-3.1%; $P=0.001$ ).		
<b>Derde et al, 2014, Europe</b>	ITS + RCT	<b>ITS:</b> Universal chlorhexidine bathing plus hand hygiene improvement <b>RCT:</b> Rapid vs. conventional screening	13 ICUs ITS: 41 558 hand hygiene opportunities RCT: colonization	HAI; hand hygiene compliance	Hand hygiene compliance: Increase from 52% to 77% ( $P$ not available). HAI data not provided.	ITS Unclear: Blinding primary outcome. RCT Unclear: Blinding primary outcome data plus contamination.  Medium risk of bias	<b>S</b>

<b>Harris et al, 2013, USA</b>	RCT	Universal glove and gown use	20 hospitals, 20 MSICUs	Hand hygiene compliance; CLABSI; CAUTI; VAP	Hand hygiene compliance Upon room entry: 56.1% vs. 50.2% in the control group; $P=0.42$ . Upon exit: 78.3% vs. 62.9% in the control group; $P=0.02$ CLABSI/CAUTI/VAP: Rates did not differ between groups (all $P >0.10$ ).	High risk: Blinding primary outcome data. Unclear: Baseline outcome.  Medium risk of bias	<b>S</b>
<b>Huang et al, 2013, USA</b>	RCT	Targeted vs. universal decolonization (no screening, universal decolonization)	43 hospitals (74 ICUs, 74 256 patients)	CLABSI	In pairwise comparisons, universal decolonization resulted in a significantly greater reduction in the hazard of infection (hazard ratio: 0.56; 95% CI: 0.49–0.65) than either screening or isolation (hazard ratio: 0.99; 95% CI: 0.84–1.16; $P<0.001$ ) or targeted decolonization (hazard ratio: 0.78; 95% CI: 0.66–0.91; $P = 0.03$ ).	Unclear: Allocation (sequence generation) + blinding primary outcome data.  Medium risk of bias	<b>S</b>
<b>Kampiatu et al, 2014, Kenya</b>	CBA	Single intervention; hand rub with sustained effect vs. handwashing	1 hospital, 3 wards 13 544 patient days (total)	HAI (all)	No HAI were reported during hand rub use ( $P<0.0005$ ).	High risk: Allocation (sequence generation) plus allocation concealment plus baseline characteristics. Unclear: Blinding	<b>S</b>

						primary outcome data. High risk of bias	
<b>Lin et al, 2015, China</b>	RCT	Preoperative chlorhexidine 0.2%	94 patients, 15 VAPs	VAP	VAP occurred in 8.5% of the patients in the chlorhexidine group compared to 23.0% in the control group ( $P<0.049$ ).	High risk: Contamination. Unclear: Baseline outcome.	<b>S</b>
						Medium risk of bias	
<b>Liu et al, 2013, China</b>	RCT	Mechanical cleaning with sterile urethral catheters	45 children	VAP	The occurrence of VAP was significantly reduced by endotracheal tube cleaning.	High risk: Contamination. Unclear: Allocation (sequence generation) plus concealment plus baseline outcome plus blinding of primary outcome data.	<b>S</b>
						High risk of bias	
<b>Milstone et al, 2013, USA</b>	RCT	Daily chlorhexidine bathing	5 hospitals, 10 paediatric ICUs, 4947 admissions	<b>Primary:</b> BSI <b>Secondary:</b> CLABSI	<b>Primary:</b> A non-significant reduction in the incidence of bacteraemia was noted with chlorhexidine bathing (3.52/1000 days; 95% CI: 2.64–4.61) compared with standard practices (4.93/1000 days – adjusted incidence rate ratio: 0.71; 95% CI: 0.42–	Unclear: Baseline outcomes plus contamination. Medium risk of bias	<b>S</b>

					1·20). <b>Secondary:</b> In the ITT population, the risk of CLABSI did not differ between treatment and control units (incidence rate ratio: 0·52; 95% CI 0·25–1·08).			
<b>Noto et al, 2015, USA</b>	RCT	Daily chlorhexidine bathing	Medical centre, 5 ICUs, 9340 patients	105 infections	HAI (CLABSI, CAUTI, VAP, <i>C. difficile</i> )	No difference between groups (2.86 to 2.90/1000 patient-days; rate difference: -0.04; 95% CI: -1.09– 1.01; <i>P</i> =0.95)	Unclear: Baseline outcome plus contamination.  Medium risk of bias	<b>S</b>
<b>Reisinger et al, 2014 USA</b>	RCT	Point-of-use reminder signs using theoretically grounded messages	Multicentre (11 wards) 16 712 hand hygiene observations		Hand hygiene compliance	No change in hand hygiene compliance between intervention and control wards/units: similar improvements at entry (4.2% vs. 7.5%; <i>P</i> = 0.79) and exit (5.1% vs. 5.5%; <i>P</i> =0.54).	High risk: Blinding primary outcome data. Unclear: Baseline characteristics plus incomplete primary outcome data.  High risk of bias	<b>S</b>
<b>Roisin et al, 2014, Belgium</b>	RCT	Rapid (PCR) MRSA detection	1 hospital 2511 patients		HAI (MRSA infection)	Only 7 cases of MRSA infections (control: 2; intervention: 5); cumulative incidence of 1.57 and 4.06 infection/1000 patients	Unclear: Baseline outcome plus blinding primary outcome data plus contamination.  High risk of bias	<b>S</b>

respectively; $P=0.281$							
<b>Sarma et al, 2013, England</b>	ITS	Universal MRSA screening and decolonization	Acute National Health Service trust 40 000 screening specimens	HAI (MRSA infection)	MRSA bacteraemia decreased from 15 to 6 cases ( $\beta$ -2: -0.577; $P<0.001$ ), followed by a continued declining trend reaching zero, but it was not statistically significant ( $\beta$ -2: -0.216; $P=0.298$ )	High risk: Intervention independent plus intervention affects data collection. Unclear: Blinding primary outcome plus incomplete primary outcome data.	<b>S</b>
						High risk of bias	
<b>Seguin et al, 2014, France</b>	RCT	6x daily povidone-iodine oral care	Multicentre, 6 ICUs, 179 patients	VAP	24 VAPs (31%) in the povidone-iodine group and 20 (28%) in the control group (relative risk: 1.11 [95% CI: 0.67–1.82]; $P=0.69$ ).	Unclear: Allocation (sequence generation) plus baseline outcome plus incomplete primary outcome data.	<b>S</b>
						Medium risk of bias	

PCR: polymerase chain reaction; HAI: health care-associated infection; CLABSI: central line-associated bloodstream infection/s; CRBSI: catheter-related bloodstream infection/s; ICU: intensive care unit; MICU: medical intensive care unit; SICU: surgical intensive care unit; EMR(-based): electronic health record(-based); NICU: neonatal intensive care unit; CVC: central venous catheters; CCU: cardiac/coronary care unit; MRSA: methicillin-resistant *Staphylococcus aureus*; OR: odds ratio; CI: confidence interval; MSICU: medical/surgical intensive care unit; IPC: infection prevention and control; SSI: surgical site infection/s; VAP: ventilator-associated pneumonia; CAUTI: catheter-associated urinary tract infection(s); CDI: *Clostridium difficile* infection; RCT: randomized control trial; ITS: interrupted time series; CBA: controlled before-and-after (study); ATP (audits): adenosine triphosphate.

**Appendix 5: Risk of bias for cluster randomized trials, non-randomized cluster trials and controlled before-and-after studies**

	Allocation - sequence	Allocation - concealment	Baseline outcome	Baseline characteristics	Incomplete primary	Blinding primary	Contamination	Selective reporting	Other risks of bias
Derde (2014)	+	+	+	+	+	?	?	+	+
Noto (2015)	+	+	?	+	+	+	?	+	+
Huang (2013)	?	+	+	+	+	?	+	+	+
Harris (2013)	+	+	?	+	+	++	+	+	+
Roisin (2014)	+	+	?	+	+	?	?	+	+
Seguin (2014)	?	+	?	+	+	+	+	+	+

Huis (2013)	+	+	+	?	?	+	?	+	+
Lin (2015)	+	+	?	+	+	+	++	+	+
Liu (2013)	?	?	?	+	+	?	++	+	+
Milstone (2013)	+	+	?	+	+	+	?	+	+
Reisinger (2014)									
Stevenson (2014)									
Lieber (2014)		++		++					
Kampiatu (2015)	++	++	+	++	+	?	+	+	+

++ high risk; + low risk; ? unclear risk

## Appendix 6: Risk of bias for interrupted time series studies

	Intervention-independent	Intervention effect pre-specified	Intervention affects data collection on primary	Blinding to primary outcome	Incomplete primary outcome	Selective reporting of	Other risks of bias
Al-Tawfiq (2013)	?	++	+	?	?	+	+
Allen (2014)	?	+	+	?	?	+	+
Derde (2014)	+	+	+	?	+	+	+
Fisher (2013)	?	+	+	?	?	+	+
Gerolemou (2014)	+	+	+	+	?	+	+
Higgins (2013)	++	+	++	?	?	+	+

Johnson (2014)	++	+	++	++	?	+	+
Kwok (2015)	++	?	+	?	?	+	+
Mermel (2013)	?	++	++	?	?	+	+
Rodriguez (2015)	+	+	+	?	?	+	+
Sarma (2013)	++		++				
Shepherd (2015)	?		?				
Talbot (2013)	?						
Viana (2013)				++	?		

++ high risk; + low risk; ? unclear risk

## References

1. Report on the endemic burden of healthcare-associated infection worldwide. Geneva: World Health Organization; 2011.
2. Bagheri Nejad S, Allegranzi B, Syed SB, Ellis B, Pittet D. Health-care-associated infection in Africa: a systematic review. *Bull World Health Organ*. 2011;89(10):757-65.
3. Shekelle PJ, Provonost PP, Wachter RM, McDonald KM, Schoelles K, Dy SM, et al. Top 10 patient safety strategies that can be encouraged for adoption now. *Ann Int Med*. 2013;58(5):365-8.
4. The evolving threat of antimicrobial resistance - options for action. Geneva: World Health Organization; 2012.
5. Five year antimicrobial resistance strategy 2013 to 2018. London (UK): Department of Health; 2013.
6. Report on the consultative meeting on antimicrobial resistance for countries in the Eastern Mediterranean Region: from policies to action (2013). Geneva: World Health Organization; 2013.
7. Antimicrobial resistance: global report on surveillance. Geneva: World Health Organization; 2014.
8. International health regulations (2005). Geneva: World Health Organization; 2008.
9. Strengthening health systems to improve health outcomes: WHO's framework for action. Geneva: World Health Organization; 2007.
10. Core components for infection control prevention and control programmes. Geneva: World Health Organization; 2009.
11. Zingg W, Holmes A, Dettenkofer M, Goetting T, Secci F, Clack L, et al. Hospital organisation, management, and structure for prevention of health-care-associated infection: a systematic review and expert consensus. *Lancet Infect Dis*. 2015;15(2):212-24.
12. Effective practice and organisation of care (EPOC). EPOC resources for review authors. Oslo: Norwegian Knowledge Centre for the Health Services; 2015.
13. Noto MJ, Domenico HJ, Byrne DW, Talbot T, Rice TW, Bernard GR, et al. Chlorhexidine bathing and health care-associated infections: a randomized clinical trial. *JAMA*. 2015;313(4):369-78.
14. Al-Tawfiq JA, Abed MS, Al-Yami N, Birrer RB. Promoting and sustaining a hospital-wide, multifaceted hand hygiene program resulted in significant reduction in health care-associated infections. *Am J Infect Control*. 2013;41(6):482-6.
15. Allen GB, Miller V, Nicholas C, Hess S, Cordes MK, Fortune JB, et al. A multitiered strategy of simulation training, kit consolidation, and electronic documentation is associated with a reduction in central line-associated bloodstream infections. *Am Journal Infect Control*. 2014;42(6):643-8.
16. Derde LPC, Goossens H, Malhotra-Kumar S, Willems RJ, Gniadkowski M, Hryniewicz W, et al. Interventions to reduce colonisation and transmission of antimicrobial-resistant bacteria in intensive care units: an interrupted time series study and cluster randomised trial. *Lancet Infect Dis*. 2014;14(1):31-9.
17. Fisher D, Tambyah PA, Lin RT, Jureen R, Cook AR, Lim A, et al. Sustained meticillin-resistant *Staphylococcus aureus* control in a hyper-endemic tertiary acute

- care hospital with infrastructure challenges in Singapore. *J Hosp Infect.* 2013;85(2):141-8.
18. Gerolemou LF, Rose K, Cooper S, Venturanza M, Aqeel A, Han Q, et al. Simulation-based training for nurses in sterile techniques during central vein catheterization. *Am J Crit Care.* 2014;23(1):40-8.
  19. Harris ADP, Belton B, Johnson JK, Shardell M, Loeb M, Newhouse R, et al. Universal glove and gown use and acquisition of antibiotic-resistant bacteria in the ICU: a randomized trial. *JAMA.* 2013;310(15):1571-80.
  20. Higgins AH, Hannan MM. Improved hand hygiene technique and compliance in healthcare workers using gaming technology. *J Hosp Infect.* 2013;84(1):32-7.
  21. Huang SS, Septimus E, Kleinman K, Moody J, Hickok JM, Avery TR, et al. Targeted versus universal decolonization to prevent ICU infection. *New Engl J Med.* 2013;368(24):2255-65.
  22. Huis A, Schoonhoven L, Grol R, Donders R, Hulscher M, Achterberg T. Impact of a team and leaders-directed strategy to improve nurses' adherence to hand hygiene guidelines: a cluster randomised trial. *Int J Nurs Stud.* 2013;50(4):464-74.
  23. Johnson L, Grueber S, Schlotzhauer C, Phillips E, Bullock P, Basnett J, et al. A multifactorial action plan improves hand hygiene adherence and significantly reduces central line-associated bloodstream infections. *Am J Infect Control.* 2014;42(11):1146-51.
  24. Kampiatu P, Cozean J. A controlled crossover study of a persistent antiseptic to reduce hospital-acquired infection. *Afr J Infect Dis.* 2014;9(1):6-9.
  25. Kwok YL, Callard M, McLaws ML. An automated hand hygiene training system improves hand hygiene technique but not compliance. *Am J Infect Control.* 2015;43(8):821-5.
  26. Lieber SR, Mantengoli E, Saint S, Fowler KE, Fumagalli C, Bartolozzi D, et al. The effect of leadership on hand hygiene: assessing hand hygiene adherence prior to patient contact in 2 infectious disease units in Tuscany. *Infect Control Hosp Epidemiol.* 2014;35(3):313-6.
  27. Lin YJ, Xu L, Huang XZ, Jiang F, Li SL, Lin F, et al. Reduced occurrence of ventilator-associated pneumonia after cardiac surgery using preoperative 0.2% chlorhexidine oral rinse: results from a single-centre single-blinded randomized trial. *J Hosp Infect.* 2015;91(4):362-6.
  28. Liu WZ, Zuo Z, Ma R, Zhang X. Effect of mechanical cleaning of endotracheal tubes with sterile urethral catheters to reduce biofilm formation in ventilator patients. *Pediatr Crit Care Med.* 2013;14(7):e338-43.
  29. Mermel LA, Jefferson J, Blanchard K, Parenteau S, Mathis B, Chapin K, et al. Reducing *Clostridium difficile* incidence, colectomies, and mortality in the hospital setting: a successful multidisciplinary approach. *Jt Comm J Qual Pat Saf.* 2013;39(7):298-305.
  30. Milstone AM, Elward A, Song X, Zerr DM, Orscheln R, Speck K, et al. Daily chlorhexidine bathing to reduce bacteraemia in critically ill children: a multicentre, cluster-randomised, crossover trial. *Lancet.* 2013;381(9872):1099-106.
  31. Reisinger HS, Perencevich EN, Morgan DJ, Forrest GN, Shardell M, Schweizer ML, et al. Improving hand hygiene compliance with point-of-use reminder signs designed using theoretically grounded messages. *Infect Control Hosp Epidemiol.* 2014;35(5):593-4.
  32. Rodriguez V, Giuffre C, Villa S, Almada G, Prasopa-Plaizier N, Gogna M, et al. A multimodal intervention to improve hand hygiene in ICUs in Buenos Aires, Argentina: a stepped wedge trial. *Int J Qual Health Care.* 2015;27(5):405-11.

33. Roisin SL, Laurent C, Denis O, Dramaix M, Nonhoff C, Hallin M, et al. Impact of rapid molecular screening at hospital admission on nosocomial transmission of methicillin-resistant *Staphylococcus aureus*: cluster randomised trial. *PloS One*. 2014;9(5):e96310.
34. Sarma JB, Marshall B, Cleeve V, Tate D, Oswald T. Impact of universal screening on MRSA bacteremias in a single acute NHS organisation (2006-12): interrupted time-series analysis. *Antimicrob Resist Infect Control*. 2013;2(1):2.
35. Seguin PL, Laviolle B, Dahyot-Fizelier C, Dumont R, Veber, B, Gergaud S, et al. Effect of oropharyngeal povidone-iodine preventive oral care on ventilator-associated pneumonia in severely brain-injured or cerebral hemorrhage patients: a multicenter, randomized controlled trial. *Crit Care Med*. 2014;42(1):1-8.
36. Shepherd EG, Kelly TJ, Vinsel JA, Cunningham DJ, Keels E, Beauseau W, et al. Significant reduction of central-line associated bloodstream infections in a network of diverse neonatal nurseries. *J Pediatr*. 2015;167(1):41-6.e1-3.
37. Stevenson KB, Searle K, Curry G, Boyce JM, Harbarth S, Stoddard GJ, et al. Infection control interventions in small rural hospitals with limited resources: results of a cluster-randomized feasibility trial. *Antimicrob Resist Infect Control*. 2014;3(1):10-17.
38. Talbot TR, Johnson JG, Fergus C, Domenico JH, Schaffner W, Daniels TL, et al. Sustained improvement in hand hygiene adherence: utilizing shared accountability and financial incentives. *Infect Control Hosp Epidemiol*. 1129;34(11):1129-36.
39. Viana WN, Bragazzi C, Couto de Castro JE, Alves MB, Rocco JR. Ventilator-associated pneumonia prevention by education and two combined bedside strategies. *Int J Qual Health Care*. 2013;25(3):308-13.