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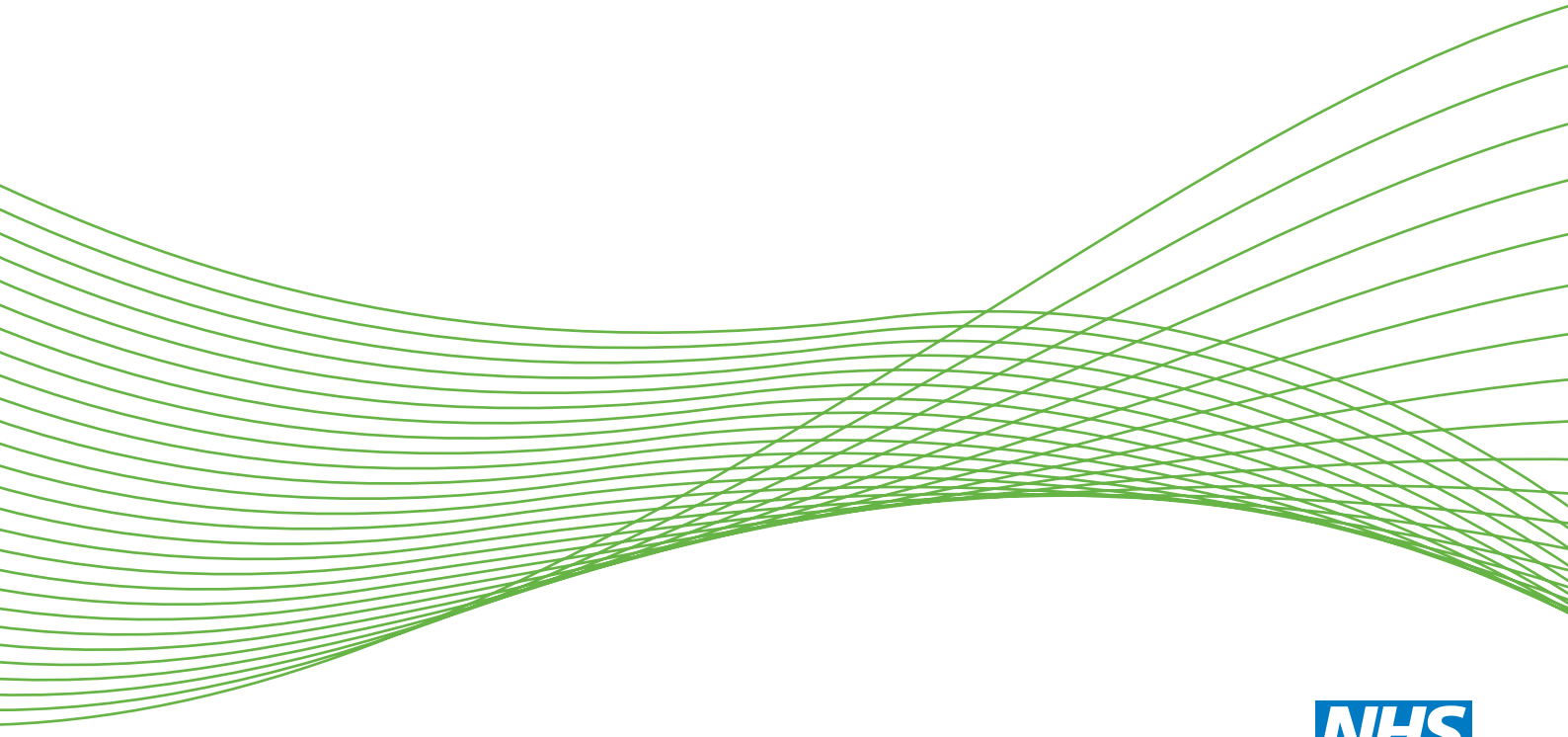

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Abstract

Educational interventions for preventing vascular catheter bloodstream infections in critical care: evidence map, systematic review and economic evaluation

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Background: Bloodstream infections resulting from intravascular catheters (catheter-BSI) in critical care increase patients' length of stay, morbidity and mortality, and the management of these infections and their complications has been estimated to cost the NHS annually £19.1–36.2M. Catheter-BSI are thought to be largely preventable using educational interventions, but guidance as to which types of intervention might be most clinically effective is lacking.

Objective: To assess the effectiveness and cost-effectiveness of educational interventions for preventing catheter-BSI in critical care units in England.

Data sources: Sixteen electronic bibliographic databases – including MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, Cumulative Index to Nursing and Allied Health Literature (CINAHL), NHS Economic Evaluation Database (NHS EED), EMBASE and The Cochrane Library databases – were searched from database inception to February 2011, with searches updated in March 2012. Bibliographies of systematic reviews and related papers were screened and experts contacted to identify any additional references.

Review methods: References were screened independently by two reviewers using a priori selection criteria. A descriptive map was created to summarise the characteristics of relevant studies. Further selection criteria developed in consultation with the project Advisory Group were used to prioritise a subset of studies relevant to NHS practice and policy for systematic review. A decision-analytic economic model was developed to investigate the cost-effectiveness of educational interventions for preventing catheter-BSI.

Results: Seventy-four studies were included in the descriptive map, of which 24 were prioritised for systematic review. Studies have predominantly been conducted in the USA, using single-cohort before-and-after study designs. Diverse types of educational intervention appear effective at reducing the incidence density of catheter-BSI (risk ratios statistically significantly < 1.0), but single lectures were not effective. The economic model showed that implementing an educational intervention in critical care units in England would be cost-effective and potentially cost-saving, with incremental cost-effectiveness ratios under worst-case sensitivity analyses of < £5000/quality-adjusted life-year.

Limitations: Low-quality primary studies cannot definitively prove that the planned interventions were responsible for observed changes in catheter-BSI incidence. Poor reporting gave unclear estimates of risk of bias. Some model parameters were sourced from other locations owing to a lack of UK data.

Conclusions: Our results suggest that it would be cost-effective and may be cost-saving for the NHS to implement educational interventions in critical care units. However, more robust primary studies are needed to exclude the possible influence of secular trends on observed reductions in catheter-BSI.

Study registration: The study is registered with PROSPERO as CRD42012001840.

Funding: The National Institute for Health Research Health Technology Assessment programme.

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Glossary

Catheter-associated bloodstream infection A primary laboratory-confirmed bloodstream infection in a patient with a central line at the time of (or within 48 hours prior to) the onset of symptoms, and which is not related to an infection from another site. Synonyms include central line-associated bacteraemia and central line-associated bloodstream infection.

Catheter-bloodstream infection (catheter-BSI) An umbrella term referring to catheter-associated bloodstream infections, catheter-related bloodstream infections or catheter-suspected bloodstream infections and their synonyms.

Catheter-related bloodstream infection Various definitions and terms are used, and sometimes confused, in the literature to describe a bloodstream infection that has developed as a consequence of an indwelling intravascular catheter. Bloodstream infections that are proven microbiologically to result from vascular catheter use are generally referred to as catheter-related bloodstream infections. For the purposes of this report, a definition as used in the Matching Michigan programme in England is provided (see *Table 1*).

Critical care unit A specially equipped hospital area designed for the specialised care of patients whose conditions are life-threatening and who require comprehensive care and constant monitoring. For the purposes of this report, synonymous with intensive care unit, including high-dependency units, but excluding step-down units.

Device-days The total number of days that patients have one or more vascular devices in a given period. Definitions vary depending on whether multiple vascular devices per patient are counted separately.

Incidence density The standardised incidence of infection. For the purposes of this report, standardised to the number of vascular device-days and expressed per 1000 device-days.

Incidence density risk ratio The ratio of incidence densities in study and comparator groups. Values of <1 favour the study group; values of >1 favour the comparator group.

Intensive care unit See *Critical care unit*.

Matching Michigan An infection prevention strategy adapted from the US Keystone ICU ('Michigan') project intervention and implemented in English NHS trusts in 2009.

ORION Guidelines for the transparent reporting of nosocomial infections, including a 22-item checklist and summary table.

STROBE Guidelines for the reporting of observational studies in epidemiology, including a 22-item checklist and supporting information with examples.

TREND Guidelines for the reporting of non-randomised evaluations of behavioural and public health interventions, including a 22-item checklist.

List of abbreviations

AG	Advisory Group
BEME	Best Evidence in Medical Education
BSI	bloodstream infection
CABSI	catheter-associated bloodstream infection
CDC	Centers for Disease Control and Prevention
CEO	chief executive officer
CFU	colony-forming unit
CH/SSD	chlorhexidine/silver sulfadiazine
CI	confidence interval
CLAB	central line-associated bacteraemia (synonymous with CABSI)
CLABSI	central line-associated bloodstream infection (synonymous with CABSI)
CQI	continuous quality improvement
CRBSI	catheter-related bloodstream infection
CVC	central venous catheter
CVL	central venous line
ECDC	European Centre for Disease Prevention and Control
HELICS	Hospitals In Europe Link for Infection Control through Surveillance
HRG	Healthcare Resource Group
HRQoL	health-related quality of life
ICER	incremental cost-effectiveness ratio
ICU	intensive care unit
ICUAI	Intensive Care Unit-Associated Infection
IHI	Institute for Healthcare Improvement
IQR	interquartile range
ITS	interrupted time series
LCBSI	laboratory-confirmed bloodstream infection
LOS	length of stay
MeSH	medical subject heading
MHA	Michigan Health and Hospital Association
MICU	medical intensive care unit
MR	minocycline and rifampicin
MRC	Medical Research Council
MRSA	methicillin-resistant *Staphylococcus aureus*
NHSN	National Healthcare Safety Network (US CDC)
NICE	National Institute for Health and Care Excellence
NNIS	Nosocomial Infection Surveillance System (US CDC)
NSP	National Surveillance Programme
PICC	peripherally inserted central catheter
PICU	paediatric intensive care unit
PSA	probabilistic sensitivity analysis
QALY	quality-adjusted life-year
QI	quality improvement
QoL	quality of life
RCT	randomised controlled trial
RR	risk ratio
SHTAC	Southampton Health Technology Assessments Centre
SICU	surgical intensive care unit
UTI	urinary tract infection
VAP	ventilator-associated pneumonia

Scientific summary

Background

Bloodstream infections resulting from the use of intravascular catheters (catheter-BSI) are the most frequent infections in critical care units in England. Catheter-BSI increase patients' length of stay (LOS) in hospital and their risk of health complications and death, and impose a burden on health services in terms of bed occupancy and the additional costs of managing these infections and their complications. Annual costs to the NHS related to catheter-BSI in critical care units have been estimated at £19.1–36.2M. The majority of catheter-BSI are thought to be preventable using evidence-based educational interventions to ensure that doctors and nurses are committed to a culture of safety and follow best practice to achieve this. However, there is a lack of guidance as to which types of intervention might be most clinically effective and cost-effective in an NHS setting. We developed an evidence map, conducted a systematic review and performed an economic evaluation to assess the effectiveness and cost-effectiveness of educational interventions relevant to the prevention of catheter-BSI in critical care units in England.

Methods

Evidence map and systematic review of effectiveness

A two-stage process was followed: (1) development of a descriptive map of the key characteristics of studies evaluating educational interventions, followed by (2) a detailed systematic review of a subset of interventions.

Search strategies

Fifteen electronic bibliographic databases [including MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, Cumulative Index to Nursing and Allied Health Literature (CINAHL), EMBASE and Cochrane Collaboration databases] were searched from the period of database inception up to February 2011, with searches rerun in March 2012. Searches were not restricted by publication language. Bibliographies of systematic reviews and related papers were screened and experts contacted to identify additional published and unpublished references.

Study selection

Titles and abstracts were screened for eligibility by two reviewers independently using a priori pilot-tested criteria. Studies eligible for inclusion in the descriptive map were any primary research studies that included one or more planned educational interventions for preventing catheter-BSI, were conducted in critical care units, and reported the effect of the intervention(s) on the incidence density of catheter-BSI, mortality and/or LOS as an outcome. We defined education in a broad sense to include any means of information provision, and we defined catheter-BSI to include catheter-related and catheter-associated bloodstream infections (CABSIs) and their synonyms. Full papers were obtained for those titles and abstracts that appeared relevant and these were screened by two reviewers independently.

Descriptive map

Keywords were developed and systematically applied to included studies to produce a detailed map of the evidence base that was used to prioritise a subset of studies for inclusion in the systematic review in consultation with the project's expert Advisory Group (AG).

Data extraction and quality assessment

Two reviewers independently extracted data from the studies included in the systematic review using a pilot-tested data extraction form and independently assessed studies for methodological quality,

including risk of bias using prespecified criteria. Differences in judgement were resolved by discussion and involvement of a third reviewer if necessary.

Data synthesis

Studies were synthesised narratively and considered for meta-analysis.

Economic evaluation

A systematic review was conducted to identify economic evaluations of educational interventions for preventing catheter-BSI in critical care. Thirteen electronic bibliographic databases [including MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, CINAHL, EMBASE, Cochrane Collaboration databases and NHS Economic Evaluation Database (NHS EED)] were searched from the period of database inception up to February 2011, with searches rerun in March 2012. References identified were screened according to a priori criteria. Full papers were obtained for those titles and abstracts that appeared relevant and these were screened by two reviewers independently.

A decision-analytic economic model was developed to compare the costs and consequences of a central venous catheter (CVC) care bundle for the prevention of catheter-BSI against current clinical practice. The CVC care bundle was defined based upon the 'Keystone intensive care unit (ICU) project' conducted in Michigan, USA, and the 'Matching Michigan' programme in England. The CVC care bundle encompassed five elements, together with education: optimal hand hygiene, chlorhexidine skin antisepsis, maximal barrier precautions for catheter insertion, choice of optimal insertion site, and prompt catheter removal. Current clinical practice was defined as critical care that did not implement a CVC care bundle.

The model follows hypothetical cohorts of patients from their admission to the critical care unit and incorporates their risk of catheter-BSI and hospital mortality. Estimates are made of the long-term survival of patients after discharge from critical care and the total costs and quality-adjusted life-years (QALYs) gained for both cohorts, from which the model determines the cost-effectiveness of the CVC care bundle. Model parameters were derived from a systematic search of the literature on the natural history and epidemiology of catheter-BSI, health-related quality of life (HRQoL) and costs. Costs were derived from primary data from previous studies and NHS unit costs. The analysis was conducted from the perspective of the NHS and Personal Social Services, and has a lifetime horizon. Uncertainty around the model results was investigated through the use of deterministic and probabilistic sensitivity analyses.

Results of the evidence map and systematic review of effectiveness

A descriptive map of 74 studies meeting the inclusion criteria was produced. The results illustrate a predominance of North American trials of educational interventions. Studies have been conducted at a range of spatial and temporal scales with diverse types of educational intervention, ranging from individual short lectures conducted in single critical care units to multiyear regional-scale interventions that involved continuous quality improvement (CQI) approaches in over 100 critical care units. Nearly all studies used uncontrolled before-and-after study designs, with only two randomised controlled trials (RCTs) included.

Discussion with the project's AG enabled the prioritisation of a policy-relevant subset of studies for systematic review. To be included, studies had to have a clearly reported prospective design; focus on adult critical care units; and provide a definition of their catheter-BSI outcome.

A total of 24 studies met the inclusion criteria for the systematic review. Twelve studies were conducted in the USA, with only one in the UK. Nine studies were judged to be at high risk of bias. However, owing to poor reporting of the methodology, the majority of studies were judged to be at unclear risk of bias. Most studies did not report their methods of data collection. Quality criteria were not used to exclude studies from data synthesis but were taken into consideration when discussing whether studies

provided convincing evidence of clinical effectiveness. Owing to the wide heterogeneity of intervention types included in the systematic review, meta-analysis was inappropriate. Instead, incidence density risk ratios (RRs) with 95% confidence intervals (incidence of catheter-BSI expressed per 1000 catheter-days) calculated for each of the interventions were compared in a narrative synthesis.

Studies included in the systematic review were predominantly uncontrolled before-and-after studies. None of the controlled studies demonstrated clinical effectiveness. Assuming that observed changes in catheter-BSI rates in before-and-after studies were caused by the intended interventions, 12 of the 24 studies included in the systematic review reported interventions that appeared to be effective at reducing the incidence density of catheter-BSI (incidence density RRs statistically significantly < 1.0), six studies reported interventions that were clearly not effective, three lacked convincing evidence of effectiveness and three provided insufficient data to calculate incidence density RRs. Overall, there was no clear evidence that particular types of education were any more or less effective at reducing incidence densities of catheter-BSI. Interventions that included checklists, performance feedback and/or infection surveillance feedback were sometimes, but not always, clinically effective. An exception is that single lectures on infection prevention practices conducted in individual critical care units (assessed in two studies) were not clinically effective. Few studies reported effects of interventions on mortality or LOS, and no clear patterns were evident for these outcomes.

Nineteen studies reported qualitative or quantitative information on intervention processes including compliance of critical care staff with evidence-based practices. Starting compliance at study inception was highly variable. In the RCT, lack of initial data collection infrastructure appears to have been a barrier to effective implementation. Although evidence is limited to few studies, inappropriate staff attitudes appear to be a potential barrier to effective implementation of evidence-based practices for preventing catheter-BSI.

Of the interventions judged in the systematic review to be clinically effective, a regional-scale CQI programme conducted in 37 critical care units in Australia (the 'CLAB ICU project') was considered most relevant to current NHS practice. Clinical effectiveness data from this intervention were used to inform the economic model.

Results of the economic evaluation

Systematic review of cost-effectiveness studies

Three economic evaluations of educational interventions for prevention of catheter-BSI were included. However, none was appropriate for estimating the cost-effectiveness of an educational intervention for prevention of catheter-BSI in NHS critical care units in England.

Modelled cost-effectiveness analysis

The results from the model showed that the CVC care bundle would save 0.8 catheter-BSI and 0.3 lives compared with current clinical practice (per 100 patients admitted to the critical care unit), with an increased survival of 3.6 years and 2.7 QALYs. The incremental cost was –£573 per QALY gained and –£1976 per catheter-BSI averted, with negative values resulting from the CVC care bundle being both more effective and less costly than existing clinical practice (i.e. dominant). The cost saving largely arises from a reduction in the critical care LOS.

Robustness of the model results was tested using a range of sensitivity analyses as well as a scenario analysis to explore the effect of different patient starting ages. The CVC care bundle ranged from remaining cost saving to no longer being cost saving, but in all cases it would be considered cost-effective at the standard cost-effectiveness threshold of £20,000 per QALY (worst-case results were all of < £5000 per QALY). The greatest variation in the sensitivity analyses was associated with two variables – catheter-BSI incidence rate and additional length stay in critical care for patients with catheter-BSI.

There is uncertainty in the model-based analysis relating to variation in implementation of the CVC care bundle, as some of the interventions included in the bundle (to be implemented on a regional or national basis) may already be partially implemented (by individual hospitals or critical care units). However, at the least favourable values tested in sensitivity analyses to reflect extremes of implementation (a relative risk of catheter-BSI with the CVC care bundle = 0.7 and baseline incidence density of 1 per 1000 catheter-days), the incremental cost-effectiveness ratio (ICER) remained below the threshold conventionally considered as cost-effective.

For England, with 90,000 critical care patients per year, the model estimates that implementing the CVC care bundle would reduce the number of catheter-BSI infections by > 700 [interquartile range (IQR) 482–914] and save 270 lives (IQR 184–348 lives) per year. The yearly additional cost to implement the intervention used in England would be £1.4M (IQR £1.2M–£1.5M). However, if the intervention was implemented, not only would the cost of implementation be recouped but there would be a net saving from implementing the intervention of £1.5M, largely as a result of the savings in costs related to reduced LOS (£2.4M, IQR £1.4M–£3.3M). The CVC care bundle remains cost saving up to an annual implementation cost of £2.7M (equivalent to £30 per critical care patient).

Conclusions

Literature searches indicate that the evaluation of educational interventions for prevention of catheter-BSI is an active area of primary research. Economic evaluation suggests that an educational intervention based on a CVC care bundle implemented in critical care units in England would be more effective and less costly than current clinical practice, even after allowing for heterogeneity of baseline clinical practices and heterogeneity of implementation. However, there is a need for more rigorous primary research studies to be conducted, as the current evidence comes predominantly from uncontrolled before-and-after studies that may not convincingly distinguish intervention effectiveness from secular trends. Clinical practices are being addressed by a wide variety of different educational strategies that do not draw upon pedagogic, theoretical or conceptual frameworks, and, consequently, do not provide generalisable lessons to inform national guidelines. A co-ordinated and harmonised approach to the provision of education, with the involvement of educationalists in the design of research studies, would improve the generalisability and comparability of educational interventions. Improvements in the reporting of the primary studies are needed, to enable judgements about risk of bias and confounding. Definitions of catheter-related and CABSIs are used inconsistently and should be standardised.

Recommendations for practice

NHS organisations should carefully consider whether existing practice for preventing catheter-BSI may be improved by implementing educational interventions in critical care units either at local or regional scales. Although it is not possible to be specific about which type of intervention may be most appropriate, economic evaluation suggests that a variety of approaches could be cost-effective or cost-saving. Consideration should be given to the need to adopt standard definitions of CABSI and catheter-related bloodstream infection, and apply and report these consistently. When clinical practice is delivered within a research setting, for example if interventions are intended to be implemented into practice while their effectiveness is monitored, consideration should be given to ensuring that the research design is appropriate for cause–effect relationships to be determined. Co-ordinated collection of surveillance data on catheter-BSI, mortality and LOS in critical care units, and the resources required to implement and sustain an intervention, would be helpful to inform future economic evaluations.

Recommendations for research

Future evaluations of educational interventions for preventing catheter-BSI should be rigorously designed to enable causal relationships to be established and any influences of secular trends on outcomes to be controlled. Appropriate designs could include RCTs and interrupted time series. When developing educational interventions for prevention of catheter-BSI, consideration should be given to: basing

interventions on robust educational and behavioural theory; involving educationalists; including process evaluations; and integrating a cost-effectiveness evaluation. Development of educational interventions for preventing catheter-BSI (and other infections) is likely to benefit from being co-ordinated at a national level, to ensure that valid and reliable pedagogical approaches are used, which are generalisable and inform national guidelines. Researchers should be encouraged to clearly report research studies of educational interventions to provide greater confidence about the validity and generalisability of the results and to fully identify the risks of bias and confounding. Updates to this review may help to clarify the extent of the growing evidence base and to ensure that the quality controls recommended above, if implemented, are effective.

Study registration

This study is registered with PROSPERO as CRD42012001840.

Funding

Funding for this study was provided by the Health Technology Assessment programme of the National Institute for Health Research.

Chapter 1 Background

Intravascular catheters are used for the administration of medication, fluids, blood products and parenteral nutrition, as well as for patient monitoring,[1] but they are an important cause of bloodstream infections (BSIs).[2–4] The most frequently used type of intravascular catheter is a central venous catheter (CVC), also referred to as a central line. A CVC is defined as an intravascular device that terminates in one of the great veins, or in or near to the right atrium, and includes peripherally inserted central catheters (PICCs), haemodialysis catheters and parenteral nutrition catheters. Insertion sites for CVCs are usually the jugular, subclavian and femoral veins, although femoral insertion may be associated with higher risk of BSIs than insertions at other sites.[5] Intravascular catheters vary in the material from which they are made, the presence or absence of antimicrobial or anticoagulant coatings, the number of lumens present and whether they are tunnelled, and these variables may have an important bearing on the risk of BSI.[6]

Four distinct pathways may be identified in the infection process of catheter-BSI. The two major pathways are the external and internal bacterial colonisation of the catheter surface, both eventually leading to catheter-tip colonisation, with the potential for subsequent bacteraemia. Additional pathways include microbial contamination of the infusate and direct mechanical introduction of pathogens into the bloodstream.[7] A wide variety of microorganisms may cause catheter-BSI, including, among others, *Staphylococcus aureus*, *Staphylococcus epidermidis*[8] and enterococci.[9] Catheter-BSI result from inadequate hygiene and suboptimal catheter management procedures. These include inadequate hand hygiene by hospital staff; inadequate skin hygiene at the site of patients' catheter insertion; suboptimal location of catheters; and unnecessary placement of catheters.[6] Other risk factors are the patient's age and underlying disease,[6] and the duration of catheterisation.[10]

Bloodstream infections arising from the placement of vascular catheters (catheter-BSI) are a particular problem in critical care units owing to the high frequency of intravascular catheter placement and increased susceptibility to infections among critical care patients.[11] The latest (2011) point prevalence survey in England,[12] showed that 64% of all patients with a BSI had a vascular access device in the 48 hours prior to onset of infection, and 59.3% of critical care patients received a CVC compared with 5.9% of other hospital patients. A 1-month audit in a hospital in England found that 65% of patients in the critical care unit required a CVC, whereas in surgical and renal wards the proportion ranged from 3.5% to 25%.[13]

Prevalence of catheter-bloodstream infection

Prevalence of catheter-BSI is usually standardised to the number of CVC-days, and is typically expressed as the incidence density per 1000 CVC-days, although the definition of a device-day varies (multiple concurrent vascular catheters in the same patient are often not counted separately[14]). According to the 2011 point prevalence survey in England, intravascular catheter placement accounted for 29% of hospital-acquired BSI.[12] Unpublished data from presentations about the 'Matching Michigan' programme in England[15–17] (described further below) reported an incidence density of catheter-BSI of 3.7 per 1000 CVC-days for a subset of 19 critical care units in northern England sampled in mid-2009. The most recent published incidence density data available for the UK are from the Intensive Care Unit Associated Infection (ICUAI) National Surveillance Programme (NSP), based on data from May 2009 until January 2010 for 19 critical care units in Scotland. The NSP reported a catheter-BSI incidence density of 0.7 per 1000 CVC-days.[18] A 2009 report of the European Centre for Disease Prevention and Control (ECDC) estimated prevalence of catheter-BSI to be 4.3 per 1000 CVC-days, based on aggregated data from 12 European countries, which included some data from England.[19]

There is evidence that prevalence of BSI associated with vascular catheters has decreased as a result of national and local infection prevention programmes in several countries. For example, in the USA the Institute for Healthcare Improvement's '100,000 Lives Campaign (2005–6) and '5 Million Lives' Campaign (2006–8) were among a number of programmes that recruited a large number of hospitals and promoted (among other objectives) strategies for the prevention of catheter-BSI. The most recent data available from the US Centers for Disease Control and Prevention (CDC)[20] show that a 58% decrease in the prevalence of catheter-BSI occurred from 2001 to 2009. The point prevalence surveys conducted in England indicate a decline in the overall prevalence of BSI in recent years but the data are difficult to interpret owing to changes that occurred in the sampling methodology.[12]

Definitions and diagnosis of catheter-bloodstream infection

Various definitions and terms are used, and sometimes confused, in the literature to describe a BSI that has developed as a consequence of an indwelling intravascular catheter. Laboratory-confirmed bloodstream infections (LCBSIs) which are proven microbiologically to result from vascular catheter use are generally referred to as catheter-related bloodstream infections (CRBSIs). In the absence of microbiological testing and after ruling out other possible sources, BSIs that appear to be linked to vascular catheter use are referred to as catheter-associated bloodstream infections (CABSIs). The gold standard for diagnosis of CRBSI is isolation of the same microorganism from a peripheral blood culture as that obtained from the tip of the removed catheter.[21] As many patients suspected of having a BSI will not have their catheter removed, and quantitative blood cultures are not universally performed, alternative definitions to CRBSI that do not require catheter removal are often used (i.e. CABSI), and these overestimate the true incidence of CRBSI. The most widely cited definitions of CABSI and CRBSI are the surveillance definitions of the US Centers for Disease Control and Prevention (CDC) National Nosocomial Infection Surveillance System (NNIS), which operated up to 2004, and the CDC National Healthcare Safety Network (NHSN) which replaced the NNIS in 2005. The latest CDC guidelines on defining and diagnosing CABSI and CRBSI, endorsed by the Infectious Diseases Society of America, were reported by Mermel and colleagues.[22] Recently, stringent definitions of CABSI and CRBSI, based on the CDC definitions, have been developed for use in the 'Matching Michigan' programme in England[17] (see *Table 1*). As we describe below (see *Current prevention of catheter-bloodstream infections in the NHS*), Matching Michigan was a programme for prevention of catheter-BSI in critical care units in England that has direct relevance to NHS practice.

For the purposes of this report, we follow the definitions of CABSI, CRBSI and catheter-suspected BSIs, as defined in the Matching Michigan programme (*Table 1*), and these definitions are collectively referred to as catheter-BSI.

Diagnosis of CRBSI is made in various ways, depending upon both local clinical practice and, for infection surveillance purposes, the definition of infection in use. The use of different definitions of infections can dramatically alter the reported infection rate unless they are aligned with clinical practice. For example, if clinical practice is not to send a CVC line tip to the laboratory for culture, or to draw only a single set of percutaneous cultures, then any definition requiring catheter-tip culture or more than one set of cultures will never be met, potentially giving an artificially low infection rate.

Impact of catheter-bloodstream infection on patients and health services

Catheter-BSI increase patients' discomfort and length of stay (LOS) in hospital[23] and their risk of health complications and death.[24] Catheter-BSI can trigger a range of responses from systemic sepsis through to septic shock and multiple organ failure. Metastatic infection may lead to septic thrombosis, endocarditis and septic arthritis.[25] Further complications may include acute respiratory distress syndrome, disseminated intravascular coagulation and acute renal failure.[26]

TABLE 1 Definitions of BSIs used in the 'Matching Michigan' programme in England (source: J Bion; dated 20 November 2009)

Infection type	Definition
LCBSI	The patient has one or more recognised pathogens cultured from one blood culture If the microorganism is a common skin organism [i.e. diphtheroids (*Corynebacterium* spp.), *Bacillus* spp. (not *B. anthracis*), *Propionibacterium* spp., coagulase-negative staphylococci (excludes sensitive *S. aureus*), *viridans*-group streptococci, *Aerococcus* spp. or *Micrococcus* spp.], then . . . • It *must* have been cultured from two or more blood cultures drawn on separate occasions, or from one blood culture in a patient in whom antimicrobial therapy has been started, and • The patient has one of the following: fever of > 38 °C, chills or hypotension
CABSI	Criteria above must be met for LCBSI, *and*: • The presence of one or more CVCs at the time of the blood culture, or up to 48 hours following removal of the CVC *and*: • The signs and symptoms and positive laboratory results including the pathogen cultured from the blood are not primarily related to an infection at another site
CRBSI	Criteria above must be met for LCBSI, *and*: • The presence of one or more CVCs at the time of the blood culture, or up to 48 hours following removal of the CVC, *and* • One of the following: 1. a positive semiquantitative (> 15 CFUs/catheter segment) or quantitative (> 10^3 CFU/ml or > 10^3 CFU/catheter segment) culture whereby the same organism (species and antibiogram) is isolated from blood sampled from the CVC or from the catheter tip, and peripheral blood; 2. simultaneous quantitative blood cultures with a > 5 : 1 ratio of CVC vs. peripheral
Catheter-suspected BSI	*Negative* blood cultures in the presence of parenteral antimicrobials, *and* • Clinical evidence of a systemic response to infection, *and* • Clinical condition improves following removal of CVC, *and* • No other likely source of infection

CFU, colony-forming unit.

Robust data on mortality, quality of life (QoL) and long-term prognosis specifically related to catheter-BSI are not available for the UK. Recent estimates of the mortality rates of patients with catheter-BSI in critical care units in France, Germany and Italy ranged from 11% to 17.1%.[27] Estimates of the additional LOS per catheter-BSI episode in UK critical care units have ranged from 1.9 days[27] to 11 days.[23] In 2006 the National Audit Office estimated the additional cost of a BSI to be £6209 per patient.[28] The most recent (2009) estimate of the financial impact for the NHS suggests that annual costs related to catheter-BSI in critical care units are £19.1–36.2M.[27]

Educational interventions for preventing catheter-bloodstream infection

Educational interventions for preventing catheter-BSI have been trialled in critical care settings in many countries and vary considerably in their content and complexity. They range from the provision of simple fact sheets and posters[29] to complex interventions comprising multiple behavioural components.[30] Educational approaches also include continuous quality improvement (CQI), which engages front-line staff in cycles of iterative problem solving, with decision-making based on real-time process measurements.[31] Interventions differ in the number and duration of education components, whether they are didactic or interactive, and whether infection surveillance feedback and performance feedback are also present. Interventions that contain several different elements which together aim to achieve a particular outcome

are referred to as 'multifaceted', 'multicomponent' or 'bundled' interventions.[32] A care bundle is defined as a small set of practices that have been individually proven to improve patient outcomes and when implemented together are expected to result in better outcomes than when implemented individually.[33]

Multifaceted educational interventions that have been developed for preventing catheter-BSI include the Michigan Keystone ICU project in the USA[34] and the NHS 'High Impact' CVC care bundle.[28] These include, among others, specific components for ensuring appropriate staff behaviour for hand hygiene, patient skin hygiene, choice of catheter type and insertion site, and catheter ongoing care.

In general, educational interventions involve encounters between teachers and learners for one or more of the following purposes: to raise awareness; to enhance or improve knowledge; or to change behaviour.[35] Educational interventions for preventing catheter-BSI ideally should include behaviour modification components underpinned by relevant theory.[36]

We defined educational interventions as those that contain any element of information provision intended to influence catheter-BSI outcomes (i.e. by changing health-care workers' behaviour). Included within this definition are checklists, and information feedback to health-care workers. We distinguish between infection surveillance feedback whereby staff are informed in real time of catheter-BSI incidence rates, and performance feedback whereby staff are informed of their compliance with evidence-based practices or progress with learning goals. According to our definition, educational interventions are not limited to purely educational practices but may also include non-educational activities, such as the provision of supplies. Such interventions may be described as providing 'components beyond education'.[37]

Current prevention of catheter-bloodstream infections in the NHS

Catheter-BSI are believed to be largely preventable following work in the UK that has successfully reduced the number of cases of methicillin-resistant *S. aureus* (MRSA) BSI. It has been proposed that the majority of catheter-BSI could be prevented using evidence-based educational interventions to ensure that doctors and nurses are committed to a culture of safety and follow best practice to achieve this.[26,38]

Evidence-based practices that are recommended for prevention of catheter-BSI include selection of an appropriate catheter type; avoidance of the femoral insertion site; antimicrobial cleansing of the insertion site; use of maximal sterile barrier precautions and aseptic technique (gloves, mask, hat, patient drapes) during catheter insertion; and use of a sterile semipermeable transparent dressing to allow observation of the insertion site.[6,39]

To address the prevention of catheter-BSI, the NHS has developed 'Saving Lives' tools,[40] which include 'high-impact' care bundles for CVCs and peripheral intravenous cannula.[28] The High Impact No. 1 CVC bundle consists of actions for preventing catheter-BSI in relation to CVC insertion (*Table 2*) and CVC ongoing care (*Table 3*). These bundles are based on 'epic2' guidelines,[39] which stress the importance of education of hospital staff for successful implementation of infection control programmes. Similar guidelines produced by the US CDC also strongly emphasise the need for education and training in evidence-based practices for preventing catheter-BSI.[6] However, in both the epic2 guidelines[39] and US guidelines[6] there is a lack of evidence on the types of educational interventions that are most appropriate and effective, and the guidelines do not make any recommendations that specifically relate to critical care settings. Following a recommendation in the Darzi Report,[41] during 2009–11 the UK National Patient Safety Agency implemented an initiative known as 'Matching Michigan'[38,42] to prevent catheter-BSI. Matching Michigan was based on a regional-scale intervention that had successfully reduced catheter-BSI incidence density in the Keystone ICU project, conducted in 103 critical care units in Michigan, USA.[34] However, the original study in the USA[34] was not randomised and did not assess the importance of the education strategy in the effectiveness of the overall care bundle.

TABLE 2 Central venous catheter insertion actions in the High Impact No. 1 CVC bundle[28]

Catheter type	Single lumen unless indicated otherwise Consider antimicrobial impregnated catheter if duration of 1–3 weeks and risk of CRBSI high
Insertion site	Subclavian or internal jugular
Skin preparation	Preferable use 2% chlorhexidine gluconate in 70% isopropyl alcohol and allow to dry If patient has a sensitivity use a single-patient-use povidone–iodine application
Personal protective equipment	Gloves are single-use items and should be removed and discarded immediately after the care activity Eye/face protection is indicated if there is a risk of splashing with blood or body fluids
Hand hygiene	Decontaminate hands before and after each patient contact Use correct hand hygiene procedure
Aseptic technique	Gown, gloves and drapes, as indicated, should be used for the insertion of invasive devices
Dressing	Use a sterile, transparent, semipermeable dressing to allow observation of insertion site
Safe disposal of sharps	Sharps container should be available at point of use and should not be overfilled; do not disassemble needle and syringe; do not pass sharps from hand to hand
Documentation	Date of insertion should be recorded in notes

TABLE 3 Central venous catheter ongoing care actions recommended in the High Impact No. 1 CVC bundle[28]

Hand hygiene	Decontaminate hands before and after each patient contact Use correct hand hygiene procedure
Catheter site inspection	Regular observation for signs of infection, at least daily
Dressing	An intact, dry, adherent transparent dressing should be present
Catheter access	Use aseptic technique and swab ports or hub with 2% chlorhexidine gluconate in 70% isopropyl alcohol prior to accessing the line for administering fluids or injections
Administration set replacement	Following administration of blood, blood products – immediately Following total parenteral nutrition – after 24 hours (72 hours if no lipid) With other fluid sets – after 72 hours
No routine catheter placement.	

The Matching Michigan programme in England recruited 240 adult and 40 paediatric critical care units, with 97% of acute health trusts in England participating. Technical components of the Matching Michigan programme were a data collection system for infection surveillance; CVC insertion checklist; CVC trolley inventory; catheter-BSI fact sheet; and Department of Health High Impact bundles.[28] Matching Michigan also included non-technical strategies, which were to develop a culture of safety; facilitate learning from incidents; foster teamwork and collaborations; and develop executive and clinical partnerships. The Matching Michigan programme ran for 2 years and ended in 2011. Preliminary results of audits from individual participating trusts are starting to appear at conferences[15–17] and in online presentations, but, to date, a detailed formal analysis of findings from Matching Michigan has not been published.

Evidence from existing reviews

A number of narrative reviews have suggested that educational interventions including care bundles may be effective at preventing catheter-BSI in various health-care settings,[7,43–46] but no systematic reviews have specifically investigated the effectiveness of educational interventions for preventing catheter-BSI in critical care units. The most relevant systematic reviews in related areas have investigated interventions for preventing catheter-BSI (not limited to educational interventions or critical care);[47] bundled behavioural interventions to control health care-associated infections (not limited to education, catheter-BSI or critical care);[30] interventions for preventing catheter-BSI in critical care (not limited to education or behavioural interventions);[48] educational interventions for preventing health care-associated infections (not limited to educational or behavioural interventions, catheter-BSI or critical care);[37] and features of educational interventions that impact on competence in aseptic insertion technique and maintenance of CVCs by health-care workers (not limited to catheter-BSI or critical care).[49] Some of these systematic reviews included primary research studies relevant to the scope of our current evidence synthesis but the most recent of these reviews[49] did not include any studies published after August 2008.

None of the systematic reviews referred to above included economic analyses. Most of the available information on the economic impact of catheter-BSI in critical care is from work conducted in the USA.[50,51] A recent brief narrative review of epidemiological studies[27] provides an insight into the economic burden of catheter-BSI in critical care in European countries including the UK but, owing to a shortage of information on costs, its findings are based on numerous assumptions and uncertainties.

Objectives

The overall aim of this evidence synthesis is to provide a rigorous evaluation of the clinical effectiveness and cost-effectiveness of educational interventions that are relevant to the NHS for preventing catheter-BSI in critical care units in England. The types of intervention that could be relevant appear diverse, but the quantity, quality and relevance of the primary clinical effectiveness and cost-effectiveness studies are unclear. To address these uncertainties the current project has the following specific objectives:

1. To create an evidence map summarising all potentially relevant primary research studies. This is necessary as a first step to clarify the quantity, quality and potential relevance to NHS policy and practice of the existing primary research studies.
2. To conduct a systematic review of a subset of studies in the evidence map considered most relevant to inform NHS policy and practice for prevention of catheter-BSI in critical care.
3. To conduct a systematic review of cost-effectiveness studies. This is necessary to clarify the quality and relevance of any existing studies of the cost-effectiveness of interventions for preventing catheter-BSI and may help to inform the structure of a decision-analytic economic model.
4. To develop a decision-analytic model to determine and compare cost-effectiveness of relevant groups of interventions and settings. This would utilise data on clinical effectiveness from Objective 2 and, if appropriate, relevant methodology and model parameters identified from Objective 3.
5. Based on the information provided from Objectives 1–4, to identify future research needs and consider the implications of implementing educational interventions for preventing catheter-BSI that are relevant to service users in the NHS.

Chapter 2 Methods for the mapping exercise and systematic review of clinical effectiveness

The a priori methods for systematically reviewing the evidence of clinical effectiveness and cost-effectiveness are described in the research protocol (see *Appendix 1*). The protocol was sent to our expert Advisory Group (AG) for comment. Minor amendments were made as appropriate, but none of the comments we received identified specific problems with the methods of the review. Methods outlined in our protocol are briefly summarised below.

Search strategy

A sensitive search strategy was developed and refined by an experienced information scientist (see *Appendix 2*).

Searches for clinical effectiveness literature were undertaken from inception of databases to January/February 2011. No trial or study filter and no language restrictions were included in the search strategy.

The strategies were applied during February 2011 to the following databases:

- MEDLINE (Ovid; searched 1948 to 19 January 2011)
- Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations (searched to 1 February 2011)
- EMBASE (Ovid; searched to 25 January 2011)
- BIOSIS (searched 1969 to 2011)
- Health Management Information Consortium (HMIC) (searched on 1 February 2011)
- CINAHL EBSCO*host* (searched on 2 February 2011)
- Cochrane Central Register of Controlled Trials (CCRCT) (searched on 2 January 2011)
- Cochrane Database of Systematic Reviews (CDSR) (searched on 2 January 2011)
- Cochrane Database of Abstracts of Reviews of Effects (DARE) (searched on 3 February 2011)
- Education Resources Information Center (ERIC) (searched from 1966)
- Web of Science databases (searched to 1 February 2011):
    - Science Citation Index Expanded (SCIE) (searched from 1970)
    - Social Sciences Citation Index (SSCI) (searched from 1970)
    - Arts & Humanities Citation Index (A&HCI) (searched from 1975)
    - Conference Proceedings Citation Index – Science (CPCI-S) (searched from 1990)
    - Conference Proceedings Citation Index – Social Science & Humanities (CPCI-SSH) (searched from 1990).

In addition, we hand-searched reference lists of the papers retrieved and relevant systematic reviews for potential additional studies. Experts on the project AG were also asked to identify additional published and unpublished references. All search results were downloaded into a Reference Manager database version 12.0.3 (Thomson ResearchSoft, San Francisco, CA, USA). Searches were rerun using the same search strategies in March 2012 to identify any new primary research published during March 2011 to March 2012, which might impact on the findings of the report.

Inclusion criteria for descriptive mapping (stage 1)

The purpose of the mapping exercise was to facilitate a description of the evidence base so that a subset of policy-relevant studies from the map could be identified and subjected to a detailed systematic review. The following inclusion/exclusion criteria were applied to the references identified by the above search strategy to select studies eligible for inclusion in the evidence map:

- *Population* Patients in critical care with any type of vascular catheter (including CVCs, arterial catheters, cannula). Critical care was defined as any critical or intensive care unit (ICU), including high-dependency units but excluded general or specialist (e.g. cardiac, neurological, surgical) non-critical units. Patients with urinary or other non-vascular catheters were only included if vascular catheters were also present. Studies solely on patients with urinary or other non-vascular catheters were excluded.
- *Design* Interventional studies based on primary research.
- *Intervention(s)* Educational interventions with an objective to reduce or prevent catheter-BSI. An educational intervention was defined as any intervention that aimed to prevent catheter-BSI and (1) included at least an element of factual information provision related to that aim; (2) was described by the authors as educational; or (3) was described by the authors as behavioural. Checklists were eligible as an educational tool. Interventions that did not target catheter-BSI (e.g. interventions for hand hygiene alone or for infection surveillance) were excluded; provision of factual information was also excluded if it was unrelated to prevention of catheter-BSI.
- *Outcomes* Primary outcomes were BSIs, mortality or LOS associated with, related to, or suspected to result from intravascular catheter use. BSIs unrelated to vascular catheter use were excluded, as were non-vascular infections (e.g. urinary tract, organ space or skin). The following secondary outcomes were not used for study selection but were to be extracted from studies at the data collection stage if at least one primary outcome was reported: staff reaction to education; attitudes; knowledge; skills; compliance with interventions; and process evaluations (quantitative or qualitative descriptions of intervention processes, facilitators or barriers).

Study selection for descriptive mapping

Titles and abstracts of records identified by the bibliographic searches conducted in January/February 2011 were assessed independently by two reviewers for potential eligibility, using a pilot tested selection worksheet containing the above selection criteria (see *Appendix 3*). Any disagreements between the reviewers were resolved through discussion and in some cases with recourse to a third reviewer. Full-text papers were obtained for all titles and abstracts that met the selection criteria or were unclear. The full-text papers were then assessed independently by two reviewers using the same study selection worksheet. Any further disagreements between the reviewers were resolved through discussion and in some cases recourse to a third reviewer. Papers published in languages other than English were each assessed by at least one native or competent speaker of the publication language together with a member of the systematic review team.

In addition to the selection of primary research studies described above, any potentially relevant systematic reviews identified during title and abstract screening were obtained as full-text versions for detailed inspection.

Owing to lack of time, any new studies identified from the updated searches in March 2012 were not formally included in the evidence synthesis but their potential implications for interpretation of the evidence synthesis findings are considered in the discussion (see *Chapter 7*).

The process of descriptive mapping

As mentioned above, the purpose of the mapping exercise was to facilitate a description of the evidence base so that a subset of policy-relevant studies from the map could be identified and subjected to a detailed systematic review. This approach has been found to be useful in previously published systematic reviews.[52–54]

Studies that met the selection criteria reported above were coded on the basis of their key characteristics using a classification instrument developed by the project team. The classification instrument (see *Appendix 4*) consisted of a standard list of keywords for capturing information on critical care specialties, vascular devices used, types of intervention used, study designs, outcomes and the educational strategies and topics covered. The classification instrument was provided in an Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) worksheet, together with instructions on how to interpret and apply the keywords, and was piloted by each member of the project team on three studies. Some amendments were made to both the keywords and the instructions to establish good inter-reviewer reliability within the team. Once finalised, the instrument was applied to the included studies by one or two reviewers depending on the publication language. Studies published in English were classified by one reviewer. Studies published in a language other than English were classified jointly by two reviewers, at least one of whom was a competent speaker of the publication language. A random sample of 40% of all the completed classifications was then checked independently by a further reviewer to ensure good inter-reviewer reliability.

Inclusion criteria for the systematic review (stage 2)

Once all of the studies had been classified, analysis was performed to construct the descriptive map (for results of the map, see *Chapter 3*).

The results of the descriptive map were presented to the AG in September 2011 for discussion. The group assisted us in prioritising a subset of studies for systematic review that most closely resemble current UK practice, and which are most likely to address current policy and practice needs for preventing catheter-BSI in critical care. Suggestions for systematic review study selection criteria were provided by seven members of the AG and 11 members of the project team, and these were discussed at a face-to-face meeting of the project team in October 2011.

Numerous potential selection criteria for the systematic review were discussed. These included limiting the systematic review to particular study designs; geographical regions; types of catheter; population age groups; types of educational approaches; or levels of study quality. A detailed description of the issues discussed is available from the authors upon request.

Based on the discussion, the inclusion criteria for the systematic review were set as follows:

- *Population* Adults (i.e. excluding neonatal and paediatric critical care units)
- *Design* Clearly reported as prospective
- *Outcomes* Studies had to provide a definition of catheter-BSI (including any definitions given in the publication or accompanying supplementary material or hyperlinks).

Study selection for the systematic review

Once the criteria for the systematic review had been set, all of the studies classified in the map were rechecked by one reviewer to ensure that the keywords regarding the population, design and outcomes were accurate. Studies from the map which met the three inclusion criteria reported above for population, design and outcomes were then entered into the full systematic review.

Data extraction in the systematic review

A data extraction and quality assessment form was devised for the systematic review based on a standard template used by the project team for other systematic reviews. The template was adapted to take into account the reporting standards recommended by the TREND Statement for reporting non-randomised studies of behavioural interventions;[55] a Best Evidence in Medical Education (BEME) Guide for systematically reviewing educational interventions;[56] and the ORION Statement for reporting intervention studies of nosocomial infections.[57] The form was piloted on a subset of the studies to ensure good inter-reviewer reliability. Data from each study included in the systematic review were then extracted by one reviewer and were checked by a second reviewer. Any disagreements between reviewers were resolved by consensus or if necessary by arbitration by a third reviewer. The completed data extraction forms can be seen in *Appendix 5*.

Quality assessment

Using criteria specified a priori, we assessed two aspects of the quality of the included studies: (1) risk of bias, which identifies methodological deficiencies in studies that could lead to systematic errors in outcomes and (2) the reporting of the methods used to collect data, which was identified by the project AG as an important aspect of study quality that should be assessed.

Risk of bias

The concept of risk of bias indicates whether study outcomes are likely to be valid and, hence, whether they may be trusted in the data synthesis.[58] Project scoping searches indicated that before-and-after studies were likely to be the most frequent research approach used for evaluating the effectiveness of educational interventions for preventing catheter-BSI. Our quality assessment criteria therefore focused on before-and-after studies, with additional criteria provided for assessing the quality of randomised controlled trials (RCTs), where appropriate. Risk of bias criteria have been established by the Cochrane Collaboration for RCTs[58] and could, in principle, be adapted or developed for assessing some aspects of bias in non-randomised studies.[59] Before-and-after studies without a concurrent control group may be particularly at risk of performance bias, as investigators may be unable to isolate effects of their intended changes in health-care practice (e.g. implementation of an intervention) from other changes that could influence patient outcomes (e.g. intrahospital, regional or national changes in health-care practices or policies). Before-and-after studies may also be at risk of selection bias if the population characteristics of the intervention and comparator (baseline) groups differ systematically, and attrition bias if availability of data differs between the intervention and comparator groups.

Specific criteria for assessing risk of bias have not been published for before-and-after studies. We developed assessment criteria for risk of selection bias, performance bias and attrition bias (*Table 4*), based on the general format of the Cochrane risk of bias tool, in which risk of bias is judged either as low, high or unclear.[58] Judgements of 'unclear' risk of bias were made if insufficient information was reported to assess a given risk of bias criterion. The risk of bias criteria were agreed by the review team and then applied independently by two reviewers to the studies included in the systematic review. The criteria were revised in light of disagreements between the reviewers' judgements. The final risk of bias criteria (see *Table 4*) are intended to assist interpretation of the current data synthesis [see *Chapter 4*,

TABLE 4 Risk of bias criteria used to assess before-and-after studies

Type of bias	Criteria for judgement of 'low'	Criteria for judgement of 'high'
Selection bias risk: systematic differences between groups	Characteristics of the patient groups were similar in the baseline and intervention periods, or any differences would be unlikely to influence risk of catheter-BSI	Characteristics of the patient groups differed between the baseline and intervention periods to an extent that could influence risk of catheter-BSI
Performance bias risk: effects of other concurrent intervention(s)	Outcomes are interpretable in relation to a specified intervention	Outcomes could be explained by more than one intervention
Performance bias risk: other concurrent staff or policy changes	Baseline and intervention periods were similar in staff numbers and expertise; patient management policies (at hospital or critical care unit levels); and critical care unit infrastructure (e.g. bed numbers)	There were notable differences between the baseline and intervention periods in staff numbers or expertise; in patient management policies; and/or critical care unit infrastructure
Performance bias risk: outcome assessment not blinded	Staff involved in blood sampling and culturing were unaware they were in a research study	Staff involved in blood sampling and culturing were aware they were in a research study
Performance bias risk: outcome definition or measurement differences between groups	Methods for taking blood for cultures and/or criteria for diagnosing catheter-BSI did not differ between baseline and intervention periods	Methods for taking blood for cultures and/or criteria for diagnosing catheter-BSI were different in baseline and intervention periods
Attrition bias risk: imbalances between groups in missing data	Patient population clearly described and the numbers of patients who provided primary outcome data agree with the described population for baseline and intervention periods	Availability of primary outcome data differed between baseline and intervention periods; and/or reasons for missing data related to intervention effectiveness

Synthesis of effectiveness (primary outcomes)] and may not be applicable outside this current systematic review. It should be recognised that assessment of risk of bias is an imperfect science, as subjectivity of interpretation and inter-reviewer disagreements occur even with the well-established Cochrane risk of bias criteria for RCTs.[60]

For RCTs, we applied the risk of bias criteria listed in *Table 4* to before-and-after comparisons within each study arm so as to enable comparisons with the non-randomised studies; and we also assessed risks of selection bias according to the adequacy of randomisation and allocation concealment, according to the standard Cochrane risk of bias criteria for RCTs.[58]

In addition to the risks of selection, performance and attrition bias reported above which we assessed using the criteria specified a priori (see *Table 4*), any other possible sources of bias noted by the reviewers in the primary studies were recorded at the data collection stage, in a free text field of the data extraction form.

Reporting of data collection in the primary studies

We recorded whether the methods of data collection were reported for clinical outcomes, infection surveillance and staff performance. Judgements were agreed by two reviewers and were recorded as yes, no, partly or unclear, together with an explanatory statement, in the data extraction form for each study. If data collection processes were reported, we also recorded whether they were shown to be validated and reliable.

Data synthesis

Studies were synthesised narratively following a structured approach similar to one proposed by Rodgers and colleagues.[61] In addition to the narrative synthesis, we explored the possibility of calculating pooled-effect estimates across independent studies in meta-analysis, taking into consideration methodological similarities and differences between the studies.

The primary review outcome was incidence density of catheter-BSI, expressed as the number of catheter-BSI per 1000 catheter-days. Effects were expressed as incidence density risk ratios (RRs) with 95% confidence intervals (CIs), for comparisons between intervention and baseline periods in the before-and-after studies. If a RR and CI were not reported for a primary study, we calculated these from catheter-BSI incidence data and the corresponding number of catheter-days, using the method of Kirkwood and Sterne.[62] In cases when catheter-BSI incidence and catheter-days were not reported, we sought these data from the study investigators. All secondary review outcomes (including compliance and process evaluations) were synthesised narratively. For all steps of the data synthesis, calculations and narrative syntheses were conducted by one reviewer and were then checked by a second reviewer.

Chapter 3 Results of the mapping exercise

Results of the literature search

The process for identifying relevant references and selecting studies for the evidence map is shown in *Figure 1*. After excluding duplicates, we identified a total of 5013 potentially relevant references. Of these, we excluded 4805 references, as their titles and/or abstracts clearly did not meet the selection criteria. Reviewer agreement at the title and abstract screening step was 99% [Cohen's kappa (κ) = 0.90]. Sixty-seven of the records not initially excluded were conference abstracts. These were found to provide too little information to contribute to the keyword mapping exercise and were subsequently excluded. We retrieved the full-text publications for the remaining 141 records for inspection. These included 12 non-English-language publications, which we translated from Spanish,[63–69] French,[70–72] German[73] and Swedish.[74] Following this selection process, 79 of the full-text records describing 74 primary research studies were included in the evidence map.[34,50,51,64,65,68–70,75–146]

Characteristics of the studies

Geographical locations

Of the 74 primary research studies reporting educational interventions for preventing catheter-BSI which we included in the evidence map, most (65%) have been conducted in North America. Seven studies have been conducted in Spain (10%),[64,65,68,69,121,122,127] five in Brazil (7%),[108,109,112,118,132] two each in Argentina,[129,130] France,[70,117] Switzerland,[94,144] and the UK,[110,128] and one each in Australia,[83] Belgium,[111] Canada,[119] Italy,[120] South Korea[142] and Mexico.[103] The UK studies were conducted in Northern Ireland[128] and Scotland[110] in paediatric and adult critical care units, respectively. No multinational studies were identified.

Spatial and temporal scales

Most (58) studies (78%) were conducted in single hospitals, with 40 of the studies (54%) conducted in single critical care units. Of the included studies, 11 were conducted in 10 or more critical care units.[34,68,82,83,85,91,107,115,133,140,141] The largest study conducted was the Michigan Keystone ICU project,[34] which included 103 critical care units in 67 hospitals in Michigan, USA.

The duration of interventions ranged from < 1 day to 7 years. In approximately one-quarter of the studies the intervention duration was unclear owing to inadequate or ambiguous reporting (*Figure 2*).

Study designs

The designs of the interventional studies are summarised in *Table 5*, based on a classification system proposed by the Cochrane Collaboration.[58,59] The order of study designs in *Table 5* reflects a hierarchy of the reliability of evidence, with risk of bias likely to be lower in well-conducted RCTs than in cohort studies.

The most frequently used study design, in 48 studies (65%), was a prospective before-and-after study (see *Table 5*). Eight studies[81,96,111,116,134,137,141,142] were historically controlled before-and-after studies. Three studies[68,136,145] were controlled trials but only two of these were randomised.[136,145] Speroff and colleagues[136] conducted a cluster RCT in the USA, in which 60 hospitals were randomised to either a virtual collaborative quality improvement (QI) programme or a toolkit-based approach for preventing catheter-BSI. Khouli and colleagues[145] conducted a RCT in the USA in which medical residents were randomised in a simulation laboratory to simulation-based plus video training for CVC insertion or video training alone. Palomar-Martinez and colleagues[68] conducted a study in Spain in which 17 critical care units received either an intervention based on the Michigan Keystone ICU project or served as controls. Two studies used an interrupted time series approach.[88,115] In the remaining 13 of the 74 studies (18%) the design

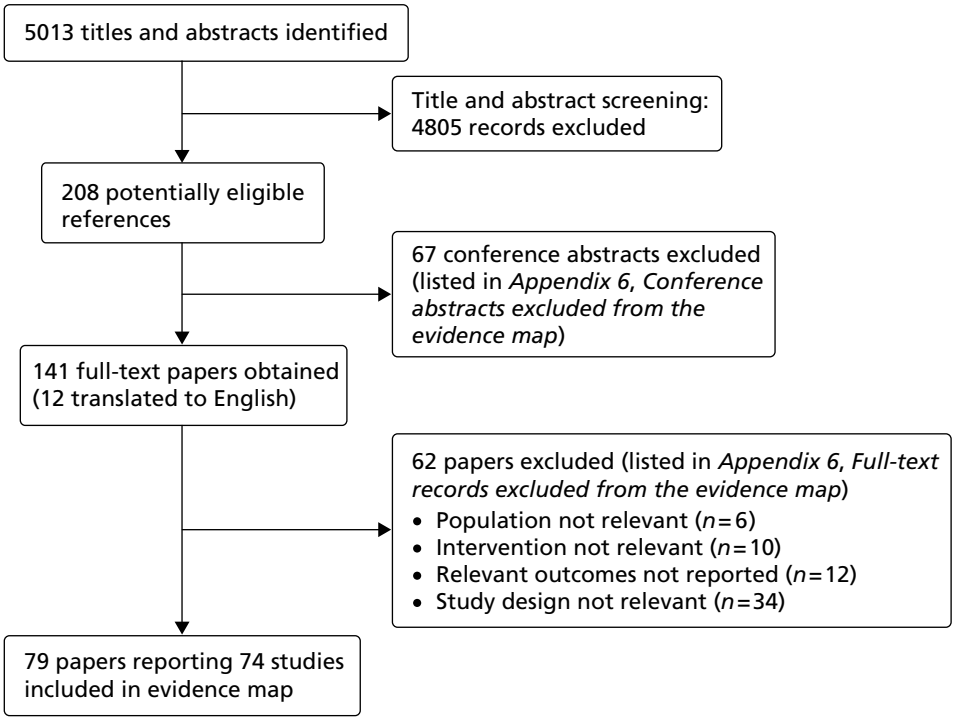

FIGURE 1 Process for selecting studies in the evidence map.

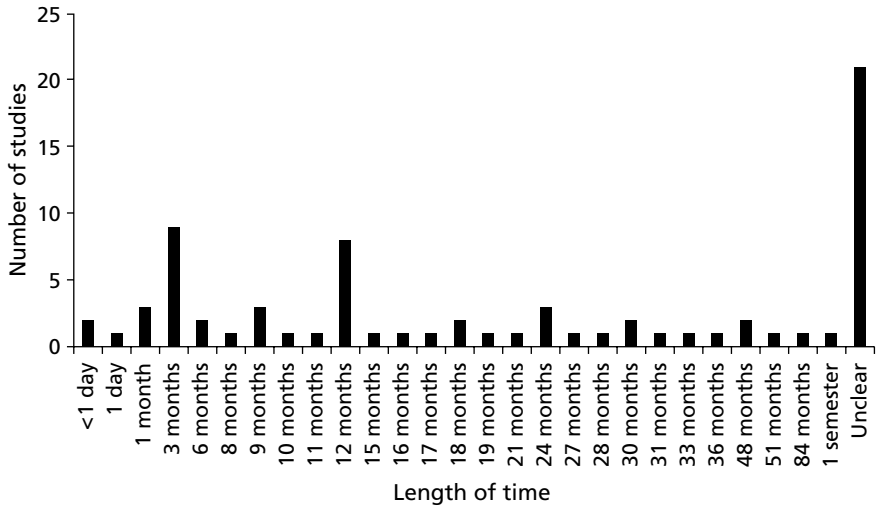

FIGURE 2 Duration of interventions.

TABLE 5 Study designs

Study design (Cochrane classification[59])	No. (rounded %) of studies (*n* = 74)
Before-and-after study – prospective	48 (65)
Design unclear	9 (12)
Before-and-after study – historically controlled	8 (11)
Controlled trial (including RCT, quasi-RCT, non-randomised)	3 (4)
Interrupted time series (controlled or uncontrolled)	2 (3)
Before-and-after study – unclear whether prospective	4 (5)

ITS, interrupted time series.

was judged unclear, either because it was unclear whether pre-intervention groups were selected prospectively or retrospectively (four studies[100,106,120,121]), or because too little information about the study methods was reported to classify the design (nine studies[78,80,82,90,101,102,105,113,125]).

Critical care specialties

The majority of studies were in adult medical, surgical and cardiac critical care units (*Table 6*).
The specialties were not described consistently in the studies and in some cases were unclear. Numbers in *Table 6* do not sum to 74, as some studies covered multiple specialties.

Intravascular devices

The studies in general provided very little information about the vascular devices used. Sixty-nine studies (93%) referred to central lines or CVCs. Five studies[65,94,105,117,131] stated that they included arterial catheters

TABLE 6 Critical care specialties

Specialty as described by the study authors	No. of studies
Medical	20
Medical–surgical	18
Surgical	18
Cardiac/coronary	17
Neonatal	11
Paediatric	8
Neurological/neurosurgical	9
Trauma	6
General or mixed	4
Burn	1
Other	6
Not reported or unclear	7

as well as CVCs, and one study[51] specifically excluded arterial catheters. Many of the studies did not report the insertion site (64% of the studies), lumen material (95%), whether antimicrobial-impregnated catheters were used (74%) or the number of lumens used (91%) (*Table 7*). Comparisons between studies are problematic, as unreported differences in vascular devices could contribute to interstudy differences in catheter-BSI incidence rates. Only three studies[83,90,131] reported catheter-BSI data separately for different types of vascular catheter.

Description and definition of catheter-bloodstream infection

In 36 of the 74 studies (49%) the authors described BSIs as catheter-associated (CABSI) and in 31 of the studies (42%) the authors described BSIs as catheter-related (CRBSI). Four studies[70,104,117,125] described BSIs in other ways and the remaining three studies[80,86,118] provided no description for the infection data they presented. Twenty-eight of the 74 studies (38%) provided a definition of catheter-BSI within their report and 56 studies (76%) cited a reference to a definition. Most of the studies defined catheter-BSI according to criteria of the US CDC NNIS, which operated up to 2004, or the CDC NHSN, which replaced the NNIS in 2005. Although the CDC definitions have changed through time, studies continued to cite old versions. For example, at least seven studies published since 2005 referred to infection definitions published in 1988.

Aims of the studies

Most (57) of the 74 studies (77%) stated that their aim was specifically to prevent catheter-BSI in critical care. The remaining studies mostly aimed to prevent catheter-BSI together with ventilator-associated pneumonia (VAP),[82,102,128,136] together with VAP and urinary tract infections (UTIs),[86,104,114,117,130,137] or together with VAP and sepsis prevention.[91,101] Five studies[89,93,94,118,120] each included prevention of catheter-BSI as part of a more general aim (*Table 8*).

TABLE 7 Vascular device characteristics potentially associated with risk of catheter-BSI

Device characteristics	No. (rounded %) of studies (*n* = 74)
Insertion site	
Fully reported	15 (20)
Partly reported	12 (16)
Not reported	47 (64)
Lumen material	
Fully reported	4 (5)
Partly reported	0 (0)
Not reported	70 (95)
Lumen coating/impregnation	
Fully reported	13 (18)
Partly reported	6 (8)
Not reported	55 (74)
Lumen number	
Fully reported	3 (4)
Partly reported	4 (5)
Not reported	67 (91)

TABLE 8 Aims of the interventions

Aim	No. (rounded %) of studies (*n* = 74)
Specifically to prevent catheter-BSI	57 (77)
Other aims	
Prevention of catheter-BSI and VAP	4 (5)
Prevention of catheter-BSI and VAP and UTI	6 (8)
Prevention of catheter-BSI and VAP and sepsis	2 (3)
Prevention of MRSA, catheter-BSI, VAP and UTI	1 (1)
Prevention of VAP, pressure ulcer, UTI, VAP, deep vein thrombosis	1 (1)
Prevention of ICU-acquired infections including catheter-BSI	1 (1)
Prevention of nosocomial infections including catheter-BSI	1 (1)
Identification of risk factors for catheter-BSI	1 (1)

Types of educational intervention

Of the 74 studies, 25 (34%) provided information on development or testing of their interventions but only three[77,102,119] (4%) reported that their interventions were based on educational theory.

The most frequently addressed clinical practices were hand hygiene (49 studies), catheter insertion site preparation (typically providing guidance on the use of chlorhexidine or povidone–iodine) (45 studies), use of full barrier precautions (43 studies), and catheter insertion site selection (typically discouraging use of the femoral site) (36 studies). The studies were variable in the extent to which they reported the clinical practices addressed by their interventions, and it was not always clear which clinical practices were included in education. For example, of the 49 studies with interventions that targeted hand hygiene behaviour, only 37 studies mentioned explicitly that intervention included education about hand hygiene (*Table 9*).

Twenty-two studies (30%) reported interventions that were purely educational and 52 studies (70%) reported that their interventions contained components beyond education (e.g. provision of antiseptic, or a catheter supplies cart).

The educational forum types (approaches to education delivery) are summarised in *Table 10*. Studies often gave rather general descriptions of educational approaches in which specific details were not reported. For this reason, the numbers of studies that used particular educational forum types may have been underestimated.

Thirty-one studies (42%) reported infection surveillance feedback and 36 studies (49%) reported performance feedback, but in nine studies[79,80,85,115,118,119,125,128,142] it was unclear whether feedback approaches were used. In several studies, feedback approaches that were described as being part of an intervention also appear to have been used during the pre-intervention period.[50,87,136,138,139]

Characteristics of the educational approaches are summarised in *Table 11* and also may have been underestimated owing to incomplete reporting by the study authors. Active learning approaches that reinforced education delivery by repeated information provision, testing and assessment and/or feedback approaches were reported in 49 of the 74 studies (66%), but in 18 studies (24%) it was unclear whether active or passive (non-reinforced) educational approaches were used. It is difficult to draw firm conclusions about the use of didactic and interactive educational approaches because often teaching sessions were described too superficially

TABLE 9 Clinical infection prevention practices reported, listed in order of the number of studies that addressed them

Clinical practice	Included in intervention	Specified as target of education
Hand hygiene	49	37
Catheter insertion site preparation, management, and/or ongoing care	45	29
Barrier precautions – full	43	28
Catheter insertion site selection (e.g. avoidance of femoral site)	36	24
Checklist (principally about catheter insertion)	35	5
Dressing care (hygiene, removal, replacement)	33	23
Catheter need review (e.g. daily inspection; removal of unnecessary catheters)	30	17
Barrier precautions – specific (e.g. drapes, gloves, gown)	27	20
Unspecified aseptic or sterile technique	22	19
Catheter device ongoing management (e.g. flushing; hub care, including 'scrub the hub')	20	19
Dressing selection (e.g. antimicrobial biopatch)	19	13
Infection prevention and/or control (including evidence-based practice; guidelines)	15	15
Central line cart use	15	1
Catheter (re)placement procedure (e.g. use of ultrasound or radiography; avoidance of guidewires)	10	8
Epidemiology of BSIs	8	8
Catheter type selection (e.g. lumen number, chemical impregnation)	5	4
Documentation and auditing of processes	5	3
Team approach to catheter care	5	4
Administration of intravenous medication or infusate	4	4
Blood draw and/or culture technique	4	4
Measurement and/or definition of infection	4	4
Catheter-BSI risk factors	2	2
Responsibilities of health-care workers	1	1
Complications of vascular catheter insertion	1	1
Isolation and contact precautions	1	1
Educational topic(s) not reported or unclear (only a very general or vague description was provided)	16	16

TABLE 10 Educational forum types (approaches to educational delivery)

Education forum	No. of studies
Checklist	35
Lecture(s), course(s) or workshop(s)	29 (+ one unclear)[a]
Printed material (leaflet, pamphlet, magazine, book, course documents)	27
Discussion group(s)	20
Poster	18
Audiovisual (video or slide show)	12
Fact sheet	11
Electronic teaching materials (multimedia resources on CD, DVD, computer, internet)	12
Champion/opinion leader (= group based)	11 (+ one unclear)
Practical demonstration of catheter technique or related activity	10
Face-to-face meetings	9
Self-study	8
Skills practice	8 (+ one unclear)
Goal sheet	7
Virtual learning (computer-mediated instruction)	6
Supervision	6
Conference calls	5
Reminders	4
Simulation	3
Mentoring, shadowing or coaching	3
Information label	2
One or more component(s) of the educational forum unclear	16
Education materials not reported or unclear	34

a Number of lectures/workshops/courses not fully deductible in 17 of these studies.

TABLE 11 Characteristics of educational approaches used

Education characteristics	No. (rounded %) of studies (*n* = 74)
Mode of learning	
Passive	7 (9)
Active	25 (34)
Both passive and active	24 (32)
Unclear	18 (24)
Mode of information presentation	
Didactic	7 (9)
Interactive	15 (20)
Both didactic and interactive	16 (22)
Unclear	36 (49)
Participation in educational sessions	
Mandatory	21 (28)
Voluntary	4 (5)
Unclear	49 (66)
Location of education/training	
In service	46 (62)
External, residential	0 (0)
External, non-residential	4 (5)
Unclear	24 (32)
Contact type	
Individual based	10 (14)
Group based	38 (51)
Both individual and group based	13 (18)
Unclear	13 (18)

for us to be sure of their approach. At least 31 of the studies (42%) used an interactive approach to learning which encourages self-discovery of information. Of the 74 studies, 21 studies (28%) made it clear that their educational sessions were mandatory, 46 studies (62%) conducted at least some of the training in-service, and group-based education appears to have been more frequently used than individual training (see *Table 11*).

Knowledge of the providers and recipients of the education (*Table 12*) and the intensity (concentration) of education (*Table 13*) is important for determining the resources that would be required if the intervention were to be replicated in another setting. Only 27 of the studies (36%) provided full information on who delivered the education, whereas 47 of the studies (64%) fully reported the intended recipients. In 42 of the studies (57%) it was unclear how many educational sessions were used and in 54 (73%) it was unclear how much time the educational sessions occupied.

TABLE 12 Education providers and recipients

Category	No. (rounded %) of studies (*n* = 74)
Education providers	
Fully reported	27 (36)
Partly reported	12 (16)
Unclear	35 (47)
Education recipients	
Fully reported	47 (64)
Partly reported	10 (14)
Unclear	17 (23)

TABLE 13 Concentration of education

Educational sessions	No. (rounded %) of studies (*n* = 74)
Frequency	
Fully reported	12 (16)
Partly reported	20 (27)
Unclear	42 (57)
Duration	
Fully reported	6 (8)
Partly reported	14 (19)
Unclear	54 (73)
Both frequency and duration fully reported	6 (8)
Frequency and duration both unclear	33 (45)

Concurrent changes in clinical practice, policy or infrastructure in addition to the intended intervention for preventing catheter-BSI were evident in 17 studies (23%). These included changes in the use of antimicrobial catheters, mechanical ventilation and/or UTI prevention bundles, hand hygiene programmes, staffing or critical care bed number. Where such changes occurred it would be difficult to isolate the effects of the intended intervention for prevention of catheter-BSI. Only 7 of the 74 studies (9%) explicitly stated that other concurrent interventions or changes in patient care did not occur during a study.[70,77,85,86,121,122,145]

Mapping exercise: summary of results

Seventy-four studies were identified that have investigated the effectiveness of educational interventions for preventing catheter-BSI in critical care. The majority of research has involved uncontrolled before-and-after studies conducted in the USA, predominantly local-scale studies in single critical care

units but also some regional-scale studies with up to 103 critical care units. Very limited information is available for the UK. Approximately half of the studies described catheter-BSI as CABSI and the other half as CRBSI, with few other descriptions reported. The most commonly targeted clinical practices were hand hygiene, preparation of the insertion site and the use of maximal sterile barrier precautions, with a wide variety of educational approaches used to address these. Interventions containing components beyond education were reported approximately twice as frequently as interventions consisting of education alone. Few studies reported the intensity of education they provided, which makes it difficult to determine resource requirements.

The evidence map highlights that secondary synthesis of educational interventions for preventing catheter-BSI is a complex area requiring appraisal of educational/behavioural strategies, complex interventions and non-randomised studies.

As mentioned earlier in *Chapter 2* (see *The process of descriptive mapping*), the results of the mapping exercise were discussed with the project's AG to identify studies relevant to NHS practice and policy for prevention of catheter-BSI. Various different inclusion criteria for the systematic review were discussed, based on the findings of the map. These discussions led to the identification of the following inclusion criteria for the systematic review:

- *Population* Adults (i.e. excluding neonatal and paediatric critical care units).
- *Design* Clearly reported as prospective.
- *Outcomes* Studies had to provide a definition of catheter-BSI (including any definitions given in the publication or accompanying supplementary material or hyperlinks).

Chapter 4 Results of the systematic review of clinical effectiveness

The inclusion criteria for the systematic review were chosen through discussion with the project's AG, to prioritise studies that were likely to be of most relevance to current NHS policy and practice for preventing catheter-BSI in critical care units in England. The agreed inclusion criteria specified that studies should have assessed interventions in adult critical care units; used and clearly reported a prospective study design; and provided a definition of catheter-BSI. Twenty-four[34,50,51,68,83,87,93,94,97,98,103,108–110,117,122,126,129,130,135,136,138,139,144] of the 74 studies included in the evidence map met these criteria and were included in the systematic review (*Figure 3*). Below, we describe the key characteristics of these 24 studies, before going on to consider their methodological quality and the effectiveness of their educational interventions for the prevention of catheter-BSI.

Characteristics of the included studies

The current systematic review focuses on studies of adult critical care units, with prospective designs, and which provided definitions of catheter-BSI, but in other respects the characteristics of the included studies are broadly representative of those included in the evidence map (*Table 14*). Half of the studies were conducted in the USA, and the majority used single-cohort before-and-after designs. One of the two UK studies in the evidence map was excluded from the systematic review because it was conducted in neonatal critical care units,[128] and one of the two RCTs in the evidence map was excluded from the systematic review because it did not provide a definition of catheter-BSI.[145] The systematic review includes studies conducted at different spatial and temporal scales, and involving different types of education, either focusing on education alone, or including additional intervention strategies beyond education (see *Table 14*). Further details of the study characteristics are presented below.

Study designs

The 24 studies included in the systematic review had the following designs. Most (20) were prospective before-and-after studies and these involved either single critical care units,[50,51,87,93,94,97,108,110,138] multiple critical care units for which results were pooled across the units,[34,83,98,126,129,130,135,139] or multiple critical care units for which results were presented separately for each unit.[103,109,122,144] One RCT[136] was based on clusters, with hospitals randomised to interventions, but implementation was at the level of the critical care unit, comparing 'Virtual Collaborative' and 'Toolkit' CQI programmes in 60 critical care units. One non-randomised study[68] compared a CQI intervention and control (no intervention) in 17 critical care units. The remaining two studies[83,117] were single-cohort CQI programmes without a true baseline period in which data from early in the intervention period served as the baseline (*Table 15*).

Populations

Characteristics of the critical care patient populations were generally reported superficially. Only 10 out of the 24 studies (42%)[50,87,93,103,109,110,129,136,139,144] reported the age and/or sex of their patient population (*Table 16*). The youngest patients reported were on average in their early 40s, in the studies by DuBose and colleagues[93] and Higuera and colleagues.[103] The oldest critical care population group reported was in the study by Rosenthal and colleagues,[129] in which the mean age was close to 72 years. Where reported, the studies included mixed-sex populations, with the proportion of men ranging from 46% to 79%. Only one study mentioned the patients' ethnicity, stating that 94% of the population was Caucasian.[139] Comorbidities were reported inconsistently, with some studies providing considerable detail and others providing no information (see data extractions in *Appendix 5*). In most studies the population characteristics either did not differ between the intervention and comparator groups or were not reported. Where differences between groups were evident we considered the risk of bias (reported below).

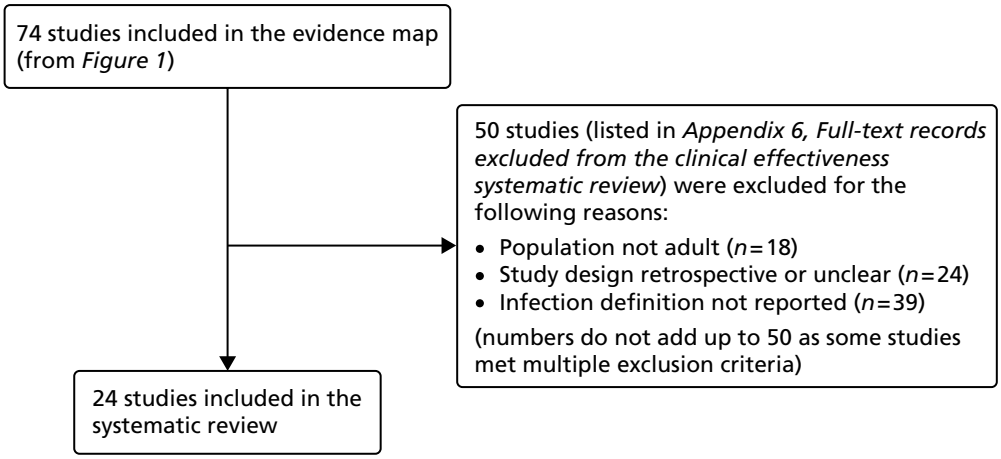

FIGURE 3 Process for selecting studies for inclusion in the systematic review.

TABLE 14 Comparison of key study characteristics between the systematic review and evidence map

Study characteristic	No. (rounded %) of studies included in the evidence map (*n* = 74)	No. (rounded %) of studies included in the systematic review (*n* = 24)
Conducted in the USA	48 (65)	12 (50)
Conducted in the UK	2 (3)	1 (4)
Prospective before-and-after study	40 (54)	20 (83)
RCT	2 (3)	1 (4)
Design unclear	13 (18)	0
Education alone	22 (30)	14 (58)
Components beyond education	52 (70)	10 (42)
Short term (≤ 12 months)	32 (43)	13 (54)
Long term (> 12 months)	21 (28)	11 (46)
Duration unclear	21 (28)	0

TABLE 15 Summary of study characteristics

Study (publication year)	Country (no.: specialty of critical care units) [duration of intervention]. Intervention summary	Study design
Burrell;[83] CEC[146] (2010, 2011)	Australia (37: not reported; included paediatric units at two hospitals) [18 months]. CQI programme based on principles of the Michigan Keystone ICU intervention,[34] including a 'clinician bundle' (hand hygiene, barrier precautions and sterile technique) and a patient bundle (skin preparation, patient draping and imaging catheter positioning during insertion) with performance feedback and infection surveillance feedback; aimed at ICU staff (staff grades not specified)	Single cohort without true baseline period
Coopersmith (2002)[50]	USA (1: surgical/burn/trauma) [6 months]. Multimodal education on CVC care and unspecified topics including in-services, posters and fact sheets, self-study and performance feedback; aimed at critical care nurses and also non-critical care staff	Prospective before-and-after study
Coopersmith (2004)[87]	USA (1: surgical) [15 months]. Multimodal education including lectures, self-study, practical demonstration, in-services and pictures of CVC maintenance, with broad topic coverage; aimed at nurses	Prospective before-and-after study
DuBose (2008)[93]	USA (1: trauma) [3 months]. Daily quality rounds checklist with 2 out of 16 checklist items relevant to CRBSI prevention; aimed at ICU fellows, residents and medical students	Prospective before-and-after study
Eggimann (2000),[94] (2005)[95]	Switzerland (1: medical) [up to 6 years]. Education based on 30-minute slideshows, bedside in-services and practical demonstration; aimed at all critical care staff (physicians, nurses and nursing assistants)	Prospective before-and-after study
Galpern (2008)[97]	USA (3: medical and surgical (mixed across three locations), one cardiac) [19 months]. Central line bundle including discussion sessions about CVC access and care, checklist, infection surveillance feedback, performance feedback and catheter cart; aimed at all ICU staff (physicians and nurses)	Prospective before-and-after study
Guerin (2010)[98]	USA (2: medical, surgical) [1 year]. Post-insertion central line care bundle including 4-hour hands-on practical sessions on CVC access and care followed by competence evaluation; included performance feedback and provision of an intravenous therapy team; aimed at all critical care unit nursing staff	Prospective before-and-after study
Higuera (2005)[103]	Mexico (2: medical surgical, neurosurgical) [9 months]. Process control intervention including 1-hour classes and provision of CDC infection control guidelines, with performance feedback and the provision of alcohol hand rub; aimed at ICU nurses, ancillary staff and physicians	Prospective before-and-after study
Lobo (2005)[108]	Brazil (2: medical) [8 months + 12 months' follow-up]. Multimodal education with infection surveillance feedback, including posters and fact sheets with emphasis on hand hygiene; aimed at all critical care staff	Prospective before-and-after study
Lobo (2010)[109]	Brazil (2: medical) [9 months]. Two educational interventions with performance feedback and infection surveillance feedback: ICU A – monthly lectures and monthly questionnaire, ICU B – single lecture, unspecified duration; aimed at all critical care staff	Prospective before-and-after study
Longmate (2011)[110]	Scotland (1: medical surgical) [up to 36 months]. CQI programme (including VAP prevention) incorporating checklist, infection surveillance feedback and performance feedback; aimed at critical care nurses and trainee doctors	Prospective before-and-after study
Misset (2004)[117]	France (1: medical surgical) [unclear, ≈ 5–6 years]. CQI programme (including VAP and UTI prevention) based on infection surveillance feedback; aimed at all ICU staff (nurses and residents)	Single cohort without true baseline period
Palomar Martinez (2010)[68]	Spain (17: not reported) [3 months]. Pilot study evaluating the feasibility of national implementation of a CQI intervention based on the Michigan Keystone ICU intervention[34]	Non-randomised controlled trial, historical baseline

continued

TABLE 15 Summary of study characteristics (*continued*)

Study (publication year)	Country (no.: specialty of critical care units) [duration of intervention]. Intervention summary	Study design
Perez Parra (2010)[122]	Spain (3: medical, general post surgery, cardiac post surgery) [15–20 minutes + 9 months' follow-up]. Short (15-minute) lecture on approaches for CVC care and maintenance; aimed at all critical care staff, with post-test 6 months after intervention	Prospective before-and-after study
Pronovost (2006),[34] (2008),[124] (2010)[123]	USA (103: including medical, cardiac surgical, neurological surgical, cardiac medical, trauma and one paediatric) [up to 3 years]. CQI programme (Michigan Keystone ICU project) using a checklist, presentations and meetings, fact sheet, infection surveillance feedback and catheter supplies cart; aimed at 'ICU colleagues' (unspecified)	Prospective before-and-after study; some ICUs without true baseline period
Render (2006)[126]	USA (8: medical) [unclear; data reported for 1 year]. Continuous QI programme based on work/learning/reporting cycles, including performance feedback and infection surveillance feedback; aimed at ICU nurses and physicians	Prospective before-and-after study
Rosenthal (2003)[129]	Argentina (4: cardiac, medical-surgical) [8–10 months]. Unspecified education and performance feedback; aimed at health-care workers (unspecified). The education period (1–2 months) was followed by a performance feedback period (7–8 months)	Prospective before-and-after study
Rosenthal (2005)[130]	Argentina (2: cardiac, medical surgical) [17 months]. Daily 1-hour educational classes and discussion groups for 1 week, followed by performance feedback during the remainder of the intervention period to enhance hand hygiene compliance; aimed at health-care workers (nurses, physicians and ancillary staff)	Prospective before-and-after study
Sherertz (2000)[135]	USA (7: general medical and surgical + 1 step down unit) [3 days in each of 2 years]. Hands-on 1-day course on infection control practices and procedures including simulation and performance feedback; aimed at third year medical students and physicians completing their first postgraduate year. Course run on 3 days in June 1996 and 3 days in June 1997, with follow-up to December 1997	Prospective before-and-after study
Speroff (2011)[136]	USA (60: not reported, but included two paediatric per arm) [18 months]. Hospitals randomised to Virtual Collaborative and Toolkit CQI approaches (including VAP prevention), with access to interactive web seminars for both groups. Virtual collaborative: monthly educational and troubleshooting conference calls, individual coaching and electronic mailing list (designed to stimulate interaction among teams). Toolkit: based on evidence based guidelines, fact sheets, review of QI and teamwork methods, educational on-line tutorials and standardised data collection/charting tools. Included performance feedback	RCT
Wall (2005)[138]	USA (1: medical) [2 years]. CQI programme involving real time feedback of infection rates and compliance with insertion practice, based on use of checklist, supervision of insertions, and web-based tutorial with competence assessment; aimed at ICU house staff (proceduralists) and nursing staff (as observers of procedures)	Prospective before-and-after study
Warren (2003)[139]	USA (2: medical, surgical) [3 months + 10 months' follow-up]. Multimodal education including lectures, self-study, bedside teaching, in-services, staff meetings, posters and fact sheets and performance feedback, with broad topic coverage; aimed at nurses and physicians	Prospective before-and-after study
Warren (2004)[51]	USA (1: medical) [1 month + 23 months' follow-up]. Multimodal education including lectures, self-study, bedside teaching, discussion groups, posters and fact sheets and performance feedback, with broad topic coverage; aimed at nurses and physicians	Prospective before-and-after study
Zingg (2009)[144]	Switzerland (5: medical, trauma, cardiovascular, general surgery) [5 months]. Multimodal education including interactive training modules and video demonstrations focusing on hand hygiene and vascular catheter care; aimed at nurses and physicians	Prospective before-and-after study

TABLE 16 Patient characteristics in 10 studies that reported patients' age and/or sex

Study	Age (years) (mean unless stated)	Sex (% male)
Coopersmith (2002)[50]	Not reported	Baseline 59.8; intervention 55.3
Coopersmith (2004)[87]	Baseline 54.5; intervention 57.4	Baseline 49.4; intervention 56.9
DuBose (2008)[93]	Baseline 41.1; intervention range 40.3–41.6	Baseline 73.0; intervention range 67.0–78.9
Higuera (2005)[103]	Baseline 44.32; intervention 45.91	Baseline 45.5; intervention 48.2
Lobo (2010)[109]	ICU A: baseline 54; intervention 53	ICU A: baseline 62; intervention 43
	ICU B: baseline 55; intervention 51	ICU B: baseline 49; intervention 50
Longmate (2011)[110]	Not reported	Baseline 56.1; intervention range 55.5–56.2
Rosenthal (2003)[129]	Baseline 71.98; intervention 71.91	Baseline 48.8; intervention 53.6
Speroff (2011)[136]	Not reported	Baseline: virtual collaborative group 50.3; toolkit group 49.7
Warren (2003)[139]	Overall study period 67	Overall study period: 52
Zingg (2009)[144]	Median: baseline 62; intervention 61	Baseline 64; intervention 67

The critical care specialties most frequently reported were medical, surgical and cardiac. Three of the regional-scale studies[33,83,136] were not conducted entirely in adult critical care units but we judged the studies to have met the population inclusion criterion for the systematic review because the proportion of non-adult critical units was small. Burrell and colleagues[83] included two paediatric critical care units (95% were adult units), Pronovost and colleagues[35] included one paediatric unit (99% were adult units) and Speroff and colleagues[136] included two paediatric units in each study arm (93% were adult units). Palomar Martinez and colleagues[68] appeared to focus on adult critical care but did not state this explicitly (the study authors were contacted but had not clarified this at the time of writing).

Vascular devices

All 24 studies included in the systematic review reported that they used CVCs, but it was not always clear whether other catheter types were also used. Misset and colleagues[117] included arterial catheters, whereas Warren and colleagues[51] specifically excluded these. Antimicrobial impregnated catheters were used routinely by DuBose and colleagues[93] and Warren and colleagues[139] but were not used by Sherertz and colleagues[135] or Warren and colleagues.[51] Longmate and colleagues[110] specified that their default catheters were non-impregnated and had four or five lumens, whereas Guerin and colleagues[98] used antimicrobial-impregnated catheters unless patients were hypersensitive to them. Coopersmith and colleagues[50,87] used four-lumen antimicrobial-impregnated catheters before their educational intervention but stated that their 'accessibility was limited' after the implementation of education (we discuss the implications of this for risk of bias below). The only other studies that reported lumen characteristics were by Wall and colleagues,[138] who used triple-lumen catheters; Render and colleagues,[126] who specified that 60% of the catheters were multilumen; and Misset and colleagues,[117] who specified that single-lumen or multilumen catheters were used as clinically required.

Definitions of bloodstream infections

Of the 24 studies, 12 defined their infections as, or equivalent to, catheter-associated (CABSI), 11 defined their infections as, or equivalent to, catheter-related (CRBSI), and the remaining study[117] gave an unclear definition (*Table 17*). Only eight studies provided definitions that agree with those of the Matching Michigan programme. In one of these studies, by Palomar Martinez and colleagues,[68] definitions equivalent to CABSI and CRBSI were both accepted but were not separated when reporting the results (see *Table 17*). In support of their reported infection definitions, 28 of the studies also cited published references to definitions of CABSI or CRBSI. However, the most frequently-cited of these references, by Garner and colleagues,[147] does not actually define CABSI or CRBSI.

TABLE 17 Comparison of catheter-associated and CRBSI definitions in the primary studies with definitions used in the Matching Michigan programme in England

Study	Reported definition	Consistent with Matching Michigan definitions?
Burrell (2011)[83,146]	CABSI	Yes – CABSI
Coopersmith (2002)[50]	CRBSI	No
Coopersmith (2004)[87]	CRBSI	No
DuBose (2008)[93]	CRBSI	No
Eggimann (2000),[94] (2005)[95]	CRBSI	No
Galpern (2008)[97]	CABSI	No
Guerin (2010)[98]	CABSI	Yes – CABSI
Higuera (2005)[103]	CABSI	No
Lobo (2005)[108]	CABSI	Yes – CABSI
Lobo (2010)[109]	CABSI	No
Longmate (2011)[110]	CRBSI	No
Misset (2004)[117]	Unclear	No
Palomar Martinez (2010)[68]	CRBSI	Yes – met either CRBSI or CABSI but not reported separately
Perez Parra (2010)[122]	CABSI	No
Pronovost (2006),[34] (2008),[124] (2010)[123]	CRBSI	No
Render (2006)[126]	CRBSI	No
Rosenthal (2003)[129]	CABSI	Yes – some met CABSI
Rosenthal (2005)[130]	CABSI	Yes – CABSI
Sherertz (2000)[135]	CRBSI	No
Speroff (2011)[136]	CABSI	Yes – CABSI
Wall (2005)[138]	CRBSI	No
Warren (2003)[139]	CABSI	No
Warren (2004)[51]	CABSI	Yes – CABSI
Zingg (2009)[144]	CRBSI	No

Types of educational intervention

The types of educational approach used in the 24 included studies are summarised in *Table 15*. As noted in the protocol (see *Appendix 1*), educational interventions were defined in a broad sense to capture any type of information provision relating to the prevention of catheter-BSI by critical care staff, including the use of checklists, performance feedback and information surveillance feedback. Fourteen of the studies (58%)[50,51,87,93,94,108,109,122,129,130,135,138,139,144] used interventions that we classified as purely educational. These ranged from the provision of single lectures[109,122] to multimodal combinations of bedside teaching,[51,94,139] in-services [50,87,94,139] self-study,[50,51,139] practical demonstrations,[87,94,144] slide shows or videos,[94,144] lectures,[51,87,109,139] discussion groups or classes,[51,130] supervision,[138] simulations,[135] and/or posters and fact sheets[50,51,87,108,139] (see *Table 15*). In one study[129] the educational approach was not reported and it is possible that other studies may not have fully reported all of the educational approaches that they used. These purely educational interventions were all implemented at a local scale, mostly in single critical care units.

A total of 10[34,68,83,97,98,103,110,117,126,136] of the 24 studies (42%) were classified as having intervention components beyond education (a classification previously used by Safdar and Abad[37] in a systematic review of interventions for preventing health care-associated infections). These studies included some of the educational approaches referred to above but, in addition, they used changes in equipment (e.g. the provision of a catheter supplies cart or alcohol for skin antisepsis) or infrastructure (e.g. the provision of a team). Five[34,68,83,126,136] of these studies implemented their interventions at a regional scale, in 8,[126] 17,[68] 37,[83] 60[136] or 103[34] critical care units (see *Table 15*). These regional-scale studies included the Michigan 'Keystone ICU' project conducted in the USA;[34,123,124] the 'CLAB ICU' project,[83] which sought to replicate aspects of the Keystone ICU project in Australia; the 'Bacteraemia Zero' project,[68] which sought to replicate aspects of the Keystone ICU project in Spain, and the RCT referred to above, which compared Virtual Collaborative and Toolkit approaches in the USA.[136] Four of these interventions could be described as CQI programmes[34,83,126,136] in which iterative improvements in clinical practices became embedded over time, whereas the fifth[68] was a short (3-month) pilot study of a CQI programme. A further two CQI programmes were implemented at a local scale in individual critical care units in France[117] and Scotland.[110] The remaining three studies[97,98,103] that implemented interventions with components beyond education at a local scale (in one to three critical care units) included a catheter insertion care bundle,[97] a catheter ongoing care bundle,[98] and an educational intervention with provision of alcohol hand rub.[103]

The duration of interventions included in the systematic review ranged from a brief 15-minute lecture reported by Perez Parra and colleagues[122] to up to 6 years in the case of a multimodal educational intervention reported by Eggimann and colleagues[94,95] (see *Table 15*). With the exception of five studies,[51,108,122,135,139] the studies monitored effects of the interventions on catheter-BSI incidence density only during the period of intervention implementation, without post-intervention follow-up. This reflects an intention in many of the studies that the interventions would become embedded into routine clinical practice.

Formal and informal education

Formal education implies that participants set aside some time for structured learning, for example to participate in classes, lectures, seminars, view slide shows, or take self-study modules. Informal education may involve passive information dissemination, for example in-service discussions during daily rounds, posters, newsletters, or supervision. The distinction is important from the perspective of resource provision since staff engaging in formal learning will be taken away from their critical care duties. Nearly all of the educational interventions contained formal education components (*Table 18*), implying that staff cover would need to be provided for those staff participating in an intervention. However, the concentration of the education (duration and frequency of sessions and whether they were periodically reinforced) was rarely reported (see data extraction forms in *Appendix 5*).

Educational theory

None of the 24 included studies specified an educational or behavioural theory. Pronovost and colleagues[124] referred to the '4E' framework proposed by Heifetz, in which the technical aspects (i.e. scientific evidence; definitions of measures standardised across hospitals) are classed as education and evaluation, whereas the adaptive elements (i.e. implementation of measures; interventions modified to fit the local context of a clinical area) are classed as engagement and execution. The authors stated only that the technical functions in the study were centralised.

Comparison of educational interventions with UK practice

The Matching Michigan programme is reflective of current NHS practice for preventing catheter-BSI (see *Chapter 1*) and educational interventions included in the systematic review shared some of the approaches used in Matching Michigan to varying degrees (*Table 19*). Of the 24 included studies, 11 studies[34,68,83,93,97,108–110,126,136,138] used checklists to improve compliance with best practices for prevention of catheter-BSI. Three studies[34,83,98] empowered their staff to halt CVC insertion procedures if protocols for

TABLE 18 Formal education approaches used in the primary studies

Study	Type of education	Main formal education method used
Burrell (2011)[83,146]	Formal + informal	Workshops
Coopersmith (2002)[50]	Formal	10-page self-study module
Coopersmith (2004)[87]	Formal + informal	Lectures
DuBose (2008)[93]	Unclear	–
Eggimann (2000),[94] (2005)[95]	Formal	Slide shows
Galpern (2008)[97]	Informal	–
Guerin (2010)[98]	Formal	4-hour mandatory training
Higuera (2005)[103]	Formal	1-hour classes
Lobo (2005)[108]	Formal	Monthly classes
Lobo (2010)[109]	Formal	Lectures
Longmate (2011)[110]	Formal	Self-guided education, including slide show
Misset (2004)[117]	Unclear	–
Palomar Martinez (2010)[68]	Formal + informal	'Kick-off' meeting, online course
Perez Parra (2010)[122]	Formal	15-minute lecture
Pronovost (2006),[34] (2008),[124] (2010)[123]	Formal + informal	PowerPoint (Microsoft Corporation, Redmond, WA, USA) presentation
Render (2006)[126]	Formal + informal	1.5-day 'kick-off' session of lectures/presentations – unclear if involved all staff
Rosenthal (2003)[129]	Formal	Unclear, other than education and training provided
Rosenthal (2005)[130]	Formal	1-hour educational classes (repeated)
Sherertz (2000)[135]	Formal	Classes on basic principles, plus skills station training
Speroff (2011)[136]	Formal	Interactive web seminars
Wall (2005)[138]	Formal	Web-based tutorial but not compulsory to complete
Warren (2003)[139]	Formal	45-minute lectures, and self-study module
Warren (2004)[51]	Formal	45-minute lectures, and self-study module
Zingg (2009)[144]	Formal + informal	45-minute classroom teaching sessions

infection prevention were not followed. Fourteen studies[34,50,83,87,97,108–110,117,126,130,136,138,139] included infection surveillance feedback in their interventions, in which catheter-BSI incidence rates were reported to critical care staff at regular intervals, either at meetings or using posters or fact sheets. However, for six of these studies, infection surveillance feedback was already in place during the baseline period and would not explain any differences in catheter-BSI incidence densities observed between baseline and intervention periods. Fourteen studies involved interventions that provided some form of performance feedback to the critical care unit staff. The feedback primarily provided information on compliance with interventions or specific intervention components (e.g. hand hygiene[110]), but in some studies feedback was given on problems encountered[109] or on staff competence assessed through tests of knowledge or skills, with staff required to repeat training if satisfactory scores were not achieved.[50,51,98] In three studies[68,122,139] the critical care staff were given tests or questionnaires, but it is unclear whether the results were fed back to the staff.

TABLE 19 Strategies used in educational interventions for prevention of catheter-BSI compared with the Matching Michigan programme

Study	Checklist	Staff empowerment	Infection surveillance feedback	Performance feedback
Burrell (2011)[83]	•	•	•	•
Coopersmith (2002)[50]			(•)	•
Coopersmith (2004)[87]			(•)	
DuBose (2008)[93]	•			
Eggimann (2000)[94]				
Galpern (2008)[97]	•		•	•
Guerin (2010)[98]		•		•
Higuera (2005)[103]				•
Lobo (2005)[108]	•		•	
Lobo (2010)[109]	•		•	•
Longmate (2011)[110]	•		•	•
Misset (2004)[117]			•	
Palomar Martinez (2010)[68]	•		?	?
Perez Parra (2010)[122]				?
Pronovost (2006)[34]	•	•	•	
Render (2006)[126]	•		•	•
Rosenthal (2003)[129]				•
Rosenthal (2005)[130]			(•)	•
Sherertz (2000)[135]				•
Speroff (2011)[136]	•		(•)	•
Wall (2005)[138]	•		(•)	•
Warren (2003)[139]			(•)	?
Warren (2004)[51]			?	•
Zingg (2009)[144]				
Matching Michigan	•	•	•	•

•, Included in intervention; (•), Included in both intervention and baseline; ?, Unclear if system was already in place before the educational intervention.

Clinical practices recommended in the Department of Health 'High Impact Intervention No. 1' for CVC insertion and maintenance[28] (see *Tables 2 and 3*) and used in Matching Michigan were included to varying degrees in the primary studies (*Table 20*). Where studies had two interventions,[109,136] the interventions within each study did not differ in the clinical practices addressed and have been summarised together in *Table 20*. The most frequently addressed of the recommended clinical practices were hand hygiene prior to patient contact, and the use of maximal sterile barrier precautions and antiseptic insertion site preparation. Only three studies[93,129,139] did not address hand hygiene practices, although in five studies[68,97,122,130,135] there was ambiguity as to whether hand hygiene was prior to or after contact with the patient (see *Table 20*).

TABLE 20 Evidence-based practices specified the UK 'High Impact Intervention No. 1' for CVC insertion and maintenance[28] that were included in the primary studies

Study	CVC insertion practices						
	Hand hygiene		Maximal barrier precautions	Skin preparation	Insertion site selection	Dressing	Documentation (date of insertion)
	Before contact	After contact					
Burrell (2011)[83]	•	•	•	•	•	•	•
Coopersmith (2002)[50]	•					?	
Coopersmith (2004)[87]	•		?	?	?	?	?
DuBose (2008)[93]							
Eggimann (2000)[94]	•	•	•	•	•	•	
Galpern (2008)[97]	○	○	•	•	•		
Guerin (2010)[98]	•		•	•	•		
Higuera (2005)[103]	•					•	•
Lobo (2005)[108]	•	•	•	•	•	•	
Lobo (2010)[109]	•	•	•	?	?	○	
Longmate (2011)[110]	•		•	•	•		
Misset (2004)[117]	•	•	•				•
Palomar Martinez (2010)[68]	○	○	•	•	•		
Perez Parra (2010)[122]	○	○		•	•		
Pronovost (2006)[34]	•	•	•	•	•		
Render (2006)[126]	•		•	•	•		•
Rosenthal (2003)[129]						•	•
Rosenthal (2005)[130]	○						
Sherertz (2000)[135]	○	○	•	•		○	
Speroff (2011)[136]	•		•	•	•		•
Wall (2005)[138]	•		•	•			
Warren (2003)[139]			•	•	•		
Warren (2004)[51]	•	•	•	•	•	•	
Zingg (2009)[144]	•	•					
Matching Michigan	•		•	•	•		•

•, included in intervention; ○, included in intervention but timing unclear in relation to patient contact (before or after) and/or care phase (device insertion or maintenance); ?, unclear whether included in intervention (limited information reported, or mentioned only as an outcome or an assessment/examination item).

CVC ongoing care practices							
Hand hygiene							
Before contact	After contact	Site inspection (daily)	Dressing	Catheter need review	Catheter access	Administration set replacement	No routine catheter replacement
•	•			•		•	
			?		?	•	
			?				
				•			
•	•		•	•		•	•
				•			
•		•	•	•	•		
•			•				
•	•		•		•	•	•
•	•		○		•	•	
•		•	?	•	•		•
•	•	•	?				•
○	○			•			
○	○		?			•	
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				•			•
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•	•		•		•	•	
•	•		•			•	
•		•		•	•		

Generally, fewer studies addressed practices related to CVC ongoing care than practices related to CVC insertion. When interpreting *Table 20*, it is important to bear in mind that authors of the primary studies might not have reported all of the clinical practices that their interventions addressed, as studies were variable in the amount of detail they provided about their methods.

The most comprehensive interventions in terms of the number of evidence-based clinical practices they included were education-only local-scale interventions reported by Eggimann and colleagues,[94] Lobo and colleagues[108] and Warren and colleagues,[51] and regional-scale interventions with components beyond education reported by Burrell and colleagues[83] and Pronovost and colleagues.[34] Among these studies, the Burrell study (the CLAB ICU project)[83] appears most relevant to current UK clinical practice, as it sought to replicate the Keystone ICU project at a regional scale.

Summary of study characteristics

Twenty-four studies were included in the systematic review. Most studies were conducted in medical, surgical and cardiac critical care units but the studies provided little information about their study populations and the vascular devices used. Where reported, patients' ages ranged from early 40s to early 70s. Half of the studies were conducted in the USA,[34,50,51,87,93,97,98,126,135,136,138,139] with only one study conducted in the UK[110] (a CQI programme in a single critical care unit in Scotland). The majority of studies used a single-cohort uncontrolled before-and-after design, with only one RCT included. The interventions evaluated in the studies were diverse in their educational approaches, ranging from single lectures in single critical care units to regional-scale CQI programmes in up to 103 critical care units. Fifty-eight per cent of the interventions reported were purely educational and 42% included components beyond education. Nearly all interventions included formal education approaches that would take staff away from bedside patient care. The interventions varied in the extent to which they addressed evidence-based clinical practices relevant to the NHS for preventing catheter-BSI. Most interventions focused on catheter insertion rather than catheter ongoing care, with hand hygiene, maximal barrier precautions and antiseptic preparation of the insertion site being the most frequently addressed practices. Different educational approaches, which were unique to individual studies, were used to address the same clinical practices. Although studies had to provide a definition of catheter-BSI to be included in the systematic review, only eight studies provided definitions consistent with those used in the NHS for the Matching Michigan programme. Two of the regional-scale interventions[68,83] aimed to replicate the Keystone ICU project intervention in different countries, and, of these, the CLAB ICU project[83] appears most relevant to NHS practice, although it was conducted in an Australian health-care setting.

Assessment of clinical effectiveness

Quality assessment: risk of bias

The included primary studies were difficult to assess for risk of bias because in most cases insufficient information was reported, resulting in a judgement of 'unclear' (*Table 21*). Methodological information supporting the judgements reached by the reviewers is given in the data extraction forms (see *Appendix 5*). When interpreting risk of bias it is important to bear in mind that, as judgements of bias are constrained by the availability of information, studies classified as having high or low risk of bias may not necessarily be at greater or lower risk of bias than those studies classified as unclear.

Studies judged to be at high risk of bias

Three studies[68,109,144] were judged to be at high risk of selection bias, as the numbers of patient-days and CVC-days were consistently lower in the intervention period than in the pre-intervention period;[109] baseline incidence of catheter-BSI was higher in control than in intervention critical care units;[68] or the McCabe rapid fatality score, number of trauma patients and number of patients who had a CVC inserted were statistically significantly higher in the intervention than in the baseline period.[144]

TABLE 21 Quality assessment: risk of bias – criteria adapted for before-and-after studies

Study	Selection bias risk (systematic differences between groups)	Performance bias risk (effects of other concurrent intervention/s)	Performance bias risk (other concurrent staff/policy changes)	Performance bias risk (outcome assessment not blinded)	Performance bias risk (outcome definition or measurement differences between groups)	Attrition bias risk (imbalances between groups in missing data)
Burrell (2011)[83]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Coopersmith (2002)[50]	Unclear	Unclear	High	High	High	Unclear
Coopersmith (2004)[87]	Unclear	Unclear	High	Unclear	Unclear	Unclear
DuBose (2008)[93]	Unclear	Unclear	Unclear	High	Low	Unclear
Eggimann (2000),[94] (2005)[95]	Low	Low	Low	Unclear	Unclear	Low
Galpern (2008)[97]	Unclear	Low	Unclear	Unclear	Unclear	Unclear
Guerin (2010)[98]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Higuera (2005)[103]	Low	Unclear	Unclear	Unclear	Unclear	Unclear
Lobo (2005)[108]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Lobo (2010)[109]	High	High	Unclear	Unclear	Unclear	Unclear
Longmate (2011)[110]	Unclear	Unclear	Unclear	High	Unclear	Unclear
Misset (2004)[117]	Unclear	Unclear	Low	Unclear	Unclear	Unclear
Palomar Martinez (2010)[68]	High	High	Unclear	Unclear	Unclear	Unclear
Perez Parra (2010)[122]	Unclear	Low	Unclear	Unclear	Low	Unclear
Pronovost (2006),[34] (2008),[124] (2010)[123]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Render (2006)[126]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Rosenthal (2003)[129]	Unclear	High	Unclear	Unclear	Unclear	Unclear
Rosenthal (2005)[130]	Unclear	High	Unclear	Unclear	Unclear	Unclear
Sherertz (2000)[135]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
[a]Speroff (2011) (RCT)[136]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Wall (2005)[138]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Warren (2003)[139]	Low	Unclear	Unclear	Unclear	Unclear	Unclear
Warren (2004)[51]	Unclear	Unclear	Unclear	High	Unclear	Unclear
Zingg (2009)[144]	High	Unclear	Unclear	Unclear	Unclear	Low

a Risk of bias criteria for the RCT refer to comparisons between baseline and intervention periods within each arm (assessment of randomisation and allocation concealment are reported separately in the text).

Four studies[68,109,129,130] were judged to be at high risk of performance bias owing to a potential influence of other concurrent or overlapping interventions as the planned intervention overlapped with different hand hygiene interventions;[129,130] staff in a critical care unit receiving one intervention moved to a different critical care unit receiving another intervention;[109] or staff in control critical care units were able to attend training for the intervention.[68]

Two studies[50,87] were judged to be at high risk of performance bias owing to staff or policy changes because they reported changes in antibiotic prescribing patterns and accessibility of quadruple-lumen catheters,[50] or reported that the number of ICU beds was higher in the intervention period (six beds; 33% increase).[87]

Four studies[50,51,93,110] were judged to be at high risk of performance bias because critical care staff assessing outcomes (the staff collecting and culturing blood samples and analysing the results) were not blinded. The remaining 19 studies did not report whether the staff were blinded but it seems unlikely that authors would have blinded study participants without reporting so.

One study[50] was judged to be at high risk of performance bias, as the authors implied that there was a procedural difference in diagnosis and/or reporting of infections between the baseline and intervention periods (it was stated that treatment of catheter colonisation could have accounted for a large number of documented infections in the pre-intervention time period).

Studies judged to be at low risk of bias

Studies were judged to be at low risk of bias if their population characteristics did not appear to differ between baseline and intervention periods[94,103,139] (low selection bias risk); they stated that no other concurrent interventions were conducted,[94,97,122] or no changes in critical care structure or staffing occurred[94,117] that could potentially affect catheter-BSI incidence; they stated that catheter-BSI definitions and diagnosis procedures did not change[93,122] (low performance bias risk); or missing data were deducible and did not appear to differ between baseline and intervention periods[94,144] (low attrition bias risk).

Risk of bias in randomised controlled trials

Only one RCT, by Speroff and colleagues,[136] was included in the systematic review. In addition to the risk of bias criteria reported above for before-and-after studies, which we used to assess before-and-after comparisons within each of the RCT arms, we assessed the risk of selection bias, according to the adequacy of randomisation and allocation concealment, using the Cochrane Collaboration criteria for risk of bias in RCTs.[58] The RCT[136] was judged to be at unclear risk of selection bias because insufficient information was provided about the methods of random sequence generation and allocation concealment.

Other bias risk

Information collected in the data extraction forms (see *Appendix 5*) suggests that studies may have been at risk of self-reporting bias (study outcomes were reported directly by the investigators without independent checking). For example, self-reporting of outcomes was routine[110,136] or dependent upon staff availability;[83] an audit tool and intervention were implemented by the same team that designed them;[87] the study co-ordinator who was involved in delivering an intervention checked data sheets for missing items and errors;[129] and it was assumed that nurses accurately captured information and completed a checklist for every insertion, without formal validity and reliability analyses.[138]

In three studies[110,117,136] the intervention as reported by the authors was not intended solely for the prevention of catheter-BSI: Longmate and colleagues[110] reported an intervention for preventing CRBSI, VAP and MRSA; Misset and colleagues[117] reported an intervention for preventing CRBSI, VAP and UTIs; and Speroff and colleagues[136] reported two interventions, each for preventing both central line-associated bloodstream infection (CLABSI) and VAP. In these studies, clinical effectiveness must be evaluated for the intervention as a whole, as effects of the individual intervention components that target the different types of infections are not separable.

Reporting of data collection in the primary studies

Of the 24 primary studies,[34,50,51,68,83,87,93–95,97,103,108–110,117,122–124,126,129,130,135,136,138,139,144,146] none provided full details of their data collection processes. The most detailed descriptions of data collection were reported by Burrell and colleagues[83] and Wall and colleagues,[138] but even their descriptions were incomplete. Burrell and colleagues[83,146] stated that data entry was manual, with an infection nurse checking data on each form. Collected data were received and collated by the Clinical Excellence Commission. Missing and invalid data were followed up and validity of reported central line-associated bacteraemia (CLAB) were confirmed with individual critical care units. However, many critical care units did not have microbiological support and reported CLAB through discussion with senior critical care staff, while improved understanding of surveillance definitions versus clinical definitions led to some CLAB cases being reclassified. Wall and colleagues[138] reported that upon completing a checklist, a nurse detached the top page (with all items readable) and dropped it in a secure lockbox. The second page remained on the patient's chart with the sensitive items blacked out. The infection control practitioners collected the checklists daily and scanned the de-identified forms into a pre-established computerised database using scanning software which read pre-established fields on the checklist into a spreadsheet database. These data were stored on a secure computer at the Center for Clinical Improvement for future statistical analyses.

Only one[94] of the 24 studies reported that their data collection approach was reliable (pre-tested and standardised in several pilot phases), for infection surveillance. One study[98] mentioned that device-day data collected by critical care unit nursing staff were compared with data collected daily by the intravascular catheter management team to confirm the accuracy of data collection but did not provide any supporting data. Three studies[110,136,138] stated explicitly that validity and/or reliability of the data collection method was not assessed. It seems improbable that validity and reliability of data collection would have been assessed in the remaining studies, as no mention was made in the publications.

Summary of quality assessment

Overall, the methodological quality of the 24 included primary studies was difficult to assess owing to limited or unclear reporting of study populations and research methods. Nine studies[50,51,68,87,93,109,110,129,130] were judged to be at high risk of bias, but, as risk of bias could be assessed only for well-reported studies, the extent of risks of bias among the studies may have been underestimated. Several different types of data were collected in the primary studies, including infection surveillance information, results of tests and assessments, and information on patient outcomes. However, none of the included studies fully reported its data collection methods and the majority of studies did not report whether data collection approaches had been shown to be valid and/or reliable. In most cases the staff who were involved in data collection were not specified, and studies may have been at risk of self-reporting bias (we did not formally assess whether staff involved in data collection were independent, but the authors of five studies[83,87,110,129,136] implied that they were not).

Synthesis of effectiveness (primary outcomes)

It was inappropriate to calculate pooled-effect estimates for study outcomes, as the primary studies included in the systematic review varied considerably in their temporal and spatial scales, objectives, and in the structure and content of their interventions. The data from the primary studies were also considered unsuitable for exploration using meta-regression to identify potential explanatory variables for intervention effects, as the data requirements for the conduct and clear interpretation of meta-regression as described by Thompson and Higgins[148] would not be met. Instead, we present a structured narrative synthesis below.

It was not possible to identify studies that could be classed as 'best' or 'worst' in terms of methodological quality and risk of bias. We have therefore not used quality criteria to exclude any studies from the data synthesis. Instead, we summarise below the effectiveness for all studies, which provided relevant outcomes data. Issues of quality and bias identified above that could influence the interpretation of clinical effectiveness for specific studies are highlighted on a case-by-case basis.

Incidence density of catheter-bloodstream infection

In 10 studies, insufficient data were reported for the calculation of incidence density RRs with 95% CIs or there were ambiguities in the published data,[83,93,94,97,117,126,130,135,136,138] and we attempted to contact the authors for clarification. Six authors responded with information, three did not respond and one responded stating that relevant data were not available. Data that were provided by the study authors in response to us contacting them are indicated in *Appendix 7*.

To enable comparisons of clinical effectiveness among the included interventions, incidence density RRs with their 95% CIs are displayed in forest plots, with the interventions grouped according to their spatial and temporal scales: regional-scale interventions (see *Figure 4*), local-scale interventions of duration ≤ 12 months (see *Figure 5*), and local-scale interventions of duration of > 12 months (see *Figure 6*). Within each forest plot, studies are ordered by effect size (larger effects of interventions relative to comparators are indicated by smaller incidence density RRs). As this is a narrative synthesis, pooled-effect estimates are not displayed in the forest plots. The amount of information available varied considerably among the studies, with some studies providing RRs for more than one intervention scenario or time period (multiple within-study effect estimates are not statistically independent but are included in the forest plots, as pooled-effect estimates are not calculated). The full data used in calculating RRs, including the baseline and intervention catheter-BSI incidence densities for each study, are given in *Appendix 7*.

Educational interventions were classified either as effective at reducing catheter-BSI incidence density, lacking convincing evidence for effectiveness, or ineffective according to the following criteria:

- *Effective* The incidence density RR for intervention compared with comparator (baseline) was < 1.0 and the 95% CI of the RR did not include 1.0.
- *Ineffective* The 95% CI of the incidence density RR for intervention compared with comparator (baseline) included 1.0.
- *Lack of convincing evidence for effectiveness* Effectiveness was marginal, or serious limitations of the study methodology cast doubt on the reliability of the results (explanations are provided below on a case-by-case basis).

Regional-scale interventions

Five studies[34,68,83,126,136] investigated regional-scale CQI interventions (*Figure 4*; for the full data see *Appendix 7, Data for forest plot: regional-scale interventions*). These studies included the Keystone ICU project,[34,123,124] the 'CLAB ICU' project,[83,146] which sought to replicate aspects of the Keystone ICU project in Australia, and the 'Bacteraemia Zero' project,[68] which sought to replicate aspects of the Keystone ICU project in Spain. Three of the studies used uncontrolled before-and-after designs, whereas two (a RCT by Speroff and colleagues[136] and the non-randomised controlled study by Palomar Martinez and colleagues[68]) included two parallel comparison groups of critical care units (virtual collaborative and toolkit groups[136] or intervention and control groups[68]). The study by Palomar Martinez and colleagues[68] reported historical baseline data on infection incidence for 3 years prior to the prospective intervention (2004–6), of which we report only the 2006 data, as these are most directly relevant for comparison with the study period (2007) (for full data see the data extraction form in *Appendix 5*). All of the regional-scale studies calculated the number of device-days based on presence/absence of vascular catheters, which does not take into account the number of concurrent catheters that a patient may have.

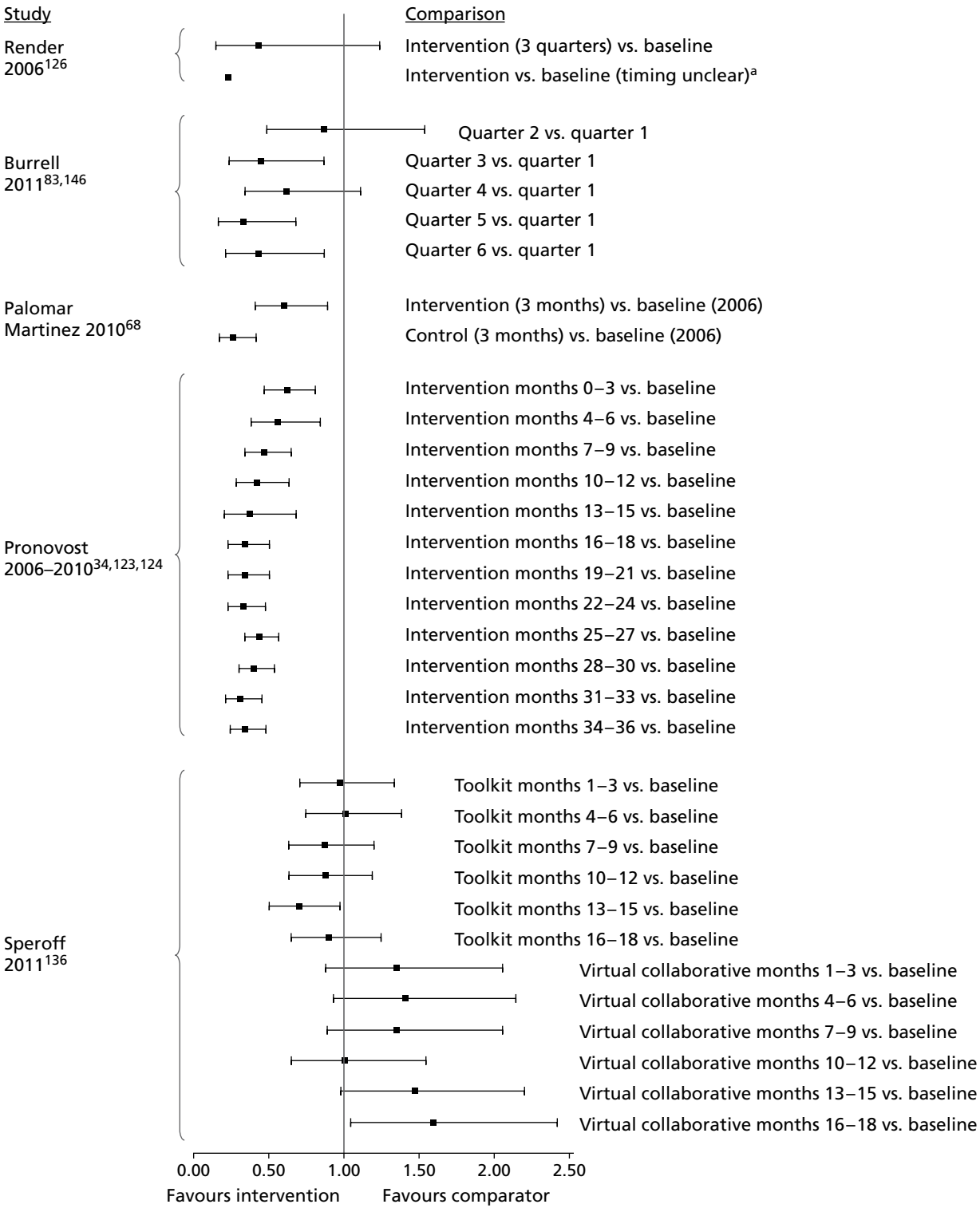

FIGURE 4 Incidence density RRs (± 95% CI) for regional-scale interventions (multiple catheters per patient not counted separately in device-days). a, CI not calculable.

Clinically effective interventions (with unclear risk of bias)

Assuming that effects displayed in the forest plots reflect those of the planned interventions, the CLAB ICU project[83,146] and Keystone ICU project[34,123,124] interventions appear to have been effective in reducing catheter-BSI incidence densities relative to baseline, although both studies had unclear risk of bias (*Box 1*). The Keystone ICU project achieved a reduction in catheter-BSI incidence density after 3 months, which subsequently persisted through the 36-month intervention monitoring period. The CLAB ICU project achieved a reduction in catheter-BSI incidence density after 6 months, which was mostly sustained until the end of the 18-month intervention monitoring period (statistically significant in quarters 3, 5 and 6) (see *Figure 4*). These studies both have some relevance to clinical practices for prevention of catheter-BSI in critical care in the NHS and are considered in more detail below.

Clinically ineffective interventions

The two interventions implemented in the RCT by Speroff and colleagues[136] were clearly not effective at reducing catheter-BSI incidence density, as acknowledged by the study authors (*Box 2*). During the 18-month study period, catheter-BSI incidence density for the virtual collaborative intervention actually increased relative to baseline (see *Figure 4*).

Process evaluation conducted by Speroff and colleagues[136] (discussed below: see *Process evaluations, facilitators and barriers*) indicated that adoption of intervention components was consistently higher in the virtual collaborative intervention arm than the toolkit approach arm, suggesting that failure of the interventions to reduce catheter-BSI incidence was not simply related to the extent of intervention implementation.

Interventions lacking convincing evidence for effectiveness

The two remaining regional-scale interventions, by Render and colleagues[126] and Palomar Martinez and colleagues,[68] appear at first sight to have been effective at reducing the incidence densities of catheter-BSI. However, upon closer inspection the findings of these studies are difficult to interpret.

Published data for the study by Render and colleagues[126] indicate an incidence density RR below 1.0 but the publication did not provide a CI or sufficient data for us to calculate one. Further data obtained on request from the author (see *Appendix 7, Data for forest plot: regional-scale interventions*) enabled

BOX 1 Regional-scale interventions at unclear risk of bias that appear effective at reducing the incidence density of catheter-BSI

- CQI programme conducted in 103 critical care units in the USA: the Keystone ICU project (duration of up to 36 months). Targeted clinicians' use of hand washing, full barrier precautions during CVC insertion, skin cleansing with chlorhexidine, avoiding the femoral site, and removing unnecessary catheters; included checklist, presentations and meetings, fact sheet, infection surveillance feedback and catheter supplies cart.[34,123,124]
- CQI programme conducted in 37 critical care units in Australia: the CLAB ICU project (duration of up to 18 months). Based on principles of the Michigan Keystone ICU project, including a 'clinician bundle' (hand hygiene, barrier precautions and sterile technique) and a patient bundle (skin preparation, patient draping and imaging catheter positioning during insertion); also included a checklist, infection surveillance feedback and catheter supplies cart.[83,146]

BOX 2 Regional-scale interventions that were not effective at reducing the incidence density of catheter-BSI or lack convincing evidence for effectiveness

Not effective: CQI programme conducted in 60 critical care units in the USA during 18 months. Hospitals were randomised to Virtual Collaborative and Toolkit CQI approaches (including VAP prevention), with access to interactive web seminars for both groups. Virtual collaborative: monthly educational and troubleshooting conference calls, individual coaching and electronic mailing list (designed to stimulate interaction among teams). Toolkit: based on evidence based guidelines, fact sheets, review of QI and teamwork methods, educational online tutorials and standardised data collection/charting tools[136] (note that hospitals were randomised but implementation was at the level of critical care units).

Lack of convincing evidence for effectiveness: Continuous QI programme, duration approximately 1 year, in a single cohort of eight critical care units in the USA, based on work/learning/reporting cycles, including performance feedback and infection surveillance feedback.[126]

Lack of convincing evidence for effectiveness: Three-month pilot study based on the Michigan Keystone ICU intervention, evaluating the feasibility of national implementation of a CQI intervention in 17 critical care units in Spain, with units allocated non-randomly to either intervention or control groups – the Bacteraemia Zero project[68] (this study was judged to be at high risk of selection and performance bias).

us to calculate an incidence density RR with a 95% CI, but the CI indicates lack of effectiveness (see *Figure 4*). On balance, the available information for the study by Render and colleagues[126] does not provide convincing evidence that the intervention was effective at reducing the incidence density of catheter-BSI (see *Box 2*).

The results of the Bacteraemia Zero project reported by Palomar Martinez and colleagues[68] are difficult to interpret because incidence density RRs were significantly lower than 1.0 both for the intervention and control groups of critical care units, with a larger effect (smaller RR) evident in the control group (see *Figure 4*). The Palomar Martinez study[68] is notable in that we judged it to be at high risk of selection bias because the control group had higher baseline incidence density of catheter-BSI than the intervention group. We also judged this study to be at high risk of performance bias because staff in control critical care units were able to attend intervention group meetings at which intervention information and materials were disseminated. On balance, this 3-month pilot study by Palomar Martinez and colleagues[68] does not provide convincing evidence of effectiveness of their CQI programme at reducing the incidence density of catheter-BSI.

Local-scale interventions of up to 12 months in duration

Twelve studies investigated local-scale interventions of up to 12 months' duration. Of these, 10 studies[50,51,98,103,108,109,122,129,139,144] provided sufficient data for the calculation of incidence density RRs (*Figure 5*; for the full data, see *Appendix 7, Data for forest plot: local-scale interventions of duration up to 12 months*). These studies all calculated the number of device-days based on the presence/absence of vascular catheters, which does not distinguish multiple concurrent catheters in a patient. The educational interventions were diverse and included single lectures on practices related to CVC care;[109,122] structured and interactive education modules focusing on hand hygiene and CVC care[144] multimodal education of various types with performance feedback;[50,51,103,129,139] multimodal education with infection surveillance feedback;[108] and a post-insertion central line care bundle.[98] Three of these studies each involved a single critical care unit;[50,51,108] three studies involved multiple critical care units and reported results pooled across the units;[98,129,139] and four studies presented results separately for different critical care units.[103,109,122,144] Lobo and colleagues[109] compared a single lecture in one critical care unit ('ICU A') with a tailored continuous educational intervention in another critical care unit ('ICU B') located at the same hospital, whereas Higuera and colleagues,[103] Perez Parra and colleagues[122] and Zingg and colleagues[144] compared results from different critical care units which had received similar interventions (see *Figure 5*).

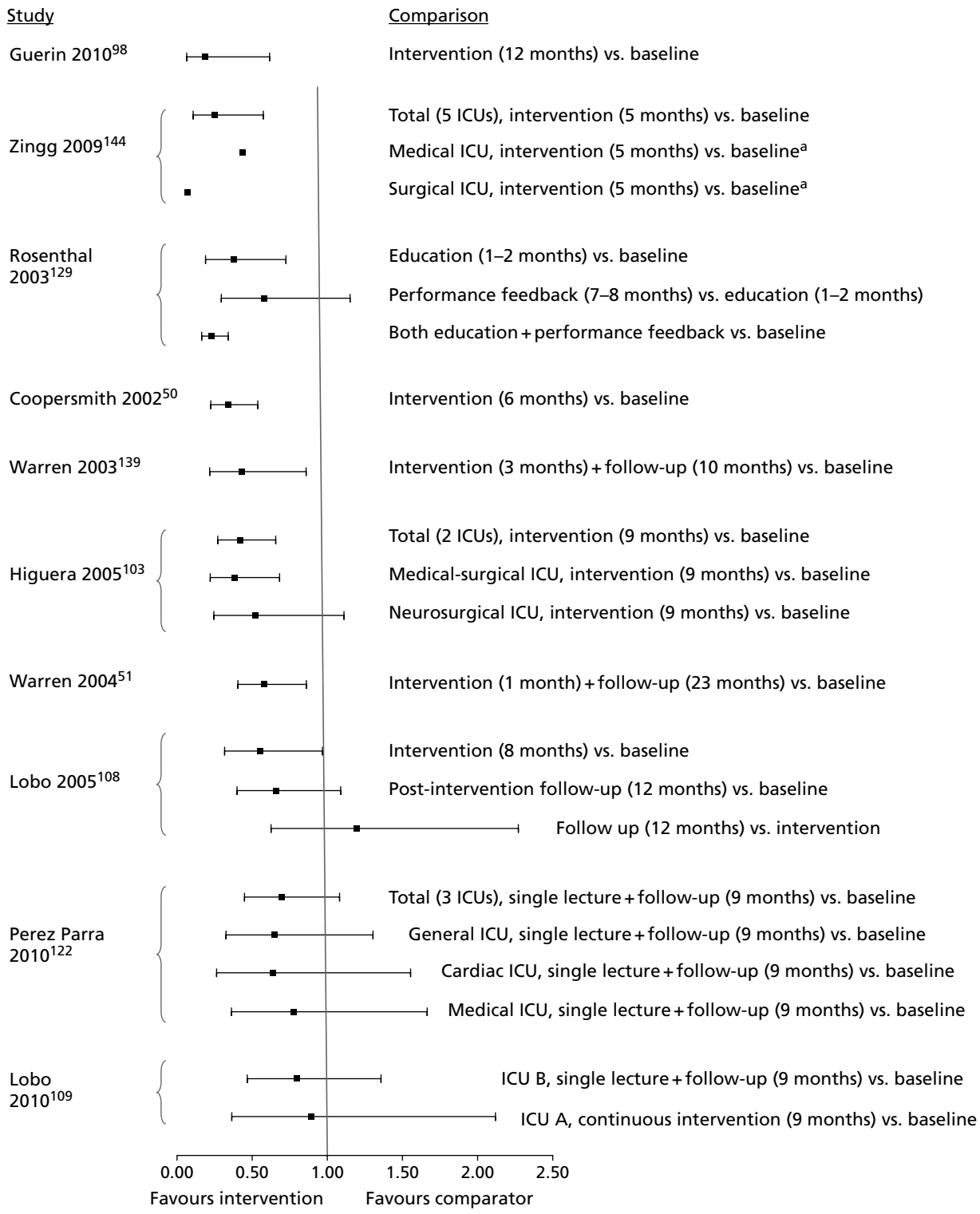

FIGURE 5 Incidence density RRs (± 95% CI) for local-scale interventions of up to 12 months in duration (multiple catheters per patient not counted separately in device-days). a, Confidence interval not calculable.

Clinically effective interventions (with unclear or high risk of bias)

Assuming that effects displayed in the forest plots reflect those of the planned interventions, seven of the interventions[50,51,98,103,129,139,144] would appear to have been effective in reducing the incidence density of catheter-BSI (*Box 3*), as incidence density RRs were significantly below 1.0 (see *Figure 5*). The studies by Coopersmith and colleagues[50] and Warren and colleagues[51] were judged to be at high risk of performance bias because the authors stated that the staff assessing outcomes were not blinded to the intervention. However, it seems unlikely that staff would have been blinded in any of the other studies, although this was not reported. Two studies[50,129] were judged to be at high risk of performance bias for other reasons. Effects of the educational intervention implemented by Coopersmith and colleagues[50] appear to have been confounded with changes in antibiotic prescribing practice and availability of four-lumen catheters, whereas effects of the educational intervention implemented by Rosenthal and colleagues[129] overlapped with a separate hand washing intervention. One study by Zingg and colleagues[144] was judged to be at high risk of selection bias, as the study characteristics of the population differed between the baseline and intervention periods.

In two[103,129] of the seven studies that appeared clinically effective, further caution on interpretation is required. In the study by Rosenthal and colleagues[129] incidence density RRs were significantly < 1.0 for education or education and performance feedback periods together but not for the performance feedback period alone. These results are difficult to interpret because the education and performance feedback

BOX 3 Local-scale interventions of up to 12 months' duration and at unclear (or, where stated, high) risk of bias that appear effective at reducing the incidence density of catheter-BSI

- Multimodal education including self-study, in-services and performance feedback in one critical care unit in the USA for 6 months, with broad topic coverage aimed at nurses; included infection surveillance feedback but this was also present in the baseline period.[50]
- Multimodal education including self-study and performance feedback, with broad topic coverage aimed at nurses and physicians in two critical care units in one hospital in the USA for 3 months; included infection surveillance feedback but this was also present in the baseline period.[139]
- Multimodal education including self-study and performance feedback, with broad topic coverage aimed at nurses and physicians in one critical care unit in the USA for 1 month; unclear whether included infection surveillance feedback.[51]
- Multimodal education focusing on hand hygiene and vascular catheter care aimed at nurses and physicians in five critical care units in one hospital in Switzerland for 5 months[144] (this study was judged to be at high risk of selection bias, as population characteristics differed between baseline and study periods).
- Unspecified education (1–2 months) followed by performance feedback (7–8 months) in four critical care units in two hospitals in Argentina[129]) (this study was judged to be at high risk of performance bias as the effects of the intervention appear to be confounded with those of a separate hand-washing intervention; also, as mentioned in the text, only the education phase can be reliably interpreted; this study also had relatively high baseline incidence density of catheter-BSI).
- Process control intervention in two critical care units in one hospital in Mexico for 9 months, including 1-hour classes and provision of CDC infection control guidelines, with performance feedback and the provision of alcohol hand rub[103] (note that this study had relatively high baseline incidence density of catheter-BSI and effectiveness was not demonstrated in all participating critical care units).
- Post-insertion central line care bundle in two critical care units in one hospital in the USA for 12 months, including 4-hour hands-on practical sessions on CVC access and care followed by competence evaluation; included performance feedback and provision of an intravenous therapy team.[98]

periods were sequential, and performance feedback may not have been independent of the effects of the preceding education. Interpretation should therefore be restricted to the education phase, which itself appeared to be clinically effective, although this was only monitored for 1–2 months (see *Figure 5*). In the study by Higuera and colleagues[103] the intervention was effective when data for two critical care units were pooled but found to be effective in only one of the units when they were analysed separately (see *Figure 5*). It is notable that the medical–surgical critical care unit had a higher baseline incidence density of catheter-BSI per 1000 catheter-days (57.4) than the neurosurgical critical care unit (32.8). These baseline incidence densities and also the baseline catheter-BSI incidence density in the study by Rosenthal and colleagues[129] (45.9 per 1000 catheter-days) are higher than typically found in European studies.

For these seven studies[50,51,98,103,129,139,144] that appeared to be effective at reducing incidence of catheter-BSI (albeit with the caveats noted above), statistical significance indicated by the CIs of RRs in *Figure 5* is consistent with the primary study publications, which, in all cases, claimed that effects of the interventions at reducing catheter-BSI incidence were statistically significant.

Two[51,139] of the studies that appeared effective at reducing catheter-BSI incidence (see *Box 3*) reported post-intervention follow-up monitoring, which may provide an indication of the longer-term persistence or attenuation of intervention effectiveness. Warren and colleagues[139] conducted 10 months of follow-up after a 3-month intervention; and Warren and colleagues[51] conducted 23 months of follow-up after an intervention of about 1 month. Although the RRs based on the whole follow-up period appear encouraging, monthly data provided for the latter study[51] (data extraction form – see *Appendix 5*) show that incidence densities varied considerably from month to month, and returned to baseline levels within the first 3 months of the 23-month follow-up period.

Clinically ineffective interventions

For two[109,122] of the local-scale short-term studies, the 95% CIs for the RRs indicate that the reduction in catheter-BSI incidence density was not statistically significant (see *Figure 5*). In contrast, the primary publications for these studies both claimed statistically significant effects of the interventions.[109,122] Lobo and colleagues[109] based their conclusion on incidence data rather than incidence density. Perez Parra and colleagues[122] stated that they initially conducted a Wilcoxon rank sum test and then to control for (unspecified) confounding effects of external events and (unspecified) secular trends that occurred during the study period they used a Poisson regression approach. The statistical significance reported[122] varied among the critical care units (overall: $p = 0.3$; general post surgical: $p = 0.05$; cardiac post surgical: $p = 0.12$; medical: $p = 0.31$) and it is not clear to which of the analytical approaches the *p*-values refer. On balance, we conclude that these two studies were not effective at reducing catheter-BSI incidence density (see *Figure 5* and *Box 4*) and the claims of statistical significance in the primary publications do not provide sufficient grounds for us to alter our conclusion.

Interventions lacking convincing evidence for effectiveness

The intervention reported by Lobo and colleagues[108] has a RR bordering on statistical non-significance (upper limit of the 95% CI 0.97) and a non-significant RR for the follow-up period suggesting that the intervention was only briefly effective (see *Box 4*) at reducing the incidence of catheter-BSI (see *Figure 5*). The publication for this study did not report statistical significance.[108]

Local-scale interventions of more than 12 months in duration

Seven studies[87,94,95,97,110,138] investigated local scale interventions of > 12 months in duration, of which five provided sufficient data for the calculation of incidence density RRs (*Figure 6*: for the full data see *Appendix 7.3, Data for forest plot: local-scale interventions of duration of > 12 months*). The studies were all conducted in single critical care units, apart from one which involved three units.[97] The interventions

BOX 4 Local-scale interventions of up to 12 months' duration that were not effective at reducing the incidence density of catheter-BSI or lack convincing evidence for effectiveness

Not effective: Single lecture (15 minutes with 9 months of follow-up) on approaches for CVC care and maintenance, with performance feedback, aimed at all staff in three critical care units in one hospital in Spain.[122]

Not effective: Single lecture (unspecified duration, with 9 months of follow-up) on CVC care aimed at all critical care staff in a single critical care ('ICU B') unit in Brazil[109] (this study was judged to be at high risk of selection bias and performance bias).

Not effective: Continuous tailored education including lectures on CVC care and hand hygiene, posters, colourful labels, and infection surveillance feedback aimed at all critical care staff in a single critical care unit ('ICU A') in Brazil for 9 months[109] (this study was judged to be at high risk of selection bias and performance bias).

Lack of convincing evidence for effectiveness: Multimodal education with emphasis on hand hygiene, aimed at all staff in two critical care units in one hospital in Brazil for 8 months, included infection surveillance feedback.[108]

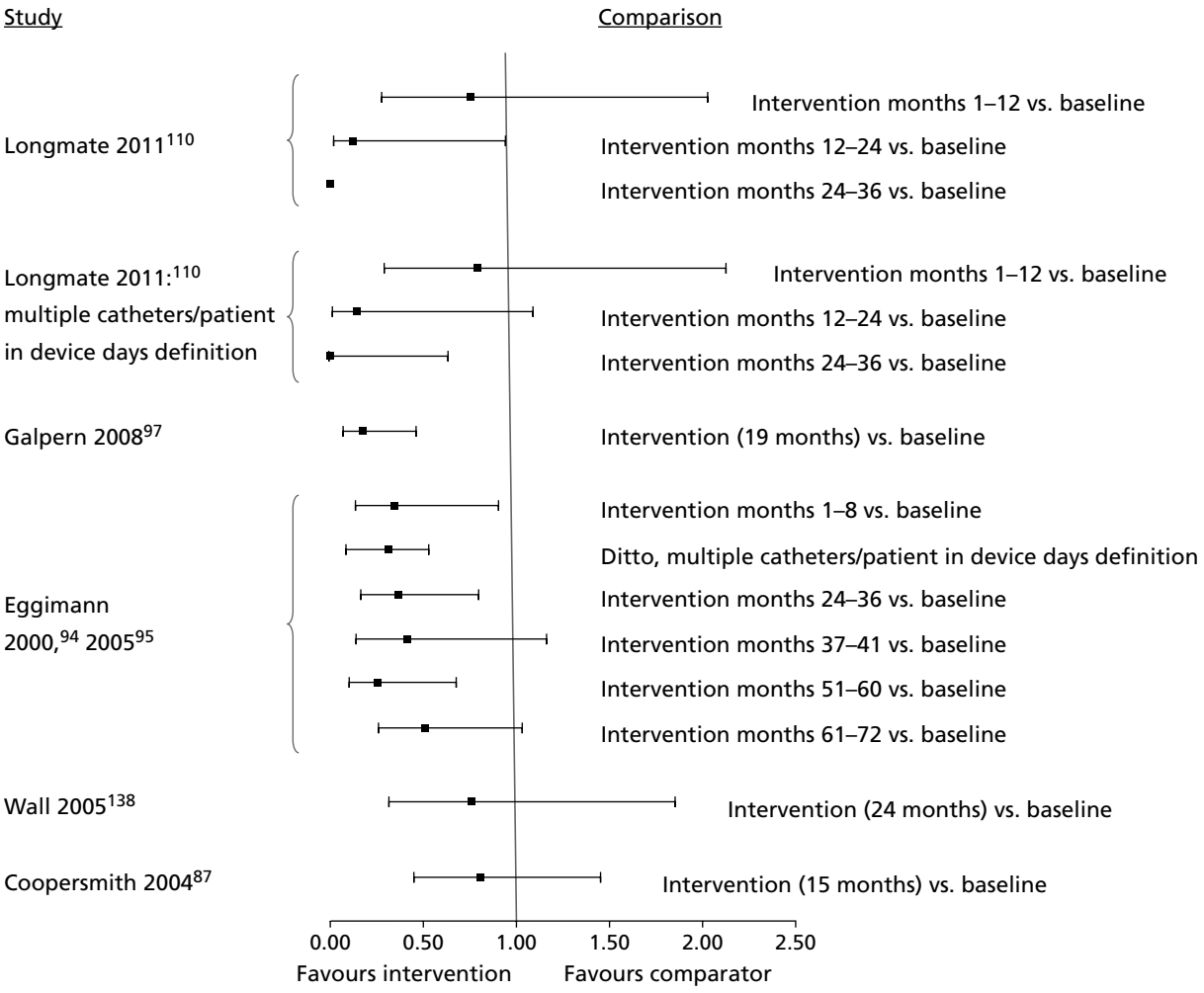

FIGURE 6 Incidence density RRs (± 95% CI) for local-scale interventions of more than 12 months in duration (multiple catheters per patient not counted separately in device-days unless stated).

included multimodal education with slide shows and bedside in-services, repeated for up to 6 years;[94,95] multimodal education with self-study, bedside in-services and performance feedback over 15 months;[87] a central line bundle deployed over 19 months, including checklist, infection surveillance feedback, performance feedback and catheter supplies cart;[97] a CQI programme implemented over 3 years, including checklist, infection surveillance feedback and performance feedback;[110] and a CQI programme focused on real-time performance feedback over 2 years, including a checklist, supervision of insertions and web-based tutorial with competence assessment.[138]

Three[87,97,138] of these five studies calculated the number of device-days based on presence/absence of vascular catheters, which does not distinguish multiple concurrent catheters in a patient. Eggimann and colleagues[94] and Longmate and colleagues[110] calculated the number of device-days in two ways: based on the presence/absence of vascular catheters; and by counting each concurrent catheter as a separate device-day. In both studies the incidence density RRs were similar for both methods of calculating the device-days (see *Figure 6*).

Clinically effective interventions (with unclear risk of bias)

Assuming that effects displayed in the forest plots reflect those of the planned interventions, three of the interventions conducted by Eggimann and colleagues,[94,95] Longmate and colleagues[110] and Galpern and colleagues[97] appear effective in reducing the incidence density of catheter-BSI (*Box 5*), with incidence density RRs significantly lower than 1.0 (see *Figure 6*). Exceptions were that the RRs were not significantly different from 1.0 on all of the monitoring dates reported by Eggimann and colleagues[94,95] and Longmate and colleagues.[110] Data from the Eggimann study[94,95] suggest that the intervention was effective for the initial 3 years of implementation but not consistently so thereafter. Data from the Longmate study[110] suggest that the intervention did not become effective at reducing catheter-BSI until the third year of implementation (see *Figure 6*). The publications reporting these three studies[94,95,97,110] either claimed statistically significant intervention effects[97,110] or did not mention the statistical significance of effects.[94,95]

The study by Longmate and colleagues[110] was judged to be at high risk of performance bias, as the authors stated that the staff assessing outcomes were not blinded. However, as mentioned above, it is unlikely that staff would have been blinded in any of the other studies, although this was not reported. The other studies were judged to be mostly at unclear risk of bias, although (as mentioned in the section on quality assessment above) the Eggimann study[94] was judged to be at low risk of bias for four of seven bias domains assessed (the other three were judged unclear).

BOX 5 Local-scale interventions of > 12 months' duration and at unclear risk of bias that appear effective at reducing the incidence density of catheter-BSI

- Multimodal education based on 30-minute slide shows and bedside in-services aimed at all critical care staff (physicians, nurses and nursing assistants) in one critical care unit in Switzerland for up to 6 years.[94,95]
- Central line bundle including discussion sessions about CVC access and care, checklist, infection surveillance feedback, performance feedback and catheter cart; aimed at all staff (physicians and nurses) in three critical care units in the USA for 19 months.[97]
- CQI programme (including VAP prevention) incorporating a CVC insertion bundle with checklist, infection surveillance feedback and performance feedback; aimed at ICU nurses and trainee doctors in one critical care unit in Scotland for up to 3 years.[110]

Clinically ineffective interventions

Two[87,138] of the five studies that implemented local-scale interventions of > 12 months' duration, by Coopersmith and colleagues[87] and Wall and colleagues,[138] were not effective at reducing catheter-BSI incidence density (*Box 6*), as the incidence density RRs were not significantly different from 1.0 (see *Figure 6*). Coopersmith and colleagues[87] acknowledged that effects of their intervention were not statistically significant. Among possible reasons for the lack of success of the intervention, Coopersmith and colleagues[87] suggested that that diffuseness of the educational message may have been a contributory factor and that ideally didactic education should be specifically targeted to support best clinical practices. Wall and colleagues[138] did not report the statistical significance of the effectiveness of their real-time process feedback approach for reducing catheter-BSI. The number of infections appeared to decrease dramatically (from 25 per 24 months to 6 per 24 months),[138] but there was also a marked decrease in the number of CVC-days during the study, which explains the lack of statistical significance when intervention effects are analysed in terms of the incidence density of catheter-BSI.

Overview of intervention effects on catheter-BSI incidence density

Assuming that the incidence density RRs reflect those of the planned interventions, then a range of different types of educational intervention would appear to have been effective at reducing catheter-BSI incidence in critical care units (*Boxes 1*, *3* and *5*). A key proviso is that some studies were judged to be at high risk of specific types of bias, but risk of bias was generally unclear and it is not possible to objectively classify the studies on bias risk. The interventions that appeared effective, subject to the caveats above, include regional-scale CQI programmes[34,83] or a local-scale CQI programme;[110] local-scale multimodal education with or without performance feedback and infection surveillance feedback;[50,51,94,103,129,139,144] a catheter insertion bundle;[97] and a catheter ongoing care bundle.[98] However, single lectures on CVC care and infection prevention were not effective as a means of reducing catheter-BSI incidence densities.[109,122] There is no clear evidence to suggest that regional-scale studies were more effective than local-scale studies, or that short-term studies (up to 12 months' duration) had different effectiveness than long-term studies (exceeding 12 months' duration). All three groups of studies (regional scale, local scale short-term and local-scale long-term) contain examples of effective interventions (*Boxes 1*, *3* and *5*) and ineffective interventions (*Boxes 2*, *4* and *6*). The studies included in the systematic review provide no clear evidence that performance feedback and/or infection surveillance feedback were influential in achieving effectiveness. Among the 12 interventions classed as clinically effective, eight (67%) included performance feedback,[50,51,83,97,98,103,110,129] four (33%) included infection surveillance feedback,[34,83,97,110] three (25%) included both types of feedback[83,97,110] and two (17%) did not include either type of feedback.[94,144] Among the eight interventions that were not classed as clinically effective, the respective proportions were similar: four (50%) included performance feedback,[109,126,136,138] three (38%) included infection surveillance feedback,[108,109,126] two (25%) included both types of feedback[109,126] and one (13%) did not include either type of feedback.[122] Apart from single lectures being ineffective, there appears to be no clear evidence

BOX 6 Local-scale interventions of more than 12 months' duration that were not effective at reducing the incidence density of catheter-BSI

- Multimodal education on CVC care and unspecified topics, including self-study, in-services and performance feedback, with broad topic coverage aimed at nurses and other staff in one critical care unit in the USA for 15 months; included infection surveillance feedback but this was also present in the baseline period[87] (this study was judged to be at high risk of performance bias).
- CQI programme involving real time feedback of infection rates and compliance with insertion practice, based on use of checklist, supervision of insertions, and web-based tutorial with competence assessment; aimed at ICU house staff (proceduralists) and nursing staff (as observers of procedures) in one critical care unit in the USA for 2 years; note that infection surveillance feedback was also present in the baseline period.[138]

that interventions which included components beyond education (e.g. provision of antiseptic or a catheter supplies cart) were more or less effective than interventions that consisted of education alone.

Most studies did not separately count multiple vascular catheters per patient when calculating the number of device-days. In two studies that compared different approaches for calculating the number of device-days, the calculation approach used did not appear to influence the incidence density RR for catheter-BSI.

Mortality

Five studies[94,103,110,139,144] reported mortality as an outcome but they did not specifically report mortality due to catheter-BSI or its sequelae.

Only one of these studies[110] reported mortality specifically for critical care patients with CVCs (those patients in the critical care unit for > 2 days with a CVC for at least part of their critical care stay). Mortality rates significantly decreased during the study period, being 21.2% during the baseline period, and 20.9% and 16% during years 3 and 4 of the intervention, respectively (year 3 vs. 1, $p = 0.328$; year 4 vs. 1, $p = 0.013$).

Three[94,103,144] of the five studies reported unadjusted mortality rates for critical care patients. Of these, two reported that there were no statistically significant differences between the baseline and intervention periods.[94,144] An exception was that mortality due to cardiac arrest was significantly more frequent during the intervention period of one study[94] ($p < 0.05$). The third study[103] reported statistically significantly lower rates of unadjusted mortality per 1000 critical care unit discharges during the intervention period than the baseline period (64/132 = 48.5% and 111/338 = 32.8%), respectively [RR = 0.68 (95% CI 0.50 to 0.91), $p = 0.01$].

The remaining study[139] reported that mortality for an ambiguous population ('in-hospital mortality rate for catheterised patients') did not differ significantly between the baseline and intervention periods.

In summary, insufficient data are available for us to draw any firm conclusions about the effects of the educational interventions, or the effects of catheter-BSI, on rates of mortality among patients in critical care units.

Length of stay

Seven studies[50,94,109,110,117,139,144] reported LOS. One of these studies[110] explicitly stated that their LOS data were for critical care unit patients who had vascular catheters. One study[144] compared LOS in patients with and without CRBSI. For the remaining five studies LOS data appear to refer to all critical care unit patients, not limited to those with vascular catheters.

Longmate and colleagues[110] reported both mean and median lengths of stay for patients who were in the critical care unit for > 2 days and had a CVC for at least part of their critical care stay. Mean (± SD) lengths of stay significantly increased [5.4 ± 3.9 days during year 1 (baseline period), 5.3 ± 3.7 days during intervention year 3, and 5.9 ± 3.7 days during intervention year 4] (differences from baseline, $p > 0.05$). The corresponding median [interquartile range (IQR)] lengths of stay decreased, and were, respectively, 9.7 (4–20) days, 8.9 (4–13) days and 6.0 (3–11) days (differences from baseline, $p < 0.05$).

Zingg and colleagues[144] reported median overall LOS for patients in five critical care units, during a 4-month baseline and 5-month intervention period. LOS was statistically significantly longer during the intervention period. The median (IQR) LOS for baseline and intervention periods respectively were 3 (2–7) days and 4 (2–9) days – difference, $p < 0.001$. Corresponding mean LOS during these periods were 5.9 days and 7.5 days, respectively. Zingg and colleagues also reported that median (IQR) LOS was 15.5 (10–25) days in patients with CRBSI and 5 (3–12) days in patients without CRBSI (difference reported as 10.5 days).

In summary, two studies[110,144] reported length of critical care unit stay in relevant populations of patients with CVCs. One study,[144] a 9-month education intervention by Zingg and Colleagues, reported significantly longer duration of stay during the intervention period, whereas the other, a 4-year continuous QI programme by Longmate and colleagues,[110] found significantly shorter duration of stay in the intervention period. In addition, Zingg and colleagues[144] reported that the median LOS for critical care patients with CRBSI was 10.5 days longer than for critical care unit patients without CRBSI (reported as 15.5 and 5 days, respectively).

Synthesis of process (secondary outcomes)

Attitudes

One of the included studies by Sherertz and colleagues[135] reported staff attitudes as a quantitative outcome. The proportions of postgraduate year 1 physicians-in-training who perceived a need for povidone–iodine, gloves, gowns and full sterile drapes increased significantly following a formal one-day education course (full data are in the data extraction form – see *Appendix 5*). However, incidence density RRs could not be calculated for this study[135] so its clinical effectiveness at reducing catheter-BSI incidence density is unclear.

Four studies[68,83,110,122] mentioned qualitative observations relating to the attitudes of critical care staff towards evidence-based infection prevention practices. Burrell and colleagues[83] observed that some clinicians considered the incidence of CLAB in New South Wales to be low and doubted the value of the project, as existing Australian practice was felt to be equal to or better than the methods informing the project. Some clinicians doubted the evidence even with supportive CDC guidelines. Hat-wearing was a contentious element of the physician bundle: clinicians cited lack of evidence for hat use and four critical care units elected to omit their use as standard practice for CVC insertion.[83] The remaining studies provided only brief mention of staff attitudes. Longmate and colleagues[110] reported that two consultant clinicians doubted the need for full aseptic technique for CVC insertion, although this was resolved after evidence sharing. Perez Parra and colleagues[122] reported that staff incorrectly assumed that small drapes were sufficient for catheter-BSI prevention, although it is not clear whether they were referring to the baseline or intervention period. Palomar Martinez and colleagues[68] reported that some practitioners expressed dissatisfaction with chlorhexidine for skin antisepsis and doubted its effectiveness.

Although limited in detail and lacking quantitative analysis, these observations of the attitudes of critical care staff highlight that staff may be liable to question the need for evidence-based infection prevention practices, even when presented with supporting evidence.

Knowledge

Two[50,122] of the included studies indirectly reported improvements in knowledge, expressed as changes in the proportion of staff with correct test scores[50] or the percentage of correctly answered questions.[122] In the latter study, the test questions most often answered incorrectly (fewer than 50% correct) were those about the need for full sterile barriers during CVC insertion and on the choice of antiseptic for skin disinfection.[122] These studies suggest that educational interventions can improve critical care staff knowledge of infection prevention practices but they did not report the types of knowledge gained through participation in the interventions.

Compliance

Compliance with evidence-based practices for preventing catheter-BSI was reported in 19 out of the 24 included studies.

Compliance with hand hygiene

Seven studies reported compliance with hand hygiene behaviour (*Table 22*). They all reported improvements in compliance relative to baseline, although these were not statistically significant in all cases. In most of the studies hand hygiene compliance rates did not reach 100% during educational interventions. In one study, the change was modest (final compliance 30%) and non-significant, possibly because hand hygiene was not a specific target of the education.[87]

TABLE 22 Compliance with hand hygiene during study baseline and intervention periods

Study	Baseline compliance (%)	Intervention compliance (%)	RR (95% CI); statistical significance	Comments
Coopersmith (2004)[87]	17	30	$p > 0.99$	
Higuera (2005)[103]	62	84.9	RR = 1.37 (1.21 to 1.51); $p = 0.0000$	Before patient contact
Lobo (2005)[108]	100	100	Not reported	CVC insertion
	5	61	RR = 12.78 (3.24 to 50.42); $P < 0.001$	Before manipulation
	38	43	RR = 1.14 (0.69 to 1.90); $p = 0.6$	After manipulation
	45	68	RR = 1.50 (0.95 to 2.37); $p = 0.072$	Before dressing
Lobo (2010)[109] (data for interventions in two critical care units – 'ICU A' and 'ICU B')	35	81	RR = 2.32 (1.62 to 3.32); $p = 0.370$	ICU A, before CVC handling
	19	84	RR = 4.42 (2.63 to 7.43); $p < 0.001$	ICU A, after CVC handling
	15	48	RR = 3.20 (1.33 to 7.72); $p = 0.008$	ICU B, before CVC handling
	9	55	RR = 6.00 (1.95 to 18.44); $p < 0.001$	ICU B, after CVC handling
	28	98	RR = 3.50 (2.24 to 5.47); $p < 0.001$	ICU A, before CVC dressing
	34	96	RR = 2.82 (1.91 to 4.17); $p < 0.001$	ICU A, after CVC dressing
	6	76	RR = 12.50 (3.22 to 48.56); $p < 0.001$	ICU B, before CVC dressing
	27	64	RR = 2.33 (1.26 to 4.31); $p < 0.006$	ICU B, after CVC dressing
Rosenthal (2005)[130]	23.1	64.5	RR = 2.79 (2.46 to 3.17); $p < 0.0001$	
Wall (2005)[138]	73	94, 89	Not reported	For last 2 quarters
Zingg (2009)[144]	59.1	65	$p = 0.466$	Overall compliance
	22.5	42.6	$p = 0.003$	Correct hand disinfection
	26	45	$p = 0.007$	Before patient contact
	21	56	$p < 0.001$	After patient contact

Five[103,108,109,130,144] of the studies that achieved statistically significant improvements in compliance had specified hand hygiene as a main[108,109,130] or joint[103,144] component of their education. High baseline variability in compliance rates is notable, both within and between the studies. For example, Lobo and colleagues[108] found baseline compliance with hand hygiene at CVC insertion was already 100% but compliance with hand hygiene before line manipulation was only 5%. Overall, these findings suggest that hand hygiene behaviour in relation to the insertion and management of CVCs is complex and variable, and can differ considerably between the stages of intravascular catheter site preparation, insertion and ongoing management. Owing to the relatively small number of studies that reported hand hygiene compliance it is unclear whether the degree of compliance with hand hygiene practices had any bearing on the effectiveness of the interventions for preventing catheter-BSI.

Compliance with barrier precautions

None of the seven studies[87,108,109,126,135,138] that measured compliance with barrier precautions (*Table 23*) had specified this as a target behaviour change, although most of the studies included an element of education about sterile barrier precautions in their interventions. Compliance with barrier precautions was highly variable at baseline, ranging from 0% to 100%. Final compliance with barrier precautions after study interventions ranged from 65% to 100%, indicating improvement, but this was reported to be statistically significant for only two out of eight comparisons.

The studies appeared to differ in their ability to detect statistically significant changes in compliance. A 30% increase in compliance with maximal sterile barrier use was not significant ($p = 0.29$) in one study,[87] whereas a 21% increase in compliance with sterile drape use was significant ($p < 0.001$) in another study.[135] Wall and colleagues[138] reported that a decline in compliance with maximal barrier precautions during the intervention period was caused by lack of use of patient drapes. Compliance with maximal barrier precautions improved after the team purchased new sterile kits pre-packaged with drapes, and confirmed providers had completed a tutorial. Wall and colleagues[138] also mentioned that use of the femoral site, compared with other insertion sites, was associated with statistically significant lower compliance with hand washing, chlorhexidine skin antisepsis and maximal barrier precautions.

TABLE 23 Compliance with barrier precautions during study baseline and intervention periods

Study	Barrier type	Baseline compliance (%)	Intervention compliance (%)	RR (95% CI); statistical significance
Coopersmith (2004)[87]	Maximal barriers	50	80	$p = 0.29$
Lobo (2005)[108]	Maximal barriers, CVC insertion	91	100	RR = 0.91 (0.80 to 1.04); $p = 0.147$
Wall (2005)[138]	Maximal barriers, for last quarter	68	86	Not reported
Lobo (2005)[108]	Glove use at CVC manipulation	40	98	RR = 2.36 (1.64 to 3.40); $p < 0.001$
	Glove use at CVC dressing	97	97	RR = 1.00 (0.91 to 1.10); $p = 1.0$.
Lobo (2010)[109]	Glove use at CVC insertion and dressing	100	100	Not reported
Render (2006)[126]	Large sterile drapes	0	83	Not reported
Sherertz (2000)[135]	Sterile drapes	44	65	$p < 0.001$

Compliance with dressing management

None of the six studies that measured compliance with dressing management (*Table 24*) explicitly specified this was a target behaviour, although dressing care was clearly stated as a topic in the educational interventions of the studies by Coopersmith and colleagues,[87] Higuera and colleagues[103] and Lobo and colleagues.[109] Compliance with various aspects of CVC dressing care ranged from 11% to 84% at baseline and improved to 21% to 97% after interventions, with the improvements all being reported to be statistically significant, although compliance with correct dating of CVC dressings reached only 21% after the intervention by Coopersmith and colleagues.[87] In the study by Rosenthal and colleagues,[129] compliance with placing gauze dressings and with checking the condition of dressings both increased by a greater degree following performance feedback than following education alone. However, as these intervention components were implemented sequentially, the effects of performance feedback may not have been independent of the education.

Compliance with skin antisepsis prior to catheter insertion

Skin antisepsis prior to CVC insertion was a common element of the education in many of the studies included in the systematic review, but no studies specified explicitly that it was a target behaviour. Baseline rates of compliance with skin antisepsis ranged from 9% to 57% in the three studies that reported this outcome, and in all cases interventions resulted in improvements, with final compliance ranging from 82% to 100%. The change was statistically significant in one study[108] but significance was not reported in the other two studies[126,138] (see *Table 25*).

Compliance with hub disinfection and catheter set dating

Compliance rates for line protection and hub disinfection were reported in two studies[108,109] and ranged from 33% to 69% at baseline and were improved by interventions, with final compliance in the range 82% to 98% (all improvements were reported statistically significant). However, there was a notable difference between two studies in compliance with the dating of intravenous administration sets, although in both cases increases in compliance occurred, which were statistically significant. Baseline compliance was only 0.57% and initially fell to 0% after education in the study by Rosenthal and colleagues[129] but then reached 74% after a phase of performance feedback. In the study by Higuera and colleagues,[103] compliance with set dating rose from 40.69% to 93.85% (see *Table 25*).

TABLE 24 Compliance with dressing management during study baseline and intervention periods

Study	Dressing action	Baseline compliance (%)	Intervention compliance (%)	RR (95% CI); statistical significance
Coopersmith (2004)[87]	Dating dressing	11	21	$p < 0.001$
Rosenthal (2003)[129]	Placing gauze	53.02	56.21 (96.53)[a]	RR = 1.06 (0.86 to 1.30); $p = 0.64$ RR[b] = 1.72 (1.40 to 2.10); $p < 0.001$
Higuera (2005)[103]	Placing gauze	84.21	97.87	RR = 1.16 (1.09 to 1.24); $p = 0.0000$
Rosenthal (2003)[129]	Checking condition	48.70	43.19 (89.56)[a]	RR = 0.89 (0.67 to 1.17); $p = 0.39$ RR[b] = 2.07 (1.65 to 2.62); $p < 0.001$
Lobo (2005)[108]	Skin antisepsis	26	58	RR = 2.25 (1.15 to 4.39); $p = 0.01$
Lobo (2010)[109]	Skin antisepsis, ICU A	54	100	RR = 1.85 (1.43 to 2.39); $p < 0.001$
	Skin antisepsis, ICU B	27	97	RR = 3.56 (2.03 to 6.23); $p < 0.001$

a During performance feedback phase.
b For education and performance feedback phases combined.

Compliance with overall bundles

Three studies[83,98,110] reported compliance with overall care bundles (*Table 25*). These were 'patient' and 'clinician' bundles[83] a CVC insertion bundle[110] and a post-insertion care bundle.[98] Compliance improved in the studies by Burrell and colleagues[83] and Longmate and colleagues[110] but was reported to be statistically significant only in the former study. The intervention by Guerin and colleagues[98] did not appear to affect compliance with the CVC post-insertion care bundle. It is notable that compliance with all four bundles was already high at baseline, ranging from 74% to 94%, and improvements appeared modest (increases of only 7% and 11% in the Burrell study[83] despite being statistically significant, and approximately 20% in the Longmate study[110]).

Burrell and colleagues[83] demonstrated relationships between compliance with the two care bundles and the effectiveness of their CQI intervention at preventing catheter-BSI (central line-associated bacteraemia). Risk of catheter-BSI was reduced if insertion was conducted by physicians compliant in both bundles [RR = 0.5 (95% CI 0.4 to 0.8); $p = 0.004$], but risk was increased if insertion was conducted by physicians not compliant with the clinician bundle [RR = 1.62 (95% CI 1.1 to 2.4); $p = 0.018$]. Most (94.0%) cases of non-compliance with the clinician bundle were due to failure to wear a hat, mask and eyewear.

TABLE 25 Compliance with other activities during study baseline and intervention periods

Study	Activity	Baseline compliance	Intervention compliance	RR (95% CI); statistical significance
Lobo (2005)[108]	Skin antisepsis at CVC insertion	9	100	RR = 11.0 (3.24 to 50.42); $p < 0.001$
Render (2006)[126]	Skin antisepsis at CVC insertion	42	82	Not reported
Wall (2005)[138]	Skin antisepsis at CVC insertion	57	100 (last quarter)	Not reported
Rosenthal (2003)[129]	Dating i.v. admin set	0.57	0 (74)[a]	$p = 0.32$ $p < 0.001$[b]
Higuera (2005)[103]	Dating i.v. admin set	40.69	93.85	RR = 2.34 (2.14 to 2.56); $p = 0.0000$
Lobo (2005)[108]	Line protection	69	98	RR = 1.38 (1.13 to 1.69); $p < 0.001$
	Hub disinfection	33	93	RR = 2.74 (1.78 to 4.22); $p < 0.001$
Lobo (2010)[109]	Hub disinfection, CVC handling, ICU A	68	97	RR = 1.42 (1.19 to 1.69); $p < 0.001$
	Hub disinfection, CVC handling, ICU B	44	82	RR = 1.80 (1.20 to 2.70); $p < 0.004$
Burrell (2011)[83]	Clinician bundle compliance	74	81	$p = 0.0006$; χ^2 of slope = 11.71
	Patient bundle compliance	81	92	$p = 0.001$; χ^2 of slope = 108.34
Guerin (2010)[98]	CVC post-insertion bundle compliance	94	93	Not reported
Longmate (2011)[110]	CVC insertion bundle compliance	80	95–100 (approximate)	Not reported

i.v., intravenous.
a During performance feedback phase.
b For education and performance feedback phases combined.

Longmate and colleagues[110] reported that all-or-nothing compliance with the CVC insertion bundle component of their CQI programme fluctuated between 80% and 100% during an 18-month period. The authors suggested that low initial compliance was attributed to a lack of checklist stickers early in the period; improved compliance later may have been due to introduction of a CVC insertion pack and the creation of subteam nurses to 'own' CVC processes, and also to greater scrutiny and follow up of episodes of incomplete compliance.[110]

In addition to the studies listed in *Table 25*, Speroff and colleagues[136] provided extensive data on the adoption of various components of flexible QI interventions in critical care units of hospitals that had been randomised to toolkit-based and virtual collaborative QI approaches (full data are given in the data extraction form: see *Appendix 5*). Adoption of intervention components was consistently higher in virtual collaborative hospitals than toolkit hospitals. However, as mentioned above, neither of these intervention approaches was successful in reducing catheter-BSI incidence density relative to baseline. Risk of catheter-BSI appeared higher under the virtual collaborative (see *Figure 4*), which had the more frequent adoption of intervention tools and strategies, suggesting that failure to reduce catheter-BSI incidence density was not simply related to the extent of intervention implementation.

Further data on compliance with evidence-based practices were reported by Coopersmith and colleagues,[50] DuBose and colleagues,[93] Lobo and colleagues,[109] Palomar Martinez and colleagues,[68] and Render and colleagues.[126] These data (see *Appendix 5*) are not discussed here as they are based on very small or unclear sample sizes, or it is unclear to which study periods they refer.

Summary of compliance

Overall, nearly all of the studies that reported compliance with evidence-based infection prevention practices reported improvements relative to the baseline period, although the uncontrolled studies cannot definitively exclude an influence of secular trends. Most of the information on compliance relates to hand hygiene, barrier precautions and CVC dressing care. The studies are difficult to compare, however, as in some studies small changes in compliance were reported to be statistically significant, whereas in other studies large changes were reported not statistically significant. Interventions targeting specific behaviours appear more likely to improve compliance but this is difficult to assess critically as target behaviours were not always clearly specified in the primary studies. Baseline compliance rates varied considerably between studies and for hand hygiene they varied markedly between the different stages of CVC site preparation, insertion and ongoing care. It is not clear from these data whether compliance with evidence-based practices was an important mediator of intervention effectiveness at preventing catheter-BSI, as baseline compliance rates were often already high. An exception is the study by Burrell and colleagues,[83] which found that compliance with two care bundles significantly reduced the risk of catheter-BSI.

Other secondary outcomes

Our systematic review protocol (see *Appendix 1*) specified two secondary outcomes that we would assess if reported in the primary studies: (1) the reaction of critical care staff to education and (2) critical care staff practical skills in relation to infection prevention. However, none of the 24 studies included in the systematic review reported these outcomes.

Process evaluations, facilitators and barriers

In addition to the assessments of attitudes, knowledge and compliance reported above, six studies[34,68,83,110,126,136] provided qualitative observations relevant to understanding intervention processes, facilitators and barriers, although none of these studies carried out a full process evaluation.

Three of the CQI studies[83,110,136] identified a lack of adequate infrastructure to support data collection and dissemination as being a barrier to successful implementation of the interventions. Burrell and colleagues[83] stated that reliable baseline data did not exist prior to the project owing to variable reporting

mechanisms. Some critical care units were hesitant to accept previously reported rates, and inadequate staffing rates in some critical care units impacted on data capture rates. Difficulties were also encountered regarding data collection and associated information technology, such that the project team resorted to hard copy receipt of checklists. The lack of a continuous and sustainable data collection system involving cross-specialty collaboration was seen as a serious risk to sustainability of the CLAB ICU project principles. Speroff and colleagues[136] commented that the lack of appropriate infrastructure to support data-driven QI was a significant barrier and that systematic standardised data collection was initially lacking in many of the study hospitals. Early effort was therefore needed to deploy a system-wide standardised infection control database registry. Longmate and colleagues[110] reported that investigators were initially unable to reach agreement on a system – which had full support of both clinicians and data analysts – for collecting process measurements.

Three studies[34,68,110] reported difficulties around the use of chlorhexidine for skin antisepsis. These related to difficulty in obtaining supplies (implying uneven compliance across critical care units)[34,68] and the fact that chlorhexidine is colourless, making the skin area prepared with antiseptic difficult to see.[68,110] In one study[110] it was agreed that povidone–iodine could be used to colour the skin, followed by chlorhexidine.

Two studies[68,136] commented that their interventions provided insufficient time for some components to be implemented. Speroff and colleagues[136] reported that implementation of checklists was slow, suggesting that beneficial translation of desired changes may take more than 18 months to achieve. Palomar Martinez and colleagues[68] reported that none of the critical care units was able to implement catheter equipment carts within the 3-month duration of their pilot study.

Other aspects of intervention process evaluation were identified in specific studies:

Burrell and colleagues[83] reported difficulty in ensuring application of, and adherence to, infection surveillance definitions. They also commented that the CLAB ICU project methodology was based on a single successful collaborative (the Keystone ICU project) without a detailed analysis of all available evidence, which allowed criticism of methodology to be an excuse for non-compliance.

Palomar Martinez and colleagues[68] reported that critical care staff were reluctant to take a test as part of the training for the CQI intervention, as the test was not mandatory, results were not anonymous and there was no credit given for participation in the training.

Pronovost and colleagues[34] reported that the Keystone ICU project intervention was modestly more effective in small hospitals, with an incidence rate ratio of 0.97 (95% CI 0.96 to 0.99, $p < 0.001$) for each 100-bed decrease in the size of the hospital. Although Pronovost and colleagues[34] did not conduct a detailed process evaluation during the Keystone ICU project, Dixon-Woods and colleagues[149] developed an ex-post theory of the processes that contributed to the project's success at preventing catheter-BSI. Although not noted by Dixon-Woods and colleagues,[149] an important difference between the Keystone ICU project[34] and other regional-scale CQI approaches that we reviewed[68,83,110,136] could be that the Keystone ICU project was based on an established data collection system.

Render and colleagues[126] provided a table of facilitators and barriers in their publication but it is unclear whether this was based on quantitative evidence. The study authors reported that after 6 months the project leader and project co-ordinator reviewed their detailed notes from the monthly reporting meetings to independently identify themes contributing to or delaying project success. The list of barriers and facilitators was then validated by the project leaders. However, the validation process was not explained.

Summary of the systematic review of clinical effectiveness

Twenty-four studies were included in the systematic review, half of which were conducted in the USA and most of which used a single-cohort uncontrolled before-and-after design. The interventions were diverse in their educational approaches, ranging from single lectures in single critical care units to regional-scale CQI programmes in up to 103 critical care units. Most interventions focused on catheter insertion rather than catheter ongoing care, with hand hygiene, maximal barrier precautions and antiseptic preparation of the insertion site being the most frequently addressed clinical practices. Different educational approaches, which were unique to individual studies, were used to address the same clinical practice. Nearly all interventions included formal education approaches that would take staff away from bedside patient care. Definitions of CABSI and CRBSI were used inconsistently and two-thirds of the studies provided infection definitions that did not agree with those used in the NHS for the Matching Michigan programme. Most studies did not separately count multiple vascular catheters per patient when calculating the number of device-days, but where different approaches for calculating the number of device-days were compared the method of calculation did not appear to influence the incidence density RRs for catheter-BSI.

Data synthesis was conducted narratively, as it was inappropriate to statistically pool effects from the different types of educational interventions, which varied in their spatial and temporal scales and intervention complexity. Some studies were identified to be at high risk of bias but, owing to deficiencies in the reporting of study methods, risk of bias was generally unclear and could not be used as a criterion for objectively excluding studies from the data synthesis. Assuming that the RRs for incidence density of catheter-BSI reflect those of the planned interventions, 12 studies reported interventions that appeared clinically effective, eight studies reported interventions judged not to be clinically effective, or not to have provided convincing evidence of effectiveness, and four studies provided insufficient data for effectiveness of their interventions to be assessed. The interventions that appeared effective (subject to caveats about possible risks of bias and establishing cause and effect in before-and-after studies) included local- and regional-scale CQI programmes; local-scale multimodal education with or without performance feedback and infection surveillance feedback; a catheter insertion bundle; and a catheter ongoing care bundle. However, single lectures on CVC care and infection prevention in single critical care units were not effective. There was no evidence to suggest that the spatial or temporal scale, intervention complexity (education alone or with components beyond education) or the presence/absence of performance feedback and/or infection surveillance feedback had any appreciable influence on the incidence density of catheter-BSI. Too few studies provided information on mortality and LOS for effects of the educational interventions on these outcomes to be assessed.

Assessments of critical care staff attitudes, knowledge, compliance with clinical practices and other aspects of intervention processes identified several barriers or potential barriers to the successful implementation of educational interventions. Although limited in detail and lacking quantitative analysis, reports of the attitudes of critical care staff suggest that staff may be liable to question the need for evidence-based infection prevention practices, even when presented with supporting evidence. Most of the information on compliance with intervention practices was related to hand hygiene, barrier precautions and CVC dressing care. However, only one study had formally tested the influence of staff compliance on intervention effectiveness, finding that staff compliance with care bundles significantly reduced the risk of catheter-BSI. In several CQI programmes a lack of existing systems and infrastructure for data collection was reported to be a barrier to effective implementation of interventions. The availability of infrastructure at intervention inception seems to be a key difference between the Keystone ICU project which was based on an existing data collection system and the other CQI programmes, which appeared to have had to develop data collection systems for their interventions.

At the time of writing this report, the only published UK study[110] to have implemented an educational intervention for adult critical care patients was conducted in Scotland by Longmate and colleagues (the results of Matching Michigan in England had not been published and so could not be included in our evidence map or systematic review). The CQI programme[110] included some elements of the Keystone ICU project but it differed from the Matching Michigan programme, in that it aimed to prevent VAP as well as catheter-BSI; it was conducted in a single critical care unit; it took 3 years to achieve effectiveness and the last year of the intervention overlapped with the Scottish Patient Safety Programme.[110] The CLAB ICU project implemented by Burrell and colleagues[83] in Australia appeared to be the most relevant of the clinically effective interventions to current NHS practice for prevention of catheter-BSI. CLAB ICU has similarities to Matching Michigan in England, as both programmes attempted to implement interventions based on the Keystone ICU project in new national settings. The CLAB ICU baseline incidence density of catheter-BSI was relatively low, consistent with the situation in English NHS trusts, and the starting infrastructure of the CLAB ICU study appears to have had some similarities with the English situation, as standard data collection strategies for infection surveillance appear not to have been in place at the start of CLAB ICU or Matching Michigan. An advantage of the CLAB ICU project, compared with most other studies included in the systematic review, is that the methods of the intervention were extensively reported. These are available in the published paper,[83] project report[146] and project website. Given the above considerations, the CLAB ICU project was used to provide some of the parameters used in the health economic model (see *Chapter 6*) to explore the cost-effectiveness of educational interventions for preventing catheter-BSI.

Chapter 5 Systematic review of cost-effectiveness studies

A systematic review of the literature was conducted to identify and assess the current evidence base for the cost-effectiveness of educational interventions for preventing catheter-BSI and to inform the most appropriate approach for the de novo economic model (see *Chapter 6*).

Search strategy

A systematic literature search was undertaken to identify economic evaluations of educational interventions for preventing CRBSIs in critical care. Sensitive search strategies (shown in *Appendix 2, Cost-effectiveness search strategy*) were developed and tested by an experienced information scientist. These strategies were used to search the following electronic bibliographic databases:

- MEDLINE (Ovid)
- MEDLINE In-Process & Other Non-Indexed Citations
- EMBASE (Ovid)
- BIOSIS
- Cochrane Central Register of Controlled Trials (CCRCT)
- Cochrane Database of Systematic Reviews (CDSR)
- Cochrane Database of Abstracts and Reviews of Effects
- Cumulative Index to Nursing and Allied Health Literature (CINAHL) EBSCO*host*
- Web of Science databases:
    - Science Citation Index Expanded (SCIE), Social Sciences Citation Index (SSCI)
    - Arts & Humanities Citation Index (A&HCI)
    - Conference Proceedings Citation Index – Science (CPCI-S)
    - Conference Proceedings Citation Index – Social Science & Humanities (CPCI-SSH)
- NHS Economic Evaluation Database [NHS EED via the Centre for Reviews and Dissemination (CRD)].

Searches were undertaken from inception of databases to February 2011 and updated in March 2012. Data from the studies that met the inclusion criteria were extracted and evaluated for quality and generalisability to the UK using a critical appraisal checklist.[150] The included studies were then described in more detail, including discussion of the main issues arising from each of the studies. The full data extraction forms for the studies are shown in *Appendix 8*.

Inclusion criteria

Titles and (where available) abstracts of references identified by the search strategy were assessed for eligibility against our inclusion criteria (*Table 26*) by two health economists. Conference abstracts were not eligible for inclusion unless sufficient detail was provided for critical appraisal. Articles published in languages other than English were eligible for inclusion. Full papers of those records that appeared relevant on title or abstract were retrieved and independently screened by two health economists. Any differences in judgement were resolved through discussion.

TABLE 26 Inclusion criteria for the systematic review of cost-effectiveness studies

Study characteristic	Inclusion criteria
Population	Patients in critical care with vascular catheter(s)
Intervention	Educational interventions with an objective to reduce or prevent CRBSIs
Outcomes	BSIs or mortality associated with, related to, or suspected to result from catheter use
Design	Full economic evaluations: cost-effectiveness, cost–utility, cost–benefit and cost–consequence

Quantity and quality of published research

A total of 767 potentially relevant articles were identified in the cost-effectiveness searches. Through inspecting the titles and abstracts of these articles, 759 non-relevant studies were excluded. The full-text records of the remaining eight studies were retrieved, but only three met all the inclusion criteria,[76,151,152] with the remaining five studies excluded because they were not full economic evaluations (*Figure 7*). A summary of the characteristics of the three included studies is given in *Table 27* and the studies are described in more detail below.

The cost-effectiveness studies were assessed using a critical appraisal checklist as shown in *Table 28*. The checklist assesses the studies for quality and their generalisability to the UK; it was adapted by the review authors from checklists originally put together by Phillips and colleagues,[150] Drummond and colleagues[153] and the National Institute for Health and Care Excellence (NICE) reference case requirements.[154] The definition of catheter-BSI provided was CRBSI in two of the studies[76,151] and CLAB in the third study.[152]

The three studies[76,151,152] specified the decision problem, the study rationale and justified the comparator. A detailed description was given of the patient groups and the health-care settings were similar to those in the UK. The health-care systems in all studies differ to that of the UK and therefore the practices may not be generalisable to the UK. The structure of the models used in the studies[76,151,152] reflect the disease process and the modelling methodologies seem appropriate.

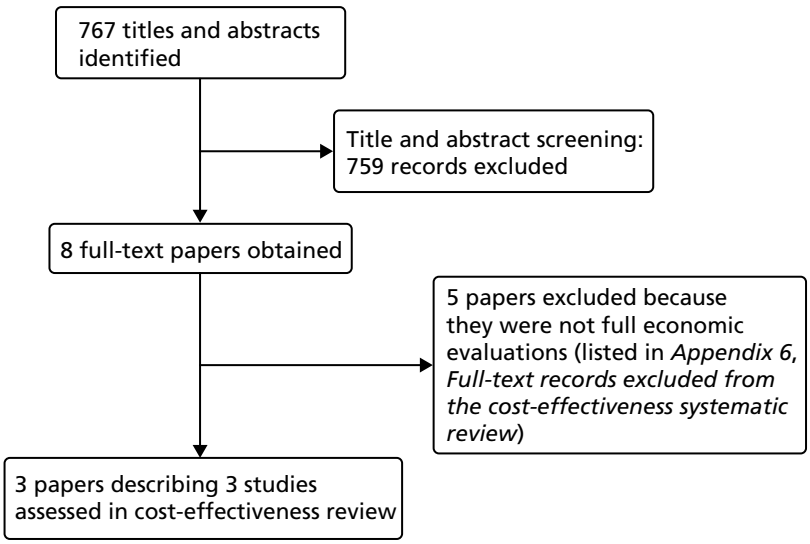

FIGURE 7 Identification of studies for inclusion in the systematic review of cost-effectiveness.

TABLE 27 Characteristics of economic evaluations

Characteristics	Halton[151]	Cohen[76]	Bond and King[152]
Publication year	2010	2010	2011
Country	Australia	USA	USA
Funding source	Queensland Health Quality and Safety programme and National Health and Medical Research Council	Not stated	None
Study type	Cost–utility analysis	Cost–consequence analysis	Cost-effectiveness analysis
Perspective	Australian health-care payer	United States health-care payer	Not stated
Study population	Adult critical care unit patients with a CVC	Adult patients with a CVC inserted in the MICU	Adult patients with a CVC
Intervention and comparator	Catheter care bundle vs. current practice	Simulated education training in catheter insertion vs. no educational intervention	CVC educational intervention vs. no educational intervention
Intervention effect	Reduction in the rate of CRBSI from 7.7 to 1.4 per 1000 line-days over an 18-month period, relative risk reduction of 0.34 (95% CI 0.23 to 0.50)	Prevented 9.95 cases of CRBSI among patients in MICU, with 14 additional hospital days (including 12 MICU days) gained	The number of CLAB was reduced from 4 to 2 per 600 CVCs inserted in a hypothetical year
Intervention cost	Unknown. A range of costs was used in the model	Total operating costs for training the medical residents, faculty and staff time, supplies and space rental were US$111,916	The total cost per patient was US$546 with the education intervention vs. US$392 without the intervention
Currency base	A$ (2006)	US$ (2008)	US$ (year not stated)
Model type, health states	Markov model	Regression model	Decision-analytic model
Time horizon	Lifetime	12 months	Hospital stay
Baseline case results	The base-case analysis shows that the care bundle is cost-effective up to an 18-month nationwide implementation cost of A$4,349,730 when compared with current practice	The intervention was highly cost-effective with overall cost savings	If the educational intervention is effective, a small increase in cost can reduce complications

MICU, medical intensive care unit.

Cohen and colleagues[76] and Bond and King[152] did not base their effectiveness estimates on a systematic review, and did not use any instruments to measure health benefit. Halton and colleagues[151] did both, using quality-adjusted life-years (QALYs) as a measure of health outcome. Data inputs for the model used in Cohen and colleagues[76] and Halton and colleagues[151] studies were adequately reported and justified, but not in the Bond and King[152] study. Cohen and colleagues[76] and Bond and King[152] did not state the uncertainty surrounding the model and the included parameters, neither did they report any form of model validation, whereas Halton and colleagues[151] reported both.

TABLE 28 Critical appraisal checklist for the economic evaluations

No.	Item	Halton 2010[151]	Cohen 2010[76]	Bond and King[152]
1	Is there a clear statement of decision problem?	Yes	Yes	Yes
2	Is the comparator routinely used in UK NHS?	Yes	Yes	Yes
3	Is the patient group in the study similar to those of interest in UK NHS?	Yes	Yes	Yes
4	Is the health-care system comparable that of the UK?	No	No	No
5	Is the setting comparable to that of the UK?	Yes	Yes	Yes
6	Is the perspective of the models clearly stated?	Yes	Yes	No
7	Is the study type appropriate?	Yes	Yes	Yes
8	Is the modelling methodology appropriate?	Yes	Yes	Yes
9	Is the model structure described and does it reflect the disease process?	Yes	Yes	Yes
10	Are the assumptions about the model structure listed and justified?	Unclear	Unclear	Yes
11	Are the data inputs for the model described and justified?	Yes	Yes	Unclear
12	Is the effectiveness of the intervention established based on systematic review?	Yes	No	No
13	Are health benefits measured in QALYs?	Yes	No	No
14	Are health benefits measured using a standardised questionnaire?	Yes	No	No
15	Are the resource costs described and justified?	Yes	Unclear	No
16	Have the costs and outcomes been discounted?	Yes	No	No
17	Has uncertainty been assessed?	Yes	No	Yes
18	Has the model been validated?	Yes	No	No

Description and results of the published economic evaluations

Full data extracted from the published economic evaluations are given in the data extraction forms (see *Appendix 8*).

Halton and colleagues

Halton and colleagues[151] conducted an economic evaluation of the effectiveness of a CVC care bundle for preventing CRBSI relative to current practice, which was defined as a non-bundled approach to central line management with the use of uncoated catheters. The study setting was an adult ICU in Australia. The intervention ran over an 18-month period. The CVC care bundle encompassed five elements: optimal hand hygiene, chlorhexidine skin antisepsis, maximal barrier precautions for catheter insertion, choice of optimal insertion site and prompt catheter removal. The intervention also included a programme to educate staff about clinical leadership and the risk of infection.

The total costs of implementing the intervention were estimated in two parts: the costs directly associated with the components of the intervention and the costs related to the monitoring, education and leadership activities. A Markov model was constructed and was used to estimate the cost-effectiveness of the CVC care bundle for different combinations of antimicrobial and uncoated catheters. The analysis was conducted from the Australian health-care payer perspective with the costs reported in Australian dollars at 2006 prices. The study used various sources including the published literature, primary data from studies, national statistics, population surveys and health-care databases to derive costs and the associated health benefits. The economic outcomes from the model were summarised in terms of QALYs and total costs.

Modelling approach

The structure of the model was based on the patient clinical pathway. A Markov state–transition decision model, which had previously been developed to evaluate the cost-effectiveness of antimicrobial CVCs in an Australian setting, was adapted.[155] The Markov model consists of short- and long-term components: short term for the hospital stay and long term for the remainder of the patients' life after hospital discharge. The patients enter the model with the CVC in situ. The short-term Markov model consists of daily cycles whereby patients may develop CRBSI, remain as an ICU patient with the CVC or have their catheter removed. Patients who develop CRBSI have an increased risk of death in hospital (*Figure 8*).

The daily probabilities of catheter removal and CRBSI were estimated by fitting a Weibull distribution to data from an epidemiological study of CVCs.[156] In the long-term Markov model, the surviving cohort was followed for the remainder of their lifetimes. Utilities associated with different health states were assigned to cycles spent in the ICU and 6 months after discharge. Costs and QALYs were discounted using a rate of 3%.

Assumptions

Several assumptions were made in the model structure. It was assumed that the catheters were inserted or removed mainly within the ICUs and that no multiple catheterisations existed. ICUs were assumed to have an existing infection control procedure in place. The consequences of CRBSI were also assumed not to be dependent on age, disease severity or causative micro-organisms. As there was no information on reduction in QALYs among CRBSI survivors, the life expectancies among this group of patients were adjusted using Australian population QoL population norms.[157]

Catheter colonisation was not included in the model, as the authors considered that this event does not carry health or economic consequences. It was assumed that preferences exist among the clinicians for the use of antimicrobial CVCs. This assumption led to comparisons between the current standard of practice using antimicrobial-impregnated catheters and adoption of the CVC care bundle.

Effectiveness of intervention

The study used estimates of the effectiveness of a catheter care bundle from the Keystone ICU project,[34] which reported an 18-month intervention aimed at reducing the incidence of CRBSI in adult ICUs in Michigan, USA (as discussed in *Chapter 4*). The intervention focused on the clinicians' use of five evidence-based procedures as highlighted by the US CDC. The intervention included a programme to educate staff about clinical leadership and risk of infection. The intervention reduced the risk of infection over 18 months with a relative risk of 0.34 (95% CI 0.23 to 0.5).

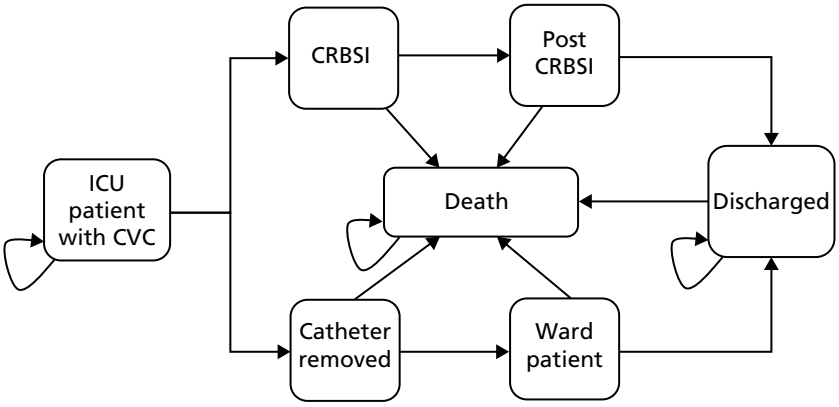

FIGURE 8 Markov model of the health states for ICU patients with a CVC.[151]

Halton and colleagues[151] estimated the effectiveness of each type of antimicrobial CVC from a systematic review of the literature conducted by Ramritu and colleagues.[158] The relative risks of contracting CRBSI with the use of a chlorhexidine/silver sulfadiazine (CH/SSD)-coated catheter, and minocycline and rifampicin (MR)-coated catheter were 0.66 and 0.39, respectively.

Estimation of quality-adjusted life-years

The health outcome in the model was expressed in QALYs. The utility weight estimates used in the model were taken from several sources. A utility value of 0.66 for the ICU stay was derived from a previous study that examined the changes in QoL before and after intensive care.[159] The study was a prospective cohort of 300 consecutive patients admitted to intensive care in a Scottish hospital. The SF-36 questionnaire was given to patients' relatives to assess the patients' health-related quality of life (HRQoL) before their current illness. The EQ-5D instrument was then used to elicit the patient's QoL over a 12-month period.

Age-related utility values were derived from a population-based survey.[157] The Australian Health Omnibus Survey was based on responses from a 3100 population using the Assessment of Quality of Life (AQoL) instrument. The data from the population based survey were stratified by age, gender and health status.

Estimation of costs

Halton and colleagues[151] included costs associated with implementing the CVC care bundle and the costs of the monitoring, educational and leadership activities. The authors were not able to estimate the cost of the care bundle itself. The estimates of the resources associated with these activities were based on descriptions from the Keystone ICU project.[34] The overall resource use estimate was based on time spent on the activities directed towards the implementation of the intervention. Time spent on activities such as mentoring by key personnel, lectures for the clinical staff and preparation of care bundle components were among the key resource estimates. The overall time spent was expressed in days and man-hours to the nearest minute.

The additional costs for the CH/SSD and MR catheters were A$11.64 and A$59.36, respectively, relative to uncoated catheters. Cost estimates for CRBSI were categorised into costs of CRBSI diagnostics, treatment and hospitalisation. Diagnostic costs for CRBSI were A$101.70 (per patient with CRBSI), based on an estimate from the Australian health-system database, whereas the cost for treatment was A$591.30. CRBSI was associated with increased hospitalisation costs and longer inpatient stays. These costs were for ICU bed-days (A$3021 per day) and hospital bed-days (A$843 per day). There were an extra 2.41 ICU days and 7.54 hospital days associated with each case of CRBSI. Other sources of cost and resource use estimates included a prior economic evaluation,[160] and costing study.[161]

Cost-effectiveness results

As the cost of implementing a CVC care bundle in Australia was unknown, deterministic threshold analyses were conducted. The maximum cost for the care bundle was identified at which it would remain cost-effective (i.e. if the cost per QALY was less than the willingness-to-pay threshold of A$64,000). The baseline analyses show the benefits for the CVC care bundle or standard practice under different scenarios. The CVC care bundle was shown to be cost-effective up to a nationwide implementation cost of A$4,349,730 for an 18-month period (or A$94,559 per ICU) compared with current practice alone. For the strategy that includes CH/SSD and MR catheters, the CVC care bundle remains costs effective up to an implementation cost of A$2,287,400 and A$1,144,465, respectively, for the same period.

Sensitivity analyses

Sensitivity analyses were conducted to compare the CVC care bundle and different forms of vascular catheters used in current practice. The analyses included a pairwise comparison between current practice and the CVC care bundle; a three-way comparison between the CVC care bundle, the CH/SSD catheters and current practice; and a four-way comparison between the CVC care bundle, MR catheters, CH/SSD catheters and current practice.

Summary of key issues

- The study estimated the cost-effectiveness of a CVC care bundle relative to current practice in an Australian setting.
- The structure of the model, assumptions and methods used in estimating the utility weights incorporated into the model were clearly stated.
- One key limitation is that the study was not able to estimate the cost of the CVC care bundle.

Cohen and colleagues

Cohen and colleagues[76] conducted a retrospective analysis of the costs from a simulation-based educational intervention in CVC insertion as a means of reducing CRBSI among patients in a medical intensive care unit (MICU) in Chicago, USA. The study estimated the financial implication of the educational intervention by comparing the rates of CRBSI during the intervention period (December 2006 to November 2007) and the year before the intervention. The intervention included a 2-hour lecture, ultrasound training and organised practice with a CVC simulator, as well as feedback from an instructor. The education intervention involved emphasis on the core evidence-based protocol for reducing CRBSI, which includes hand washing, full sterile barrier technique, chlorhexidine skin preparation, avoidance of the femoral site and prompt CVC removal.

The cost-effectiveness model used regression analyses to estimate the costs from the non-randomised before-and-after study. The resources used and cost estimates for the intervention were derived from hospital cost accounting data. The costs included were the cost of the intervention and the associated costs for the hospital stay.

Modelling approach

Two statistical methods were used in the study: the propensity score matched case–control comparison method and the linear regression method. The trial data were analysed and regression models were used to derive estimates of cost and LOS for the intervention and control group, controlling for age, sex and Charlson score (an indicator of comorbidity). To give the intervention and the control group the same infection risk, a regression-based propensity score was used. Estimates of cost differences between the matched cases and controls were then derived.

Effectiveness of intervention

The effectiveness of the intervention was estimated retrospectively by comparing the CRBSI rates for the year before the intervention to the one after the simulation-based education. Using hospital accounting data, the incremental cost and LOS associated with MICU patients with a CVC and a CRBSI during the period were estimated.

A total of 477 patients who had a CVC inserted in the MICU during the period were included in the study. The baseline infection rate before the trial was 11 cases in 239 CVC patients, i.e. 4.2 per 100 MICU CVC admissions. After the medical residents had been fully trained, the infection rate was estimated to be 0.42 per 100 MICU CVC admissions. The study estimated that 9.95 CRBSI cases were prevented in the year after the intervention. Analysis of the data (for both statistical methods) gave an additional LOS for patients with CRBSI compared with those without CRBSI of 13.8–14.2 days for the hospital and 12.1–12.2 days for the MICU.

Estimation of quality-adjusted life-years

Utility weights were not reported in the model and the study in general, and so QALYs were not estimated. The health benefit from the study had been estimated in terms of the number of CRBSI cases averted.

Estimation of costs

The cost estimates in the study were sourced primarily from the hospital cost accounting data and include the costs of supplies, faculty and staff time and space rental (as outlined in the data extraction form: see *Appendix 8*).

All the reported costs were adjusted to 2008 US dollars. The cost to train 69 medical residents was US$111,916. The predicted annual cost to maintain the intervention was US$89,455. The additional cost estimates associated with CRBSI derived from the linear regression model and the risk-adjusted model were similar: US$82,005–82,730.

Cost-effectiveness results

The total annual estimated savings for the propensity score matched case–control comparison method and the linear regression method, respectively, were US$823,164 and US$815,950, 141 and 137 patient hospital days, and 120 and 121 MICU days. The net annual saving in monetary terms from the intervention was estimated to be US$700,000. Based on the results, a 7 : 1 rate of return on investment was achieved with the intervention. The study did not report any results of sensitivity analysis.

Summary of key issues

- Data were from a before-and-after study and may not be a true reflection of the intervention effect.
- The intervention was limited to a particular hospital setting and was conducted for a limited duration. This makes it unclear if the findings are generalisable to other hospitals or countries.
- The study did not consider longer-term follow-up.
- The health outcomes of the study were not presented in QALYs.

Bond and King

Bond and King[152] conducted an economic evaluation of the theoretical impact of an educational intervention to improve the safety of CVC insertion. The study setting was a health-care system that included a tertiary care centre, a community hospital and an emergency department in the USA. The educational intervention consisted of a CVC education course. It was a day-long programme with brief introductory lectures followed by hands-on procedural simulation in CVC insertion, using training mannequins, appropriate sterile procedures, ultrasound imaging and feedback from instructors. In addition, doctors and nurses were taught the Institute for Healthcare Improvement (IHI) bundle of barrier precautions and new processes to encourage, ensure and track compliance.

A decision-analytic model was constructed and was used to estimate the cost-effectiveness of the education intervention. The authors did not state the perspective of the analysis, nor the base year for the costs. The study used various sources including data from published primary studies. The results from the model were presented in US dollars in terms of net monetary benefits of the education intervention compared with no education.

Modelling approach

A decision-analytic model was constructed in TreeAge software version 1.5 (TreeAge Software Inc., Williamstown, MA, USA) and describes the duration of the hospital stay. The model starts with the need for a CVC, with a focus on non-emergent cases, defined as those where there was sufficient time to follow sterile precautions in CVC insertion. One cohort of patients receive the education intervention and the other does not. In each cohort, a proportion receive the CVC in the internal jugular, subclavian and femoral veins. Patients then either have no complications or mechanical complications, such as iatrogenic pneumothorax or CLAB. Patients who suffer a CLAB or mechanical complication have corresponding higher costs and mortality than those without.

Effectiveness of intervention

The evaluation assumes that the educational intervention would reduce the rate of CLAB by 50% and reduce the rate of the mechanical complications by 25% in the base-case analysis. The study did not discuss the sources upon which these are based, nor the rationale behind their use. Patients with CLAB had an attributable mortality of 12%, compared with a baseline mortality risk of 10% for ICU patients, based on a review of studies.

Estimation of quality-adjusted life-years

Utility weights were not reported in the model and the study in general, and so QALYs were not estimated. The health benefit from the study had been estimated in terms of the number of CLAB cases averted.

Estimation of costs

The costs of the educational programme were presented but it is not clear how these were estimated or whether they were based upon an empirical study. The costs of the programme included the acquisition cost of mannequins and ultrasound technology, and the staff training time for the trainers and trainees. The cost of the programme was US$170,360 for the first year and an average of US$63,610 for the subsequent 4 years, for the health-care system described, in which 600 patients had CVCs inserted in each year.

The cost per CLAB case was US$16,350 based upon those reported by IHI; however, the full reference was not provided so we are unable to critique this cost. The mean excess cost of mechanical complications was US$17,312.

Cost-effectiveness results

The results were presented for the education intervention versus no intervention per individual with a CVC inserted in the ICU. The survival during the hospital stay was 89.9% for those in the education intervention cohort and 89.8% in the no-education intervention cohort. The costs with and without the education, based on the first year programme cost, were US$546 and US$392, respectively, i.e. an additional cost of US$154. For the health-care setting, the additional cost was US$92,400 to reduce the number of CLABs from 4.2 to 2.1. The study conducted a number of sensitivity analyses varying the programme cost, CLAB baseline rate and the intervention effectiveness. For the lower programme cost for years 2–5, the additional cost of the education intervention was US$44 per patient. Raising the CLAB rate to 5% gave a net monetary benefit of US$158 with an additional survival of 0.3%.

Summary of key issues

- The study estimated the cost-effectiveness of a CVC education intervention relative to no education for a US health-care setting.
- The model does not consider long-term follow-up beyond the hospital stay or include QALYs.
- The derivation of some of the model parameter estimates is unclear, particularly the cost of the CLAB, and the effectiveness of the education intervention.

Published economic evaluations: summary of methods

- A systematic review of cost-effectiveness studies identified three cost-effectiveness studies of educational interventions for preventing catheter-BSI in critical care.[76,151,152] Two studies used a decision modelling approach and the other was a trial-based economic analysis.
- Halton and colleagues[151] used a Markov decision-analytic approach to model Australian patients with CRBSI over their lifetime and the health benefits associated with a CVC care bundle. The model did not include the cost of the care bundle.

- Cohen and colleagues[76] used a trial-based cohort analysis to derive estimates of the costs and benefits associated with a simulation-based education intervention in a hospital in the USA. They used regression models to estimate the costs and health benefits for matched case and control groups with and without CRBSI. However, the intervention was limited to a particular hospital setting and for a short period of time.
- Bond and colleagues[152] used a Markov decision-analytic approach to evaluate effects of an educational intervention on CLAB among US patients. The model did not consider the long-term health benefit for the intervention.
- None of the studies was considered appropriate to estimate the cost-effectiveness of educational interventions for preventing catheter-BSI in critical care units in the UK NHS.

Chapter 6 Economic evaluation

We developed a new model to estimate the costs, benefits and cost-effectiveness of implementing a CVC care bundle for preventing catheter-BSI in adult patients in critical care units in England, compared against current clinical practice. The CVC care bundle in this analysis was defined based upon the Matching Michigan programme in England and the original US Keystone ICU project approach.[34] It encompassed five elements: optimal hand hygiene, chlorhexidine skin antisepsis, maximal barrier precautions for catheter insertion, choice of optimal insertion site, and prompt catheter removal. Current clinical practice was defined as critical care that did not implement a CVC care bundle. The model was populated with clinical effectiveness data from the study most relevant to Matching Michigan identified in our systematic review of clinical effectiveness (see *Chapter 4*). HRQoL data were derived from the published literature and cost data derived from published studies (where available), and from national and local NHS unit costs.

The economic evaluation was from the perspective of the NHS and Personal Social Services, as only these direct costs were included. The model estimates the costs during hospital stay and the lifetime benefits for the intervention and its comparator. The benefits were discounted at 3.5%, as recommended by NICE.[154] The base price year for the costs was 2011. The outcome of the economic evaluation is reported as the incremental cost per QALY gained.

Methods for cost-effectiveness modelling

Description of the model structure

A decision-analytic model was designed to estimate the cost-effectiveness of a CVC care bundle for preventing catheter-BSI in critical care units compared with remaining with current clinical practice. A diagram of the model is shown below (*Figure 9*). The model follows cohorts of patients from their admission to the critical care unit. The cohorts of patients compared are those who receive the CVC care bundle and those who receive current clinical practice. The numbers of critical care patients infected with catheter-BSI depend upon the catheter-BSI incidence rate, the proportion of patients with a CVC, and the effectiveness of the intervention (CVC care bundle or current clinical practice) for preventing infections. Patients may die during their hospital stay and the risk of mortality is greater for those with catheter-BSI. Furthermore, LOS will be greater for patients with catheter-BSI. The model estimates the number of people who contract catheter-BSI, those who die in hospital and the total LOS for the two cohorts. The long-term survival of patients after discharge from the critical care unit is estimated using a simple Markov model with states for alive and dead. Long-term QALYs are estimated for these patients using general population age-related HRQoL utility values. The model calculates the costs associated with LOS and the treatment and diagnosis of the catheter-BSI infections. There are also costs of implementing the CVC care bundle.

In the model, the total costs and discounted QALYs are calculated for both cohorts and thus the cost-effectiveness of the CVC care bundle is calculated:

$$\text{Cost effectiveness} = \frac{\text{Cost for bundle cohort} - \text{cost for current practice cohort}}{\text{QALYs for bundle cohort} - \text{QALYs for current practice cohort}} \quad (1)$$

The model is based on the following assumptions:

- We assumed for the purposes of the model that CABSI and CRBSI are synonymous, and are collectively referred to as catheter-BSI. It is not possible to distinguish between the surveillance definition of catheter-associated BSI and the clinical definition of catheter-related BSI. Although in theory CABSI

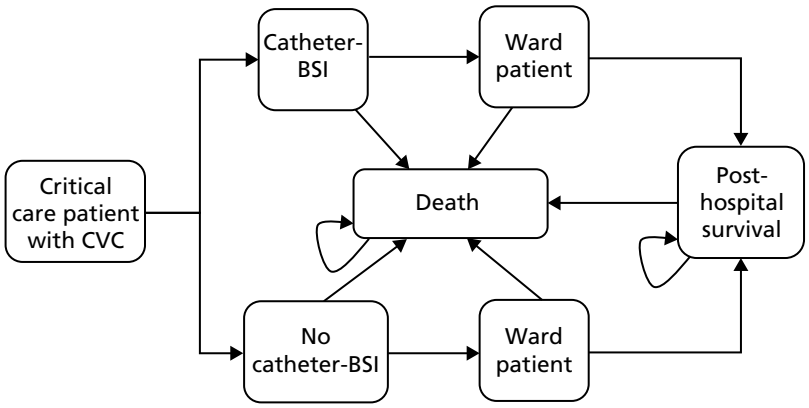

FIGURE 9 Cost-effectiveness model for the CVC care bundle to prevent catheter-BSI.

overestimates the true incidence of CRBSI (for definitions see *Chapter 1*), our review of clinical effectiveness (see *Chapter 4*) and another systematic review[21] found that the definitions are used interchangeably and inconsistently in primary research studies.

- We assumed that there is no difference in mortality during the hospital stay following critical care discharge for patients who had catheter-BSI in the critical care unit compared with those who did not. We were unable to find any data for the mortality during the hospital stay following critical care discharge for these two groups.
- We assumed that there was no difference in mortality after hospital discharge for those who had catheter-BSI in the critical care unit compared with those who did not.

The model does not consider the HRQoL of patients in critical care units, because the time spent in critical care is very small compared with the lifetime horizon, and therefore any QALY gains during this period are insignificant. In addition, non-fatal adverse events associated with catheter-BSI were included within the model as a cost, but not as a utility decrement.

The economic evaluation does not include non-tangible benefits or disbenefits associated with the intervention, such as changes to staff morale and public confidence in the health-care system.

Evaluation of uncertainty

There are uncertainties in the evaluation of the cost-effectiveness of the CVC care bundle. These reflect a lack of information about the content of interventions, their costs and resource use, and the extent to which they were implemented in primary research studies, as well as a general lack of information about the effects of catheter-BSI on patient survival and HRQoL. Uncertainty was evaluated using deterministic and probabilistic sensitivity analyses (PSAs). One-way deterministic sensitivity analyses (described below) were conducted to evaluate the influence of individual parameters on the model results and to test the robustness of the cost-effectiveness results to variations in the structural assumptions and parameter inputs.

Multiparameter uncertainty in the model was addressed using PSA.[162] In the PSA, probability distributions were assigned to point estimates of all parameters used in the base-case analysis. The model was run for 1000 iterations, with a different set of parameter values for each iteration, by sampling parameter values at random from their probability distributions. The uncertainty surrounding the cost-effectiveness of the CVC care bundle is represented according to the range of cost-effectiveness results. The parameters included in the PSA, the distribution used for sampling each parameter, and the upper and lower limits assumed for each variable are reported in *Appendix 9*.

Model validation

The economic model was validated by checking the model structure, calculations and data inputs for technical correctness by an independent health economist. The structure was reviewed by two clinical experts for its appropriateness for the disease process and the treatments considered. The robustness of the model to changes in input values was tested using sensitivity analyses to ensure that any changes to the input values produced changes to the results of the expected direction and magnitude. Finally, the model results were compared with those from previous published cost-effectiveness analyses.

Data sources

Catheter-bloodstream infection epidemiology

Catheter-bloodstream infection incidence rate

Catheter-bloodstream infection incidence data were collected from critical care units in England during the Matching Michigan programme. Matching Michigan recruited 97% of the acute health-care trusts in England, representing 216 critical care units. The main elements of the scheme involved defining and measuring infections and then reporting results on a monthly basis.[163] Although full data from the Matching Michigan programme were not available at the time of writing this report, the incidence per 1000 catheter-days was reported as 3.7 at the start of the collecting period (May 2009). For the purposes of our analyses, we have used the incidence rate from before the introduction of the Matching Michigan intervention (*Table 29*) to reflect the baseline incidence density of catheter-BSI associated with current clinical practice.

Within the model, the incidence density per 1000 catheter-days was converted to the percentage of critical care patients who contracted catheter-BSI by assuming a mean stay in critical care with a CVC of 5 days.[164]

The proportion of patients with a central venous catheter

No estimate was found of the proportion of patients in critical care requiring a CVC in England (or anywhere else in the UK). However, a pilot surveillance study[166] reported infection control data for nine hospitals in Irish critical care units between November 2010 and January 2011. The characteristics of the Irish units were assumed to be similar to those in the UK. The proportion of patients with a CVC was defined as the percentage of patients in the critical care unit who had one or more CVC inserted. Nationally, it was 71% and ranged between individual units from 49% to 96%.

Clinical effectiveness

Central venous care bundle effectiveness

At the time of constructing the model, full results of the Matching Michigan programme had not been published. An estimate of the effectiveness of the CVC care bundle was derived from our systematic review of clinical effectiveness (see *Chapter 4*). In this review the most relevant studies in terms of geographical scale for providing clinical effectiveness data were the five regional-scale projects[34,68,83,126,136] as they most closely resemble the regional multicentre approach used in Matching Michigan in England. We considered the 'CLAB ICU' study by Burrell and colleagues in Australia[83] to be the most appropriate for the following reasons: (1) it appeared to closely reflect the strategic approach used in Matching Michigan in England (provision of a CVC insertion kit, checklist, infection surveillance feedback and staff empowerment among other components); (2) sufficient details of the intervention were reported for the intervention to be classified by the reviewers as reproducible based on the published information; (3) costs of the intervention were reported; (4) the intervention was, like Matching Michigan, specifically intended to replicate the original US Keystone ICU project approach[34] in a new national setting. The study by Burrell and colleagues[83] is reported in more detail in *Chapter 4*. Burrell and colleagues[83] used a definition of CABSI during the hospital stay, rather than CRBSI, as used with other model parameters. However, as noted above, we assume that CABSI and CRBSI are synonymous and are collectively referred to as catheter-BSI.

TABLE 29 List of parameters included in the model

Parameter name	Base case	Higher estimate	Lower estimate	Source
Catheter-BSI epidemiology				
Catheter-BSI incidence rate, per 1000 catheter-days for current clinical practice	3.7	5.0	1.3	NPSA[163]
Critical care mortality, no catheter-BSI	0.169	0.203	0.135	ICNARC 2011[164]
RR for critical care mortality due to catheter-BSI	3.25	3.6	2.7	Lambert *et al.*[165]
Proportion of patients with a CVC	0.71	0.96	0.49	ICCTG[166]
Costs				
Ward bed-day, £	246	295.2	196.8	HRG 2010/11[167]
Critical care bed-day, £	1440	1171	1657	HRG 2010/11[167]
Catheter-BSI diagnosis and treatment costs, £	518	622	415	Halton *et al.*[151]
CVC care bundle (per critical care patient), £	15.48	20.13	10.84	Various
Clinical effectiveness				
Bundle effectiveness, RR	0.4	0.67	0.22	Burrell *et al.*[83]
Additional critical care LOS for catheter-BSI, days	1.5	2.5	0.0	Lambert *et al.*[165]
Additional ward LOS for catheter-BSI, days	5.13	8.68	1.58	Warren *et al.*[168]
Other parameters				
Starting age, years	60	70	50	ICNARC[164]
	Intercept	**Age coefficient**		
HRQoL utility coefficients	1.0604	–0.0043		Ward *et al.*[169]

HRG, Healthcare Resource Group; National Patient Safety Agency; ICCTG, Irish Critical Care Trials Group; ICNARC, Intensive Care National Audit & Research Centre.

Burrell and colleagues[83] reported a 60% reduction in the number of catheter-BSI in critical care, i.e. a relative risk of 0.4 compared with baseline clinical practice.

Our model compares a CVC care bundle against remaining with current clinical practice, where those elements from the CVC care bundle have not been implemented on a co-ordinated, national or regional basis. However, it may be the case that some hospitals (or individual critical care units) would have incorporated some elements of the CVC care bundle into current clinical practice, prior to implementation of a co-ordinated, national or regional programme. The baseline catheter-BSI incidence data used in the model, based on the rate reported in acute health-care trusts in England prior to the implementation of Matching Michigan, should reflect such partial implementation. It should also be noted that there may be variation in the degree to which aspects of the bundle are implemented between different hospitals. Similar variability would likely have been present in the regional-scale CLAB ICU project[83] that provides an estimate of clinical effectiveness of the CVC care bundle.

Increased length of stay due to infection

Length of stay was reported in seven studies[50,94,109,110,117,139,144] in our clinical effectiveness review (see *Chapter 4*). Only one of these studies, by Zingg and colleagues,[144] reported LOS data separately for patients with and without catheter-BSI, and we have therefore additionally searched the literature for further supporting information on the additional LOS due to catheter-BSI.

Estimates for increased LOS due to catheter-BSI vary widely in the literature. However, some of these studies[170,171] have overestimated the additional LOS due to the acquired infection by ignoring the timing of the infection. This leads to 'time-dependent bias' in multiplicative hazard ratios. A more appropriate method to estimate LOS due to an infection is to use a multistate or longitudinal model that accounts for the time of the infection.[170–172]

Barnett and colleagues[170] demonstrated the effect of time-dependent bias on LOS. They used a multistate model that accounted for the time of infection and compared that to a commonly used model that ignores the time of infection (a generalised linear model assuming a gamma distribution). They applied the two methods to a large prospective cohort of hospital admissions from Argentina and validated their results using a simulation study. The additional critical care LOS due to nosocomial infection was 11.23 days when ignoring time dependence and only 1.35 days after accounting for the time of infection. The simulation results showed that ignoring time dependence consistently overestimated the additional LOS.

We found four studies[165,168,170,173] that used the appropriate methodology to estimate the additional LOS attributable to BSIs in the critical care unit. From these, we considered a study by Lambert and colleagues[165] to be most relevant and appropriate as it was a large European study. Lambert and colleagues[165] analysed data for 119,699 patients collected prospectively from 537 critical care units in 10 participating countries during 2005–8, using a standard European protocol for the surveillance of infections [Hospitals In Europe Link for Infection Control through Surveillance (HELICS)-ICU].[174] They assessed the excess mortality and critical care LOS associated with BSI (and pneumonia). They focused on the most frequent causative microorganisms for BSI and pneumonia (*Acinetobacter baumannii, Escherichia coli, Pseudomonas aeruginosa* and *S. aureus*). The risk of death in the critical care unit was modelled with a time-dependent regression model assuming proportional hazards, taking into account the indirect effect on mortality of (a potentially) extended stay due to the infection. The study[165] reported analyses separately for infections caused by pathogens with and without antimicrobial resistance (sensitive or resistant). The time adjusted excess LOS for all four microorganisms varied from 1.1 days to 2.5 days for sensitive and resistant pathogens, respectively. The excess LOS for all patients was not reported and so we estimated the pooled population excess LOS using the proportions of patients with sensitive (71%) and resistant (29%) microorganisms, to give an estimate of 1.5 days.

We found one study[168] that used the appropriate methodology to estimate the additional LOS attributable to catheter-BSI during hospital stay, after discharge from the critical care unit. Warren and colleagues[168] prospectively collected data on all patients admitted to the medical–surgical critical care units of the Missouri Baptist Medical Centre in St Louis during 1998–2000. They analysed data for patients who had required a CVC during their critical care stay. Two multiple regression models were created to evaluate hospital LOS and critical care LOS due to catheter-BSI using the backward stepwise method. Compared with non-infected patients, those patients with catheter-BSI had longer critical care and total hospital LOS. The unadjusted mean difference in overall LOS was 21.8 days for the critical care unit and 51.7 days for hospital stay. After controlling for confounding factors, the attributable critical care LOS due to catheter-BSI was 2.41 days and the attributable hospital LOS was 7.54 days (95% CI 3.99 to 11.09). Warren and colleagues[168] used a definition of CABSI, rather than CRBSI but, as noted above, it is not possible to isolate the effect of using different definitions and therefore catheter-BSI used in the model does not distinguish between CABSI and CRBSI.

Critical care unit mortality

General population data for patients in UK critical care units are collated by the Intensive Care National Audit & Research Centre (ICNARC).[163] The latest data available were for the period for April 2009 to March 2010, from 188 NHS critical care units with 96,810 patients admitted. The mean patient age was 60.5 years and the mortality rate reported for critical care was 16.9%. Mean LOS in the unit was 5 days. The mean mortality rate during the hospital stay (outside the critical care unit) was 8.3%.

As with estimates for LOS, estimates for the attributable mortality for catheter-BSI vary widely according to the methodology adopted. Mortality was reported in five studies[94,103,110,139,144] in our clinical effectiveness review (see *Chapter 4*); however, none of the studies reported mortality data separately for patients with and without catheter-BSI. As with LOS, we considered the study by Lambert and colleagues[165] to be the most appropriate. Their findings suggest that BSI caused by all four microorganisms treble the risk of mortality for patients in the critical care unit. The fully adjusted hazard ratios for critical care deaths were 3.1 and 3.6 for sensitive and resistant microorganisms, respectively. We used the same method as for LOS to estimate an overall hazard ratio for critical care mortality of 3.25.

We found no evidence for any differences between mortality risks for patients with catheter-BSI during their hospital stay, outside the critical care unit, and therefore assumed there was no additional mortality risk during this period.

Estimation of costs

The costs included in the model were critical care unit and ward bed-day costs, catheter-BSI diagnostic and treatment costs and the cost of the CVC care bundle. The base year for the analysis was 2011; where necessary, costs were inflated to that year using the inflation indices from the Unit Costs of Health and Social Care.[175]

Critical care unit and ward bed-days

Critical care unit and ward bed-day costs were taken from Healthcare Resource Group (HRG) costs.[176] The cost of a critical care bed-day was estimated based upon the cost for the number of organs supported (zero to six). We assumed that for our cohort of patients there would be the equivalent of an average of three organs supported (HRG code XC03Z), and we tested this assumption in the sensitivity analysis. The HRG bed-day cost for patients after they leave the critical care unit is dependent upon the reason for their critical care admission. We used the median cost for all non-elective inpatient (long-stay) excess bed-days reported.

Catheter-bloodstream infection diagnostic and treatment costs

Halton and colleagues[151] estimated the consumable costs associated with catheter-BSI in Australia and these prices reflected the cost to Queensland Health decision-makers. These costs included the price of the catheters, catheter-BSI diagnosis (one catheter tip culture and two blood cultures) and catheter-BSI treatment. Treatment costs were a weighted average of the costs of standard regimens for causative organisms observed within the surveillance system: i.e. 2 weeks of vancomycin, 10 days of ticarcillin and clavulanate or 4 weeks of fluconazole. We converted these costs to UK pounds sterling (£) and inflated them to our analysis base year (exchange rate £1 = A$1.477).

Central venous catheter care bundle cost

The cost of the CVC care bundle used in the model refers to the additional costs – above those of current clinical practice – of implementing the bundle. For the purposes of the analysis the costs of current clinical practice are assumed to be zero. The cost of the CVC care bundle consists of the national programme and local implementation costs. The programme grant for implementing Matching Michigan in England was £1,750,000 for a 2-year period. The programme grant costs covered the costs of the support for central training days and web-based data collection tools, but did not cover any payments to local health professionals. Thus, the annual cost would be £875,000 per annum. The local training costs were calculated based on clinical advice we received about the implementation of Matching Michigan in one local centre. In this centre, one Band 6 nurse trained and monitored ICU staff in three critical care units and this took 20% whole time equivalent. Using the assumptions above, the CVC care bundle costs were estimated as £15.48 per patient attending critical care (see *Table 29*) and these are shown in *Appendix 10*. The CLAB ICU project,[83] which provides our estimate of clinical effectiveness, included 37 critical care units at a total cost of A$508,831. Assuming critical care patient admissions were similar to those in the UK, this would equate to an average cost per critical care patient of about £15, which is consistent with the cost used for the CVC care bundle in our analysis.

Estimation of health-related quality of life and long-term survival

The long-term survival of patients after discharge from the critical care unit was estimated based on England and Wales population mortality rates[177] using a simple Markov model with states for alive and dead. Survival of patients after discharge from critical care is lower than for the general population as reported by Williams and Dobb.[178] We multiplied the general population mortality rates by the relative risks of mortality reported in their study:[178] 2.9 in the first year and 1.5 thereafter. Long-term QALYs were estimated using general population utility values stratified for age as derived in a previous Health Technology Assessment (HTA) report for statins[169] (utility = 1.0604 – 0.0043*x*, where *x* is the person's age). We used the mean age of a critical care patient of 60 years, according to the ICNARC data.[164] The calculated mean discounted life expectancy for a typical patient aged 60 years from hospital discharge was 11.8 years, and the mean discounted QALY was 9.1.

Results of the modelling

This section reports the cost-effectiveness results for cohorts of 100 adult patients aged 60 years admitted to the critical care unit. The analysis evaluates a CVC care bundle compared with remaining with current practice, where current practice relates to the period before the introduction of the Matching Michigan programme. Results are presented for costs and QALYs for the CVC care bundle cohort and the current clinical practice cohort with undiscounted costs and health outcomes discounted at 3.5%.

The base-case results show that there are 0.79 fewer catheter-BSI in the CVC care bundle cohort than in the current clinical practice cohort (*Table 30*), a corresponding 0.3 fewer deaths during critical care, which leads to an increased survival of 3.55 years and 2.72 QALYs. The bundle dominates current practice, i.e. it is more effective and less costly. The cost savings are largely as a result of the savings from reduced LOS in the critical care unit. The incremental cost per QALY gained was –£573 (*Table 31*). The incremental cost per catheter-BSI averted was –£1976.

Sensitivity analysis

Deterministic sensitivity analysis

One-way deterministic sensitivity analyses were performed, in which model parameters were systematically and independently varied, using realistic minimum and maximum values. The sensitivity analyses

TABLE 30 Summary of the model results for cohorts of 100 adult patients admitted to critical care

Outcome	Current practice	CVC care bundle	Difference
Patients with catheter-BSI in critical care (per 100 adult critical care patients)	1.31	0.53	0.79
Total mortality, critical care unit (per 100 adult critical care patients)	17.40	17.10	0.30
Total survivors, hospital discharge (per 100 adult critical care patients)	74.30	74.60	0.30
Additional critical care LOS for catheter-BSI (days per 100 adult critical care patients)	1.97	0.79	–1.18
Additional ward LOS for catheter-BSI (days per 100 adult critical care patients)	6.74	2.70	–4.04
Discounted life-years	879	883	3.55
Discounted QALYs	674	677	2.72
Extra inpatient bed-day cost, £	4494	1798	–2697
Cost diagnosis + treatment catheter-BSI, £	681	272	–408
Intervention cost, £	0	1548	1548
Total cost, £	5175	3618	–1557

TABLE 31 Base-case cost-effectiveness results for cohorts of 100 adult patients admitted to critical care

Strategy	Cost, £	Life-years	QALYs	ICER (£/QALY)
Current clinical practice	5175	879.3	674.0	–
CVC care bundle	3618	882.8	676.7	–
Difference	–1557	3.55	2.72	–573

ICER, incremental cost-effectiveness ratio.

investigated the effect of uncertainty around the model assumptions, structure and parameter values on the cost-effectiveness results to highlight the most influential parameters. The effects of uncertainty in multiple parameters were addressed using PSA (reported below). Where possible, the parameters were varied according to the ranges of their CIs, based on published estimates. Where these data were not available an alternative suitable range was chosen, based upon expert opinion. The same ranges were used in the deterministic analyses and PSA (see *Appendix 9*).

Tables 32–34 show the results of the deterministic sensitivity analyses for the incremental cost-effectiveness ratios (ICERs), incremental costs and incremental QALYs. As the ICERs are negative in the base case, some of the results appear counterintuitive owing to the nature of the cost-effectiveness ratio, and care is needed in their interpretation. As an example to illustrate the nature of a negative ICER, readers may consider two results from hypothetical cost-effectiveness analyses comparing two treatments: (1) a saving of £1000 and a gain of 0.5 QALYs (ICER = –£2000/QALY) and (2) the same saving and a gain of 1 QALY (ICER = –£1000/QALY). The negative ICERs would appear to suggest that (1) is more cost-effective than (2). However, (1) is actually *less* cost-effective than (2).

The cost-effectiveness results are robust to changes in all parameters in the deterministic sensitivity analysis. The cost-effectiveness estimates for the CVC care bundle vary from –£990 to £479 per QALY gained for all analyses (see *Table 32*). With the exception of catheter-BSI incidence rate and additional critical care LOS for patients with catheter-BSI, the model results are cost saving for all parameter values, and the results are most sensitive to changes in these two parameters. For changes to the values of the

TABLE 32 Deterministic sensitivity analyses results for ICERs for cohorts of 100 adult critical care patients

Parameter	Baseline	Upper value	Lower value	Upper value ICER (£/QALY)	Lower value ICER (£/QALY)	Range (£)
Catheter-BSI incidence rate	3.7	5	1.3	–721	479	1200
Additional critical care LOS for catheter-BSI	1.5	2.5	0.001	–990	53	1043
CVC care bundle effectiveness	0.4	0.67	0.22	–107	–704	597
Additional ward LOS for catheter-BSI	5.13	8.68	1.58	–826	–320	506
Proportion of patients with CVC	0.71	0.96	0.49	–721	–317	404
Cost of CVC care bundle (per critical care patient), £	15.48	20.13	10.84	–402	–744	342
RR for critical care mortality due to catheter-BSI	3.25	3.6	2.7	–496	–758	262
Critical care mortality, no catheter-BSI	0.169	0.2028	0.1352	–477	–716	239
Critical care unit bed-day cost, £	1440	1171	1657	–456	–667	212
Ward bed-day cost, £	246	295	197	–646	–500	146
Catheter-BSI diagnosis and treatment cost, £	518	622	415	–603	–543	60

TABLE 33 Deterministic sensitivity analyses results for incremental costs for cohorts of 100 adult critical care patients

Parameter	Baseline	Upper value	Lower value	Upper value incremental cost, £	Lower value incremental cost, £	Range
Catheter-BSI incidence rate	3.7	5	1.3	–2648	£457	3105
Additional critical care LOS for catheter-BSI	1.5	2.5	0.001	–2692	£144	2836
CVC care bundle effectiveness	0.4	0.67	0.22	–160	–2488	2329
Proportion of patients with CVC	0.71	0.96	0.49	–2650	–595	2056
Additional ward LOS for catheter-BSI	5.13	8.68	1.58	–2245	–869	1376
Cost of CVC care bundle (per critical care patient), £	15.48	20.13	10.84	–1092	–2021	929
Critical care bed-day cost, £	1440	1171	1657	–1239	–1814	575
Ward bed-day cost, £	246	295	197	–1756	–1358	398
Catheter-BSI diagnosis and treatment cost, £	518	622	415	–1639	–1475	163

TABLE 34 Deterministic sensitivity analysis results for incremental QALYs for cohorts of 100 adult critical care patients

Parameter	Baseline	Upper value	Lower value	Upper value QALYs	Lower value QALYs	Range
Catheter-BSI incidence rate	3.7	5	1.3	3.67	0.96	2.72
CVC care bundle effectiveness	0.4	0.67	0.22	1.50	3.53	2.04
Proportion of patients with CVC	0.71	0.96	0.49	3.68	1.88	1.80
Critical care mortality, no catheter-BSI	0.169	0.203	0.135	3.26	2.17	1.09
RR for critical care mortality due to catheter-BSI	3.25	3.6	2.7	3.67	0.96	2.72

catheter-BSI incidence rate and the additional critical care LOS for patients with catheter-BSI, the cost-effectiveness estimates vary between –£721 and £479 and between –£990 and £53, respectively.

The most influential parameters on the incremental cost are the catheter-BSI incidence rate, the additional critical care LOS for patients with catheter-BSI and the CVC care bundle effectiveness (see *Table 33*). The incremental cost varies between –£2692 and £457 for all analyses. The most influential parameters on the incremental QALYs are the catheter-BSI incidence rate and the CVC care bundle effectiveness (see *Table 34*). The incremental QALYs vary between 0.96 and 3.68 for all analyses.

Probabilistic sensitivity analyses

In the PSA, all parameters were sampled probabilistically from an appropriate distribution[162] using similar ranges as used in the deterministic sensitivity analyses (see *Appendix 9*). The parameters sampled were: catheter-BSI incidence rate, critical care mortality, catheter-BSI mortality risk, catheter utilisation, critical care unit and ward bed-day costs, treatment costs for catheter-BSI, critical care and ward LOS and CVC care bundle effectiveness and cost.

One thousand simulations were run. The PSA results are presented in *Table 35* and show similar results to the deterministic analyses (see *Tables 32–34*) with an ICER of –£488 per QALY gained. The variability of the results is explored in more detail in *Table 36*, by showing the IQRs for model outputs. The CVC care bundle

cost varies between £1377 and £1702, and this is offset by the savings from the inpatient bed-day cost (–£3647 to –£1553). The scatterplots and histogram for cost and health outcomes for the PSA are shown in *Figures 10* and *11*. The majority (83%) of the results show that the bundle is cost saving compared with current clinical practice. The cost-effectiveness of the bundle was < £5000 per QALY gained for all simulation results.

TABLE 35 Baseline PSA cost-effectiveness results

	Cost, £		Life-years		QALYs		ICER (£/QALY)	
Strategy	Median	IQR	Median	IQR	Median	IQR	Median	IQR
Current clinical practice	4903	3351–6831	878.9	865–894	673.7	663–685	–	–
CVC care bundle	3489	2817–4462	882.7	868–897	676.6	666–688	–	–
Difference	–1414	–2582 to –293	3.78	2.43–4.58	2.90	1.83–3.51	–488	–827 to –131

TABLE 36 Summary of PSA cost-effectiveness results for the difference between the CVC care bundle cohort and the current clinical practice cohort

Outcome	Median	IQR
Patient with catheter-BSI in critical care (cases per 100 adult critical care patients)	0.76	0.54–1.02
Total mortality, critical care (cases per 100 adult critical care patients)	0.28	0.20–0.39
Additional critical care LOS for catheter-BSI (days per 100 adult critical care patients)	–0.93	–1.60 to –0.49
Additional ward LOS for catheter-BSI (days per 100 adult critical care patients)	–3.98	–5.81 to –2.63
Inpatient bed-day cost, £	–2358	–3647 to –1553
Intervention cost, £	1542	1377–1702

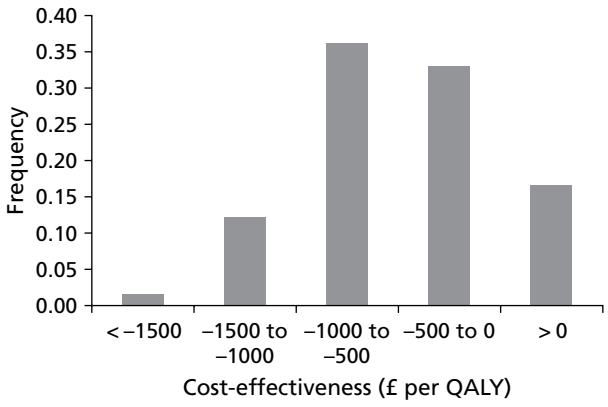

FIGURE 10 Histogram of ICERs for CVC care bundle compared with current clinical practice from the PSA simulation runs.

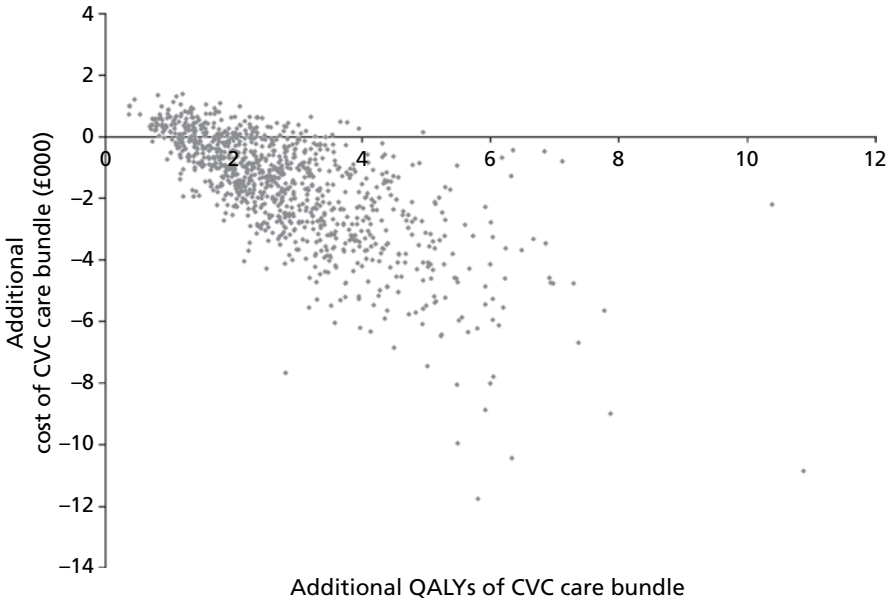

FIGURE 11 Scatterplot for PSA.

Scenario analyses

In addition to the sensitivity analyses, additional scenario analyses were undertaken to investigate the uncertainty in the model results for simultaneous changes to more than one parameter.

Effect of changing the age of patients in critical care

A scenario analysis was conducted for alternative mean starting ages for patients in the critical care unit, using the analysis described above (see the section 'Estimation of HRQoL and long-term survival'). The calculated mean discounted life expectancy from hospital discharge for a typical patient of age 50 and 70 years was 15.8 and 7.6 years respectively and the corresponding mean discounted QALY was 12.6 and 5.6.

For a cohort of patients with mean age of 50 years, the cost-effectiveness is slightly improved at –£413 per QALY gained. At mean age of 70 years, the cost-effectiveness is slightly worse at –£926 per QALY gained.

Threshold analysis

Table 37 shows the results of a threshold analysis in which all parameters were varied until the CVC care bundle became more costly than the current clinical practice. For this scenario, the CVC care bundle would only be more expensive for any feasible changes to four of the parameters, and would remain cost saving

TABLE 37 Model scenario analysis results

Parameter	Value at which CVC care bundle becomes more expensive than current practice
Catheter-BSI incidence, per 1000 catheter-days	< 1.8
Proportion of patients with CVC	< 0.35
CVC care bundle cost, per patient, £	> 30
CVC care bundle effectiveness	> 0.7

for the other parameters. The results show that the bundle would no longer be cost saving if the bundle cost per patient was > £30, the bundle effectiveness incidence density RR was > 0.7, the catheter-BSI incidence density of < 1.8 per 1000 catheter-days, or the proportion of critical care patients with a CVC of < 0.35.

Two-way sensitivity analysis comparing central venous catheter care bundle cost versus effectiveness

Figure 12 shows a two-way sensitivity analysis of the effect on the model results of simultaneously varying both bundle cost and bundle effectiveness. These results show that, even when using extreme values for the parameters, for example with a bundle effectiveness of 0.7 and bundle cost of £85 per critical care patient, the bundle (although no longer cost saving) remains cost-effective with an ICER of < £5000 per QALY gained.

Two-way sensitivity analysis comparing catheter-bloodstream incidence versus additional critical care length of stay

Figure 13 shows a two-way sensitivity analysis of the effect of simultaneously changing both catheter-BSI incidence and additional critical care LOS for catheter-BSI on the model results. These results show that

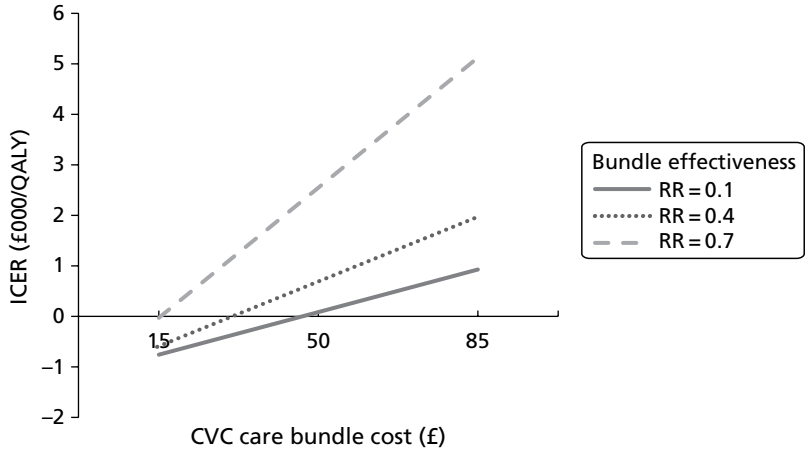

FIGURE 12 Two-way sensitivity analysis comparing CVC care bundle cost vs. effectiveness.

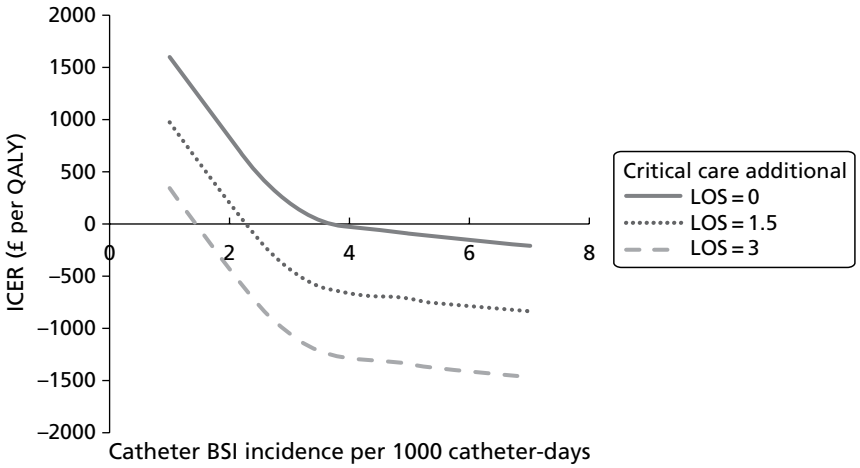

FIGURE 13 Two-way sensitivity analysis comparing CRBSI incidence vs. critical care additional LOS.

even when using extreme values for the parameters, for example with an incidence density of 1.0 catheter-BSI per 1000 catheter-days and no additional critical care LOS for catheter-BSI, the CVC care bundle is no longer cost-saving, but remains cost-effective with an ICER of < £2000 per QALY gained.

Two-way sensitivity analysis comparing catheter-bloodstream infection incidence versus bundle effectiveness

Figure 14 shows a two-way sensitivity analysis of the effect of simultaneously changing both catheter-BSI incidence and CVC bundle effectiveness on the model results. These results show that, even when using extreme values for the parameters, for example with a bundle effectiveness of 0.7 and incidence density of 1.0 catheter-BSI per 1000 catheter-days, the bundle, although no longer cost saving, remains cost-effective with an ICER of about £3000 per QALY gained.

Estimating the cost of national implementation

The national costs and benefits of implementing the CVC care bundle were estimated using the model based on the total annual number of admissions to critical care units during 1 year (2009/10) (ICNARC). In that year, there were 96,810 admissions to 188 NHS adult general critical care units in England, Wales and Northern Ireland. Note that this may slightly underestimate the total number of admissions, as not all critical care units participated in the data collection. The results are shown in *Table 38*.

For England, with 90,000 critical care patients per year, the model estimates that implementing the CVC care bundle would reduce the number of catheter-BSI infections by > 700 (IQR 482–914) and save 270 (IQR 184–348) lives per year. The yearly additional cost to implement the intervention used in England would be £1.4M (IQR £1.2M–£1.5M). However, if the intervention was implemented, not only would the cost of implementation be recouped, but also there would be a net saving from implementing the intervention of £1.5M, largely as a result of the savings in costs related to reduced LOS (£2.4M, IQR £1.4M–£3.3M). The CVC care bundle remains cost saving up to an annual implementation cost of £2.7M (equivalent to £30 per critical care patient).

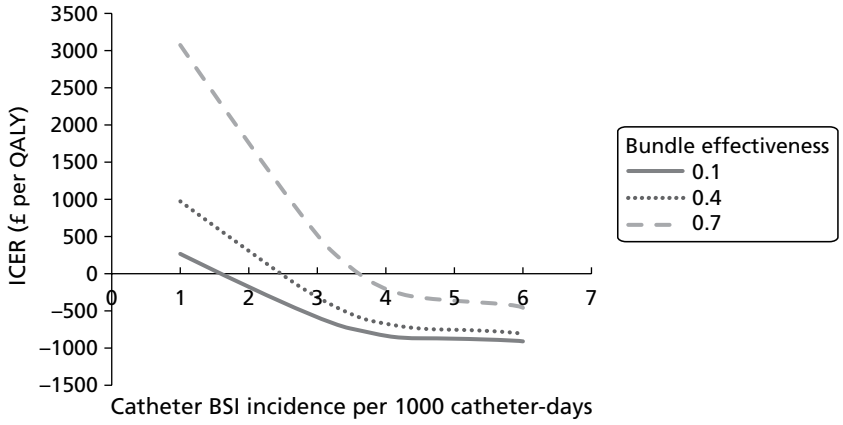

FIGURE 14 Two-way sensitivity analysis comparing catheter-BSI incidence vs. bundle effectiveness.

TABLE 38 Base-case cost-effectiveness results extrapolated for all critical care units in England

Outcome	Current clinical practice	CVC care bundle	Difference	Difference, 25% percentile	Difference, 75% percentile
No. of patients	90000	90000			
Health outcomes					
Catheter-BSI cases	1182	473	709	482	914
Total critical care mortality	15,660	15,390	270	184	348
Additional critical care LOS due to catheter-BSI, days	1773	709	–1064	–1439	–439
Additional ward LOS due to catheter-BSI, days	6064	2426	–3639	–5232	–2365
Discounted life-years	879,665	882,856	3192	2183	4118
Discounted QALYs	674,267	676,713	2447	1673	3156
Costs					
Inpatient bed-day cost, £	4,045,018	1,618,007	–2,427,011	–3,282,553	–1,397,455
Intervention cost, £	0	1,393,409	1,393,409	1,239,459	1,532,181
Total cost (£)	4,657,753	3,256,510	–1,401,243	–2,323,724	–263,726

Summary of cost-effectiveness

We developed a decision-analytic model to assess the cost-effectiveness of a CVC care bundle compared with current clinical practice. The model followed cohorts of patients from their admission to critical care and estimated the associated costs, mortality and lifetime QALYs. The results from the model showed that the CVC care bundle saved 0.8 catheter-BSI and 0.3 lives per 100 patients admitted to critical care compared with current clinical practice, and led to an increased survival of 3.55 years and 2.72 QALYs. The CVC care bundle is more effective and less costly than current clinical practice, largely as a result of the saving from the reduced length of critical care stay.

The effects of a range of parameter values in the economic model were evaluated in sensitivity analyses. The model results were found to be robust to changes in the parameter values. The model results are most sensitive to changes in catheter-BSI incidence and the additional critical care LOS for catheter-BSI.

There is uncertainty in the model-based analysis relating to variation in implementation of the CVC care bundle. Some of the interventions included in the bundle (to be implemented on a regional or national basis) may already be partially implemented (by individual hospitals or ICUs). The effect of this would, all other things being equal, be to lower the baseline incidence of catheter-BSI (prior to regional or national implementation of the CVC care bundle). In addition, there is likely to be variation in the success or completeness of implementing the CVC care bundle which would be expected – all other things being equal – to result in a lower reduction in catheter-BSI following implementation. We conducted a two-way sensitivity analysis on these variables, which indicated that implementing the CVC care bundle was less cost-effective at lower catheter-BSI incidence density. However, even at the least favourable values tested (a relative risk of catheter-BSI with the CVC care bundle = 0.7 and baseline incidence density of 1.0 per 1000 catheter-days) the ICER remained below the threshold conventionally considered as cost-effective.

The PSA estimated the probability that the CVC care bundle is cost-effective at different willingness-to-pay thresholds. The majority (83%) of the results show that the CVC care bundle would be cost saving compared with current clinical practice.

Chapter 7 Discussion

Discussion of the systematic review of clinical effectiveness

A wide range of educational approaches has been used in interventions for preventing catheter-BSI in critical care units. Results of updated literature searches (discussed further below) suggest that this is an active area of primary research. Many of the interventions appear to have potential relevance to NHS practice, as they addressed clinical practices for infection prevention recommended in the 'epic2' national evidence-based guidance for NHS hospitals in England[39] to varying degrees. The intervention that has attracted the most attention and publicity is the Keystone ICU project, which achieved a reduction in catheter-BSI incidence density in 103 critical care units in the USA during 3 years of implementation.[34,123,124] Owing to the apparent success of the Keystone ICU project, there have been several attempts to replicate it in other countries, including the Matching Michigan programme in England, the CLAB ICU project in Australia[83] and the Bacteraemia Zero project in Spain.[68] Given that the Bacteraemia Zero project[68] did not provide convincing evidence of effectiveness, and the Matching Michigan programme results had not been published, we considered the CLAB ICU project to be most relevant to NHS practice. As noted in *Chapter 4*, one of the interventions included in the systematic review was conducted in the UK (in Scotland) but this had limitations including delayed effectiveness at reducing catheter-BSI and overlap with a national patient safety programme, and the intervention appeared less relevant than the Australian CLAB ICU project to NHS practice.

Study designs

The only studies with concurrent control groups[68,109,136] included in the systematic review did not demonstrate clinical effectiveness of their interventions. The entire evidence base for clinical effectiveness thus comes from single-cohort studies that would be classed as low quality according to the criteria for grading quality of evidence and strength of recommendations (GRADE).[179]

A problem with these poor-quality studies is that they cannot usefully inform infection prevention guidelines such as 'epic2', which need to be based on reliable evidence. More rigorous study designs are needed to enable the determination of cause–effect relationships. In the Bacteraemia Zero project, for example, the intervention was no more effective than the control (i.e. no-intervention group), but within the intervention group of critical care units catheter-BSI incidence density was significantly lower during the intervention period than at baseline. This example illustrates how potentially misleading single-cohort studies can be for deducing effectiveness, as they do not control for secular trends. It is important that the study design employed is appropriate for the research question and capable of determining causality. Although not always feasible, RCTs may be appropriate for, and have been used in, evaluations of the effectiveness of educational interventions.[180] As there are often two or three levels of infrastructural organisation, i.e. critical care units grouped within hospitals, and hospitals grouped within regions, a cluster RCT design may be appropriate. Scales and colleagues[181] provided an example of the utility of a cluster RCT approach for evaluating the effectiveness of a QI improvement programme on adoption of evidence-based practices in critical care units. An alternative approach to the use of concurrent control groups is to use an interrupted time series (ITS) design. An ITS design requires sufficiently fine resolution of temporal monitoring of outcomes (e.g. weekly or monthly) to enable detection of any changes in outcomes when an intervention is implemented, against any background secular trends. However, there is no clear consensus on how many temporal outcome assessments would be needed for a study to be classified as ITS. Only two[88,115] of the 74 studies included in the evidence map (none of which was included in the systematic review) employed an ITS approach (a further study[127] claimed to use an ITS approach but was reported as a single-cohort before-and-after study design).

Study reporting

Studies that have been conducted need to be more clearly and fully reported. Guidance on the reporting of observational studies of educational interventions is available from several sources, including the STROBE checklist (strengthening the reporting of observational studies in epidemiology),[182] the TREND checklist (improving the reporting quality of nonrandomised evaluations in behavioural and public health interventions)[55] and the ORION statement (reporting intervention studies of nosocomial infections).[57] Item 7 in the STROBE checklist encourages study authors to report all potential confounders and effect modifiers. This item should be particularly emphasised by peer reviewed journals as, in this review, a failure of authors to disclose this information was a major reason why many primary studies were judged to be at unclear risk of performance bias. Another key deficiency in the primary studies was the failure to report whether valid and reliable data collection methods had been used. A potential problem with these checklists and statements is that when reporting non-randomised educational interventions for preventing catheter-BSI it may not be obvious which checklist(s) the authors should use. Our assessment of study quality suggested non-compliance of authors with the checklists and statements is frequent.

Populations

The eligibility criteria for the systematic review developed in consultation with the project AG focused on adult critical care patients, who make up the majority of the critical care population and were identified in the evidence map as having the most primary evidence. Neonatal critical care units were not specified in the systematic review eligibility criteria as they are very different to those of adult specialties and experience higher rates of BSI-related mortality.[24] In practice it was not feasible for us to completely exclude children from the systematic review since some adult critical care specialties may include a small proportion of children, but the studies rarely reported this level of detail about their populations. Three of the regional-scale interventions[34,83,136] were not conducted entirely in adult critical care units but we judged them to have met the population inclusion criterion for the systematic review because the proportion of paediatric critical units they included was small (in all cases < 9%), whereas a fourth regional-scale intervention did not explicitly state the population but we assumed it to be primarily adult.[68] If we had strictly limited the systematic review to entirely adult critical care patients then we would have excluded several studies of relevance to NHS practice, notably the Keystone ICU project,[34] CLAB ICU project[83] and Bacteraemia Zero project.[68]

Primary outcomes

All 24 of the studies included in the systematic review reported the incidence of catheter-BSI but 10 studies did not report sufficient data for us to calculate the incidence density RR and its 95% CI, and we therefore had to contact the study authors for this information. The incidence density expressed per 1000 catheter-days is a common metric used to compare infection prevalence, but studies reporting catheter-BSI incidence density typically follow the NNIS and CDC approach,[22] which does not count separately any individual catheters present in the same patient during a 24-hour period. A more precise definition employed by HELICS[174] defines a catheter day as a patient having a single catheter for a whole or part 24-hour period, whereas two catheters for a part or whole 24-hour period would be defined as two device-days. Only two of the studies included in the systematic review[94,110] used both definitions of catheter-days, enabling comparisons. The limited data available from these two studies suggest that the definition of catheter-days did not have an appreciable impact on incidence density RRs.

The temporal and spatial resolution of outcome assessments varied considerably among the studies, illustrating why standardisation to catheter-days is necessary to enable comparisons. Most studies reported incidence density RRs for the cumulative number of catheter-BSI and catheter-days registered during a single intervention period compared with a single baseline period. Where additional finer-resolution (e.g. monthly) data were also provided,[50,51,103,109,122,139] (data in *Appendix 5*) these illustrated considerable short-term temporal variability in catheter-BSI incidence density that was not reflected in overall estimates for intervention and baseline periods. Studies which included multiple critical care units usually provided pooled estimates of catheter-BSI incidence density for all the units combined. Where catheter-BSI incidence density was also reported separately for different critical care units[103,122,144] considerable spatial variability

in catheter-BSI incidence density was evident, which would be obscured when pooling incidence densities across units. We recommend that primary studies should always provide estimates of the temporal and spatial variability of their data when reporting outcomes.

Relatively limited data were provided about mortality and LOS in the primary studies. It would be helpful in future studies for records to be kept of the mortality and LOS for critical care patients with and without catheter-BSI, to clarify the burden of catheter-BSI in settings relevant to the NHS.

Secondary outcomes and process evaluations

The Medical Research Council (MRC) guidance on developing and evaluating complex interventions[183] stresses the importance of conducting process evaluations to help in understanding the reasons why complex interventions may or may not be effective. Assessments of attitudes, knowledge, compliance and other aspects of intervention processes identified several barriers or potential barriers to the successful implementation of the educational interventions included in the systematic review. Staff attitudes towards the need for evidence-based infection-prevention practices appear to be a barrier, as several studies reported staff resistance to the use of sterile drapes, gloves, masks and hats, with some staff questioning evidence-based guidance. In the CQI programmes a notable issue was a lack of existing systems and infrastructure for data collection. This seems to be an important difference between the Keystone ICU project, which was based on an existing data collection system, and the other CQI programmes that appeared to have had to develop data collection systems for their interventions. These observations of process improve understanding of potential facilitators and barriers to the successful implementation of educational interventions for preventing catheter-BSI but they were primarily based on ad hoc observations reported by the study authors, and it may be that other important facilitators or barriers were identified but not reported.

Educational approaches

Although many of the interventions included in the systematic review addressed similar sets of clinical practices, these were often addressed using very different, and often unclear, educational approaches. In many cases educational interventions were described superficially and it was difficult to tell whether all of the educational approaches used had been fully reported. Ideally, educational interventions should be reported in sufficient detail, and the resource requirements needed to implement the education elucidated, so they could be replicated. The information needed would include, for example, the total staff time involved and the cost of all materials, preferably itemised to allow interpretation of how costs might vary if intervention concentration (i.e. frequency and duration of sessions) were varied. The types of education should be clearly reported, as formal educational approaches that take staff away from bedside patient care will have associated opportunity costs. An example of good reporting of the education frequency/duration and staffing requirements was provided by Zingg and colleagues.[144] Educational interventions tend to evolve once they are implemented,[149,184] so it is important that any differences between the intended and actual implementation are reported. Where possible, primary outcomes research studies should include an integral cost-effectiveness evaluation.

Instead of each intervention using its own unvalidated educational approach, as was the case in the studies we reviewed, there is a good case to be made for educational approaches to be developed in a more co-ordinated way so that they integrally support the national guidance on care bundles and can be deployed in a more consistent and similar manner. The educational interventions which we reviewed do not draw upon pedagogical, theoretical or conceptual frameworks that would enable understanding of why a particular approach works, or does not work. Consequently there are no generalisable lessons to inform the 'epic2' guidelines on which types of educational approach should be used in support of infection prevention practices. Unless some action is taken to effect a change, it seems likely that the current primary research activity in this area will continue to develop further ad hoc and unvalidated educational approaches. A necessary first step to address this issue would be to determine a responsible organisation for considering the harmonisation of educational approaches (e.g. an evidence-based-practice

guidelines development group). Involvement of educationalists in the design of interventions would help to ensure that the interventions are well supported by relevant theory and are reliable and generalisable.

Information feedback approaches

Infection surveillance feedback, in which results of infection surveillance are provided to health-care workers to inform their clinical practices, is thought to be an effective strategy for reducing nosocomial infection incidence.[185] Our clinical effectiveness findings suggested that infection surveillance feedback and/or performance feedback were not essential for effecting reductions in catheter-BSI incidence density. However, the feedback approaches varied considerably among the primary studies, with some studies providing active feedback (e.g. at meetings), whereas others provided passive feedback (e.g. in wall charts) and none of the studies clearly reported the data collection methods used or whether they were valid and reliable. It may be that the interventions included in our systematic review were too heterogeneous in their intervention characteristics for any underlying influences of feedback approaches on catheter-BSI to have been detectable. For some studies, it became apparent only when the publications were scrutinised in detail that infection surveillance feedback was already practised in the pre-intervention period, and would therefore not explain any observed changes in catheter-BSI incidence when interventions were implemented.

Definitions of catheter-bloodstream infection

During the preparation of this report we identified citations to more than 15 different published sources of CDC definitions in support of CABSI or CRBSI. The most frequently cited publications containing CDC definitions were by Garner and colleagues,[147] NNIS[186] and Horan and colleagues.[187] However, although two of these references define LCBSI,[147,187] none of them actually defines CABSI or CRBSI. A systematic review on 191 studies of patients with cancer published by Tomlinson and colleagues in 2011[21] found that CABSI and CRBSI are defined inconsistently in primary research studies. Our findings (see *Chapter 4*) provide further evidence that CABSI and CRBSI are inconsistently defined in primary research. For the NHS, the definitions of CABSI and CRBSI that were used during Matching Michigan (see *Table 1*) appear appropriate and could be formally recommended for wider use.

Influence of updated literature searches on the clinical effectiveness results

Bibliographic searches, which were rerun in March 2012 using the original search strategy, identified 933 potentially relevant new titles and abstracts published between February 2011 and March 2012, of which 19 full-text publications met the criteria for inclusion in the evidence map (see *Appendix 6, Clinical effectiveness full-text records identified in search updates*) and 12 potentially relevant new conference abstracts were identified (see *Appendix 6, Clinical effectiveness conference abstracts identified in search updates*).

Of the 19 new full-text publications, 18 reported 18 new primary research studies and one publication[188] reported on an existing study already in the evidence map.[83] The new studies published during February 2011 to March 2012 would increase the size of the evidence map from 74 studies to 92 studies (i.e. a 24% increase), indicating that the evaluation of educational interventions for preventing catheter-BSI is an active area of research. This appears to be particularly the case for paediatric and neonatal critical care (60% increase and 36% increase, respectively).

Among the 18 new studies identified that would be eligible for inclusion in the evidence map, three studies would appear to also meet the inclusion criteria for the systematic review, although this was not assessed formally. Render and colleagues[189] evaluated a regional-scale CQI programme conducted in 174 critical care units in 123 hospitals in the USA, which was based on a centralised infrastructure to support the co-ordinated implementation of care bundles containing infection prevention learning modules and five evidence-based practices (hand hygiene, maximal barrier precautions, skin antisepsis, avoidance of femoral insertions, removal of unnecessary CVCs). Kim and colleagues[190] evaluated a catheter care bundle in six critical care units in a hospital in the USA, including checklist, supplies cart, catheter need review, avoidance of the femoral site, staff empowerment to halt incorrect procedures, staff education, and

infection surveillance and performance feedback. Seddon and colleagues[191] evaluated a CQI programme in a single critical care unit in New Zealand based on a care bundle, insertion and maintenance checklists and performance feedback but we noted that this intervention coincided with a major expansion of the critical care unit, which could be a confounding factor.

These three newly published studies all used before-and-after designs and claimed statistically significant reductions in the incidence density of catheter-BSI, although we did not check their calculations or methodological quality. The Render study[189] is notable in being the largest study we have come across in terms of the number of critical care units involved (174 units were included). The Seddon study[191] is notable in being the only study conducted in New Zealand. If these studies were, upon more rigorous scrutiny, shown to be clinically effective at preventing catheter-BSI then their findings would be broadly consistent with those of our systematic review which demonstrated both local-scale and regional-scale CQI programmes including CVC care bundles appear effective at preventing catheter-BSI. However, as with all the before-and-after studies, a key assumption is that the observed effects were a result of the planned interventions.

Searches of databases of ongoing research did not identify any other relevant primary research studies taking place up to May 2012.

In summary, the updated searches indicate that educational interventions for preventing catheter-BSI is an active area of research, but did not identify any new evidence that would appear to change the conclusions of our systematic review.

Findings from other systematic reviews

Systematic reviews of interventions for preventing health care-associated infections identified before this project commenced are summarised in *Chapter 1*. The most directly relevant and recent of these were published in 2008 by Safdar and Abad[37] and in 2010 by Cherry and colleagues.[49]

Safdar and Abad[37] conducted a systematic review of educational interventions for preventing health-care associated infections, not limited to catheter-BSI or critical care. Of 26 primary studies they included, 10 were also included in our evidence map. The main conclusion from their systematic review, which was limited to English-language publications, was that implementation of educational interventions may reduce health care-associated infections considerably but the before-and-after design of studies precluded drawing firm conclusions. Safdar and Abad[37] recommended cluster randomised trials using validated educational interventions and costing methods should be developed to determine the independent effect of education on reducing healthcare-associated infections and the cost-savings that may be realised with this approach.

Cherry and colleagues[49] aimed to determine individual features of educational interventions that impact on competence in aseptic insertion technique and maintenance of CVCs by health-care workers. Their review was not limited to catheter-BSI or critical care and it is unclear whether they applied publication language restrictions. Of 47 primary studies included, 28 were also included in our evidence map. Their main conclusions were that educational interventions appear to have the most profound and prolonged effect when used in conjunction with audit, feedback, and availability of new clinical supplies consistent with the content of the education provided, and if baseline compliance to best practice is low. Cherry and colleagues[49] did not include informal learning and they did not explicitly report data to support their conclusions concerning audit and feedback.

Our searches did not find any more recent relevant systematic reviews than those by Safdar and Abad[37] and Cherry and colleagues.[49] These reviews are now relatively old, with searches conducted up to November 2006 and August 2008, respectively. Our current evidence synthesis is more rigorous than these preceding systematic reviews in that we were not limited to English-language publications and we formally assessed study quality using risk of bias criteria. In contrast, Cherry and colleagues[49] used a composite quality score expressed as a percentage which is difficult to interpret. The quality score focused on the

quality of education rather than other aspects of methodological quality and some studies that were also included in our systematic review[50,108] received a maximum quality score (100%) from Cherry and colleagues[49] despite having methodological limitations (see *Chapter 4*).

Discussion of the economic evaluation

Our systematic review of cost-effectiveness studies identified only three economic evaluations of educational interventions to prevent CRBSIs. One of the studies did not include the cost associated with the care bundle in the analysis; another study used a trial-based cohort analysis to derive estimates of the costs and benefits associated with a simulation-based education intervention in a hospital in the USA, whereas the third study did not consider long-term health benefits beyond the hospital stay. It was not possible to conclude from any study what the likely cost-effectiveness of the intervention would be in a UK setting. Literature searches updated in March 2012 did not identify any further relevant studies.

The model developed in this study allows us to estimate the cost-effectiveness of a CVC care bundle versus current clinical practice to prevent catheter-BSI. The CVC care bundle was found to be more effective and cheaper than current practice, i.e. a dominant strategy. The model results were robust to changes in the model parameters. The model results were most sensitive to the catheter-BSI incidence rate and the additional length of critical care stay associated with catheter-BSI. The PSA showed that the probability that the CVC care bundle dominated current practice was 0.85.

For the purposes of the model, we assumed that CABSI and CRBSI were synonymous and were collectively referred to as catheter-BSI. Although in theory CABSI overestimates the true incidence of CRBSI, our review of clinical effectiveness and another systematic review[21] found that the definitions are used interchangeably and inconsistently in primary research studies.

Experience from a clinical member of the review team (TC) working in English health-care trusts suggested that implementation of evidence-based practices would vary between hospitals, and may even vary between critical care units within the same hospital. There is uncertainty about the uptake of evidence-based practices before Matching Michigan was introduced, although many English health-care trusts would likely have followed 'epic2' guidelines[39] and the Department of Health 'High Impact Intervention'[28] for best practice in prevention of catheter-BSI. It is possible that current clinical practice in some critical care units already incorporated some elements of the CVC care bundle. This variation was not reported in primary studies and cannot be directly quantified. However, there is likely to have been similar variability in implementing evidence-based practices among the critical care units in the CLAB ICU study by Burrell and colleagues[83] that we have chosen for providing an estimate of the clinical effectiveness of the CVC care bundle.

Much of the primary evidence relating to educational interventions for preventing catheter-BSI is from studies conducted in the USA, whilst the study used for the clinical effectiveness estimate for the economic model was conducted in Australia. Critical care in the USA is believed to be significantly different from practice in the UK with regard to bed number, staffing, resource and case mix.[192] The UK has the lowest number of critical care beds per capita in the developed world whereas the USA has the highest. Differences also exist for general health care and critical care expenditure.[192,193] Australian critical care is believed to lie somewhere between these two outlier nations.

Despite being populated with some data from outside the UK, there are two aspects of the model that provide reassurance that the model outputs are relevant to critical care units in English NHS trusts. First, the clinical effectiveness estimate from the Australian CLAB ICU study is similar to clinical effectiveness estimates from other primary studies conducted in different countries, suggesting that clinical effectiveness may not be strongly dependent on the geographical variations in critical care infrastructure and case mix noted above. Second, as the model outputs are robust to sensitivity analyses it seems likely that variation

that would result from geographical differences in critical care delivery approaches will already have been captured.

As the model was restricted to adult critical care, it is unclear whether the current results are generalisable to paediatric critical care or especially to neonatal critical care which has different risk factors for and prognosis of catheter-BSI. In principle, the model structure is likely to also be applicable to neonatal and paediatric populations and could be rerun using parameter estimates from studies conducted specifically on these populations. A question relevant to the primary evidence is whether effective educational interventions for preventing catheter-BSI in paediatric and neonatal populations are any different to those used in adult populations. Results of updated clinical effectiveness literature searches (described above) suggest that an increasing proportion of the primary research is being conducted in paediatric and neonatal critical care units and that at least 16 studies in paediatric and 15 studies in neonatal critical care units have been published that could be assessed.

In the NHS, although national patient safety initiatives are intended to be implemented throughout England, variations in infrastructure and resource availability (e.g. staffing) mean that in practice local interventions are often implemented in a small scale way, frequently without good baseline data collection. Many of the different educational interventions reported in *Chapter 4* may therefore reflect actual practice. The model results indicate that a range of educational intervention types for preventing catheter-BSI could be cost-saving, meaning that the NHS could consider implementing smaller-scale interventions that appear effective, as listed in *Boxes 3* and *5* in *Chapter 4*.

At present there is no information available on how the individual components of a care bundle contribute to the overall cost-effectiveness of the bundle. An assumption is made that all components are necessary for clinical effectiveness and, hence, cost-effectiveness, and care bundles are intended to be implemented on an all-or-nothing basis.[33]

Strengths, limitations and uncertainties of this report

Systematic review of clinical effectiveness

One of the strengths of this review is its adherence to rigorous systematic review methods. We conducted exhaustive searches that were not limited to English-language publications, applied explicit inclusion criteria to the search results, critically appraised the included studies, and used transparent methods to synthesise study findings. A further strength is our inclusion of an initial descriptive mapping stage followed by a systematic review of a subset of studies. This process facilitated the involvement of clinical experts in the design of the review. The review team included clinical experts in infection prevention, critical care and medical education and was supported by an AG that included clinical experts directly involved in implementing NHS policies for the prevention of catheter-BSI.

Despite its strengths the review had limitations. It was preferable for the subset of the studies in the systematic review to be homogeneous in terms of the intervention characteristics to ensure that their aggregation statistically would be meaningful and appropriate (i.e. comparing like with like) but, in accordance with the systematic review eligibility criteria developed in consultation with clinical experts, a wide variety of intervention types was included. Although this diversity of interventional approaches does appear relevant to NHS practice, it was not appropriate to pool outcomes for different interventions in a quantitative meta-analysis and so we instead conducted a narrative synthesis. The systematic review was restricted to studies that defined catheter-BSI so that we could investigate any impact of differing infection definitions on study outcomes. However, upon scrutiny of the studies we found that definitions of CABSI and CRBSI were applied inconsistently and generally did not agree with the definitions used in NHS practice. Therefore, we could not explore the potential influence of different infection definitions on effectiveness outcomes.

There are some uncertainties in our systematic review of clinical effectiveness. All studies that appeared to demonstrate clinical effectiveness of their educational interventions were single-cohort studies without concurrent control groups. The extent to which secular trends might have played a part in determining the observed changes in catheter-BSI incidence densities is unclear. The systematic review focused on adult critical care specialties that represent the majority of critical care specialties in the NHS, but it is not known whether similar findings would have been obtained for studies in paediatric and neonatal critical care units (it was not feasible to conduct a systematic review on all specialties in this project owing to the review team resources that would be required). Other uncertainties concerned poor reporting in the primary study publications: intervention details, especially the concentration of education and resources needed to implement education were often unclear or not reported, and nearly all of the studies were judged to be at unclear risk of bias owing to inadequate reporting of key methodological information.

Although it would have been preferable to have included the Matching Michigan programme in our evidence map and systematic review of clinical effectiveness (subject to meeting the inclusion criteria), this was not feasible as results from Matching Michigan were not available at the time of our analyses. However, where possible we have used interim information from Matching Michigan to inform our economic evaluation.

Economic evaluation

Our economic evaluation is the only published example of an assessment of the cost-effectiveness of educational interventions for prevention of catheter-BSI in the UK. The model specifically addresses clinical practices in critical care units in NHS trusts in England but the results are probably generalisable to the wider UK. The economic evaluation was informed by systematic reviews of effectiveness and cost-effectiveness, and systematic searches for input parameter data. The model was developed following a structured and objective process in accordance with standard NICE practice, and the model structure and data inputs are clearly presented in this report to facilitate replication and testing of our model assumptions.

Despite these strengths, the economic evaluation has some limitations. Owing to lack of data, we had to assume that mortality rates during the hospital stay following critical care discharge, and after hospital discharge, do not differ between patients who have catheter-BSI in the critical care unit and those who do not. We also had to assume that CABSI and CRBSI are synonymous, as the systematic review of clinical effectiveness had indicated that these definitions were not meaningfully separable in the primary research literature. The model does not consider the HRQoL of patients in critical care units because the time spent in critical care is very small compared with the lifetime horizon, and therefore any QALY gains during this period are insignificant. In addition, non-fatal adverse events associated with catheter-BSI were included within the model as a cost but not as a utility decrement. The economic evaluation does not include non-tangible benefits or disbenefits associated with the intervention, such as changes to staff morale and public confidence in the health-care system.

There are uncertainties around the cost of the CVC care bundle intervention. The implementation of the intervention is likely to vary widely in practice between critical care units. Different critical care units are also likely to vary in the extent to which they would have already implemented components of the CVC care bundle at baseline. Some model input parameters could not be sourced from the UK and clinical effectiveness estimates were obtained from a relevant Australian study. Where possible we conducted sensitivity analyses to illustrate the influence of these uncertainties on the cost-effectiveness estimates produced by the model.

Chapter 8 Conclusions

The evaluation of educational interventions for preventing catheter-BSI is an active area of primary research, but there are concerns about the reliability of the evidence, which comes predominantly from uncontrolled before-and-after studies and may not convincingly distinguish intervention effectiveness from background secular trends. Very limited primary research has been conducted in the UK and at the time this report was prepared none had been published from England.

Our economic evaluation suggests that an educational intervention based on a CVC care bundle implemented in critical care units in England would be more effective and less costly than current clinical practice, even after allowing for heterogeneity of baseline clinical practices and heterogeneity of implementation. The model results are robust to variations in cost of the CVC care bundle and clinical effectiveness, indicating that a variety of other educational interventions could potentially be cost-saving if implemented at local or regional scales. More robust primary studies of clinical effectiveness are needed, however, to clarify cause and effect to ensure that model input parameters for clinical effectiveness truly reflect intervention impacts rather than secular trends.

There is general agreement about the types of evidence-based practices that should be employed for preventing catheter-BSI, as reflected in the UK 'epic2' guidelines (and also the US IHI guidelines). These guidelines emphasise the need for education to support the evidence-based clinical practices for infection prevention but cannot make recommendations about which educational practices are appropriate as the primary research studies are of insufficient quality to be informative. Primary study investigators should be informed of the limitations of uncontrolled cohort studies and encouraged to use more robust methods that can identify causality. These could include RCTs and ITS designs.

The same core sets of clinical practices for infection prevention in relation to CVC insertion and ongoing care are currently being addressed by a wide variety of different educational strategies. The educational approaches do not draw upon pedagogic, theoretical or conceptual frameworks and, consequently, do not provide generalisable lessons to inform the 'epic2' (or IHI) guidelines. Harmonisation of education, using validated approaches (that could link to national curricula) would improve the relevance of primary research for informing national guidelines, and improve the comparability and analysis of the primary research studies. It seems appropriate that the evaluation of whether and how to standardise educational approaches could be considered by a relevant evidence-based-practice guideline development group.

Despite the existence of several checklists and statements relevant to the reporting of educational interventions for infection prevention (e.g. STROBE, TREND, ORION), the standard of reporting primary studies appears very poor. Consideration should be given to why these statements/checklists may not have been effective at improving reporting standards, and whether the compliance of study investigators with the reporting standards could be improved.

Recommendations for practice

NHS organisations should carefully consider whether existing practice for preventing catheter-BSI may be improved by implementing educational interventions in critical care units either at local or regional scales. Although it is not possible to be specific about which type of intervention may be most appropriate, economic evaluation suggests that a variety of approaches could be cost-effective or cost-saving. As potential cost savings could be achieved, implementation of educational interventions may be compatible with organisational cost reduction plans.

Consideration should be given to the need to adopt standard definitions of CABSI and CRBSI, and apply and report these consistently. Definitions used by the NHS during the Matching Michigan programme (and presented in *Table 1* of this report) may be appropriate.

When clinical practice is delivered within a research setting, for example if interventions are intended to be implemented into practice while their effectiveness is monitored, consideration should be given to ensuring that the research design is appropriate for cause–effect relationships to be determined (as discussed in this report). To assist future economic evaluations, the resources required to implement and sustain an intervention should be clearly reported.

Coordinated collection of surveillance data on catheter-BSI, mortality and LOS in critical care units would be helpful to inform future economic evaluations, particularly to assist in establishing the extent to which infection with catheter-BSI influences these outcomes.

Recommendations for research

To ensure that future primary studies of the effectiveness of educational interventions for prevention of catheter-BSI provide useful evidence to inform national guidelines, researchers should give careful consideration to the choice of study design. Uncontrolled single-cohort study designs are unlikely to provide information of sufficient quality to inform national guidelines, unless a detailed ITS analysis can be undertaken to exclude any influences of secular trends on study outcomes.

It is important that the study design is appropriate for the research question and can identify causality. Where feasible, the preferred research design may be a RCT.

When developing educational interventions for prevention of catheter-BSI, consideration should be given to the MRC guidance on the development and evaluation of complex interventions. To ensure generalisability, educational interventions should be supported by educational and behavioural theory, and educationalists should be involved in their design. Outcome evaluations should be accompanied by process evaluations and have an integral cost-effectiveness evaluation.

Development of educational interventions for preventing catheter-BSI (and other infections) is likely to benefit from being co-ordinated at a national level, to ensure that valid and reliable approaches are employed that yield findings which are generalisable and inform national guidelines.

Research commissioners, journal editors and other relevant research stakeholders should encourage researchers to clearly report research studies of educational interventions to provide greater confidence about the validity and generalisability of the results and to fully identify the risks of bias and confounding. Consideration should be given to whether current reporting guidelines (e.g. the STROBE, TREND and ORION checklists/statements) are being adequately followed, and whether steps could be taken to improve authors' compliance with recommended reporting standards.

Updates to this review may help to clarify the extent of the growing evidence base and to ensure that the quality controls recommended above, if implemented, are effective. Given that there is current research interest in the effectiveness of educational interventions for preventing catheter-BSI in paediatric and neonatal populations, a more detailed review of the evidence for these populations would be appropriate.

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Geoff K Frampton (Research Fellow, SHTAC) was the Principal Investigator and chaired the project meetings and AG. He scoped the research question, prepared the draft protocol and contributed to the writing of the protocol; screening studies for inclusion in the descriptive map; piloting and applying mapping keywords; extracting data from studies included in the systematic review of clinical effectiveness; assessing the quality of the included studies; conducting the analysis of the descriptive map; conducting the synthesis of outcome data in the systematic review of effectiveness; and writing the final report.

Petra Harris (Research Fellow, SHTAC) contributed to discussions at project meetings; writing of the protocol; screening studies for inclusion in the descriptive map; piloting and applying mapping keywords; extracting data from studies included in the systematic review of clinical effectiveness; assessing the quality of the included studies; conducting the analysis of the descriptive map; conducting the synthesis of outcome data in the systematic review of effectiveness; and writing the final report.

Keith Cooper (Senior Research Fellow, Health Economics, SHTAC) contributed to discussions at project meetings; piloting and applying mapping keywords; screening studies for inclusion in the systematic review of cost-effectiveness; extracting data from studies included in the systematic review of cost-effectiveness; assessing the quality of the included studies; developing the economic model and conducting the cost-effectiveness analysis; and writing the final report.

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Karen Welch (Information Specialist, SHTAC) conducted the literature searches for the systematic reviews of clinical effectiveness and cost-effectiveness, and commented on a draft version of the final report.

Brian H Cuthbertson (Professor of Critical Care, Sunnybrook Health Sciences) contributed to the writing of the protocol; piloting and applying mapping keywords; and writing the final report.

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Appendix 1 Protocol for Technology Assessment Report 9/01/25

COMMISSIONED BY THE NIHR HTA PROGRAMME MARCH 2011

1. Title of the project

A systematic review and economic evaluation of the effectiveness and generality of educational interventions for preventing CRBSIs in critical care

2. Protocol version: 2

This version of the protocol was amended on 14th April 2011. The inclusion criteria for participants in *Table 1* were slightly modified and the updated criteria were applied to all titles and abstracts.

3. Plain English summary

Catheters are very important for the treatment of patients in critical care but provide a route of entry for bacteria and other micro-organisms into the bloodstream, and are frequently associated with serious infections. These infections increase patients' discomfort, length of stay in hospital, the cost of their treatment and risk of death.

Education is important for ensuring that hospital staff understand how to maintain hygiene and follow practices that reduce the risk of infections. Education may be part of a 'care bundle', alongside other activities designed to reduce infections. Types of education are very diverse, ranging from simple leaflets or posters to seminars and group discussions and complex strategies designed to encourage staff to follow more hygienic procedures. Although some of these education strategies can prevent infections and potentially save lives, the effectiveness of most has not been evaluated in detail, especially whether infection prevention can be maintained in the longer term, and whether education carried out in one critical care setting is applicable to other settings.

This project (an evidence synthesis) will rigorously and systematically assess the evidence to determine which types of educational intervention can help prevent infections in critical care patients who have a vascular catheter, whether they can maintain long-term prevention of infections, and whether they are cost-effective. To address the difficulty of evaluating complex educational strategies, the project will employ an evidence mapping technique that can help to visualise the different parts of complex strategies and enable them to be assessed and compared. A decrease in the frequency of CRBSIs will be the key measure of the effectiveness of education. Where available, information will also be collected on the extent to which education strategies are followed and implemented by nurses and doctors.

This project will help the NHS to implement educational procedures for reducing infections that are the most effective and the best value for money. The project is particularly relevant to a strategy that was implemented during 2009–2011 in critical care units in some NHS trusts in England. The strategy, known as 'Matching Michigan', was originally developed in the USA and has not previously been evaluated to see if it has similar findings in the UK. The project will link to the Matching Michigan team in England to

ensure that the assessment of cost-effectiveness is directly relevant to NHS trusts in England. The findings of this project could assist future planning of infection prevention strategies related to Matching Michigan.

4. Decision problem

The aim of this health technology assessment project is to assess the clinical effectiveness and cost-effectiveness of different educational schemes for preventing catheter-related bloodstream infections (CRBSI) in patients in critical care. Initial scoping searches for this project suggest that research on educational interventions for preventing CRBSI appears to be mostly from studies that may not have optimal study designs and may not be representative of critical care settings and practices in the UK. Uncertainty remains about the extent of the evidence and effectiveness of interventions. There is therefore a need to systematically synthesise all relevant evidence about these educational interventions to clarify their effectiveness, strengths and limitations, and their relevance to the NHS. Results of this evidence synthesis will help to inform future research and policy for implementing educational infection prevention schemes.

5. Background

5.1 Catheter-related bloodstream infections (CRBSI) in critical care

Intravascular catheter placement is an important cause of bloodstream infections (BSI)[1,2], and is the commonest source of hospital-acquired bacteraemia in hospitals in England[3]. CRBSIs (CRBSI) are a particular problem in critical care due to the high frequency of intravascular catheter placement and increased susceptibility to infections among critical care patients. CRBSI are associated with morbidity and, especially in paediatric critical care, also mortality[4]. Estimates of the additional length of stay per CRBSI episode in UK critical care units have ranged from 1.9 days[5] to 11 days[6]. Owing to a lag in the publication of infection rates, there is uncertainty as to whether these published data are representative of current rates of CRBSI in UK critical care units.[1]

([1] Recent unpublished data from UK critical care units suggest that CRBSI rates may in some cases be much lower than those reported in the published literature (Dr D. Wyncoll, personal communication). In the current project, as indicated in section 8.2, the most relevant data to UK critical care units will be used to evaluate cost-effectiveness of educational interventions.)

CRBSI result from inadequate hygiene and suboptimal catheter management procedures. These include among others inadequate hand hygiene of hospital staff, inadequate skin hygiene at the site of patients' catheter insertion, suboptimal location of catheters, and unnecessary placement of catheters. CRBSI are believed to be largely preventable following work in the UK that has successfully reduced the number of cases of MRSA BSI. It has been proposed that the majority of CRBSI could be prevented using evidence-based educational interventions to ensure that doctors and nurses are committed to a culture of safety and follow best practice to achieve this[7,8].

5.1.1 Definitions of CRBSI

Various definitions and terms are used, and sometimes confused, in the literature to describe a bloodstream infection that has developed as a consequence of an indwelling intravascular catheter. To define CRBSI (sometimes also referred to as CRBI), both a percutaneously drawn blood culture, and a catheter tip culture (or blood drawn through the catheter itself) should quantitatively or semiquantitatively confirm the same organism up to 48 hours after removal of the catheter, together with clinical manifestations of systemic infection (e.g., fever, chills, hypotension)[9,10].

Catheter-associated BSI (CABSI), sometimes also referred to as CABI or central line associated bacteraemia (CLAB), are defined as all BSI in patients with central venous catheters (CVC) after excluding other sites of infection by medical review[9,10]. CLAB means a bloodstream infection with no other apparent focus of infection where a central line (i.e. CVC) has been in situ within 48 hours of the event.

According to these strict definitions, CABSI overestimates the true incidence of CRBSI. However, these definitions are not always rigidly adhered to.

These various definitions make direct comparison of rates of infection difficult and at times misleading, and care will be taken when reviewing studies that report rates of infection based upon the different definitions. The Matching Michigan project provides clear quantitative criteria for defining CABSI, CRBSI, and catheter-suspected BSI; these may assist classification of infections in the current work.

5.1.2 Diagnosis of CRBSI

Diagnosis of CRBSI is made in various ways, depending upon both local clinical practice and, for infection surveillance purposes, the definition of infection in use. Diagnostic criteria for surveillance purposes are rigorously applied and take account of multiple factors including:

- The number of blood culture specimens performed, and whether these cultures are percutaneously-drawn, or drawn via the CVC
- Whether the CVC has been removed, and if so whether culture of the line tip demonstrates significant quantities of the same micro-organism as is detected in percutaneously drawn blood
- Identification of a known pathogen in a single blood culture, or a common skin organism identified in two or more sets of blood cultures

Presentation of identified signs of systemic infection in a patient, linked to one or more positive blood cultures.

Use of different definitions of infections can dramatically alter the reported infection rate unless they are aligned with clinical practice. For example, if clinical practice is not to send a CVC line tip to the laboratory for culture, or to draw only a single set of percutaneous cultures, then any definition requiring catheter-tip culture or more than one set of cultures will never be met, potentially giving an artificially low infection rate. However, provided that an infection definition is applied consistently over time, then the impact of interventions aimed at improving practice and reducing infection rates should still be reliably demonstrated. Care will be taken when reviewing studies to ensure that infection definitions have been applied consistently.

5.1.3 Impact of CRBSI on patients and health services

CRBSI increases patients' discomfort and length of stay in hospital[6] and their risk of health complications and death[4]. Complications include acute respiratory distress syndrome, disseminated intravascular coagulation, acute renal failure, and shock[7]. However, data on mortality, quality of life and long-term prognosis specifically related to CRBSI are not available for the UK. Recent estimates of the mortality rates of patients with CRBSI in critical care units in France, Germany and Italy ranged from 11% to 17.1%[5]. The most recent (2009) estimate of the financial impact for the NHS suggests that annual costs related to CRBSI in intensive care units are £19.1 to £36.2 million[5].

5.2 Educational interventions for preventing CRBSI

5.2.1 Definition of educational interventions

In general, educational interventions involve the communication of information to a specific target group for one or more of the following purposes: to raise awareness; to enhance or improve knowledge; or to change behaviour[11]. Educational interventions for preventing CRBSI ideally should include behaviour modification components underpinned by relevant theory[12]. For the purposes of this project our working

definition of an educational intervention is any intervention that aims to prevent CRBSI and: (a) includes at least an element of factual information provision related to that aim; (b) is described by the authors as educational; or (c) is described by the authors as behavioural. Project scoping searches indicated that behaviour-modifying interventions to prevent CRBSI are often called 'educational' rather than 'behavioural' interventions, and behaviour modification components of interventions are not always mentioned in the titles and abstracts of studies. We define educational interventions broadly in this project to ensure that relevant behavioural interventions are not missed at the study selection step.

5.2.2 Types of intervention

Educational interventions for preventing CRBSI have been trialled in critical care settings in many countries and vary considerably in their content and complexity. They range from the provision of simple fact sheets and posters[13] to complex interventions comprising multiple behavioural components[14]. Interventions differ in the number and duration of education components, whether they are didactic or interactive, and whether surveillance and performance feedback are also present. Interventions that contain several different elements which together aim to achieve a particular outcome are referred to as 'multi-faceted', 'multi-component', or 'bundled' interventions[15]. Multi-faceted educational interventions that have been developed for preventing CRBSI include the Michigan project in the USA[16] and the NHS Central Venous Catheter Care Bundle[17]. These include, among others, specific components for ensuring staff hand hygiene, patient skin hygiene, appropriate choice of catheter type and insertion site, and appropriate ongoing catheter care.

5.2.3 Current usage in the NHS

To address the prevention of CRBSI, the NHS has recently developed 'Saving Lives' tools[18] which include the 'High-Impact' care bundles for central venous catheters and peripheral intravenous cannula[17]. These bundles are based on 'EPIC-2' guidelines[19], which stress the importance of education of hospital staff for successful implementation of infection control programmes. However, in the EPIC-2 guidelines there is a lack of evidence on the types of educational interventions that are most appropriate and effective, and the guidelines do not make any recommendations that specifically relate to critical care settings. EPIC-2 guidelines are also inconsistent with US guidelines[9] in interpreting the quality of evidence. Following a recommendation in the Darzi Report[20], during 2009–2011 the UK National Patient Safety Agency implemented an initiative known as 'Matching Michigan'[8,21] to reduce CRBSI, based on a care bundle that has successfully reduced CRBSI in over 100 intensive care units (ICU) in the Michigan study in the USA[16]. However, the original study in the USA was not randomised and did not assess the importance of the education strategy in the effectiveness of the overall care bundle[16]. Guidance is needed from the wider literature on how to implement educational strategies to optimise the clinical effectiveness and cost-effectiveness of this and other related bundled interventions, but the evidence to support such guidance has not been critically synthesised.

6. Planned investigation

6.1 Existing research

6.1.1 Clinical effectiveness of educational interventions

Studies have suggested that the introduction of interventions involving staff education alone or in combination with performance feedback can reduce the frequency of CRBSI in ICU by 40% to 89%[16,22–29]. Various multi-faceted interventions involving staff education alongside other strategies have also been shown to reduce the frequency of CRBSI in ICU[30–32]. However, most of the evidence has not been critically appraised and appears to be mainly from non-randomised studies of relatively short duration. These may give an over optimistic picture of infection control, as they do not consider longer-term attenuation of the effectiveness of interventions. Some multi-component bundled interventions involving staff education in critical care may provide sustained (3-year) reductions in infections[33], whereas other bundled interventions appear to have had no effect[34]. Although prevention of infections in some critical care units may be

enhanced using staff interventions with education reinforcement, surveillance, performance feedback and process control[23], the cost-effectiveness and wider generalisability of these is unclear. Strategies that combine both education and behaviour change stimuli would be expected to have greater impact, by providing a paradigm in which education includes components to target change in the knowledge, beliefs and skills which influence practice[35,36]. However, health agencies also have to consider how to avoid overwhelming staff with new initiatives and deal with competing demands for safer care with higher throughput[9], particularly as increased staff workload negatively affects the care of critically ill patients[37]. The most complex interventions might not therefore necessarily be the most clinically and cost-effective[38].

6.1.2 Cost-effectiveness of educational interventions

Based on the estimated annual costs of CRBSI to the NHS above[5], the potential cost reduction to the NHS that could be made by preventing CRBSI would clearly be substantial. The costs of implementing educational interventions to achieve this however are rather unclear. The Michigan intervention[16] could prevent up to 15 deaths and save around $2 million annually in one intensive care unit (ICU) based on rates of CRBSI in the USA[39] (which might not be representative of current rates of CRBSI in the UK – section 6.1), but there are many uncertainties about how to transfer this type of intervention to UK practice. For example, it is unclear whether interventions tested in ICU in specific localities are generalisable to different geographic regions and healthcare systems, and whether education reinforcement works in situations of high staff turnover and staff shortage as often occur in the UK. The purported simplicity and cost of some interventions is also questionable, for example the Michigan intervention was described as simple and inexpensive but appears to require the delivery of at least 16 lectures by trained staff[39], the overall cost of which has not been explored.

6.1.3 Evidence scoping

Scoping searches for this proposal (which are likely to underestimate the true extent of the evidence) identified more than 20 prospective cohort studies of potentially relevant educational interventions (some of which are cited above) but no randomised controlled trials (RCTs). Eight potentially relevant narrative reviews were identified in scoping, but no systematic reviews have directly assessed the clinical effectiveness of educational strategies for preventing CRBSI in critical care. The most relevant systematic reviews in related areas have investigated: the effectiveness of bundled behavioural interventions to control healthcare associated infections (not limited to education, CRBSI or critical care)[14]; the effectiveness of interventions for preventing CRBSI in critical care (not limited to education or behavioural interventions)[40]; and educational interventions for preventing healthcare associated infections (not limited to educational or behavioural interventions, CRBSI, or critical care)[41].

None of these systematic reviews included economic analyses. Most of the available information on the economic impact of CRBSI in critical care is from work conducted in the USA[22,42]. A recent brief narrative review of epidemiological studies, referred to above[5], provides an insight into the economic burden of CRBSI in critical care in European countries including the UK but, due to a shortage of information on costs, its findings are based on numerous assumptions and uncertainties.

The scoping search highlights the need for an evidence synthesis assessing both the clinical and cost-effectiveness of educational interventions for preventing CRBSI in critical care, to assist decision making in the NHS.

6.2 Research objectives

The aim of this project is to conduct an evidence synthesis of the clinical and cost-effectiveness of educational interventions aimed at hospital staff in critical care (doctors and nurses) for preventing CRBSI. An economic model will be devised by adapting an existing cost-effectiveness model or constructing a new one using the best available evidence to determine cost-effectiveness in a UK critical care setting. The project aims also to provide recommendations that will be sufficiently specific to be of use to those implementing infection-prevention strategies in the NHS and for further research.

The main objectives will be as follows:

1. To systematically review: (a) the clinical effectiveness; and (b) the cost-effectiveness of educational interventions for the prevention of CRBSI.
2. To use an evidence mapping approach to describe the scope of the clinical effectiveness evidence base in terms of the different types of educational interventions, critical care settings, study designs and their theoretical basis, types and duration of education reinforcement, and outcomes reported including evidence of sustainability of effect. The evidence map would: (a) provide an overview, classification and characterisation of relevant educational interventions to enable complex interventions to be visualised and, where appropriate, compared; (b) provide a classification and report of other key study attributes, for example illustrating how CRBSI and CABSI are defined and applied in the studies; and (c) use recognised criteria to screen studies in terms of their relevance to the NHS.
3. To apply the evidence mapping exercise results to prioritise a subset of studies of highest relevance for detailed appraisal in the systematic review of clinical effectiveness.
4. To develop a decision-analytic model to determine and compare cost-effectiveness of relevant groups of interventions and settings identified through evidence mapping, either by adapting an existing economic model or constructing a model for the UK de novo.
5. To identify future research needs and make specific recommendations about the implementation of educational interventions for preventing CRBSI that are relevant to service users in the NHS.

7. Research methods

The project will involve a systematic review of the clinical effectiveness (section 8.1) and a systematic review and economic evaluation of the cost-effectiveness (section 8.2) of educational interventions for preventing CRBSI in critical care (*Figure 1*). The purpose of the cost-effectiveness systematic review will be twofold: to assess whether an appropriate economic evaluation has been undertaken and, if not, to provide evidence to develop and populate a de novo economic evaluation.

7.1 Systematic review of clinical effectiveness

7.1.1 Literature search

Literature will be identified from several sources including:

1. General health and biomedical databases including BIOSIS, the British Nursing Index, CINAHL, EMBASE, MEDLINE, the Science Citation Index, and the Social Sciences Citation Index (also others if considered relevant);
2. Specialist electronic databases (e.g. The Cochrane Library; Database of Abstracts and Reviews of Effectiveness);
3. Unpublished literature and conference proceedings;
4. Contact with individuals with expertise in the field;
5. Checking of reference lists;
6. Research in progress databases (e.g. the UK Clinical Research Network website, Current Controlled Trials, and Clinical trials.gov);
7. Relevant websites identified by the project team and Advisory Group.

All databases will be searched from their inception to the current date. Hand searching will focus on key journals and meeting abstracts published in the past two years, with the key journals identified in consultation with experts and from analyses of search results. Based on the scoping searches, we do not envisage that many non-English-language studies will be found (studies conducted in other countries were usually reported in English). We will include relevant non-English language as well as English-language studies in the project, irrespective of their geographical location. The search strategy will be developed and applied by an experienced information specialist to ensure that as many relevant foreign-language studies

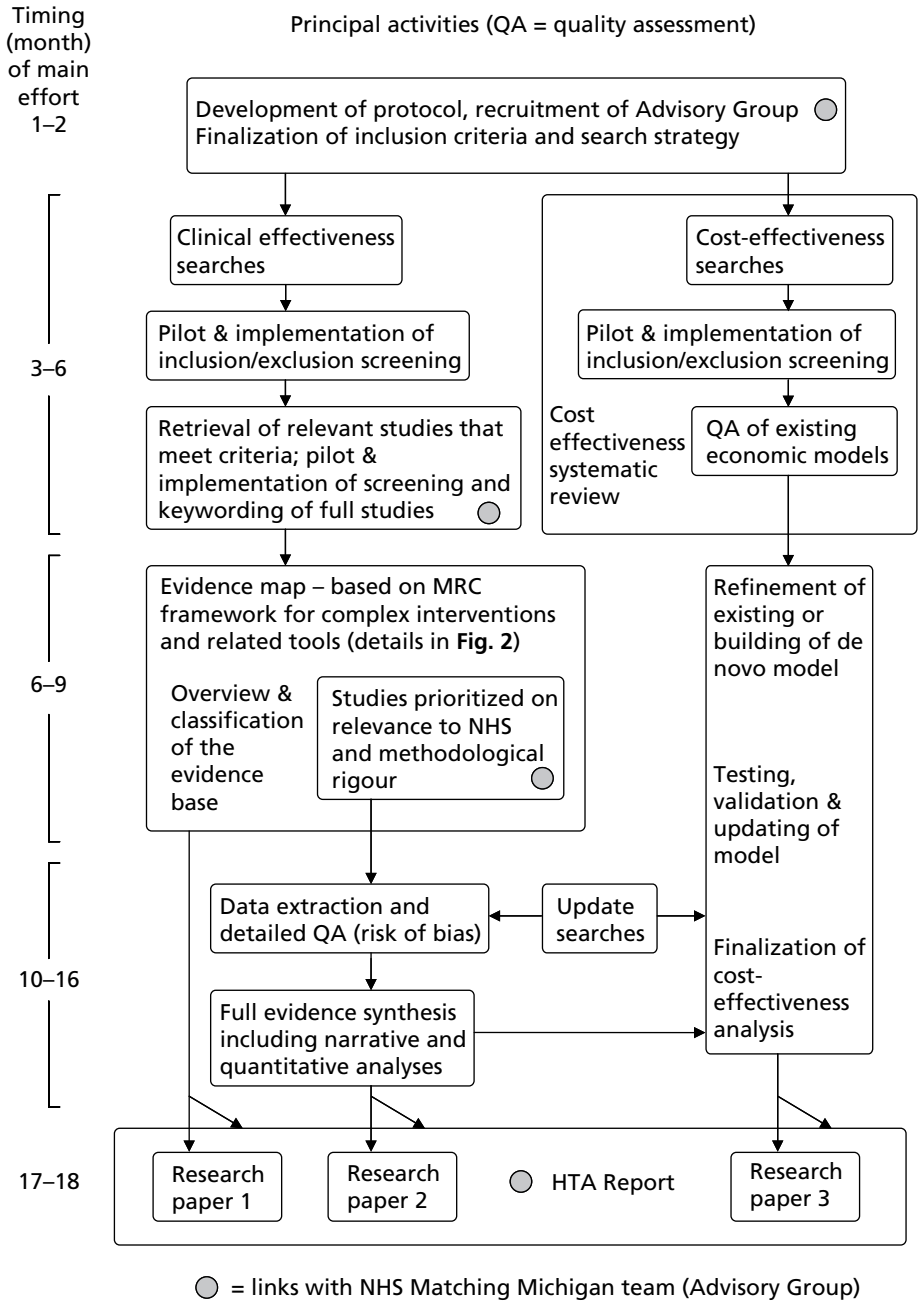

FIGURE 1 Overview of the project approach.

as possible are identified. Where required, translation will be done by native speakers of the language within the project team's research institutions. If an excessive number of foreign-language studies requires translation, we will contact the HTA programme to advise of the situation, in case provision of additional resources is considered appropriate.

A comprehensive database of relevant published and unpublished articles will be constructed using Reference Manager bibliographic software.

7.1.2 Inclusion criteria and search strategy

Inclusion criteria for the systematic review of clinical effectiveness will be based on the PICOD scheme (Population, Intervention, Outcome, Comparator, Design) and are shown in *Table 1*. Inclusion criteria for the systematic review of cost-effectiveness are reported below (section 8.2). Note that although the target for educational interventions is critical care staff (doctors and nurses), it is the patients that are the relevant population for inclusion in evidence synthesis. This is because the relevant primary outcomes (CRBSI) are reported for patients.

Care will be taken to ensure that the search strategy can adequately capture educational interventions, given that these may be very diverse, inconsistently or poorly reported, or that education may make up a relatively small component of multi-faceted interventions. The search strategy will also be developed to capture the different possible variants, acronyms, synonyms and definitions of CRBSIs (including CRBSI, CABSI), taking into consideration that these might not have been used consistently and correctly in the literature. A search strategy for studies of cost-effectiveness will also be developed, following standard procedures (section 8.2).

Understanding how and why interventions work is an integral part of the appraisal of complex interventions[43]. Process evaluations and secondary outcomes (e.g. knowledge, behaviour, attitudes or compliance of staff) may help to explain intervention mechanisms. Process evaluations and secondary outcomes will be included provided that relevant primary (infection) outcomes are also reported (*Table 1*). If reported in sufficient detail, process evaluations will be assessed following a systematic approach, to be agreed by the project team (e.g. an approach employed in a recent synthesis of evidence on sexually transmitted infections[44] may be suitable).

The study designs which will be included are not limited to controlled trials (*Table 1*). This is because in a scoping exercise much of the evidence found was from cohort studies. For the systematic review of

TABLE 1 Inclusion criteria for the systematic review of clinical effectiveness

Participants (P)	Patients in any critical care units who receive vascular catheters of any type whilst in critical care (including tunnelled and non-tunnelled catheters, subcutaneous catheter ports, peripherally inserted central catheters and cannula) for any medical purposes.
Intervention (I)	Any educational interventions for preventing CRBSI in critical care as defined in section 6.2.1. Studies that do not explicitly state an aim to prevent infections, but which report educational interventions that could prevent CRBSI in critical care, will be included if they meet the other inclusion criteria and report relevant outcomes.
Comparator (C)	Relevant comparators are: usual care (no active intervention) or any educational intervention that differs from the primary intervention in one or more educational components.
Outcomes (O)	Primary outcomes will be used for study selection decisions. Primary outcomes: (1) The frequency of CRBSIs, expressed as infection rates per device-days (usually expressed as BSI per 1000 catheter-days), per hospital days, as a proportion of the study population, or relative to a comparator. Any related infection definitions will be accepted for inclusion screening (e.g. CRBSI, CABSI) as the accuracy and appropriateness of these will be scrutinised at the evidence mapping step. (2) Mortality due to CRBSI. Secondary outcomes: These will be assessed if relevant primary outcomes are reported, and may include: knowledge; attitudes; behaviour; and compliance of critical care staff. Process evaluations: These will be assessed if relevant primary outcomes are reported.
Design (D)	Interventional studies only. Randomised controlled trials, non-randomised or quasi-randomised controlled clinical trials, prospective cohort studies, retrospective cohort studies, controlled before-and-after studies, and interrupted time series studies will be included if they evaluate a relevant intervention. Case–control studies, case series, cross-sectional studies, and descriptive studies will be excluded. Where there is evidence from different types of study design for a specific intervention, only those studies with the most rigorous designs will be included and data extracted.

cost-effectiveness, studies will only be included if they report the results of full economic evaluations [cost-effectiveness, cost–utility, cost–benefit or cost–consequence analyses].

7.1.3 Study selection

Studies will be selected for inclusion through a two-stage process using the pre-defined and explicit criteria outlined in *Table 1*. The full literature search results will be screened by two reviewers to identify all citations that may meet the inclusion criteria. Full manuscripts of all selected citations will be retrieved and assessed by two reviewers against the inclusion criteria. Studies published as abstracts or conference presentations will only be included if sufficient details are presented to allow an appraisal of the methodology and the assessment of results to be undertaken. To ensure that studies are screened consistently, an inclusion decision checklist will be developed and used for each manuscript assessed. Any disagreements over study inclusion will be resolved by consensus or if necessary by arbitration by a third reviewer.

7.1.4 Evidence mapping

All studies that meet the inclusion criteria will be entered into a mapping exercise in order to clarify the structure of educational interventions and identify those that are potentially of most relevance to the NHS.

The mapping exercise is summarised in *Figure 2* and will follow principles developed by the Global Evidence Mapping Initiative[45] to classify and summarise the evidence base as well as guidance from the Medical Research Council[43] and the National Institute for Health and Clinical Excellence (NICE)[46] on the reporting and evaluation of complex interventions. The key objectives of this step will be to: (a) provide an overview, classification and characterisation of relevant educational interventions to enable complex interventions to be visualised and, where appropriate, compared; (b) provide a classification and report of other key study attributes, for example illustrating how CRBSI and CABSI are defined and applied in the studies, and whether studies included process evaluations, information on potential facilitators or barriers to implementation, or other secondary outcomes; and (c) identify studies that are of most relevance to the NHS which should be prioritised for full evidence synthesis. The mapping exercise will be conducted as follows (*Figure 2*):

1. With assistance from the Project Advisory Group (section 10), the characteristics of studies to be included in the descriptive map will be determined and made into a list;
2. In a pilot exercise involving two researchers, keywords will be developed that reliably and reproducibly describe each of the study characteristics in the list;
3. Each included study will be mapped by one researcher and the agreed keywords relevant to describe the characteristics of each study will be entered into a Microsoft Excel or Access database such that study interventions and keywords can be cross-tabulated;
4. Keyword assignments and database entries for each study will be checked by a second researcher;
5. Entries in the database will be used to concisely summarise the structure and composition of the study interventions using numerical, graphical and/or narrative methods where appropriate.

Depending upon the overall quality and quantity of evidence available, the evidence mapping exercise could include a preliminary appraisal of methodological quality to help decide which studies are prioritised for detailed full evidence synthesis (e.g. based on study design and sample size). A thorough appraisal of methodological quality, using risk of bias criteria, will be applied later to those studies that are identified as being of most relevance to the NHS and which proceed for full data extraction (section 8.1.5).

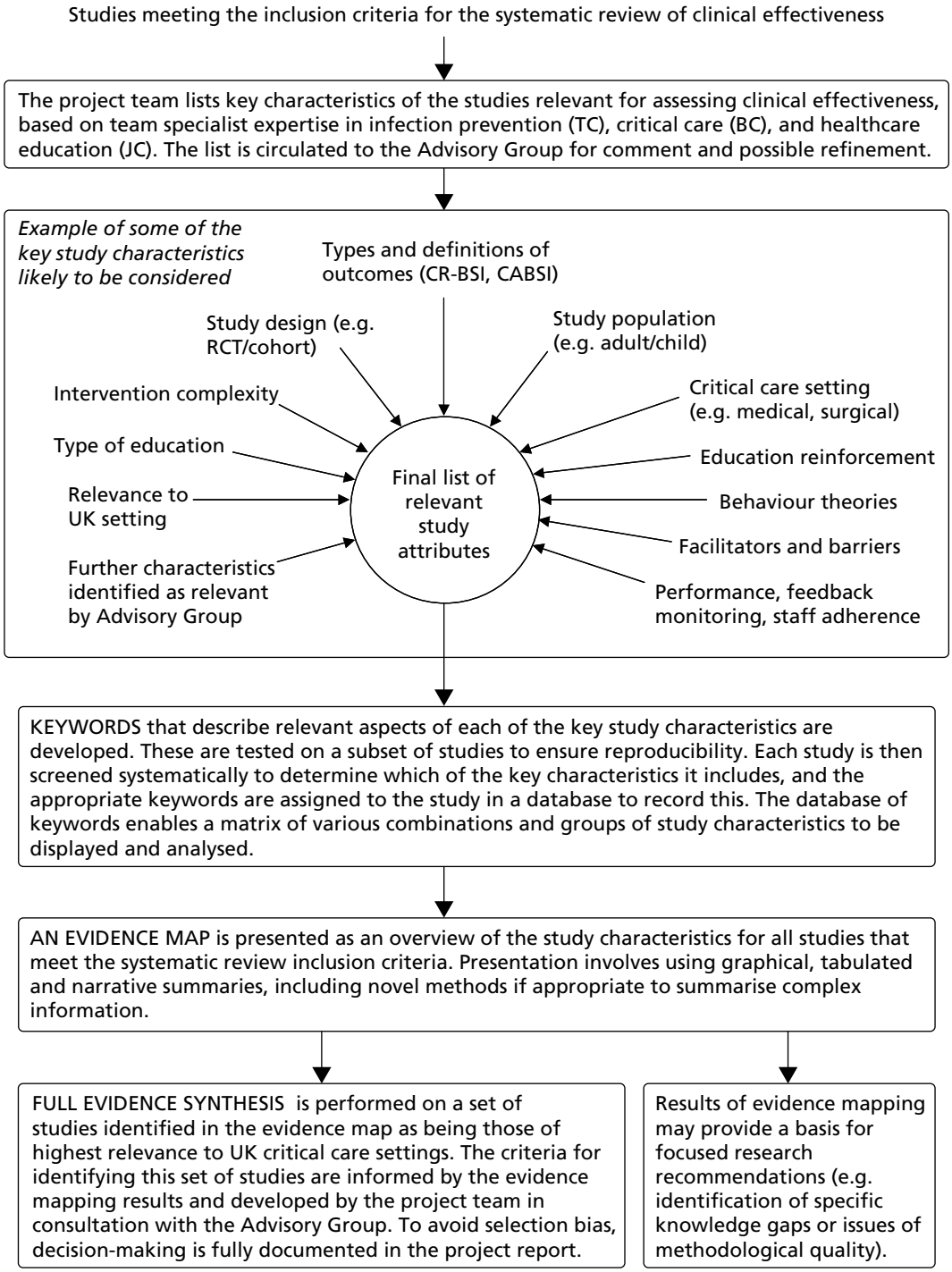

FIGURE 2 Overview of the evidence mapping procedure for studies of clinical effectiveness.

7.1.5 Data extraction and quality assessment

The extraction of studies' findings will be conducted by one reviewer and independently checked by a second reviewer using a pre-designed and piloted data extraction form to avoid any errors. The data extraction form will be based on the PICOD scheme to clearly record and report all relevant aspects of the populations (P), interventions (I), comparators (C) outcomes (O), as well as methodological aspects of the study designs (D). Any disagreements between reviewers will be resolved by consensus or if necessary by arbitration involving a third reviewer. This process will be applied to those studies identified in the mapping exercise (section 8.1.4) as being of highest relevance in the context of current practice in the NHS. The methodological quality of these included studies, including their internal and external validity, will be appraised using established criteria for studies of clinical effectiveness[47] and recognised quality assessment approaches for studies of cost-effectiveness and economic models (section 8.2). Missing information will be obtained from investigators of the primary studies if possible, so as to maximise the information about the educational interventions that can be extracted from each study.

7.1.6 Data synthesis

Studies will be synthesised through a narrative review with tabulation of results of included studies. If feasible, the results from individual studies will be synthesised through meta-analysis using established methods[47], with causes of heterogeneity of results examined.

7.2 Economic evaluation

The cost-effectiveness of educational interventions in preventing CRBSI in critical care will be assessed in two stages: a systematic review of cost-effectiveness and development of a decision-analytic economic model (*Figure 1*).

7.2.1 Systematic review of cost-effectiveness

Searches of general health and biomedical databases (as listed in section 8.1.1), specialist electronic databases (e.g. the NHS Economic Evaluation Database; The Cochrane Library), and unpublished literature and conference proceedings will be carried out to identify relevant studies. The systematic review will focus on economic evaluations of educational interventions to prevent CRBSI. To inform development of our economic evaluation we will also include any studies that report model-based economic evaluations of other (non-educational) interventions, if they were published since a 2007 review of the economics of preventing CRBSI[48]. Experts will be contacted to ask if they know of any relevant published or unpublished studies that we have not identified. Studies will be included in the systematic review if they are full economic evaluations (cost utility or cost-effectiveness studies) that report both measures of costs and consequences, and include outcomes expressed as CRBSI cases avoided, or life years or quality-adjusted life years gained. The methodological quality of included cost-effectiveness studies will be appraised using accepted criteria for appraising economic evaluations[49,50]. Studies will be synthesised through a narrative review that includes: a clear explanation of the assessment process; a detailed critical appraisal of study methods; tabulation of the results of the included studies; a summary indicating which data are used in the economic model; and an explanation of any knowledge gaps and assumptions.

7.2.2 Decision-analytic model

Evidence from both the systematic review of cost-effectiveness and the systematic review of clinical effectiveness (section 8.1) will be used to develop the economic model. Existing economic models of interventions to prevent CRBSI identified in the systematic review of economic evaluations will be assessed for their relevance and quality. If these are not suitable, a *de novo* decision-analytic model will be developed. Development of model structure will be informed by previously published models (such as that developed by one of the applicants[51]) and validated through discussion with clinical and methodological advisors. Accepted guidelines for good practice in decision-analytic modelling[52] and the general principles outlined in the NICE 'reference case'[53] will be followed. Clinical effectiveness parameters in the model will be taken from the systematic review of clinical effectiveness. Additional targeted literature searches will be required to populate other parameters in the model, such as the baseline risk of CRBSI. Expert opinion will

be used where suitable data to populate the model cannot be identified from the literature. Where expert opinion has been used, this will be clearly identified in the report of the model.

The model will provide a cost-consequences analysis, reporting the costs of alternative educational interventions (broken down by key components, such as staff training, administration, consumables etc. where possible) and their consequences in terms of patient outcomes, principally any effect on the risk of CRBSI. The outcome of the model will be presented as the incremental cost per CRBSI avoided. We will consider the feasibility of developing also a cost-utility analysis model incorporating final outcomes (life expectancy or quality-adjusted life expectancy – i.e. QALYs). This will require estimating excess mortality attributable to CRBSI in patients admitted to ICU and the impact of such infections on patients' quality of life. The model will adopt a UK NHS and Personal Social Services perspective.

The resources necessary for providing the educational interventions will be estimated from studies included in the systematic review of effectiveness (section 8.1), and from discussion with expert advisors. The costing will concentrate on costing studies that were conducted in health systems with similar institutional arrangements to the NHS, and those including educational interventions that are similar to those being introduced in the NHS (for example, 'Matching Michigan'). Unit costs will be developed based on published evidence, official sources such as NHS Reference Costs[54] and Unit Costs of Health and Social Care[55], and from the Costing Unit at Southampton General Hospital. Costs will be inflated to current prices as necessary. If no published data on resource use are available, estimates will be based on information from expert advisors.

Uncertainty relating to key parameters will be explored using deterministic and, where appropriate, probabilistic sensitivity analyses. If it is feasible to develop a full cost-utility model, probabilistic sensitivity analyses will be conducted and the results expressed using cost-effectiveness acceptability curves (CEACs). The key variables to be explored will include: effectiveness of educational interventions, baseline risk of CRBSI, cost and duration of CRBSI, mortality attributable to CRBSI, and QALYs.

The model will be developed using standard software including Excel and TreeAge Pro to ensure transparency and would be flexible in terms of permitting different estimates to be used for key input parameters. Any structural assumptions underlying the model would be transparently reported. The model could therefore be updated in response to new information about critical care (intensive care) practices. We propose to consult the project's Advisory Group, which will include clinicians working in critical care, to identify which of the possible changes in critical care practices are likely to be most relevant. This will ensure that appropriate, modifiable, input parameters and structural assumptions are included in the model.

8. Project timetable and milestones

The project will take 18 months, commencing 4th January 2011. Twelve milestones and three proposed research publications arising from the project are detailed in the full project proposal (see also Fig 1). Interim reports will be prepared and submitted at dates to be confirmed by the HTA programme. A final project report will be completed and disseminated by 30 June 2012.

9. Advisory Group

Julian Bion – Professor of Critical Care; clinical lead of Matching Michigan project

Andrew Jackson – Consultant Nurse IV Therapy & Care; Infection Prevention Society

Annette Richardson – Nurse Consultant Critical Care; British Association of Critical Care Nurses

Trudie Roberts – Professor of Medical Education; Association for the Study of Medical Education

Katie Scales – Consultant Nurse Critical care; National Infusion and Vascular Access Society

Barry Williams – Critical Care Patient Liaison Committee (CritPal)

Duncan Wyncoll – Consultant Intensivist; Intensive Care Society

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Appendix 2 Search strategies

Clinical effectiveness search strategy

Database, date searched, host, years, keywords	Search strategy	Results
MEDLINE (Ovid) 1948–2010 Searched 19 January 2011	1. exp Critical Care/ (36,392) 2. exp Intensive Care/ or exp Intensive Care Units/ (56,613) 3. ("acute care" or "critical care" or "critically ill" or "critical illness").tw. (39,816) 4. (high dependency adj1 (care or unit*1)).tw. (334) 5. "intensive care".tw. (64,078) 6. (intensive adj therapy adj unit*).tw. (470) 7. (ITU or ICU or CCU or CICU or CITU).tw. (20,600) 8. ("level 2 care" or "level 3 care").tw. (10) 9. Catheterization, Central Venous/ or Catheterization/ or Catheterization, Peripheral/ (43,836) 10. Catheters, Indwelling/ (13,995) 11. exp catheters/ (14,041) 12. (catheter* adj5 (venous or intravenous or arterial or vascular or intravascular or central or indwelling or peripheral or peripherally)).tw. (24,337) 13. (tunnel* adj5 (venous or intravenous or arterial or vascular or intravascular or central or indwelling or peripheral or peripherally)).tw. (567) 14. (device* adj5 (venous or intravenous or arterial or vascular or intravascular or central or indwelling or peripheral or peripherally)).tw. (4016) 15. (CVC or PICC or JICC or SICC or SBCC or PVC or IVI).tw. (5474) 16. ("Porta-cath" or Portacath or Hickman* or Broviac or Venflon or Groshong).tw. (1046) 17. ("implantable port" or "access port").tw. (421) 18. cannula*.tw. (28,306) 19. exp Bacterial Infections/ (621,883) 20. exp Bacteremia/ (16,592) 21. septicemia/ (35,825) 22. Sepsis/ (35,825) 23. Asepsis/ (1371) 24. cross infection/ (38,455) 25. Infectious Disease Transmission, Professional-to-Patient/ (1298) 26. Communicable Diseases/ (14,197) 27. exp bacteria/ (898,770) 28. fungemia/ (2236) 29. exp Staphylococcal Infections/ (43,061) 30. Staphylococcus aureus/ (37,167) 31. Methicillin Resistance/ (8874) 32. Staphylococcus/ or Staphylococcus epidermidis/ (25,893) 33. exp Streptococcus/ or exp Streptococcal Infections/ (93,168) 34. Pseudomonas aeruginosa/ (26761)	2383 *Updated 13 March 2012*: 215

Database, date searched, host, years, keywords	Search strategy	Results
MEDLINE (*continued*)	35. Escherichia coli/ (199,341) 36. exp Enterobacter/ (5257) 37. exp Klebsiella/ or exp Klebsiella Infections/ (14,273) 38. exp Corynebacterium/ or exp Corynebacterium Infections/ (11,752) 39. exp Acinetobacter/ or exp Acinetobacter Infections/ (4555) 40. exp Enterococcus/ (12,385) 41. exp Candida/ (29,862) 42. exp Blood-Borne Pathogens/ (2208) 43. exp Enterobacteriaceae Infections/ (69,490) 44. equipment contamination/ (7863) 45. colony count microbial/ (24,932) 46. exp Infection/bl [Blood] (11,976) 47. bacter?emia.tw. (16,603) 48. (infection* or acinetobacter* or asepsis or bacter?emia* or bacteria* or candida or coloni?ation or contaminat* or cfu or colony or colonies or corynebacterium or escherichia or enterococc* or enterobacter* or fungi or fungus or fungal or fung?emia or klebsiella or met?icillin or microorganism* or micro-organism* or microbial* or microbe* or microbiologic* or mycology or mycological or organism* or nosocomial* or pathogen* or sepsis or septic or septic?emia septicemia or staphylococc* or streptococc*).tw. (1,829,791) 49. (blood?stream adj infection*).tw. (2725) 50. (blood-stream adj infection*).tw. (321) 51. (blood* adj3 infect*).tw. (12,628) 52. ("healthcare associated" adj infection*).tw. (434) 53. (HAI or HAIs or "HAI's" or HCAI or HCAIs or "HCAI's").tw. (1965) 54. (extraluminal adj infection*).tw. (2) 55. (MRSA or MSSA).tw. (9036) 56. (blood adj culture*).tw. (13,853) 57. (positive adj2 culture*).tw. (18,147) 58. (positive adj isolate*).tw. (1274) 59. Infection Control/ (15,889) 60. Catheter Related infections/ (550) 61. Catheters/mi [Microbiology] (8) 62. Catheters, Indwelling/mi [Microbiology] (916) 63. ("CR-BSI" or "CR-BSIs" or CRBSI or CRBSIs or CABI or CABIs or CABSI or CABSIs or CLABSI or CLABSIs or CRI or CRIs or BSI or BSIs or "AC-CRI " or "AC-CRIs").tw. (3189) 64. (line adj3 (infection* or sepsis or bacter?emia)).tw. (871) 65. (catheter* and blood* and infection*).tw. (3333) 66. (catheter* and (sepsis or bacter?emia*)).tw. (4544) 67. exp Education, Medical/ (111,037) 68. exp Education, Nursing/ (63,596) 69. education continuing/ (6798) 70. Education, Department Hospital/ (203) 71. Educational Measurement/ (22,708) 72. Internal Medicine/ed [Education] (3666) 73. Nursing Staff, Hospital/ed [Education] (7762) 74. exp Health Education/ (116,581) 75. Health Knowledge, Attitudes, Practice/ (51,711) 76. Inservice training/ or Training Support/ or Instruction/ (19,943)	

Database, date searched, host, years, keywords	Search strategy	Results
MEDLINE (*continued*)	77. Preceptorship/ (3313) 78. Mentors/ (5422) 79. Interdisciplinary communication/ (5646) 80. Teaching Rounds/ or Hospitals, Teaching/ or Teaching Materials/ or Teaching/ (56,353) 81. Personnel, Hospital/ed [Education] (2314) 82. Emergency Medicine/ed [Education] (2971) 83. exp Critical Care/ed [Education] (30) 84. Curriculum/ (49,213) 85. Program Evaluation/ (36,217) 86. Program Development/ (17,654) 87. Infection Control/mt, og, st [Methods, Organization & Administration, Standards] (8562) 88. Equipment Contamination/pc, st [Prevention & Control, Standards] (2540) 89. Safety Management/mt, og, st [Methods, Organization & Administration, Standards] (6730) 90. Intensive Care Units/mt, st [Methods, Standards] (1456) 91. Point-of-Care Systems/og, st [Organization & Administration, Standards] (797) 92. Clinical Competence/st [Standards] (10,874) 93. Total Quality Management/mt, og [Methods, Organization & Administration] (5517) 94. (educat* or awareness or bundle* or collaborat* or campaign* or communicat*).tw. (520,606) 95. (feedback or "feed back" or "feeding back" or course* or instruct* or inform* or impart* or knowledge or learn* or "e-learn" or "e-learning" or lecture*).tw. (1,375,734) 96. (module* or modular or session* or study or studies or studying or studies).tw. (4,597,782) 97. ("self study" or re-educat* or "self-educat*").tw. (1322) 98. (assess* or apprais* or competenc* or competent* or curriculum* or evaluat* or seminar* or test* or teach* or taught or train* or simulat* or refresh* or tool* or meeting* or presentation* or skill* or drill* or workshop*).tw. (4,262,387) 99. (link* adj2 (staff or nurs*)).tw. (395) 100. (preceptor* or mentor*).tw. (7136) 101. (component* or "multi-component" or "multi-faceted" or "multi-modal" or initiative* or intervention*).tw. (883,237) 102. (session* or strategy or strategies or initiative or program* or package*).tw. (823,678) 103. "blended learning".tw. (65) 104. "self-learn*".tw. (372) 105. (shar* adj3 practice*).tw. (685) 106. (risk* adj3 (reduc* or management)).tw. (66,351) 107. (booklet* or workbook* or checklist* or library or libraries or literature or questionnaire* or sheet* or pamphlet* or poster* or pictorial* or verbal* or video* or audiovisual* or podcast or telemedicine or teleconferenc*).tw. (909,308) 108. ("scrub the hub" or "Matching Michigan" or "Michigan project" or "Michigan Intervention" or "NHS Venous Catheter Care" or EPIC or "EPIC-2" or "saving lives").tw. (1608) 109. (behavio?r* adj2 chang*).tw. (19,294) 110. (behavio?r adj2 alter*).tw. (3091)	

Database, date searched, host, years, keywords	Search strategy	Results
MEDLINE (*continued*)	111. (chang* adj5 (hygien* or handwash* or hand wash* or disinfect* or sterilisation or sterilization)).tw. (747) 112. (alterat* adj5 (hygien* or handwash* or hand wash* or disinfect* or sterilisation or sterilization)).tw. (31) 113. (management adj5 (contaminat* or hygien* or handwash* or hand wash* or disinfect* or sterilisation or sterilization)).tw. (787) 114. (precaution* adj5 (hygien* or handwash* or hand wash* or disinfect* or sterilisation or sterilization)).tw. (319) 115. (behavio?r* adj2 management).tw. (2099) 116. (risk* adj (manage* or assess*)).tw. (26,622) 117. governance.tw. (3690) 118. or/1-8 (129,513) 119. or/9-18 (95,966) 120. or/19-59 (2,461,905) 121. or/60-66 (11,112) 122. or/67-117 (8,445,986) 123. 118 and 119 and 120 and 122 (1919) 124. 118 and 121 and 122 (1643) 125. 123 or 124 (2418) 126. (editorial or letter or comment).pt. (1,024,427) 127. 125 not 126 (2383) 128. from 127 keep 1-1000 (1000) 129. from 127 keep 1001-2000 (1000) 130. from 127 keep 2001-2383 (383)	
Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations Searched 1 February 2011	Adapted from MEDLINE strategy	92 *Updated 13 March 2012*: 71
EMBASE (Ovid) Searched 25 January 2011	1. exp intensive care/ (324,789) 2. exp intensive care unit/ (53,595) 3. ("acute care" or "critical care" or "critically ill" or "critical illness").tw. (52,785) 4. (high dependency adj1 (care or unit*1)).tw. (469) 5. ("intensive care" or "intensive medical care").tw. (83,359) 6. (intensive adj therapy adj unit*).tw. (556) 7. (ITU or ICU or CCU or CICU or CITU or SCBU).tw. (31,316) 8. ("level 2 care" or "level 3 care").tw. (24) 9. or/1-8 (407,797) 10. exp catheterization/ (100,116) 11. INTRAVENOUS CATHETER/ or ARTERY CATHETER/ or CATHETER/ or INDWELLING CATHETER/ or PERIPHERALLY INSERTED CENTRAL VENOUS CATHETER/ or CENTRAL VENOUS CATHETER/ or INTRAVASCULAR CATHETER/ (36,464) 12. (catheter* adj5 (venous or intravenous or arterial or vascular or intravascular or central or indwelling or peripheral or peripherally)).tw. (28,927) 13. (tunnel* adj5 (venous or intravenous or arterial or vascular or intravascular or central or indwelling or peripheral or peripherally)).tw. (727)	2944 *Updated 13 March 2012*: 659

Database, date searched, host, years, keywords	Search strategy	Results
EMBASE (*continued*)	14. (device* adj5 (venous or intravenous or arterial or vascular or intravascular or central or indwelling or peripheral or peripherally)).tw. (5087) 15. (CVC or PICC or JICC or SICC or SBCC or PVC or IVI).tw. (7571) 16. ("Porta-cath" or Portacath or Hickman* or Broviac or Venflon or Groshong).tw. (1244) 17. ("implantable port" or "access port").tw. (514) 18. cannula*.tw. (31,388) 19. or/10-18 (176,786) 20. catheter infection/ (6889) 21. ("CR-BSI" or "CR-BSIs" or CRBSI or CRBSIs or CABI or CABIs or CABSI or CABSIs or CLABSI or CLABSIs or CRI or CRIs or BSI or BSIs or "AC-CRI " or "AC-CRIs").tw. (4339) 22. (line adj3 (infection* or sepsis or bacter?emia)).tw. (1112) 23. (catheter* and blood* and infection*).tw. (4439) 24. (catheter* and (sepsis or bacter?emia*)).tw. (5609) 25. "catheter-related bloodstream infection*".tw. (705) 26. "catheter-associated bloodstream infection*".tw. (131) 27. or/20-26 (17,675) 28. 9 and 27 (4542) 29. exp INFECTION/ or GRAM POSITIVE INFECTION/ or STAPHYLOCOCCUS INFECTION/ or BACTERIAL INFECTION/ or GROUP A STREPTOCOCCAL INFECTION/ or ENTEROCOCCAL INFECTION/ or KLEBSIELLA INFECTION/ or HOSPITAL INFECTION/ or STREPTOCOCCUS INFECTION/ or GRAM NEGATIVE INFECTION/ or METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS INFECTION/ or GROUP B STREPTOCOCCAL INFECTION/ or DEVICE INFECTION/ or ENTEROBACTERIACEAE INFECTION/ or BLOODSTREAM INFECTION/ or CROSS INFECTION/ (2,002,322) 30. FUNGAL CONTAMINATION/ or BACTERIUM CONTAMINATION/ or VIRAL CONTAMINATION/ or MICROBIAL CONTAMINATION/ (13,226) 31. bacteremia/ or sepsis/ (86,693) 32. (infection* or acinetobacter* or asepsis or bacter?emia* or bacteria* or candida or coloni?ation or contaminat* or cfu or colony or colonies or corynebacterium or escherichia or enterococc* or enterobacter* or fungi or fungus or fungal or fung?emia or klebsiella or met?icillin or microorganism* or micro-organism* or microbial* or microbe* or microbiologic* or mycology or mycological or organism* or nosocomial* or pathogen* or sepsis or septic or septic?emia or staphylococc* or streptococc*).tw. (2,124,000) 33. (MRSA or MSSA).tw. (12,771) 34. or/29-33 (3,293,446) 35. CLINICAL EDUCATION/ or NURSING EDUCATION/ or CONTINUING EDUCATION/ or EDUCATION PROGRAM/ or RESEARCH BASED NURSING EDUCATION/ or CONTINUING EDUCATION PROVIDER/ or INTERDISCIPLINARY EDUCATION/ or EMERGENCY MEDICAL SERVICES EDUCATION/ or MEDICAL EDUCATION/ or HEALTH EDUCATION/ or EDUCATION/ or "OUTCOME OF EDUCATION"/ (482,831) 36. IN SERVICE TRAINING/ or TRAINING/ or STAFF TRAINING/ (67,556) 37. (educat* or awareness or bundle* or collaborat* or campaign* or communicat*).tw. (627,949) 38. (feedback or "feed back" or "feeding back" or course* or instruct* or inform* or impart* or knowledge or learn* or "e-learn" or "e-learning" or lecture*).tw. (1,706,178) 39. (module* or modular or session*).tw. (126,951) 40. ("self study" or re-educat* or "self-educat*").tw. (1752)	

Database, date searched, host, years, keywords	Search strategy	Results
EMBASE (*continued*)	41. (assess* or apprais* or competenc* or competent* or curriculum* or evaluat* or seminar* or test* or teach* or taught or train* or simulat* or refresh* or tool* or meeting* or presentation* or skill* or drill* or workshop*).tw. (5,171,099) 42. (link* adj2 (staff or nurs*)).tw. (427) 43. (preceptor* or mentor*).tw. (8258) 44. (component* or "multi-component" or "multi-faceted" or "multi-modal" or initiative* or intervention*).tw. (1,069,468) 45. (session* or strategy or strategies or initiative or program* or package*).tw. (1,023,638) 46. "blended learning".tw. (93) 47. "self-learn*".tw. (438) 48. (shar* adj3 practice*).tw. (878) 49. (risk* adj3 (reduc* or management)).tw. (86,429) 50. ("scrub the hub" or "Matching Michigan" or "Michigan project" or "Michigan Intervention" or "NHS Venous Catheter Care" or EPIC or "EPIC-2" or "saving lives").tw. (2080) 51. (booklet* or workbook* or checklist* or library or libraries or literature or questionnaire* or sheet* or pamphlet* or poster* or pictorial* or verbal* or video* or audiovisual* or podcast* or telemedicine or teleconferenc*).tw. (1,109,759) 52. (behavio?r* adj2 chang*).tw. (23,225) 53. (behavio?r adj2 alter*).tw. (3549) 54. (chang* adj5 (hygien* or handwash* or hand wash* or disinfect* or sterilisation or sterilization)).tw. (828) 55. (alterat* adj5 (hygien* or handwash* or hand wash* or disinfect* or sterilisation or sterilization)).tw. (36) 56. (manag* adj5 (contaminat* or hygien* or handwash* or hand wash* or disinfect* or sterilisation or sterilization)).tw. (1241) 57. (precaution* adj5 (hygien* or handwash* or hand wash* or disinfect* or sterilisation or sterilization)).tw. (424) 58. (behavio?r* adj2 manag*).tw. (3687) 59. (prevent* adj5 (measure* or control*)).tw. (54,004) 60. (risk* adj (manage* or assess* or contain*)).tw. (35,159) 61. infection control practitioner/ (61) 62. (infection* and prevent*).tw. (87,720) 63. RISK REDUCTION/ or BEHAVIORAL RISK FACTOR SURVEILLANCE SYSTEM/ or HIGH RISK BEHAVIOR/ or RISK ASSESSMENT/ or RISK MANAGEMENT/ (304,788) 64. or/35-63 (8,009,274) 65. 28 and 64 (3151) 66. (bloodstream or blood-stream or "blood stream").tw. (13,990) 67. 9 and 19 and 34 and 64 and 66 (759) 68. 65 or 67 (3182) 69. bacteremia/ or bloodstream infection/ or sepsis/ (87,784) 70. 9 and 19 and 64 and 69 (1376) 71. 68 or 70 (3460) 72. (comment or letter or editorial).pt. (1,078,117) 73. 71 not 72 (3396) 74. limit 73 to embase (2944)	

Database, date searched, host, years, keywords	Search strategy	Results
Web of Science Time span = all years Searched on 1 February 2011 *Databases*: Science Citation Index Expanded (SCI-E): 1970–present Social Sciences Citation Index (SSCI): 1970–present Arts & Humanities Citation Index (A&HCI): 1975–present Conference Proceedings Citation Index - Science (CPCI-S): 1990–present Conference Proceedings Citation Index - Social Science & Humanities (CPCI-SSH): 1990–present	Databases=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH # 1 83,956 TS=("intensive care" or "critical care" or "intensive therapy unit" or ITU or ICU or CCU or CICU or CITU) # 2 24,167 TS=(catheter* SAME (venous or intravenous or arterial or vascular or intravascular or central or indwelling or peripheral or peripherally)) # 3 1511 TS=(tunnel* SAME (venous or intravenous or arterial or vascular or intravascular or central or indwelling or peripheral or peripherally)) # 4 7870 TS=(device* SAME (venous or intravenous or arterial or vascular or intravascular or central or indwelling or peripheral or peripherally)) # 5 1193 TS=("central line") # 6 19,168 TS=(CVC or PICC or JICC or SICC or SBCC or PVC or IVI) # 7 1434 TS=("Porta-cath" or Portacath or Hickman* or Broviac or Venflon or Groshong) #8 22,666 TS=("implantable port" or "access port" or cannula*) # 9 5752 TS=(infection* SAME ("bloodstream" or "blood stream" or "blood-stream")) # 10 > 100,000 TS=(sepsis or asepsis or septic* or bacteremia or bacteraemia) # 11 1873 TS=(healthcare associated infection*) # 12 5279 TS=("CR-BSI" or "CR-BSIs" or CRBSI or CRBSIs or CABI or CABIs or CABSI or CABSIs or CLABSI or CLABSIs or CRI or CRIs or BSI or BSIs or "AC-CRI " or "AC-CRIs") # 13 72,693 (#2 or #3 or #4 or #5 or #6 or #7 or #8) # 14 > 100,000 (#9 or #10 or #11 or #12 or #13) # 15 3003 (#1 and #13 and #14) # 16 464 (#1 and #12) # 17 3178 (#15 or #16) # 18 >100,000 TS=(educat*) # 19 137 (#17 and #18) # 20 > 100,000 TS=(train* or teach* or program* or feedback or lean* or instruct*) # 21 > 100,000 TS=(strateg* or component* or initiative*) #22 > 100,000 TS=(booklet* or workbook* or checklist* or library or libraries or questionnaire* or pamphlet* or poster* or pictorial* or verbal* or video* or audiovisual* or podcast* or telemedicine or teleconferenc* or website*) # 23 9557 TS=("scrub the hub" or "Matching Michigan" or "Michigan project" or "Michigan Intervention" or "NHS Venous Catheter Care" or EPIC or "EPIC-2" or "saving lives") # 24 > 100,000 (#20 or #21 or #22 or #23) # 25 807 (#17 and #24) # 26 838 (#19 or #25)	838 *Updated 13 March 2012*: 138
BIOSIS 1969–2011 Searched 1 February 2011	Same strategy as Web of Science	449 *Updated 13 March 2012*: 11 BIOSIS Previews 82 BIOSIS Citation Index Total *N* = 93

Database, date searched, host, years, keywords	Search strategy	Results
HMIC Searched 1 February 2011	As MEDLINE search – HMIC download filter would not work easily – only 37 imported but remainder checked and were duplicates so 37 were downloaded	43 (37 downloaded) DATABASE NO LONGER SUBSCRIBED TO SO NO UPDATE WAS FEASIBLE
The Cochrane Library Searched 2 January 2011	#1 Medical subject heading (MeSH) descriptor Intensive Care explode all trees (1050) #2 MeSH descriptor Critical Care explode all trees (1704) #3 MeSH descriptor Intensive Care Units explode all trees (2344) #4 ("acute care" or "critical care" or "critically ill" or "critical illness") (9593) #5 "high dependency care" or "high dependency unit" (51) #6 high next dependency next unit* (41) #7 "intensive care" (11,969) #8 (ITU or ICU or CCU or CICU or CITU) (2595) #9 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8) (19,362) #10 MeSH descriptor Catheterization, Central Venous explode all trees (667) #11 central near catheter* (1867) #12 central near cannul* (182) #13 central near3 line (298) #14 central near3 device (198) #15 central near3 device (198) #16 (catheter NEAR (venous or intravenous or arterial or vascular or intravascular or indwelling or peripheral or peripherally)) (2518) #17 (catheterization NEAR (venous or intravenous or arterial or vascular or intravascular or indwelling or peripheral or peripherally)) (1494) #18 (catheterisation NEAR (venous or intravenous or arterial or vascular or intravascular or indwelling or peripheral or peripherally)) (1494) #19 (tunnel near (venous or intravenous or arterial or vascular or intravascular or central or indwelling or peripheral or peripherally)) (262) #20 (device near (venous or intravenous or arterial or vascular or intravascular or central or indwelling or peripheral or peripherally)) (1098) #21 (CVC or PICC or JICC or SICC or SBCC or PVC or IVI or CVL or PCVC or CVAD or TCVC) (475) #22 umbilical near catheter* (94) #23 umbilical near cannul* (6) #24 umbilical near3 line* (8) #25 (Portacath or Hickman* or Broviac or Venflon or Groshong) (195) #26 port next cath* (9) #27 porta next cath* (2) #28 (#10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27) (5519) #29 blood next stream next infection (50) #30 bloodstream near infection* (273) #31 blood stream near infection* (56) #32 bacteria* near infection* (5699) #33 MeSH descriptor Infection explode all trees (15,511) #34 MeSH descriptor Communicable Diseases explode all trees (126)	

Database, date searched, host, years, keywords	Search strategy	Results
Cochrane databases (*continued*)	#35 MeSH descriptor Bacterial Infections and Mycoses explode all trees (24,790) #36 MeSH descriptor Infectious Disease Transmission, Professional-to-Patient explode all trees (29) #37 MeSH descriptor Bacteremia explode all trees (670) #38 (sepsis or asepsis or septic* or bacteremia* or bacteraemia* or bacteria* or endotoxin*) (24,032) #39 blood near poison* (177) #40 culture near3 (blood or positive) (2428) #41 "healthcare associated" next infection* (22) #42 (HAI or HAIs or "HAI's" or HCAI or HCAIs or "HCAI's") (471) #43 (MRSA or MSSA) (259) #44 infection*:ti,ab (28,643) #45 (#29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44) (52,153) #46 MeSH descriptor Catheter-Related Infections, this term only 49 #47 catheter* near3 infect* (719) #48 catheter* near3 microb* (138) #49 (catheter* and blood and infection*):ti,ab (208) #50 ("CR-BSI" or "CR-BSIs" or CRBSI or CRBSIs or CABI or CABIs or CABSI or CABSIs or CLABSI or CLABSIs or CRI or CRIs or BSI or BSIs or "AC-CRI" or "AC-CRIs") (316) #51 (#46 OR #47 OR #48 OR #49 OR #50) (1110) #52 MeSH descriptor Education explode all trees (15,114) #53 MeSH descriptor Inservice Training explode all trees (441) #54 MeSH descriptor Training Support, this term only (14) #55 (awareness or bundle* or collaborat* or campaign* or communicat*):ti,ab (9811) #56 (feedback or "feed back" or "feeding back" or course* or instruct* or inform* or impart* or knowledge or learn* or "e-learn" or "e-learning" or lecture*) (111,227) #57 (module* or modular or message* or session* or curriculum* or evaluat* or seminar* or test* or teach* or taught or train* or simulat* or refresh* or tool* or meeting* or presentation* or skill* or drill* or workshop* or outreach) (335,667) #58 (booklet* or workbook* or checklist* or library or libraries or questionnaire* or sheet* or pamphlet* or poster* or pictorial* or verbal* or video* or audiovisual* or podcast or telemedicine or teleconferenc* or symposia or symposium) (61,099) #59 change next management (35) #60 ((change or changing) near (process or procedure)) (1161) #61 early next warning next system* (23) #62 ("scrub the hub" or "Matching Michigan" or "Michigan project" or "Michigan Intervention" or "NHS Venous Catheter Care" or EPIC or "EPIC-2" or "saving lives") (124) #63 educat* (30,296) #64 (chang* near (hygien* or handwash* or hand wash* or disinfect* or sterilisation or sterilization)) (85) #65 (alter* near (hygien* or handwash* or hand wash* or disinfect* or sterilisation or sterilization)) (53) #66 (management near (contaminat* or hygien* or handwash* or hand wash* or disinfect* or sterilisation or sterilization)) (45)	

Database, date searched, host, years, keywords	Search strategy	Results
Cochrane databases (*continued*)	#67 (precaution* near (hygien* or handwash* or hand wash* or disinfect* or sterilisation or sterilization)) (13) #68 prevent* near infect* (10,190) #69 (quality near (strateg* or intervention* or management or initiative*)) (4354) #70 (risk near (management or prevention or intervention*)) (8647) #71 (precaution near infect*) (25) #72 (#52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71) (387,381) #73 (#9 AND #28 AND #45 AND #72) (325) #74 (#9 AND #51 AND 72) (48) #75 (#73 OR #74) (340)	
CINAHL EBSCO*host* Searched 2 February 2011	S1 (MH "Intensive Care Units") OR (MH "Intensive Care Units, Pediatric") OR (MH "Intensive Care, Neonatal") OR (MH "Neonatal Intensive Care Nursing") OR (MH "Critical Care") OR (MH "Critical Care Nursing") OR (MH "Intensive Care Units, Neonatal") (33,939) S2 TX (ITU or ICU or CCU or CICU or CITU) (9272) S3 S1 or S2 (38,088) S4 (MH "Central Venous Catheters") OR (MH "Catheters, Vascular") OR (MH "Catheters+") OR (MH "Catheters and Tubes") OR (MH "Peripherally Inserted Central Catheters") OR (MH "Catheterization") OR (MH "Catheter Care") OR "catheter*" (21,661) S5 TX (CVC or PICC or JICC or SICC or SBCC or PVC or IVI or CVL or PCVC or CVAD or TCVC or Portacath or Hickman* or Broviac or Venflon or Groshong) (1654) S6 TX (central n3 cannul* or central n3 line* or central n3 device (1166) S7 TX (Portacath or "Port-A-Cath" or Hickman or Broviac or Venflon or Groshong) (540) S8 S4 or S5 or S6 or S7 (22,929) S9 (MH "Infection") OR "infection" OR (MH "Bacterial Infections) (64,326) S10 (MH "Bacteremia") (2044) S11 TX (bacteremia or bacteraemia or sepsis or asepsis or septic* or "blood poison*") (11,692) S12 (MH "Endotoxins") OR "endotoxin" OR (MH "Endotoxemia") (840) S13 (MH "Toxemia") OR "toxemia" (51) S14 TX bloodstream infection* (1127 S15 TX blood-stream infection* (98) S16 (MH "Bacterial Colonization") OR "colonization" (3085) S17 S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16 (73,507) S18 (MH "Catheter-Related Infections") (2447) S19 TX (catheter related bloodstream infection*) (298) S20 TX (CRBSI or CLABSI or CABSI or BSI or CRI) (1812) S21 S18 or S19 or S20 (4115) S22 (MH "Education, Clinical") OR (MH "Education, Competency-Based") OR (MH "Education, Allied Health") OR "education*" (306,068) S23 (MH "Hygiene/ED") OR (MH "Handwashing/ED") (250) S24 TX ("scrub the hub" or "Matching Michigan" or "Michigan project" or "Michigan Intervention" or "NHS Venous Catheter Care" or EPIC or "EPIC-2" or "saving lives") (650) S25 (learn* or teach* or train* or feedback) (170,039)	209 *Updated 13 March 2012*: 78

Database, date searched, host, years, keywords	Search strategy	Results
CINAHL (*continued*)	S26 S22 or S23 or S24 or S25 (395,945) S27 S3 and S8 and S17 and S26 (199) S28 S3 and S21 and S26 (150) S29 S27 or S28 (209)	
CRD Searched 3 February 2011	# 1 ("intensive care" OR "critical care" OR "critical illness" OR "critically ill") (2133) # 2 MeSH Critical Care EXPLODE 1 2 (484) # 3 MeSH Intensive Care EXPLODE 1 2 (313) # 4 MeSH Intensive Care Units, Neonatal EXPLODE 1 (107) # 5 MeSH Intensive Care Units, Pediatric EXPLODE 1 (157) # 6 (ITU OR ICU OR CCU OR CICU OR CITU) (464) # 7 #1 or #2 or #3 or #4 or #5 or #6 (2435) # 8 MeSH Catheterization, Central Venous EXPLODE 1 (154) # 9 MeSH Catheterization, Peripheral EXPLODE 1 (68) # 10 MeSH Catheters, Indwelling EXPLODE 1 (123) # 11 (CVC OR PICC OR JICC OR SICC OR SBCC OR PVC OR IVI OR CVL OR PCVC OR CVAD OR TCVC) (56) # 12 (catheter* OR cannul*) (1084) # 13 #8 or #9 or #10 or #11 or #12 (1162) # 14 MeSH Bacterial Infections EXPLODE 1 (1999) # 15 MeSH Bacteremia EXPLODE 1 2 3 (147) # 16 MeSH Sepsis EXPLODE 1 2 (390) # 17 MeSH Asepsis EXPLODE 1 (3) # 18 MeSH Fungemia EXPLODE 1 2 3 (20) # 19 (infection* OR acinetobacter* OR asepsis OR bacter?emia* OR bacteria* OR candida OR coloni?ation OR contaminat* OR cfu OR colony OR colonies OR corynebacterium OR escherichia OR enterococc* OR enterobacter* OR fungi OR fungus OR fungal OR fung?emia OR klebsiella OR met?icillin OR microorganism* OR micro-organism* OR microbial* OR microbe* OR microbiologic* OR mycology OR mycological OR organism* OR nosocomial* OR pathogen* OR sepsis OR septic OR septic?emia AND septicemia OR staphylococc* OR streptococc*) (6148) # 20 (HAI OR HAIs OR "HAI's" OR HCAI OR HCAIs OR "HCAI's") (15) # 21 (MRSA OR MSSA) (85) # 22 #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 (6993) # 23 ("CR-BSI" OR "CR-BSIs" OR CRBSI OR CRBSIs OR CABI OR CABIs OR CABSI OR CABSIs OR CLABSI OR CLABSIs OR CRI OR CRIs OR BSI OR BSIs OR "AC-CRI " OR "AC-CRIs") (77) # 24 catheter AND related AND infection* (170) # 25 (line AND (infection* OR sepsis OR bacter?emia)) (292) # 26 (catheter* AND (sepsis OR septic OR bacter?emia*)) (56) # 27 #23 or #24 or #25 or #26 (518) # 28 (educat* OR train* OR teach* OR feedback OR bundle OR course* OR learn* OR lecture* OR workshop*) (7927) # 29 (component* OR "multi-component" OR "multi-faceted" OR "multi-modal" OR initiative* OR intervention* OR program* OR strateg*) (24,642) # 30 (booklet* OR checklist* OR library OR libraries OR literature OR questionnaire* OR sheet* OR pamphlet* OR poster* OR pictorial* OR verbal* OR video* OR audiovisual* OR podcast OR telemedicine OR teleconferenc* OR workbook) (20,644)	Results cross checked manually against database – nothing new to add *Updated 13 March 2012*: 0 relevant to education Taking education out of the equation 3

Database, date searched, host, years, keywords	Search strategy	Results
CRD (*continued*)	# 31 ("scrub the hub" OR "Matching Michigan" OR "Michigan project" OR "Michigan Intervention" OR "NHS Venous Catheter Care" OR EPIC OR "EPIC-2" OR "saving lives") (20) # 32 #25 or #26 or #27 or #28 or #29 or #30 or #31 (33,207) # 33 7 AND 13 AND 22 AND 32 (82) # 34 7 AND 27 AND 32 (187) # 35 #33 or #34 (237) # 36 #2 OR #3 OR #4 OR #5 (620) # 37 #13 AND #22 AND #32 AND #36 (17) # 38 #27 AND #32 AND #36 (18) # 39 #37 OR #38 (23) 40 ("intensive care" OR "critical care") (2038) # 41 27 AND 32 AND 40 (125) # 42 catheter* AND educat* (42) # 43 (catheter* AND educat* AND intensive AND unit*) (12) # 44 (catheter* AND educat* AND critical AND unit*) (7) # 45 #43 or #44 (17)	

Cost-effectiveness search strategy

Database	Search strategy	Results
MEDLINE Ovid Serached 22 February 2011	1. exp Critical Care/ 2. exp Intensive Care/ or exp Intensive Care Units/ 3. ("acute care" or "critical care" or "critically ill" or "critical illness").tw. 4. (high dependency adj1 (care or unit*1)).tw. 5. "intensive care".tw. 6. (intensive adj therapy adj unit*).tw. 7. (ITU or ICU or CCU or CICU or CITU).tw. 8. ("level 2 care" or "level 3 care").tw. 9. Catheterization, Central Venous/ or Catheterization/ or Catheterization, Peripheral/ 10. Catheters, Indwelling/ 11. exp catheters/ 12. (catheter* adj5 (venous or intravenous or arterial or vascular or intravascular or central or indwelling or peripheral or peripherally)).tw. 13. (tunnel* adj5 (venous or intravenous or arterial or vascular or intravascular or central or indwelling or peripheral or peripherally)).tw. 14. (device* adj5 (venous or intravenous or arterial or vascular or intravascular or central or indwelling or peripheral or peripherally)).tw. 15. (CVC or PICC or JICC or SICC or SBCC or PVC or IVI).tw. 16. ("Porta-cath" or Portacath or Hickman* or Broviac or Venflon or Groshong).tw. 17. ("implantable port" or "access port").tw. 18. cannula*.tw. 19. exp Bacterial Infections/ 20. exp Bacteremia/ 21. septicemia/ 22. Sepsis/ 23. Asepsis/ 24. cross infection/ 25. Infectious Disease Transmission, Professional-to-Patient/ 26. Communicable Diseases/ 27. exp bacteria/ 28. fungemia/ 29. exp Staphylococcal Infections/ 30. Staphylococcus aureus/ 31. Methicillin Resistance/ 32. Staphylococcus/ or Staphylococcus epidermidis/ 33. exp Streptococcus/ or exp Streptococcal Infections/ 34. Pseudomonas aeruginosa/ 35. Escherichia coli/ 36. exp Enterobacter/ 37. exp Klebsiella/ or exp Klebsiella Infections/ 38. exp Corynebacterium/ or exp Corynebacterium Infections/ 39. exp Acinetobacter/ or exp Acinetobacter Infections/ 40. exp Enterococcus/ 41. exp Candida/ 42. exp Blood-Borne Pathogens/ 43. exp Enterobacteriaceae Infections/ 44. equipment contamination/ 45. colony count microbial/	266 *Updated 14 March 2012*: 43

Database	Search strategy	Results
MEDLINE (*continued*)	46. exp Infection/bl [Blood] 47. bacter?emia.tw. 48. (infection* or acinetobacter* or asepsis or bacter?emia* or bacteria* or candida or coloni?ation or contaminat* or cfu or colony or colonies or corynebacterium or escherichia or enterococc* or enterobacter* or fungi or fungus or fungal or fung?emia or klebsiella or met?icillin or microorganism* or micro-organism* or microbial* or microbe* or microbiologic* or mycology or mycological or organism* or nosocomial* or pathogen* or sepsis or septic or septic?emia septicemia or staphylococc* or streptococc*).tw. 49. (blood?stream adj infection*).tw. 50. (blood-stream adj infection*).tw. 51. (blood* adj3 infect*).tw. 52. ("healthcare associated" adj infection*).tw. 53. (HAI or HAIs or "HAI's" or HCAI or HCAIs or "HCAI's").tw. 54. (extraluminal adj infection*).tw. 55. (MRSA or MSSA).tw. 56. (blood adj culture*).tw. 57. (positive adj2 culture*).tw. 58. (positive adj isolate*).tw. 59. Infectioan Control/ 60. Catheter Related infections/ 61. Catheters/mi [Microbiology] 62. Catheters, Indwelling/mi [Microbiology] 63. ("CR-BSI" or "CR-BSIs" or CRBSI or CRBSIs or CABI or CABIs or CABSI or CABSIs or CLABSI or CLABSIs or CRI or CRIs or BSI or BSIs or "AC-CRI " or "AC-CRIs").tw. 64. (line adj3 (infection* or sepsis or bacter?emia)).tw. 65. (catheter* and blood* and infection*).tw. 66. (catheter* and (sepsis or bacter?emia*)).tw. 67. exp Education, Medical/ 68. exp Education, Nursing/ 69. education continuing/ 70. Education, Department Hospital/ 71. Educational Measurement/ 72. Internal Medicine/ed [Education] 73. Nursing Staff, Hospital/ed [Education] 74. exp Health Education/ 75. Health Knowledge, Attitudes, Practice/ 76. Inservice training/ or Training Support/ or Instruction/ 77. Preceptorship/ 78. Mentors/ 79. Interdisciplinary communication/ 80. Teaching Rounds/ or Hospitals, Teaching/ or Teaching Materials/ or Teaching/ 81. Personnel, Hospital/ed [Education] 82. Emergency Medicine/ed [Education] 83. exp Critical Care/ed [Education] 84. Curriculum/ 85. Program Evaluation/ 86. Program Development/ 87. Infection Control/mt, og, st [Methods, Organization & Administration, Standards]	

Database	Search strategy	Results
MEDLINE (*continued*)	88. Equipment Contamination/pc, st [Prevention & Control, Standards] 89. Safety Management/mt, og, st [Methods, Organization & Administration, Standards] 90. Intensive Care Units/mt, st [Methods, Standards] 91. Point-of-Care Systems/og, st [Organization & Administration, Standards] 92. Clinical Competence/st [Standards] 93. Total Quality Management/mt, og [Methods, Organization & Administration] 94. (educat* or awareness or bundle* or collaborat* or campaign* or communicat*).tw. 95. (feedback or "feed back" or "feeding back" or course* or instruct* or inform* or impart* or knowledge or learn* or "e-learn" or "e-learning" or lecture*).tw. 96. (module* or modular or session* or study or studies or studying or studies).tw. 97. ("self study" or re-educat* or "self-educat*").tw. 98. (assess* or apprais* or competenc* or competent* or curriculum* or evaluat* or seminar* or test* or teach* or taught or train* or simulat* or refresh* or tool* or meeting* or presentation* or skill* or drill* or workshop*).tw. 99. (link* adj2 (staff or nurs*)).tw. 100. (preceptor* or mentor*).tw. 101. (component* or "multi-component" or "multi-faceted" or "multi-modal" or initiative* or intervention*).tw. 102. (session* or strategy or strategies or initiative or program* or package*).tw. 103. "blended learning".tw. 104. "self-learn*".tw. 105. (shar* adj3 practice*).tw. 106. (risk* adj3 (reduc* or management)).tw. 107. (booklet* or workbook* or checklist* or library or libraries or literature or questionnaire* or sheet* or pamphlet* or poster* or pictorial* or verbal* or video* or audiovisual* or podcast or telemedicine or teleconferenc*).tw. 108. ("scrub the hub" or "Matching Michigan" or "Michigan project" or "Michigan Intervention" or "NHS Venous Catheter Care" or EPIC or "EPIC-2" or "saving lives").tw. 109. (behavio?r* adj2 chang*).tw. 110. (behavio?r adj2 alter*).tw. 111. (chang* adj5 (hygien* or handwash* or hand wash* or disinfect* or sterilisation or sterilization)).tw. 112. (alterat* adj5 (hygien* or handwash* or hand wash* or disinfect* or sterilisation or sterilization)).tw. 113. (management adj5 (contaminat* or hygien* or handwash* or hand wash* or disinfect* or sterilisation or sterilization)).tw. 114. (precaution* adj5 (hygien* or handwash* or hand wash* or disinfect* or sterilisation or sterilization)).tw. 115. (behavio?r* adj2 management).tw. 116. (risk* adj (manage* or assess*)).tw. 117. governance.tw. 118. or/1-8 119. or/9-18 120. or/19-59 121. or/60-66 122. or/67-117	

Database	Search strategy	Results
MEDLINE (*continued*)	123. 118 and 119 and 120 and 122 124. 118 and 121 and 122 125. 123 or 124 126. (editorial or letter or comment).pt. 127. 125 not 126 128. exp economics/ 129. exp economics hospital/ 130. exp economics pharmaceutical/ 131. exp economics nursing/ 132. exp economics medical/ 133. exp "Costs and Cost Analysis"/ 134. Cost Benefit Analysis/ 135. exp models economic/ 136. exp fees/ and charges/ 137. exp budgets/ 138. (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic*).tw. 139. (value adj1 money).tw. 140. budget$.tw. 141. or/128-140 142. ((energy or oxygen) adj cost).tw. 143. (metabolic adj cost).tw. 144. ((energy or oxygen) adj expenditure).tw. 145. or/142-144 146. 141 not 145 147. (letter or editorial or comment or historical article).pt. 148. 146 not 147 149. 127 and 148 ADDED IN BEHAVIO?R AS FREE TEXT WORD – NOTHING NEW IDENTIFIED (1 March 2011) 150. 150 behavio?r*.tw. (536,358) 151. 151 118 and 119 and 120 and 148 and 150 (4) 152. 152 118 and 121 and 148 and 150 (4) 153. 153 151 or 152 (5) 154. 154 153 not 149 (0)	
MEDLINE in Process & Other Non-Indexed Citations **Ovid** Searched 22 February 2011	As per MEDLINE	9 *Updated 14 March 2012*: 38

Database	Search strategy	Results
EMBASE Ovid Searched 22 February 2011	1. exp intensive care/ 2. exp intensive care unit/ 3. ("acute care" or "critical care" or "critically ill" or "critical illness").tw. 4. (high dependency adj1 (care or unit*1)).tw. 5. ("intensive care" or "intensive medical care").tw. 6. (intensive adj therapy adj unit*).tw. 7. (ITU or ICU or CCU or CICU or CITU or SCBU).tw. 8. ("level 2 care" or "level 3 care").tw. 9. or/1-8 10. exp catheterization/ 11. INTRAVENOUS CATHETER/ or ARTERY CATHETER/ or CATHETER/ or INDWELLING CATHETER/ or PERIPHERALLY INSERTED CENTRAL VENOUS CATHETER/ or CENTRAL VENOUS CATHETER/ or INTRAVASCULAR CATHETER/ 12. (catheter* adj5 (venous or intravenous or arterial or vascular or intravascular or central or indwelling or peripheral or peripherally)).tw. 13. (tunnel* adj5 (venous or intravenous or arterial or vascular or intravascular or central or indwelling or peripheral or peripherally)).tw. 14. (device* adj5 (venous or intravenous or arterial or vascular or intravascular or central or indwelling or peripheral or peripherally)).tw. 15. (CVC or PICC or JICC or SICC or SBCC or PVC or IVI).tw. 16. ("Porta-cath" or Portacath or Hickman* or Broviac or Venflon or Groshong).tw. 17. ("implantable port" or "access port").tw. 18. cannula*.tw. 19. or/10-18 20. catheter infection/ 21. ("CR-BSI" or "CR-BSIs" or CRBSI or CRBSIs or CABI or CABIs or CABSI or CABSIs or CLABSI or CLABSIs or CRI or CRIs or BSI or BSIs or "AC-CRI " or "AC-CRIs").tw. 22. (line adj3 (infection* or sepsis or bacter?emia)).tw. 23. (catheter* and blood* and infection*).tw. 24. (catheter* and (sepsis or bacter?emia*)).tw. 25. "catheter-related bloodstream infection*".tw. 26. "catheter-associated bloodstream infection*".tw. 27. or/20-26 28. 9 and 27 29. exp INFECTION/ or GRAM POSITIVE INFECTION/ or STAPHYLOCOCCUS INFECTION/ or BACTERIAL INFECTION/ or GROUP A STREPTOCOCCAL INFECTION/ or ENTEROCOCCAL INFECTION/ or KLEBSIELLA INFECTION/ or HOSPITAL INFECTION/ or STREPTOCOCCUS INFECTION/ or GRAM NEGATIVE INFECTION/ or METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS INFECTION/ or GROUP B STREPTOCOCCAL INFECTION/ or DEVICE INFECTION/ or ENTEROBACTERIACEAE INFECTION/ or BLOODSTREAM INFECTION/ or CROSS INFECTION/ 30. FUNGAL CONTAMINATION/ or BACTERIUM CONTAMINATION/ or VIRAL CONTAMINATION/ or MICROBIAL CONTAMINATION/ 31. bacteremia/ or sepsis/	305 *Updated 20 March 2012*: 116

Database	Search strategy	Results
EMBASE (*continued*)	32. (infection* or acinetobacter* or asepsis or bacter?emia* or bacteria* or candida or coloni?ation or contaminat* or cfu or colony or colonies or corynebacterium or escherichia or enterococc* or enterobacter* or fungi or fungus or fungal or fung?emia or klebsiella or met?icillin or microorganism* or micro-organism* or microbial* or microbe* or microbiologic* or mycology or mycological or organism* or nosocomial* or pathogen* or sepsis or septic or septic?emia or staphylococc* or streptococc*).tw. 33. (MRSA or MSSA).tw. 34. or/29-33 35. CLINICAL EDUCATION/ or NURSING EDUCATION/ or CONTINUING EDUCATION/ or EDUCATION PROGRAM/ or RESEARCH BASED NURSING EDUCATION/ or CONTINUING EDUCATION PROVIDER/ or INTERDISCIPLINARY EDUCATION/ or EMERGENCY MEDICAL SERVICES EDUCATION/ or MEDICAL EDUCATION/ or HEALTH EDUCATION/ or EDUCATION/ or "OUTCOME OF EDUCATION"/ 36. IN SERVICE TRAINING/ or TRAINING/ or STAFF TRAINING/ 37. (educat* or awareness or bundle* or collaborat* or campaign* or communicat*).tw. 38. (feedback or "feed back" or "feeding back" or course* or instruct* or inform* or impart* or knowledge or learn* or "e-learn" or "e-learning" or lecture*).tw. 39. (module* or modular or session*).tw. 40. ("self study" or re-educat* or "self-educat*").tw. 41. (assess* or apprais* or competenc* or competent* or curriculum* or evaluat* or seminar* or test* or teach* or taught or train* or simulat* or refresh* or tool* or meeting* or presentation* or skill* or drill* or workshop*).tw. 42. (link* adj2 (staff or nurs*)).tw. 43. (preceptor* or mentor*).tw. 44. (component* or "multi-component" or "multi-faceted" or "multi-modal" or initiative* or intervention*).tw. 45. (session* or strategy or strategies or initiative or program* or package*).tw. 46. "blended learning".tw. 47. "self-learn*".tw. 48. (shar* adj3 practice*).tw. 49. (risk* adj3 (reduc* or management)).tw. 50. ("scrub the hub" or "Matching Michigan" or "Michigan project" or "Michigan Intervention" or "NHS Venous Catheter Care" or EPIC or "EPIC-2" or "saving lives").tw. 51. (booklet* or workbook* or checklist* or library or libraries or literature or questionnaire* or sheet* or pamphlet* or poster* or pictorial* or verbal* or video* or audiovisual* or podcast* or telemedicine or teleconferenc*).tw. 52. (behavio?r* adj2 chang*).tw. 53. (behavio?r adj2 alter*).tw. 54. (chang* adj5 (hygien* or handwash* or hand wash* or disinfect* or sterilisation or sterilization)).tw. 55. (alterat* adj5 (hygien* or handwash* or hand wash* or disinfect* or sterilisation or sterilization)).tw. 56. (manag* adj5 (contaminat* or hygien* or handwash* or hand wash* or disinfect* or sterilisation or sterilization)).tw. 57. (precaution* adj5 (hygien* or handwash* or hand wash* or disinfect* or sterilisation or sterilization)).tw. 58. (behavio?r* adj2 manag*).tw. 59. (prevent* adj5 (measure* or control*)).tw. 60. (risk* adj (manage* or assess* or contain*)).tw.	

Database	Search strategy	Results
EMBASE (*continued*)	61. infection control practitioner/ 62. (infection* and prevent*).tw. 63. RISK REDUCTION/ or BEHAVIORAL RISK FACTOR SURVEILLANCE SYSTEM/ or HIGH RISK BEHAVIOR/ or RISK ASSESSMENT/ or RISK MANAGEMENT/ 64. or/35-63 65. 28 and 64 66. (bloodstream or blood-stream or "blood stream").tw. 67. 9 and 19 and 34 and 64 and 66 68. 65 or 67 69. bacteremia/ or bloodstream infection/ or sepsis/ 70. 9 and 19 and 64 and 69 71. 68 or 70 72. (comment or letter or editorial).pt. 73. 71 not 72 74. limit 73 to embase 75. exp Health Economics/ 76. monte carlo method/ 77. markov.ti,ab. 78. (financial or finance or finances or financed).ti,ab. 79. cost/ 80. cost minimization analysis/ 81. cost of illness/ 82. cost utility analysis/ 83. budget/ 84. "resource use".ti,ab. 85. (decision adj1 (tree* or analys* or model*)).tw. 86. (resource? adj1 allocat*).tw. 87. exp economic evaluation/ 88. exp "health care cost"/ 89. exp pharmacoeconomics/ 90. (cost adj3 (util* or effective* or efficac* or benefit* or consequence* or analys* or minimi* or saving* or breakdown* or lowering or estimate* or variable* or allocation* or control* or illness* or instrument* or technolog*)).tw. 91. (econom* or pharmacoeconomic* or "pharmaco economic*").ti,ab. 92. or/75-91 93. 74 and 92 94. (letter or editorial or note).pt. 95. 93 not 94	
CINAHL EBSCO*host* Searched 22 February 2011	*Following COST FILTER Added on to clinical search*: S30 (MH "Economics+") (341,991) S31 (MH "Financial Management+") (26,259) S32 (MH "Financial Support+") (217674) S33 (MH "Financing, Organized+") (67782) S34 (MH "Business+") (50121) S35 S31 or S32 or S33 or S34 (337744) S36 S30 NOT S35 (35930) S37 (MH "Health Resource Allocation") (4520) S38 (MH "Health Resource Utilization") (6625)	41 *Updated 20 February 2012*: 24

Database	Search strategy	Results
CINAHL (*continued*)	S39 S37 or S38 (10,914) S40 S36 or S39 (43,151) S41 TI (cost or costs or economic* or pharmacoeconomic* or price* or pricing) OR AB (cost or costs or economic* or pharmacoeconomic* or price* or pricing*) (64,812) S42 S40 or S41 (93,923) S43 S29 and S42 (41)	
Web of Science Searched 23 March 2011	*Following COST FILTER added on to clinical search*: # 27 > 100,000 TI=(cost* or economic* or pharmacoeconomic*) # 28 > 100,000 TS=("cost effective*" or "cost benefit*" or "cost saving*" or "cost analys*" or "cost utili*" or "cost mimimi*" or "cost consequence*" or "cost comparison*" or "cost identificat*") # 29 15,887 TS=("health economic*" or "healthcare cost*" or "health care cost*" or "economic evaluation*") # 30 32,009 TS=(economical) # 31 > 100,000 (#27 or #28 or #29 or #30) #32 45 (#26 and #31)	45 *Updated 21 March 2012*: 12
BIOSIS Searched 23 February 2011	Same as Web of Science Strategy	6 *Updated 21 March 2012*: 17
The Cochrane Library Searched 23 February 2011	#1 MeSH descriptor Intensive Care explode all trees #2 MeSH descriptor Critical Care explode all trees #3 MeSH descriptor Intensive Care Units explode all trees #4 ("acute care" or "critical care" or "critically ill" or "critical illness") #5 "high dependency care" or "high dependency unit" #6 high next dependency next unit* #7 "intensive care" #8 (ITU or ICU or CCU or CICU or CITU) #9 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8) #10 MeSH descriptor Catheterization, Central Venous explode all trees #11 central near catheter* #12 central near cannul* #13 central near3 line #14 central near3 device #15 central near3 device #16 (catheter NEAR (venous or intravenous or arterial or vascular or intravascular or indwelling or peripheral or peripherally)) #17 (catheterization NEAR (venous or intravenous or arterial or vascular or intravascular or indwelling or peripheral or peripherally))	50 in total 11 CENTRAL 4 DARE 35 NHSEED 2 CDSR not downloaded not relevant) *Updated 21 March 2012*: 1 Cochrane HTA 4 Cochrane CDSR

Database	Search strategy	Results
Cochrane databases (*continued*)	#18 (catheterisation NEAR (venous or intravenous or arterial or vascular or intravascular or indwelling or peripheral or peripherally))	
	#19 (tunnel near (venous or intravenous or arterial or vascular or intravascular or central or indwelling or peripheral or peripherally))	
	#20 (device near (venous or intravenous or arterial or vascular or intravascular or central or indwelling or peripheral or peripherally))	
	#21 (CVC or PICC or JICC or SICC or SBCC or PVC or IVI or CVL or PCVC or CVAD or TCVC)	
	#22 umbilical near catheter*	
	#23 umbilical near cannul*	
	#24 umbilical near3 line*	
	#25 (Portacath or Hickman* or Broviac or Venflon or Groshong)	
	#26 port next cath*	
	#27 porta next cath*	
	#28 (#10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27)	
	#29 blood next stream next infection	
	#30 bloodstream near infection*	
	#31 blood stream near infection*	
	#32 bacteria* near infection*	
	#33 MeSH descriptor Infection explode all trees	
	#34 MeSH descriptor Communicable Diseases explode all trees	
	#35 MeSH descriptor Bacterial Infections and Mycoses explode all trees	
	#36 MeSH descriptor Infectious Disease Transmission, Professional-to-Patient explode all trees	
	#37 MeSH descriptor Bacteremia explode all trees	
	#38 (sepsis or asepsis or septic* or bacteremia* or bacteraemia* or bacteria* or endotoxin*)	
	#39 blood near poison*	
	#40 culture near3 (blood or positive)	
	#41 "healthcare associated" next infection*	
	#42 (HAI or HAIs or "HAI's" or HCAI or HCAIs or "HCAI's")	
	#43 (MRSA or MSSA)	
	#44 infection*:ti,ab	
	#45 (#29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44)	
	#46 MeSH descriptor Catheter-Related Infections, this term only	
	#47 catheter* near3 infect*	
	#48 catheter* near3 microb*	
	#49 (catheter* and blood and infection*):ti,ab	
	#50 ("CR-BSI" or "CR-BSIs" or CRBSI or CRBSIs or CABI or CABIs or CABSI or CABSIs or CLABSI or CLABSIs or CRI or CRIs or BSI or BSIs or "AC-CRI " or "AC-CRIs")	
	#51 (#46 OR #47 OR #48 OR #49 OR #50)	
	#52 MeSH descriptor Education explode all trees	
	#53 MeSH descriptor Inservice Training explode all trees	
	#54 MeSH descriptor Training Support, this term only	
	#55 (awareness or bundle* or collaborat* or campaign* or communicat*):ti,ab	
	#56 (feedback or "feed back" or "feeding back" or course* or instruct* or inform* or impart* or knowledge or learn* or "e-learn" or "e-learning" or lecture*)	

Database	Search strategy	Results
Cochrane databases (*continued*)	#57 (module* or modular or message* or session* or curriculum* or evaluat* or seminar* or test* or teach* or taught or train* or simulat* or refresh* or tool* or meeting* or presentation* or skill* or drill* or workshop* or outreach) #58 (booklet* or workbook* or checklist* or library or libraries or questionnaire* or sheet* or pamphlet* or poster* or pictorial* or verbal* or video* or audiovisual* or podcast or telemedicine or teleconferenc* or symposia or symposium) #59 change next management #60 ((change or changing) near (process or procedure)) #61 early next warning next system* #62 ("scrub the hub" or "Matching Michigan" or "Michigan project" or "Michigan Intervention" or "NHS Venous Catheter Care" or EPIC or "EPIC-2" or "saving lives") #63 educat* #64 (chang* near (hygien* or handwash* or hand wash* or disinfect* or sterilisation or sterilization)) #65 (alter* near (hygien* or handwash* or hand wash* or disinfect* or sterilisation or sterilization)) #66 (management near (contaminat* or hygien* or handwash* or hand wash* or disinfect* or sterilisation or sterilization)) #67 (precaution* near (hygien* or handwash* or hand wash* or disinfect* or sterilisation or sterilization)) #68 prevent* near infect* #69 (quality near (strateg* or intervention* or management or initiative*)) #70 (risk near (management or prevention or intervention*)) #71 (precaution near infect*) #72 (#52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71) #73 (#9 AND #28 AND #45 AND #72) #74 (#9 AND #51 AND 72) #75 (#73 OR #74) #76 ("cost effective*" or "cost benefit*" or "cost saving*" or "cost analys*" or "cost utili*" or "cost mimimi*" or "cost consequence*" or "cost comparison*" or "cost identificat*"):ti,ab,kw #77 (cost* or economic* or pharmacoeconomic*):ti #78 ("health economic*" or "healthcare cost*" or "health care cost*" or "economic evaluation*"):ti,ab,kw #79 (economical):ti,ab #80 MeSH descriptor Costs and Cost Analysis explode all trees #81 MeSH descriptor Cost-Benefit Analysis explode all trees #82 MeSH descriptor Models, Economic, this term only #83 MeSH descriptor Economics, Hospital explode all trees #84 MeSH descriptor Economics, Medical explode all trees #85 MeSH descriptor Economics, Nursing explode all trees #86 MeSH descriptor Health Care Costs explode all trees #87 (#76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82 OR #83 OR #84 OR #85 OR #86) #88 (#75 AND #87)	

Database	Search strategy	Results
CRD Searched 23 February 2011	# 1 ("intensive care" OR "critical care" OR "critical illness" OR "critically ill") # 2 MeSH Critical Care EXPLODE 1 2 # 3 MeSH Intensive Care EXPLODE 1 2 # 4 MeSH Intensive Care Units, Neonatal EXPLODE 1 # 5 MeSH Intensive Care Units, Pediatric EXPLODE 1 # 6 (ITU OR ICU OR CCU OR CICU OR CITU) # 7 #1 or #2 or #3 or #4 or #5 or #6 # 8 MeSH Catheterization, Central Venous EXPLODE 1 154 # 9 MeSH Catheterization, Peripheral EXPLODE 1 # 10 MeSH Catheters, Indwelling EXPLODE 1 # 11 (CVC OR PICC OR JICC OR SICC OR SBCC OR PVC OR IVI OR CVL OR PCVC OR CVAD OR TCVC) # 12 (catheter* OR cannul*) # 13 #8 or #9 or #10 or #11 or #12 # 14 MeSH Bacterial Infections EXPLODE 1 # 15 MeSH Bacteremia EXPLODE 1 2 3 # 16 MeSH Sepsis EXPLODE 1 2 # 17 MeSH Asepsis EXPLODE 1 3 # 18 MeSH Fungemia EXPLODE 1 2 3 # 19 (infection* OR acinetobacter* OR asepsis OR bacter?emia* OR bacteria* OR candida OR coloni?ation OR contaminat* OR cfu OR colony OR colonies OR corynebacterium OR escherichia OR enterococc* OR enterobacter* OR fungi OR fungus OR fungal OR fung?emia OR klebsiella OR met?icillin OR microorganism* OR micro-organism* OR microbial* OR microbe* OR microbiologic* OR mycology OR mycological OR organism* OR nosocomial* OR pathogen* OR sepsis OR septic OR septic?emia AND septicemia OR staphylococc* OR streptococc*) # 20 (HAI OR HAIs OR "HAI's" OR HCAI OR HCAIs OR "HCAI's") # 21 (MRSA OR MSSA) # 22 #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 # 23 ("CR-BSI" OR "CR-BSIs" OR CRBSI OR CRBSIs OR CABI OR CABIs OR CABSI OR CABSIs OR CLABSI OR CLABSIs OR CRI OR CRIs OR BSI OR BSIs OR "AC-CRI " OR "AC-CRIs") # 24 (catheter AND related AND infection*) # 25 (line AND (infection* OR sepsis OR bacter?emia)) # 26 (catheter* AND (sepsis OR septic OR bacter?emia*)) # 27 #23 or #24 or #25 or #26 # 28 (educat* OR train* OR teach* OR feedback OR bundle OR course* OR learn* OR lecture* OR workshop*) # 29 (component* OR "multi-component" OR "multi-faceted" OR "multi-modal" OR initiative* OR intervention* OR program* OR strateg*) # 30 (booklet* OR checklist* OR library OR libraries OR literature OR questionnaire* OR sheet* OR pamphlet* OR poster* OR pictorial* OR verbal* OR video* OR audiovisual* OR podcast OR telemedicine OR teleconferenc* OR workbook) # 31 ("scrub the hub" OR "Matching Michigan" OR "Michigan project" OR "Michigan Intervention" OR "NHS Venous Catheter Care" OR EPIC OR "EPIC-2" OR "saving lives") # 32 #25 or #26 or #27 or #28 or #29 or #30 or #31	38 *Updated 21 March 2012*: 36

Database	Search strategy	Results
CRD (*continued*)	# 33 7 AND 13 AND 22 AND 32 # 34 7 AND 27 AND 32 # 35 #33 or #34 # 36 #2 OR #3 OR #4 OR #5 # 37 #13 AND #22 AND #32 # 38 #27 AND #32 AND #36 # 39 #37 OR #38 # 40 #13 AND #22 AND #32 AND #36 # 41 #38 or #40 # 42 (catheter* AND educat* AND intensive AND unit*) # 43 (catheter* AND educat* AND critical AND unit*) # 44 #41 or #42 or #43	

Appendix 3 Study inclusion worksheet for titles and abstracts

Selection criteria worksheet to be used on titles and abstracts

Educational intervetntions for preventing catheter-related bloodstream infections in critical care

Lead author name and ref. ID number:			
Population Patients in critical care[a] with vascular catheter(s)[b]	Yes ↓ Next question	Unclear ↓ Next question	No → EXCLUDE
Design Interventional study, primary research	Yes ↓ Next question	Unclear ↓ Next question	No → EXCLUDE
Intervention Educational interventions[c] with an objective to reduce or prevent CRBSIs	Yes ↓ Next question	Unclear ↓ Next question	No → EXCLUDE
Outcomes BSIs, or mortality associated with, related to, or suspected to result from catheter use.[d]	Yes ↓ Next question	Unclear ↓ Next question	No → EXCLUDE
Final decision	**INCLUDE**	**UNCLEAR (discuss)**	**EXCLUDE**

a Any critical or intensive care[e] including high-dependency units. Excludes general wards and specialist (e.g. cardiac, neurological, surgical) non-critical units.
b Excludes studies that are solely on urinary or other non-vascular catheters. Patients with urinary or other non-vascular catheters may be included only if vascular catheters[e] are also present.
c For the purposes of this systematic review, an educational intervention is defined as any intervention that aims to prevent CRBSI and (a) includes at least an element of factual information provision related to that aim; (b) is described by the authors as educational; or (c) is described by the authors as behavioural. Includes checklists. Excludes interventions that do not target CRBSIs (e.g. interventions for hand hygiene alone). Excludes surveillance unless a relevant intervention is also reported. Excludes provision of factual information if it is unrelated to the intervention.
d Excludes BSIs[e] that are not related to vascular catheter use. Excludes non-vascular infections (e.g. urinary tract, skin), unless relevant BSIs are also reported.
e There are many possible synonyms for critical care, vascular catheters, education, and BSIs – refer to the search strategy for a full list (see *Appendix 2*).

Appendix 4 Keyword tool for evidence map study classification

1. Study identification

Reference ID:	Reviewer:
Lead author:	
Publication year:	
Intervention implementation date(s):	
Country (if USA, also the state): *Recording the state here (USA studies only) helps us to identify linked studies. Write 'multistate' if more than one, or 'state not reported' if appropriate*	
No. of critical care units:	
No. of centres (specify if not hospitals): *'Centres' here refers to the hospitals in which critical care units are sited (not the departments within hospitals, or clusters of hospitals within administrative regions). Please write the type of unit here if not a hospital*	
If one centre only, name of centre: *This information helps us to identify linked studies (it will not be systematically collected for evidence mapping)*	

2. Critical care specialties

Cardiac		*If 'Other' is selected please write the type(s) of critical care here (this will be used to update the list)*
Medical		
Neonatal		
Neurological		
Paediatric		
Surgical		
Trauma		
Mixed		
Other		
Unclear		

3. Vascular devices

Device type(s) reported		Device type refers to what type of catheter it is (e.g. CVC, PICC)
Insertion site(s) reported		Insertion site refers to the specific blood vessel in which the catheter is inserted
Lumen material reported		Lumen material refers to what the catheter tubing is made of
Lumen coating reported		Lumen coating refers to any chemical coating or impregnation of the catheter, e.g. catheters with antimicrobial or anticoagulant surfaces
Lumen no. and use reported		The number of catheter lumens can affect risk of CRBSI (unused lumens can act as a conduit for microorganisms). Select this option only if the use of all reported lumens is explained
Device changes reported		Changing catheters can increase risk of infections and other complications (e.g. pneumothorax). Select this option if any information about device changes (e.g. number, frequency, interval or reasons for changes) is reported
Device purpose(s) stated		Device purpose refers to what the catheter(s) lumen(s) are used for (e.g. drug provision, nutrition provision, haemodynamic monitoring or haemodialysis)
None of the above reported		This is a required response if none of the other options applies, to help ensure that you have systematically checked the paper and not inadvertently missed information

4. Device placement

Precritical care		Patients arrive in critical care with vascular catheters already in situ
In critical care unit		Vascular catheters are placed while patients are in the critical care unit. Select both options if catheters are placed both before and during critical care stay
Unclear		

5. Concurrent invasive devices

Urinary catheter	
Other non-vascular	
None	
Unclear	

6. Population information

Sample size: patients		This refers to the number of patients for whom relevant outcome data are presented. It may or may not reflect the number of critical care beds
Sample size: critical care staff		This refers to the number of critical care staff who receive the relevant intervention(s) (not necessarily the same as the number of critical care staff)
Attrition: patients		
Attrition: critical care staff		
None of the above reported		This is a required response if none of the other options applies, to help ensure that you have systematically checked the paper and not inadvertently missed information

7. Length of follow-up (months)

Insert a number, or state if follow-up timing is not reported or unclear

8. Type of intervention

- A 'bundle' is defined as two or more interventions that are implemented together and aim to influence the same outcome(s).
- An 'initiative' refers to two or more interventions delivered together or in a linked way such that the structure and process may appear rather complex and does not clearly fit the description of a bundle. Initiatives may include additional components in support of intervention implementation (e.g. provider collaboration strategies).

Education alone		Select this option if the intervention is purely educational
Single intervention with education component(s) or support		Select this option if there is a single intervention that contains a mix of educational and non-educational components, or a single non-educational intervention supported by education provided separately (i.e. education that supports the intervention but is not part of it)
Bundle or initiative with discrete education component(s)		Select this option if a relevant bundle or initiative to prevent BSIs is reported *and*: • one or more of the bundle or initiative components involves education, *or* • the bundle or initiative components do not themselves involve education but education is provided separately to support part or all of the bundle or initiative
Bundle or initiative with unspecified/unclear education component(s)		Select this option if a relevant bundle or initiative to prevent BSIs is reported and education is provided to support the bundle or initiative, but it is unclear to which part(s) of the bundle or initiative the education relates
Unclear		Select this option if none of the above options can be ascertained (e.g. owing to inadequate or ambiguous reporting)

9. Aim of intervention

Specifically to prevent CRBSI	
Other	

10. Study design

Select one from 'a' to 'j'; select 'k' if appropriate.

This classification is consistent with chapter 13 of the Cochrane Handbook.[58]

a. Controlled trial (including RCT, quasi-RCT, non-randomised)		A study with two or more parallel groups recruited simultaneously and matched for population characteristics, at least one of which receives a relevant intervention and at least one of which acts as a relevant comparator (e.g. no-intervention control group). As we expect to find relatively few controlled trials, this option covers both randomised and non-randomised designs
b. ITS (controlled or uncontrolled)		A study that uses observations at multiple time points before and after an intervention (the 'interruption'). The design attempts to detect whether the intervention has had an effect significantly greater than any underlying trend over time. There is no clear consensus on how many measurements are required in order to classify the design as an ITS (as the number and spacing of measurements is determined by the hypothesis of individual studies). Only select this option if the study authors call the design an ITS
c. Controlled cohort before-and-after study (CchBA) – prospective		A study with two or more separately-recruited concurrent groups (cohorts), at least one of which receives a relevant intervention, and at least one of which acts as a relevant comparator (e.g. no-intervention control group). A 'prospective' controlled cohort study recruits participants before any intervention and follows them into the future
d. Controlled cohort before-and-after study (CchBA) – retrospective		A study with two or more separately-recruited concurrent groups (cohorts), at least one of which receives a relevant intervention and at least one of which acts as a relevant comparator (e.g. no-intervention control group). A 'retrospective' controlled cohort study identifies subjects from past records describing the interventions received and follows them from the time of those records
e. Controlled cohort before-and-after study (CchBA) – unclear		A controlled cohort before-and-after study for which it is unclear whether the study was done prospectively or retrospectively
f. Cohort before-and-after study (ChBA) – prospective		A study on a single group, which is monitored before and after a relevant intervention is implemented. A 'prospective' cohort study recruits participants before any intervention and follows them into the future
g. Cohort before-and-after study (ChBA) – retrospective		A study on a single group, which is monitored before and after a relevant intervention is implemented. A 'retrospective' cohort study identifies subjects from past records describing the interventions received and follows them from the time of those records
h. Cohort before-and-after study (ChBA) – unclear		A cohort before-and-after study for which it is unclear whether the study was done prospectively or retrospectively
i. Historically controlled study		A study that compares a group of participants who received an intervention with a similar group from the past who did not

j. Design unclear		
k. Incremental or phased implementation of intervention(s)		This option identifies studies in which parts of an intervention are implemented at different times, or different interventions are introduced in a staggered or sequential fashion. It can apply to different study designs. Please select the study design above

11. Concurrent interventions

Yes		Concurrent interventions are interventions that overlap in time with the educational intervention of interest. Examples include simultaneous or overlapping implementation of interventions for CRBSI, VAP, pressure ulcers, sepsis, or glycaemic control. This option identifies studies in which confounding of interventions might be a problem
No		
Unclear		

12. Intervention appraisal

Evidence base specified		We are seeking any justification given in the paper for why this intervention is being applied in this population and setting. A statement merely that the intervention is 'evidence-based' would not be acceptable as a justification unless supported by relevant citations
Educational theory specified		
Previous development and/or testing reported		This refers only to previous primary research that has evaluated this intervention or its precursors. If only secondary research is available to justify the use of this intervention, select 'Evidence base specified' instead
Facilitators reported		Facilitators are variables measured in the study that could contribute to the intervention working as (or better than) intended (i.e. at preventing CRBSI). Examples could include positive attitudes, good compliance, possession of relevant clinical skills, or high intervention implementation fidelity
Barriers reported		Barriers are variables measured in the study that could contribute to the intervention not working as intended (i.e. not preventing CRBSI). Examples could include negative attitudes, poor compliance, lack of relevant clinical skills, high staff turnover, or low intervention implementation fidelity
Other process evaluation		A process evaluation seeks to establish why an intervention works (or does not). By definition, analysis of facilitators and barriers is part of process evaluation. 'Other process evaluation' refers to any aspects of evaluating why the intervention works (or does not) that do not clearly fit under the headings of facilitators or barriers
None of the above reported		This is a required response if none of the other options apply, to help ensure that you have systematically checked the paper and not inadvertently missed information

13. Education messages (targets)

Antimicrobial use		
Barrier precautions – full		
Barrier precautions – specific (e.g. drapes, gloves, gown)		
Catheter type selection (e.g. lumen number, chemical impregnation)		
Catheter placement procedure (e.g. use of ultrasound or X-ray; avoidance of guidewires)		
Catheter insertion site selection (e.g. avoidance of femoral site)		
Catheter insertion site preparation (e.g. chlorhexidine)		
Catheter ongoing management (e.g. flushing; hub care, including 'scrub the hub')		
Catheter need review (e.g. daily inspection; removal of unnecessary catheters)		
Checklist use [i.e. education on how to use checklist(s)]		
Central line cart use		
Documentation and auditing of processes		
Dressing selection (e.g. antimicrobial bioptach)		
Dressing care (hygiene, removal, replacement)		
Hand hygiene		
Infection prevention and/or control (including evidence-based practice; guidelines)		
Micro-organism epidemiology		
Nurse empowerment (in critical care or infection prevention)		
Team approach to catheter care		
Other		
Unclear		

14. Type(s) of education

Checklist with factual information		
CD or DVD		
Device training		
Discussion group		
Fact sheet		
Goal sheet		
In-service training		
Lecture		
Mentor led		
Peer led		
Poster		
Practical demonstration		
Residential course		
Skills practice		
Self-study module		
Simulation based		
Slide show		
Supervision		
Website		
Workshop		
Written material		
Unclear component(s)		

15. Education delivery

Providers specified		The provider is the person or technology (e.g. computer) delivering the intervention (i.e. the communicator of the information provision or practical skills training)
Recipients specified		The recipient is the staff member (or group) within the critical care unit to whom the educational intervention is directed
Neither of the above reported		This is a required response if none of the other options applies, to help ensure that you have systematically checked the paper and not inadvertently missed information

16. Education contextual support

Performance feedback (including assessment/testing)		Performance feedback refers to the provision of feedback to the person or group receiving the educational intervention on how well they are progressing with the intended learning outcomes. This includes tests or assessments (e.g. of knowledge, behaviour or skills)
Infection surveillance feedback		Infection surveillance feedback is any process whereby real-time or recent information on CRBSI infection rates is provided in support of an educational intervention. The information may be made available to intervention providers and/or recipients

17. Duration of education

Fully reported		Select this option if all educational components associated with the intervention(s) are reported sufficiently well that the total amount of time needed to implement the education can be ascertained (e.g. total number of hours required for lectures, tests and practical skills training sessions)
Partially reported		Select this option if there are several educational components associated with the intervention(s) but the duration is only reported for some of them
Unclear		Select this option if the duration is not reported for any educational components associated with the intervention(s), or is reported but unclear

18. Bloodstream infections outcomes reported

Catheter related (CRBSI)		Select this option if catheter- or central line-related BSIs are reported, irrespective of how they are defined
Catheter associated (CABSI, CLAB, CLABSI)		Select this option if catheter- or central line-associated BSIs are reported, irrespective of how they are defined
Catheter suspected BSI		Select this option if catheter- or central line-associated BSIs are reported, irrespective of how they are defined
Other or unclear		Select this option if outcomes do not match any of the above categories

19. Bloodstream infections outcome units

Rate/1000 device-days		
Rate/no. of admissions		
Rate/no. of patient-days		
Relative risk reduction		
Absolute risk reduction		
Number needed to treat		
Infections prevented		
Percentage change infection rate		
Incidence rate ratio		

20. Secondary outcomes

Attitudes		
Compliance		
Knowledge		
Skills		

21. Other outcomes

Mortality		Select this option if any type of mortality is reported (e.g. catheter related, BSI related, all cause)
Adverse events		Select this option if adverse events due to catheter use and/or BSIs are reported
LOS		Select this option if any LOS is reported (critical care or total hospital stay)

Appendix 5 Data extraction forms for clinical effectiveness studies

BURRELL (2011)[83]

Methods

Study characteristics

Lead author, publication year(s) and reference ID(s)	Burrell (2011);[83] CEC (2010)[146]
Summary of approach	A state-wide collaborative QI programme (CLAB ICU project) in Australia based on the principles of the Michigan Keystone ICU project, with top-down and bottom-up drivers of change
Location	Australia: New South Wales
Language	English
Critical care specialty	Not specified other than ICUs were primarily adult (2/37 units were paediatric)
No. of critical care units	37 ICUs (10 tertiary, 12 metropolitan, 13 rural, 2 paediatric)
No. of hospitals	Not reported
Study design	Variant of a cohort before-and-after study in which true pre-intervention data were not collected but instead the first 12 months of intervention were considered to be the baseline ('run-in' period)
Study time periods	**Pre-intervention:** No data reported **Total duration of intervention:** 18 months (July 2007 to December 2008) • 'Run-in period': July 2007 to June 2008: 12-month period from start of intervention implementation • 'Analysis period': July 2008 to December 2008: final 6-month period (assumed full implementation of intervention occurred by 12 months) **Follow-up:** None (continuous QI programme) Uptake of the project was staggered, with a small (unspecified) percentage of units late to start[146]
Funding source	New South Wales Department of Health provided funding for the CEC to implement and support the project
Conflicts of interest	Stated that none were identified

CEC, Clinical Excellence Commission.

Population and setting

Critical care unit characteristics

Not reported. General information on the characteristics of most of the participating ICUs including staffing and bed number is available in cited surveys[194,195] but the survey data cover the whole study period, not discriminating the 'run-in' and 'analysis' periods. From the surveys it appears that in addition to the two paediatric intensive care units (PICUs), adult units in New South Wales also included some paediatric patients.[194] Adult ICUs in New South Wales also appear to have included some high-dependency beds.[194]

Data are from the subset of checklists that reported insertion site (10,850 of 11,575 checklists; 93.7%).

Population and setting characteristics	Run-in period (months 1–12) (24 critical care units in month 1)	Analysis period (months 13–18) (up to 34 critical care units)	Difference between analysis and run-in periods
Patient population characteristics	Not reported	Not reported	Not reported
Device characteristics			
Insertion site – jugular	1119 (33.0%)	2452 (32.9%)	Overall effect of insertion site $p = 0.998$ (ridit analysis)
Insertion site – subclavian	999 (29.4%)	2082 (27.9%)	
Insertion site – femoral	772 (22.8%)	1875 (25.1%)	
Insertion site – cubital fossa	400 (11.8%)	809 (10.8%)	
Insertion site – other/unknown	103 (3.0%)	239 (3.2%)	
Total available data for insertion site (93.7% of the checklists that were returned)	3393 (100%)	7457 (100%)	
Insertion site antisepsis used	Not reported. A project update in an ICCMU newsletter (February 2008) noted that for one-third of central lines in the project database the line coating was not specified		
Dressing type and duration/frequency	Not reported		

ICCMU, Intensive Care Coordination and Monitoring Unit.

Intervention characteristics

Objective	To achieve a measurable reduction of CLAB in New South Wales ICUs. Initially defined by health service agreements as a 20% reduction by January 2008 and a further 80% by January 2010[146]
Main focus of education	Catheter insertion. Focusing on the preparation of the clinician (hand hygiene, barrier precautions and sterile technique) and patient [skin preparation, patient draping and catheter positioning during insertion (imaging)]. Referred to as a clinician bundle and a patient bundle, respectively
Trainers (providers)	CEC and ICCMU promoted the intervention to ICU clinicians. Project governance was provided by a steering committee, with stakeholder representation. The steering committee members and their contributions to meetings during 2007–9 are listed in the final project report.[146] ICUs developed improvement teams with physician and nursing representation from existing staff
Training of trainers	Not reported
Learners (recipients)	ICU staff ('proceduralists') who were permitted or being trained to insert CVLs (staff grades not specified)
Target behaviour change	Sterile catheter insertion procedure
Development and testing	A multidisciplinary expert group was convened to develop a guideline for CVL insertion based on existing guidelines. A checklist including the 'patient bundle' and the 'clinician bundle' was developed to support the compliance with the guideline and to collect data. The intervention was based in principle on the Michigan Keystone ICU project intervention. As a QI initiative, some aspects of development and testing ran concurrently with implementation
Educational or behavioural theory	Not reported

Educational strategies and topics targeted	Principal focus on catheter insertion guidelines supported by an insertion checklist and awareness campaign. The guideline, checklist, training framework, posters, newsletters and data collection document are available at: www.cec.health.nsw.gov.au/programs/clab-icu#resources2 (accessed October 2012) **Evidence-based percutaneous catheter insertion guideline:** Emphasised importance of hand hygiene, skin preparation and full barrier precautions (displayed prominently in some ICUs) **Checklist:** Developed and revised based on feedback from learning sessions. To facilitate data collection and ensure compliance with the guideline. Observer empowered to stop procedure if a significant breach of aseptic technique by the proceduralist. Check items were: staff competency; hat, mask and protective eyewear, hand hygiene, sterile gloves and gown, skin preparation with alcoholic chlorhexidine; full patient draping with sterile sheets; maintenance of sterile technique throughout procedure; documentation of guidewire removal; securing and dressing catheter; confirmation of catheter vascular position; complications **Education and training workshops:** Two large initial workshops in June 2007 (introduction and forging links) and November 2007 (feedback and sharing initial successes). Included open discussion of barriers to implementation and suggestions for improvement. Subsequently, smaller workshops were held to develop standard education and training approaches and an e-learning package. Some ICUs had weekly or biweekly multidisciplinary meetings to review CLABs (e.g. as reported in November 2008 ICCMU newsletter) **Training framework** (developed and improved during October 2007 to August 2008): Defining the minimum knowledge and practical skills required for CVC insertion, with catheter insertion competence assessed under supervision and documentation of feedback and learning needs in a logbook. Supported by a 1-page training support tool listing 56 competence/knowledge criteria **Posters of three types:** (1) explained the definition of CLAB; (2) explained the process for confirming CLAB including need for multidisciplinary team consultation; (3) bullet point reminders of appropriate site selection; hand hygiene; aseptic technique; maximal barrier precautions; securing and dressing of catheter; and daily assessment of need for catheter **Data collection document:** Provided an explanation of CLAB definitions; emphasised that collection and submission of CLAB data are a multidisciplinary activity involving intensive care, microbiology and infection control practitioners **Unstructured teleconferences:** Monthly for first year then bimonthly, held by the project co-ordinator **Electronic updates:** Articles in bimonthly newsletters of the ICCMU, Listserv circulars and ad hoc e-mails from the project team to participating sites
Infection surveillance feedback approach	Checklists were submitted by ICUs to the CEC project co-ordinators who prepared and disseminated surveillance reports to ICUs as they were received. The project team conducted data integrity checks and followed up missing or improbable data, and confirmed the validity of reported CLABs with individual ICUs. Outliers were identified based on CLAB numbers or incidence rates, with identified ICUs subjected to additional analyses to provide insight into causes and to promote improvement
Performance feedback approach	Monthly reports of compliance with the patient bundle and clinician bundle were provided to ICUs, starting in October 2007. Reports were also issued monthly to area health service clinical governance units and quarterly to New South Wales Health. Checklist submission was used as a proxy for participation. Validation and reliability of the reporting process not stated Within the training framework undertaken by new or unqualified staff, proceduralists were supervised before performing independent CVL insertions. The supervisor recorded feedback and learning needs in a log book
Concentration of education	Owing to the complex nature of the collaborative intervention, in which the methods adopted varied among the participating ICUs and were continuously implemented, the precise frequency and duration of all education activities cannot be established. However, sufficiently detailed information is given (if the online supporting documents are consulted) to allow numerous aspects of the programme to be repeated or adapted (including the guideline, checklist, posters and training framework). The frequency and type of meetings required is largely discernible from the information given
Non-educational intervention components	Standard sterile equipment pack made available for use across all New South Wales adult ICUs; staff empowerment to halt procedure
Costs reported	Yes. Detailed costs of the intervention for 2008 are given in an appendix to the project report

CEC, Clinical Excellence Commission; CVL, central venous line; ICCMU, Intensive Care Coordination and Monitoring Unit.

Outcome characteristics

Catheter-BSI definition
Reference cited:
O'Grady *et al.*[196]
	Based on New South Wales Department of Health 2005 and CDC surveillance definitions for CLAB (reference cited), except that only CLABs occurring in patients in the critical care unit or within 24 hours of transfer out were recorded
	• The cultured organism is not related to an infection at another site *and*
	• The presence of a recognised pathogen cultured from one or more blood cultures *or*
	• The presence of fever (> 38 °C), chills or rigors; or hypotension (episode), within 24 hours of a positive blood culture being collected and at least one of the following:
	  ○ Isolation of the same potential contaminant from two or more blood cultures drawn on separate occasions within a 48-hour period (isolates identified by suitable microbiological techniques) *or*
	  ○ Isolation of a potential contaminant from a single blood culture drawn from a patient with an intravascular line (within 48 hours of the episode) and appropriate antimicrobial therapy against the isolate is commenced

Outcomes reported	Not referred to as primary or secondary, but stated that the main outcomes were compliance with aseptic CVL insertion and rates of CLAB CLAB incidence: per 1000 central line-days; % change No. of catheters used Catheter dwell time Compliance with clinician bundle Compliance with patient bundle Adverse events (retained and broken guidewires) (data not extracted by reviewers)

CVL, central venous line.

Results data

Primary outcomes

Data are from the subset of checklists that reported central venous line (CVL) type (10,890 of 11,575 checklists; 94.1%). Date of discharge from ICU was used as a proxy for date of CVL removal if a CVL was still present at discharge. Simultaneous CVLs in the same patient were counted as a single device.

Outcome	Baseline (run-in period) (months 1–12) (24 critical care units in month 1)	Intervention (analysis period) (months 13–18) (up to 34 critical care units)	Difference between baseline (run-in) and intervention (analysis) periods
Device utilisation			
CVLs used			
Centrally inserted	2432	5289	Statistical comparison not reported
Peripherally inserted	475	992	
Dialysis	397	865	
Other and unspecified	43	82	
Total	3347	7228	
Total (range) line duration, days*			
Centrally inserted	13,174 (1–58)	29,331 (1–104)	Statistical comparison not reported
Peripherally inserted	1352 (1–37)	3365 (1–242)	
Dialysis	2215 (1–130)	4434 (1–52)	
Other and unspecified	210 (1–25)	290 (1–21)	
Total	16,951 (1–130)	37,420 (1–248)	

*Includes only inserted CVLs for which data on CVL type and line-days were available

Outcome	Baseline (run-in period) (months 1–12) (24 critical care units in month 1)	Intervention (analysis period) (months 13–18) (up to 34 critical care units)	Difference between baseline (run-in) and intervention (analysis) periods
Median (IQR) in situ period, days			
Centrally inserted	8 (8)	8 (8)	Statistical comparison not reported
Peripherally inserted	6 (10)	8 (15)	
Dialysis	9 (9)	8 (8)	
Other and unspecified	8 (10)	6 (10)	
Total	8 (8)	8 (8)	
Device-days (not reported; e-mailed by author)	First quarter 9308	Second quarter 7684	
		Third quarter 9634	
		Fourth quarter 9725	
		Fifth quarter 9589	
		Sixth quarter 8773	
No. of devices/patient	Not reported	Not reported	Not reported
CLAB incidence rate	Not reported	Not reported	Not reported
CLAB incidence per 1000 catheter-days: (a) reported; (b) e-mailed by the author	(a) First quarter 3.0 (95% CI 2.0 to 4.3)[a]	(a) Sixth quarter 1.2 (95% CI 0.6 to 2.2)[a]	(a) 60% reduction; $p = 0.0006$; χ^2 of slope = 11.71
	(b) First quarter 3.0	(b) Second quarter 2.6	
		(b) Third quarter 1.3	
		(b) Fourth quarter 1.9	
		(b) Fifth quarter 1.0	
		(b) Sixth quarter 1.3	
CLAB incidence per 1000 patient-days	Not reported	Not reported	Not reported
LOS	Not reported	Not reported	Not reported
Mortality	Not reported	Not reported	Estimated only, not measured

a Further incidence rate data reported by quarter in a graph but not extracted by reviewers.

Secondary outcomes

Outcome	Baseline (run-in period) (months 1–12) (24 critical care units in month 1)	Intervention (analysis period) (months 13–18) (up to 34 critical care units)	Difference between baseline (run-in) and intervention (analysis) periods
Reaction to education	Not a study outcome		
Attitudes	Not a study outcome		
Compliance with clinician bundle	74% (reported for a quarter but unclear which one)	81% (for last quarter of project)	7% improvement; $p < 0.0001$; χ^2 of slope = 118.83
Compliance with patient bundle	81% (reported for a quarter but unclear which one)	92% (for last quarter of project)	11% improvement; $p < 0.001$; χ^2 of slope = 108.34
Compliance with both bundles	Not reported	Not reported	1.4 times more likely in analysis period; $p = 0.0001$; χ^2 of slope = 14.325
Knowledge	Not a study outcome		
Skills	Not a study outcome		

Process evaluation

Internal evaluation revealed:[83]

- Reduced risk of CLAB if insertion was conducted by physicians compliant in both bundles: RR = 0.5 (95% CI 0.4 to 0.8); $p = 0.004$
- Increased risk of CLAB if insertion was conducted by physicians not compliant with the clinician bundle: RR = 1.62 (95% CI 1.1 to 2.4); $p = 0.018$
- Reduced risk of CLAB associated with centrally inserted CVLs: RR = 0.5 (95% CI 0.3 to 0.9); $p = 0.01$
- Increased risk of CLAB if patient had a centrally inserted CVL *and* insertion was conducted by physicians not compliant with the clinician bundle: RR = 1.99 (95% CI 1.2 to 3.2); $p = 0.004$
- Increased (but not statistically significant) risk of CLAB if patient had a peripherally inserted CVL *and* insertion was conducted by physicians not compliant with the clinician bundle: RR = 5.08 (95% CI 1.03 to 25); $p = 0.059$
- No significant difference in risk whether physicians complied with the clinician bundle but not the patient bundle, or complied with both bundles ($p = 0.891$)
- No significant risk change associated with using peripherally inserted CVLs ($p = 0.07$) or other CVL types ($p = 1.0$)
- 94.0% of cases of non-compliance with the clinician bundle were due to failure to wear a hat, mask and eyewear

Attendance at teleconferences by expert group and month was recorded and reported[146]

The following potential or actual barriers to implementation were reported, but not quantified:[146]

- Some clinicians considered the incidence of CLAB in New South Wales to be low and doubted the value of the project, as Australian practice was considered to be equal to, or better than, the methods informing the project
- Some clinicians doubted the evidence even with supportive CDC guidelines. Methodology was based on a single successful collaborative (Pronovost and colleagues[34,123,124]) without a detailed analysis of all available evidence. This allowed criticism of methodology to be an excuse for non-compliance
- Hat wearing was a contentious element of the physician bundle – clinicians cited lack of evidence for their use and four ICUs elected to omit their use as standard practice for CVL insertion
- Inadequate staffing rates in some ICUs impacted on data capture rates. Some units resisted a requirement for staff to follow up on CVLs and submit checklists. Some checklists were self-completed by proceduralists as assistance was not always available
- Difficulty was encountered in ensuring that infection surveillance definitions were applied and adhered to
- Difficulties were encountered regarding data collection and associated information technology such that the project team resorted to hard copy receipt of checklists in October 2007 and manual data entry in August 2008. The lack of a continuous and sustainable data collection system involving cross-specialty collaboration was seen as a serious risk to sustainability of the CLAB ICU principles
- Reliable baseline data did not exist prior to the project, owing to variable reporting mechanisms. Some units were hesitant to accept previously reported rates
- Frequently CLAB was reported without discussion with senior ICU staff, despite dissemination of posters and concise definition notes

Critical appraisal

Potential for bias

Group selection	Were there systematic differences between the baseline and intervention groups? NOT REPORTED If YES, were the differences between the groups adjusted for in statistical analyses (e.g. as covariates or subgroups, or stratification by propensity scores)? NOT APPLICABLE
Intervention administration	Were any confounding variables identified that could influence the effect estimate for the overall intervention? NOT REPORTED. No state-wide changes in related health policy or practice concurrent with the intervention were mentioned by the authors but it was not explicitly stated that such changes did not occur. However, although most ICUs formed improvement teams, there was variable engagement of key personnel Was the effect of educational practice separable from effects of non-educational practice? NO. Although the intervention was primarily based on educational approaches, other non-education components were included, notably a standard sterile equipment pack made for use across all New South Wales adult ICUs Were the intervention component(s) implemented as planned? PARTIALLY. Reported all-or-nothing compliance with patient and clinician bundles improved from baseline and reached 81% and 92%, respectively. However, difficulties were encountered regarding data collection and associated information technology such that the project team resorted to hard copy receipt of checklists in October 2007 and manual data entry in August 2008
Missing data	Were there systematic differences between the baseline and intervention groups in attrition or exclusions (includes withdrawal due to mortality; missing outcome data)? UNCLEAR. Device utilisation data differed between the two study periods but it is unclear whether this reflects real differences in device utilisation and/or differences in checklist returns
Outcome measurement	Were there systematic differences between the baseline and intervention groups in how outcomes were determined (including differences in how outcomes were defined)? UNCLEAR. This intervention encouraged standardisation of how outcomes were defined, detected and reported so it is difficult to identify possible bias in outcome measurement Was any blinding of personnel and/or outcome assessors reported (including assessors of blood cultures)? NO
Other possible sources of bias	Self-reporting bias: some checklists were filled in by the proceduralist, as assistance was not always available. Authors stated that as this was a QI initiative and not a study, these factors could not be controlled. Data on CVL type and line-days not available for all CVLs – unclear whether this is a possible source of bias as reasons for data non-availability not given

Other critical appraisal criteria

Methods	Intervention described in sufficient detail to be replicated? YES
	Justification given for sample size? NOT REPORTED
	Data collection process reported? PARTIALLY. Stated that data entry was manual, with an infection nurse checking data on each form. Collected data were received and collated by the CEC
	If YES or PARTIALLY, was the data collection process shown to be valid? PARTIALLY. Authors state that missing and invalid data were followed up and validity of reported CLAB were confirmed with individual ICUs. However, a quality test to review data capture was not completed by all sites and at least one tertiary unit had low data capture
	If YES or PARTIALLY, was the data collection process shown to be reliable? NO. Many ICUs did not have microbiological support and reported CLAB with discussion with senior ICU staff. Improved understanding of surveillance definitions vs. clinical definitions led to some CLABs cases to be reclassified
	Statistical tests described? PARTIALLY. Not all outcome analyses (e.g. ridit) were reported in the methods section
Results	Educational significance or effect size assessed? NOT REPORTED
	Target behaviour change achieved? PARTIALLY. Some aspects of catheter insertion procedure were complied with more extensively than others. Changing sterile hat-wearing behaviour seemed to be a particular obstacle

CEC, Clinical Excellence Commission.

Additional comments

- The project involved collaboration between the New South Wales Department of Health, the NSW Clinical Excellence Commission (CEC), ICCMU and individual ICUs.
- Following the project, an independent external project evaluation was conducted by the Centre for Clinical Governance Research University of New South Wales. This led to seven key recommendations for the operation of similar collaborative projects.
- The data reported above are from the primary research publication,[83] final project report[146] and extensive online material associated with the project: a catheter insertion guideline, checklist, training framework, posters, data collection document, and newsletters, available at: www.cec.health.nsw.gov.au/programs/clab-icu#resources2 (accessed October 2012).

COOPERSMITH (2002)[50]

Methods

Study characteristics

Lead author, publication year(s) and reference(s)	Coopersmith (2002)[50]
Summary of approach	Single unit, education initiative to decrease the primary BSI rate, based on a self-study module aimed primarily at full-time ICU nursing staff (to provide continuity given the rotation of residents and fellows in the ICU)
Location	USA, Missouri
Language	English
Critical care specialty	Surgical/burn/trauma Intensive Care Unit (ICU)
No. of critical care units	1
No. of hospitals	1
Hospital name (unless multicentre); city	Barnes-Jewish Hospital, St Louis, MO, USA
Study design	Single cohort before-and-after study
Study time periods	Baseline: January 1998 to June 1999 (18 months) Intervention: July to December 1999 (6 months) Follow-up: none (only intervention monitored)
Funding source	Stated that work was supported in part by funding from the Centers for Disease Control and Prevention Cooperative Agreement, the BJC Hospital Epidemiology and Infection Control Consortium and the National Institutes of Health
Conflicts of interest	Not reported

Population and setting

Critical care unit characteristics

University-affiliated teaching hospital with 18 ICU beds, with an average of 1400 patients admitted per year

Mean LOS: 3.8 days

Nurse to patient ratio 2 : 1, but with very high acuity levels may be 1 : 1 (at the discretion of the charge nurse)

Clinical practice: nursing staff have primary responsibility for catheter maintenance and function as bedside assistants when physicians place CVCs. CVCs placed throughout the length of the study were inserted by residents from the departments of surgery (PGY-1, PGY-2), anaesthesiology (PGY-2, PGY-3) and emergency medicine (PGY-2) as part of their 4- to 6-week rotation through the ICU. CVC placement was supervised by surgery, anaesthesiology or pulmonary critical care fellows

Use of antibiotics and antiseptics: Not reported

Stated that nursing and technician staffing patterns were similar throughout the length of the study

Patient population characteristics (not stated whether mean or median)	Baseline	Intervention	Difference between baseline and intervention
Patient census per month	121.6	115.6	Statistical significance of acuity score not mentioned; stated all other *p*-values were not statistically significant
Bed occupancy, %	85.8	83.7	
Ventilated patients per month	68.3	66.3	
Length of mechanical ventilation, days	2.5	2.8	
Patient acuity score (average of 36-indicator Medicus system)	2.9	2.9	
Male, %	59.8	55.3	
Weight, kg	78.0	80.2	
CVCs placed per month	40.2	40.4	
Device characteristics	Devices reported as CVC; PICCs were excluded from analysis. Chlorhexidine and silver sulfadiazine-impregnated catheters were inserted when patients were clinically judged to need four CVC lumens for access purposes (around 1–2%). Quadruple-lumen, antibiotic-impregnated catheters were used pre and post interventions but accessibility was 'specifically limited' after the implementation of the education		
Insertion site antisepsis used	Not reported		
Dressing type and duration/ frequency	Not reported		

Intervention characteristics

Objective	To determine whether an education initiative aimed at improving CVC insertion and care in a surgical/burn/trauma ICU can decrease the rate of primary BSIs
Main focus of education	Detailed module covering CVC insertion and maintenance, and prevention of primary BSI; aimed primarily at nurses
Trainers (providers)	Not applicable for self-study module; providers of in-service and lectures not reported
Training of trainers	Not reported
Learners (recipients)	All registered nurses in the ICU [the self-study module and tests were mandatory – but note that compliance (reported below) was not 100%]. All new nurses hired after 1/7/1999 were required to complete the study module and post test but no critical care fellow hired after this date took part in the programme; no residents placing CVCs participated in the full education module
Target behaviour change	Multiple hygienic practices associated with catheter insertion and maintenance
Development and testing	Comparison of hospital policy with CDC recommendations on insertion and care of CVCs by a multidisciplinary task force (a physician and infection control practitioners) consisting of representatives from nine hospitals in the Barnes-Jewish-Christian Health System (13 acute-care hospitals located in the St Louis area). Nurses in the ICU completed a 17-question survey about their own CVC care practice and a 13-question observation survey on physician practice that they witnessed during CVC insertion. Based on the information obtained, the task force designed an education module to improve practices related to CVC insertion and care. No pilot testing of the module was reported
Educational or behavioural theory	Not reported
Educational strategies and topics targeted	**Ten-page self-study module:** topics included epidemiology and scope of the problem, risk factors, aetiology, definition and methods to decrease risk. Risk factors specifically addressed included length of both hospitalisation and catheterisation, colonisation of insertion site and hub, and anatomical location of CVC placement. Specific risk reduction strategies addressed included hand washing and aseptic technique; methods for detecting potential clinical signs and symptoms of local infection; technique for sending catheter tip culture; routine catheter site care; replacing administration sets and fluids; cleaning and changing injection ports and Luer-lock caps; how to handle parenteral fluids and multidose vials; and procedure for drawing blood cultures. **Guidelines covered in the module:** included changing injection caps and intravenous tubing for fluids and medications every 72 hours (or immediately if blood accumulated around the cap or its integrity was compromised); replacing transparent line dressings every 7 days or gauze dressings (used solely if bleeding or oozing at the insertion site) every 48 hours; and immediate replacement of dressings that were soiled or no longer occlusive **Staff-wide in-service training:** implied that staff listened to this; content not reported Six **fact sheets** and one **poster** from the study module were displayed in the ICU **Lectures:** Given to a subset of attending physicians, fellows and a single group of residents rotating through the ICU (content, providers, duration and frequency not reported)
Infection surveillance feedback approach	Conducted during both baseline and intervention periods: Monthly updates on the ICU's infection rate and comparisons to NNIS data were presented at staff meetings
Performance feedback approach	Mandatory 20-question examination on knowledge of catheter-related bacteraemia before and after the self-study module and in-service training. Details of the examination topics were provided in a table (data not extracted by reviewers). Nurses who scored < 80% in the post-test were required to repeat the module
Concentration of education	Total time for two tests, reading the self-study module and listening to the in-service was around 1 hour (variations between staff mentioned but no further details reported). Staff scoring below 80% had to repeat the self-study module (time taken unclear). Apart for monthly BSI rate updates in the ICU, paper states that no formal programme aimed at reinforcing the material in the education module was required
Non-educational intervention components	Quadruple-lumen, antibiotic-impregnated catheters were used pre and post interventions, but accessibility was 'specifically limited' after the implementation of the education
Costs reported	No. Only a crude estimate of cost saving reported

Outcome characteristics

Catheter-BSI definition Reference cited: Pearson[197]	Infections were classified as primary or secondary based upon CDC NNIS definitions (reference cited) Primary BSI (bacteraemia) was defined as (1) recognised pathogen isolated from blood culture not related to infection at another site or (2) fever of > 38.5 °C, chills or hypotension, and either of the following: (a) common skin contaminant isolated from two blood cultures drawn on separate occasions, within 24 hours, unrelated to infection at another site, or (b) common skin contaminant isolated from a blood culture from a patient with an intravascular device and the physician institutes appropriate antimicrobial therapy Secondary bacteraemia was defined as BSI, which develops as a result of a documented infection with the same microorganism at another body site
Outcomes reported	Not stated whether primary or secondary: BSIs per 1000 catheter-days; % decrease of BSIs; primary BSIs in 6-month intervals pre and post intervention; total number of catheter-days; number of isolates and % decrease of total isolates; bacteraemia; acuity; compliance; average % correct on pre-intervention test; improvement in test scores; average increase in pre to post-test scores; identical average scores pre and post-test, average decrease scores from pre to post-test Monthly rate per 1000 CVC-days of BSIs from January 1998 to December 2000 displayed in graph format (not data extracted)

Results data

Primary outcomes

Outcome	Baseline 2188 patients; 18 months	Intervention 2095 patients; 6 months	Difference between baseline and intervention (statistics not reported unless stated)
Device duration	Not reported	Not reported	
Total device utilisation, days	6874	7044	
No. of devices/patient	Not reported	Not reported	
Total no. of primary BSI	74	26	
BSI incidence per 1000 catheter-days	10.8	3.7	66% decrease; $p < 0.0001$
BSI incidence per 1000 patient-days	Not reported	Not reported	
LOS, days	3.7	4.0	
Mortality	Not reported	Not reported	

Outcomes data for 6-month periods

	Infections per 1000 CVC-days (no. of primary BSI)	
Reporting period[a]	Baseline	Intervention
January to June 1998	11.6 (25) (for 2150 CVC-days)	
July to December 1998	11.9 (28) (for 2355 CVC-days)	
January to June 1999	8.9 (21) (for 2369 CVC-days)	
July to December 1999		5.1 (12) (for 2358 CVC-days)
January to June 2000		2.4 (6) (for 2455 CVC-days)
July to December 2000		3.6 (8) (for 2231 CVC-days)

a Monthly infection incidence per 1000 catheter-days also reported in a graph (not extracted by reviewers).

Secondary outcomes

Reaction to education	Not a study outcome		
Attitudes	Not a study outcome		
Compliance	Overall 52/66 staff (78.8%) completed the entire education module, comprising 49/56 full-time nurses (87.5%); 1/6 attending physicians (17%); and 2/4 critical care fellows (50%); 5 (9%) nurses read the study module and took only the post test 2 (3.5%) nurses read the study module but did not take any tests		
Knowledge, test scores	**Baseline**	**Intervention**	**Difference between baseline and intervention**
Average score, % correct ± SD	78.3% ± 12.9%	89.9% ± 8.3%	$p < 0.0001$ (95% CI 7.97 to 15.30)
No. (%) with higher score on post test	36 (69.2%)		Not reported
Average test score increase, % ± SD	74.0% ± 11.7% to 91.7% ± 6.9%		$p < 0.0001$ (95% CI 13.8 to 21.5)
No. (%) with identical baseline and post-intervention scores (average score 87% correct)	12 (23.1%)		Not applicable
No. (%) with decrease on % correct post intervention	4 (7.7%)		Change in average correct score from 92.5% to 85%
Average score for five nurses who took module and post test only	86%		Not reported
Skills	Not a study outcome		
Process evaluation	Compliance assessed (data above). No other process evaluation reported		

Critical appraisal

Potential for bias

Group selection	Were there systematic differences between the baseline and intervention groups? UNCLEAR. Patient age was not reported
	If YES, were the differences between the groups adjusted for in statistical analyses (e.g. as covariates or subgroups, or stratification by propensity scores)? NOT APPLICABLE
Intervention administration	Were any confounding variables identified that could influence the effect estimate for the overall intervention? YES. Authors stated that decreases in catheter-related fungaemia from 9 to 0 cases may be a reflection of changes in antibiotic prescribing patterns. The accessibility of quadruple-lumen antibiotic-coated catheters changed during the study; it was 'specifically limited' after the implementation of the education, with the authors stating they could not rule this out as a confounding influence
	Was the effect of educational practice separable from effects of non-educational practice? YES (educational intervention), assuming that the potential confounders noted above would be of negligible importance
	Were the intervention component(s) implemented as planned? PARTIALLY. Education was mandatory but compliance was not 100%
Missing data	Were there systematic differences between the baseline and intervention groups in attrition or exclusions (includes withdrawal due to mortality; missing outcome data)? NOT REPORTED
Outcome measurement	Were there systematic differences between the baseline and intervention groups in how outcomes were determined (including differences in how outcomes were defined)? YES. The authors stated: Because one definition of infection was 'common skin contaminant isolated from blood culture from patient with intravascular device and physician institutes appropriate antimicrobial therapy,' treatment of catheter colonisation could have accounted for a large number of documented infections in the pre-intervention time period. Although the meaning is unclear, it implies a procedural difference occurred between the baseline and intervention periods
	Was any blinding of personnel and/or outcome assessors reported (including assessors of blood cultures)? ICU staff not blinded, no further details reported
Other possible sources of bias	Authors stated that treatment of catheter colonisation could have accounted for a large number of documented infections in the pre-intervention period

Other critical appraisal criteria

Methods	Intervention described in sufficient detail to be replicated? NO. The content of the self-study module and tests was reasonably well described but did not precisely list the test questions asked. The in-service training and lectures were not described at all. The reported completion time of one hour on average for two 20-question tests, a 10-page self-study module and unspecified in-service training suggests that only superficial coverage of the content could have been achieved
	Justification given for sample size? NOT REPORTED
	Data collection process reported? NOT REPORTED
	If YES or PARTIALLY, was the data collection process shown to be valid? NOT APPLICABLE
	If YES or PARTIALLY, was the data collection process shown to be reliable? NOT APPLICABLE
	Statistical tests described? YES
Results	Educational significance or effect size assessed? NOT REPORTED
	Target behaviour change achieved? NOT REPORTED. The authors stated that improvement in test scores led to a change in behavioural pattern but this was based on an assumption, not on measured changes in bedside practice

Additional comments

- Monthly infection incidence data per 1000 catheter-days were reported in figure 1 of the primary study (full data not extracted by reviewers). These data indicate high month-to-month variability in incidence rates. During July, August and September 1998 baseline incidence rates were, respectively, about 5, 24 and 12 per 1000 catheter-days (data estimated from graph). During July and August 1999, incidence rates (around 9 per 1000 catheter-days) exceeded some of the monthly incidence rates in the baseline period.
- No information on what proportion of patients in either time period were completely monitored with regard to BSIs.
- Unclear whether BSI monitoring was based on blood culture monitoring in response to clinical signs or whether there was routine monitoring of factors, such as catheter tip removal.
- Unclear how long after the education module the post test was, and unclear how long the knowledge gained persisted.
- The target nurses were not involved in the development of the intervention that was aimed primarily at them.
- Rationale of intervention was that educating nurses may have had a knock-on effect on practitioners who inserted CVCs but this was not tested.
- Very limited, almost no, information on the use of antibiotics and antiseptics.
- Unclear whether staff were advised of the existence of the study.
- During development of the intervention the views of physicians who insert CVCs were not included.
- Coopersmith (2004)[87] provides additional follow-up data and suggests that compliance with evidence-based practices was poor following the initial intervention.

COOPERSMITH (2004)[87]

Methods

Study characteristics

Lead author, publication year(s) and reference ID(s)	Coopersmith (2004)[87]
Summary of approach	Single unit behavioural intervention to improve compliance with all facets of best practice of CVC insertions and maintenance (followed, but independent of, a previous intervention reported by Coopersmith (2002)[50])
Location	USA, Missouri
Language	English
Critical care specialty	SICU
No. of critical care units	1
No. of hospitals	1
Hospital name (unless multicentre); city	Barnes-Jewish Hospital, St Louis
Study design	Single cohort before-and-after study
Study time periods	Baseline: July 1999 to June 2001 (24 months)* Pre-intervention audit: November 2000 to January 2001 Intervention: July 2001 to September 2002 (15 months) Post-intervention audit: November 2001 to February 2002 Follow-up: None (continuous intervention implementation) [*Previous education intervention implemented July 1999 and monitored up to December 1999; reported by Coopersmith (2002)[50]]
Funding source	Funding received from the Centers for Disease Control and Prevention Cooperative Agreement, the BJC Hospital Epidemiology and Infection Control Consortium and the National Institutes of Health
Conflicts of interest	Not reported

SICU, surgical intensive care unit.

Population and setting

Critical care unit characteristics

Eighteen beds (staffed by 69 nurses during previous educational programme implementation), with around 1400 patients admitted per year. Extended to 24 beds by the end of the study (exact time of change not reported), with 12 attending physicians (final number of nursing staff not reported)

Average LOS: 4.3 days

Clinical practice based on an educational programme aimed at preventing CRBSIs: reported by Coopersmith *et al.*[50] (Note that there was relatively poor compliance with this – details below)

During the whole study period, CVC maintenance and site care were performed by registered nurses only. The CVCs were placed by residents from the departments of surgery (PGY-1, PGY-2), anaesthesiology (PGY-2, PGY-3) and emergency medicine (PGY-2) as part of their 4- to 6-week rotation through the ICU and a full-time nurse practitioner. CVC placement was supervised by surgery, anaesthesiology or pulmonary/critical care fellows or by ICU attending staff. CVCs were not routinely changed over guidewires at any time during the study

		Baseline	Intervention
Patient population characteristics	Male, %	49.4	56.9
	Mean age, years	54.5	57.4
	Contact isolation, %	25.2	25.0
Device characteristics (% of CVCs)		(171 CVCs in 99 patients)	(138 CVCs in 72 patients)
Insertion site	Subclavian	53	53
	Internal jugular	41	41
	Femoral	6	6
Location of catheter insertion	SICU	73	84
	Operating room	21	10
	Emergency department	1	2
	Other (hospital ward, outside hospital)	5	4
Insertion site antisepsis used:		(171 CVCs in 99 patients)	(138 CVCs in 72 patients)
Antibiotic ointment (% of CVCs)		3	4
Dressing type (% of CVCs):		(171 CVCs in 99 patients)	(138 CVCs in 72 patients)
Transparent		93	98
Gauze		3	1
Both		4	1

SICU, surgical intensive care unit.

Intervention characteristics

Objective	To improve compliance with evidence-based guidelines for CVC insertion and maintenance
Main focus of education	Specified behaviours associated with CVC insertion and maintenance (hand hygiene; barrier precautions; antibiotic ointment and dressing use; dating dressings; avoiding stopcocks)
Trainers (providers)	One or two named study authors gave lectures and hands-on demonstrations
Training of trainers	Not reported
Learners (recipients)	Nurses received lectures and hands-on demonstrations as part of their annual skills sessions. The entire resident staff of surgery and emergency medicine departments received lectures. Monthly lectures were given to all residents rotating through the ICU
Target behaviour change	Compliance with best practice for CVC maintenance for nursing staff and CVC insertion for physicians including preferred insertion site and no stopcocks, hand hygiene, maximal sterile barrier, type of catheter site dressing, and avoidance of antibiotic ointment
Development and testing	Audit tool: Development of flow charts of evidence-based best practice, detailing maintenance and insertion of CVC by a multidisciplinary team of physicians (an infection control specialist, nurses, a pharmacist and a QI specialist). Team used literature-based determination of risk factors involved in catheter infections to develop an audit tool and behaviours on the audit sheet were marked as 'yes' or 'no' (e.g. did the person inserting the CVC use appropriate hand hygiene before insertion?) Behavioural intervention: Stated only that this was based on the results of the bedside audits
Educational or behavioural theory	Not reported
Educational strategies and topics targeted	Referred to as a behavioural intervention; stressed compliance with all facets of best practice of CVC insertions and maintenance **Pictures:** Placed at end of every patient's bed, throughout the ICU, and in the manual each resident received when they rotated through the ICU. These demonstrated each step of CVC insertion (aimed at physicians) and maintenance (aimed at nursing staff) **Lectures:** Topics not reported **Hands-on demonstrations:** Topics not reported
Infection surveillance feedback approach	During both the baseline and intervention periods: BSI rates and comparison with national rates using NNIS data were presented on a monthly basis at multidisciplinary staff meetings
Performance feedback approach	Not included in intervention. Audits of compliance informed the development of the intervention but audit results were not reported to have been directly fed back to the ICU teams
Concentration of education	Lectures and hands-on demonstrations were given to nurses as part of their annual skills sessions. Lectures of unspecified frequency were given to the entire resident staff in the departments of surgery and emergency medicine and monthly lectures were given to all residents rotating through the ICU. Frequency and duration of sessions not reported. Reinforcement of sessions (e.g. whether annual repetition) not reported
Non-educational intervention components	None – intervention purely educational
Costs reported	Not reported

Outcome characteristics

Catheter-BSI definition Reference cited: Pearson[197]	BSIs were classified as primary or secondary on the basis of NNIS definitions (reference cited). CRBSI defined as: a microorganism isolated from a blood culture not related to distant infection, or: 1. a fever > 38.5 °C, chills, or hypotension, and either: 2. a common skin contaminant (typically a coagulase-negative *Staphylococcus* species) isolated from two blood cultures drawn at separate times within 24 hours unrelated to distant infection or isolated from a blood culture in a patient with a CVC and treated by the attending ICU physician with a full course of antibiotics. BSIs with documented distant infection with the same pathogen were characterised as secondary bacteraemias
Outcomes reported	*Primary outcome*: Compliance with practices known to decrease CRBSI (appropriate hand hygiene, sterile gown, mask, sterile gloves, large sterile drape, absence of antibiotic ointment, catheter sutured in, transparent dressing appropriately placed) *Secondary outcome*: CRBSI rate for all ICU patients

Results data

Primary outcomes

Outcome		Baseline (24 months), 2716 patients, 9353 catheter-days	Intervention (15 months), 1773 patients, 6152 catheter-days	Difference between baseline and intervention
Device duration (days), %	< 7 days	62.9	57.8	
	7–10 days	29.4	35.9	
	> 10 days	7.7	6.3	
	Days in place, mean	6.0	6.3	
Total device utilisation, CVC-days		9353 (*n* = 2716)	6152 (*n* = 1773)	
No. of devices/patient		Not reported	Not reported	
CRBSI incidence rate		32	17	
Incidence per 1000 catheter-days		3.4	2.8	*p* = 0.40
Incidence per 1000 patient-days		Not reported	Not reported	
LOS		Not reported	Not reported	
Mortality		Not reported	Not reported	

Additional primary outcomes data

Device duration (% of CVCs) – data from randomly selected subsets of patients	Baseline (3 months), 99 patients, 171 CVCs	Intervention (4 months), 72 patients, 138 CVCs	Difference between baseline and intervention (not reported unless indicated)
< 7 days	62.9%	57.8%	Statistics not reported
7–10 days	29.4%	35.9%	
> 10 days	7.7%	6.3%	
Mean duration, days	6.0	6.3	

Secondary outcomes

Compliance with target behaviour (number (%) of CVCs) – data from randomly selected subsets of CVCs	Baseline (3 months), six CVCs, six patients	Intervention (4 months) 10 CVCs, 10 patients	Difference between baseline and intervention
Appropriate hand hygiene	1 (17%)	3 (30%)	Statistics not reported
Sterile gown	6 (100%)	10 (100%)	
Mask	6 (100%)	10 (100%)	
Sterile gloves	6 (100%)	10 (100%)	
Large sterile drape	3 (50%)	8 (80%)	
Absence of antibiotic ointment	6 (100%)	10 (100%)	
Catheter sutured in	5 (83%)	10 (100%)	
Transparent dressing appropriately placed	6 (100%)	10 (100%)	

Compliance with target behaviour associated with CVC insertion (% of CVCs) – data from randomly selected subsets of patients	Baseline (3 months), 99 patients, 171 CVCs	Intervention (4 months), 72 patients, 138 CVCs	Difference between baseline and intervention
Properly dating the CVC dressing	11%	21%	$p < 0.001$
Stopcock use (avoidance of)	70%	24%	$p < 0.001$
Appropriate hand hygiene use	17%	30%	$p > 0.99$
Maximal sterile barrier precautions	50%	80%	$p = 0.29$
Reaction to education	Not a study outcome		
Attitudes	Not a study outcome		
Knowledge	Not a study outcome		
Skills	Not a study outcome		
Process evaluation	No other process evaluation apart from the random audits, which suggested lack of compliance with target behaviours may have been a barrier (data above)		

Critical appraisal

Potential for bias

Selection bias	Were there systematic differences between the baseline and intervention groups? UNCLEAR. Authors stated that patient demographics were similar throughout the course of the study but limited data were reported, with no indication of patients' health status. Random subsets of patients and CVC insertions were used for reporting outcomes in the baseline and intervention groups but no information was provided on how random selection was achieved
	If YES, were the differences between the groups adjusted for in statistical analyses (e.g. as covariates or subgroups, or stratification by propensity scores)? NOT APPLICABLE
Intervention administration	Were any confounding variables identified that could influence the estimate for the overall intervention? YES. There were six additional ICU beds in the intervention period (33% increase) but staff numbers and staff to patient ratios were not reported. The number CVCs inserted in the ICU increased by 9%, whereas those inserted in the operating room decreased by 11%
	Was the effect of educational practice separable from effects of non-educational practice? YES. The intervention comprised purely educational components. However, the reduction in infection rates was not statistically significant
	Were the intervention component(s) implemented as planned? UNCLEAR. Stated in methods section that lectures and hands-on demonstrations were given to nurses as part of their annual skills sessions by two of the authors and also to all staff in departments of emergency medicine and surgery, and monthly lectures were given to all residents rotating through the ICU. However, no details of attendance for lectures or hands-on demonstrations were reported
Missing data	Were there systematic differences between the baseline and intervention groups in data availability? UNCLEAR. For CRBSI data it appears that all patients in the ICU were monitored. However, for behavioural outcomes subgroups of patients and CVCs were randomly selected but no details were provided on how random selection was carried out
Outcome measurement	Were there systematic differences between the baseline and intervention groups in how outcomes were determined (including differences in how outcomes were defined)? NOT REPORTED
	Was any blinding of personnel and/or outcome assessors reported (including assessors of blood cultures)? NOT REPORTED
Other possible sources of bias	Were any other sources of bias present? YES. The authors reported a potential investigator bias, as the audit tool was administered by members of the team that designed the intervention and audit tool. Authors stated that knowledge of observations alone could alter staff behaviours. Intervention took place 24 months after a previous educational programme targeting CRBSIs

Other critical appraisal criteria

Methods	Intervention described in sufficient detail to be replicated? NO. Pictures of the CVC insertion process were mentioned but no details of the content of lectures and hands-on demonstrations were reported so the mechanisms for eliciting the target behaviour changes are unclear
	Justification given for sample size? NOT REPORTED
	Data collection process reported? NOT REPORTED. The authors stated only that the audit tool was administered by members of the team who designed the intervention and the audit tool
	If YES or PARTIALLY, was the data collection process shown to be valid? NOT APPLICABLE
	If YES or PARTIALLY, was the data collection process shown to be reliable? NOT APPLICABLE
	Statistical tests described? YES
	Educational significance or effect size assessed? NOT REPORTED
	Target behaviour change achieved? PARTIALLY. Compliance with all target behaviours increased following implementation of the intervention but for hand hygiene and dating of dressings the improvements were small, and post-intervention compliance was only 30% and 21%, respectively

Additional comments

- Authors commented that the diffuseness of the behavioural intervention message may have reduced the impact on CRBSI rates.
- Monthly infection incidence data reported in a graph – illustrates high temporal variability in BSI incidence, with incidence rates in some months post intervention implementation being higher than some baseline rates.
- Unclear whether staff were advised of the existence of the study.

DUBOSE (2008)[93]

Methods

Study characteristics

Lead author, publication year(s) and reference(s)	DuBose (2008)[93]
Summary of approach	Single-unit daily quality rounds checklist to increase compliance with prophylactic measures for prevention of VAP, deep venous thrombosis or pulmonary embolism, central line infection and other ICU complications
Location	USA: California
Language	English
Critical care specialty	Trauma
No. of critical care units	1
No. of hospitals	1
Hospital name (unless multicentre); city	Division of Trauma Surgery and Surgical Critical Care, University of Southern California, Los Angeles
Study design	Single cohort before-and-after study
Study time periods	Baseline: 1 month (date not reported) Intervention: 3 months (date not reported) Follow-up: None (monitoring only during intervention)
Funding source	Not reported
Conflicts of interest	Not reported

Population and setting

Critical care unit characteristics (stated only that unit was a high-volume level I trauma centre)		Baseline (1 month)	Intervention month 1	Intervention month 2	Intervention month 3
Patient population characteristics	ICU patient-days surveyed	244	185	188	193
	Mean age, years	41.1	41.0	41.6	40.3
	Gender, % male	73.0	76.8	67.0	78.9
	Mean injury severity score	17.3	20.9	15.0	16.1
Device characteristics		CVCs routinely used were antimicrobial-coated (ARROWgard Blue PLUS Multi-lumen, antimicrobial surface-coated using chlorhexidine, chlorhexidine acetate, and silver sulfadiazine) and placed directly through an introducer (ARROW percutaneous sheath introducer kit 8.5 Fr). All routine catheters were placed with full barrier precautions, and catheters placed in emergency situations where the use of full barrier precautions was not documented were removed within 24 hours			
Insertion site antisepsis used		Not reported			
Dressing type and duration/frequency		Not reported			

Intervention characteristics

Objective	To increase compliance with measures that aim to reduce ICU complications and identify areas for improvement in quality of care
Main focus of education	General: to reduce ICU complications. Prevention of CRBSI was a relatively minor part (2/16 checklist items were relevant)
Trainers (providers)	Not explicitly stated; appears to have involved the multidisciplinary team noted below under development and testing and/or the trauma and surgical critical care QI committee. Stated surgical critical care fellows acted as 'champions' of daily prophylaxis
Training of trainers	Not reported
Learners (recipients)	Checklists were completed by ICU fellows and their team of residents and medical students on the daily rounding basis
Target behaviour change	General: Sixteen different activities for reducing complications in the ICU
Development and testing	A multidisciplinary team of care providers that included intensivists, trauma surgeons, nursing staff and a biostatistician conducted a comprehensive review of best-practices data to identify items to be included in the checklist
Educational or behavioural theory	Not reported
Educational strategies and topics targeted	**Daily quality rounds checklist.** Listed 16 evidence-based measures for preventing ICU complications. Of these, two were relevant to prevention of central line infections: checking the central line day and checking the continued need for invasive devices **Monthly review of deficiencies** by a multidisciplinary team of intensivists, trauma surgeons, nursing staff and a biostatistician resulted in the highlighting of those measures most clearly requiring more focused effort. Improvements were then designed and implemented following discussion Training on new protocol strategies and improvement of existing approaches (no details given)
Infection surveillance feedback	Not included
Performance feedback	Unclear. Some feedback of process was mentioned for insulin management; results appear to have been fed back monthly to the trauma and surgical critical care QI committee – unclear whether and how disseminated to ICU staff. Paper checklists were completed by an ICU fellow and manually entered into an Excel database
Concentration of education	The initial time required for completion of the checklist and institution of corrective changes averaged approximately 1 hour per day. With familiarity, after the first few weeks of use, the time decreased to 20–30 minutes per day. This equated to approximately two additional minutes per patient
Non-educational intervention components	None. However, the majority of checklist topics were not directly relevant to catheter BSIs
Costs reported	No, but authors stated that the cost was quite minimal: the completion of the checklist represented little additional burden on the ICU fellow and did not significantly alter nursing workloads

Outcome characteristics

Catheter-BSI definition	Central-line related infection: Positive blood cultures with a recognised pathogen without evidence of alternative septic source must be documented, and the catheter must have been in place for > 48 hours
Outcomes reported	Not stated whether primary or secondary: • CLABSI rate • CVC duration • VAP rate[a] • Self-extubation rate[a] • Mechanical ventilation duration[a] • Compliance with VAP bundle (head of bed angle, sedation holiday, peptic ulcer disease prophylaxis, deep-vein thrombosis prophylaxis)[a]

a Data not extracted by reviewers.

Results data

Primary outcomes

Outcome		Baseline (3 months; dates not reported)	Intervention (3 months; dates not reported)	Difference between baseline and intervention
CVC duration	% lines > 24 hours	89.4	88.4 (86.2 = result for first month of intervention)	Statistical test of difference not reported
	% lines > 48 hours	74.1	68.4 (64.1 = result for first month of intervention)	
	% lines > 72 hours	62.4	52.8 (49.1 = result for first month of intervention)	
Total device utilisation		Not reported	Not reported	Not reported
No. of devices/patient		Not reported	Not reported	Not reported
Mean monthly central line-associated BSI [central line-related infection] incidence rate per 1000 device-days[a]		8.9[b] 11.3[b]	5.8	Statistical test of difference not reported
Incidence per 1000 patient-days		Not reported	Not reported	Not reported
LOS		Not reported	Not reported	Not reported
Mortality		Not reported	Not reported	Not reported

a Two descriptions (device-related and device-associated infections) were given for the same outcome.
b Two different values were reported for the same outcome (the value of 11.3 appeared both in the abstract and results; the value of 8.9 in the results only).

Secondary outcomes

Reaction to education	Not a study outcome
Attitudes	Not a study outcome
Compliance	Compliance with daily CVC site evaluation according to a previously established quality assurance pathway exceeded 95% [not stated which time period(s) this referred to] Compliance was reported in more detail for VAP prevention (data not extracted by reviewers)
Knowledge	Not a study outcome
Skills	Not a study outcome
Process evaluation	Not a study outcome

Critical appraisal

Potential for bias

Group selection	Were there systematic differences between the baseline and intervention groups? UNCLEAR. Reported that demographic characteristics 'remained constant' between groups but limited data given (the maximum difference in mean age between the baseline and intervention periods was 1.3 years; the maximum difference in injury severity score was 4.8; and the maximum difference in the proportion male was 11.9%) If YES, were the differences between the groups adjusted for in statistical analyses (e.g. as covariates or subgroups, or stratification by propensity scores)? NOT APPLICABLE
Intervention administration	Were any confounding variables identified that could influence the effect estimate for the overall intervention? NOT APPLICABLE Was the effect of educational practice separable from effects of non-educational practice? YES. Only a checklist (i.e. educational) was used (although only 2 of the 16 checklist items concerned catheter BSIs) Were the intervention component(s) implemented as planned? NOT REPORTED. Compliance with the checklist was not reported
Missing data	Were there systematic differences between the baseline and intervention groups in data availability? UNCLEAR. The number of checklists completed and entered into the database was not reported
Outcome measurement	Were there systematic differences between the baseline and intervention groups in how outcomes were determined (including differences in how outcomes were defined)? NO. States that a standard definition of infections was used throughout the study and all potential nosocomial infections, central line-related infections and VAP were diagnosed by the hospital epidemiology service Was any blinding of personnel and/or outcome assessors reported (including assessors of blood cultures)? YES. The checklist was used by an ICU fellow not directly involved in patient care for 1 month during the baseline period to establish pre-intervention compliance. During this period only, nursing and clinical staff were blinded to the use of the checklist
Other possible sources of bias	No other sources of bias were reported by the authors or identified by the reviewers based on the information presented

Other critical appraisal criteria

Methods	Intervention described in sufficient detail to be replicated? YES. The intervention consisted principally of a checklist that could be reproduced or adapted Justification given for sample size? NOT REPORTED Data collection process reported? NOT REPORTED. Stated only that compliance of the nursing staff in the completion of specified measures was ensured by the monitoring of a unit nurse manager through a previously established quality assurance pathway (details not reported) If YES or PARTIALLY, was the data collection process shown to be valid? NOT REPORTED If YES or PARTIALLY, was the data collection process shown to be reliable? NOT REPORTED Statistical tests described? NO
Results	Educational significance or effect size assessed? NOT REPORTED Target behaviour change achieved? UNCLEAR. Some aspects of practice for reducing complications in the ICU were complied with more extensively than others. Primarily reported compliance data for a VAP intervention (data not extracted by reviewers). Compliance with daily CVC site evaluation (assessed according to a previously established quality assurance pathway) was reported to have only exceeded 95%, but it is not clear by how much compliance had increased or to which time period(s) of the study this refers

EGGIMANN (2000–5)[94,95]

Methods

Study characteristics

Lead author, publication year(s) and reference(s)	Eggimann (2000);[94] Eggimann (2005)[95]
Summary of approach	Single unit educational intervention consisting primarily of short slide shows and bedside education
Location	Switzerland
Language	English
Critical care specialty	Medical
No. of critical care units	1
No. of hospitals	1
Hospital name (unless multicentre); city	University of Geneva Hospital; Geneva
Study design	Single cohort before-and-after study
Study time periods	Baseline: October 1995 to February 1997 (16 months) Intervention: March 1997 to October 1997 (8 months)[94] Intervention continuation: March 1997 to 2002 (month unspecified) (total duration approximately 6 years)[95] Follow-up: None (continuous monitoring of intervention)
Funding source	Lead author was supported in part by a grant from G and L Hirsch, Geneva, Switzerland during the preparation of the paper. Co-author (Harbarth) was supported by a grant from the Max-Kade Foundation, New York, USA during the preparation of the paper. The intervention continuation was supported in part by a grant from the Swiss National Science Foundation
Conflicts of interest	Stated in the intervention continuation report[95] that no potential financial conflicts of interest were disclosed

Population and setting

Critical care unit characteristics	18 beds in a MICU at a 1500-bed primary care and tertiary care centre Average of 1400 patients per year admitted to the ICU Mean LOS 4 days (further data in Results section) All vascular lines were inserted by advanced internal medicine residents or fellows in the MICU; there was no change in the physicians' profile between the study periods Device insertion and management were based on institutional written guidelines promulgated by the nursing department *Material preparation*: Based on physicians' individual preferences *Patient positioning*: According to nursing habits acquired elsewhere *Skin preparation*: Hair shaving *Barrier precautions*: Sterile gloves, small fenestrated sheets, paper mask *Insertion technique*: Various techniques; no specific training *Device replacement*: Every 24 hours for all administration sets and devices. *Device removal*: Peripheral line after 3–5 days; no specific recommendation for central lines *Hand hygiene*: With surgical soap in sink before and after each patient care, or hand disinfection

Patient population characteristics: all adult patients admitted to the MICU for more than 48 hours	Baseline: October 1995 to February 1997 (16 months), 2104 patients	Intervention: April to November 1997 (8 months), 1050 patients	Difference between baseline and intervention: total patient-days for baseline and intervention = 13,200
No. of patients			
Unstable angina	554 (26%)	296 (28%)	Difference in number of patients not statistically significant
Myocardial infarction	406 (19%)	218 (21%)	
Cardiac monitoring	222 (11%)	116 (11%)	
Cardiac arrest	48 (2.3%)	32 (3.0%)	
Hypertensive crisis	76 (3.6%)	25 (2.3%)	
Acute heart failure	55 (2.6%)	41 (3.9%)	
Acute respiratory insufficiency	122 (5.8%)	74 (7.1%)	
Asthma	54 (2.6%)	19 (1.8%)	
COPD	54 (2.6%)	15 (1.4%)	
ARDS	20 (1.0%)	9 (0.9%)	
Neurological – intoxication	106 (5.0%)	55 (5.2%)	
Neurological – miscellaneous	105 (5.0%)	42 (4.0%)	
Infections	98 (4.7%)	32 (3.0%)	
Other disorders	184 (8.7%)	76 (7.2%)	
Total patients	2104	1050	
Age, years, mean (SD)			
Unstable angina	66 (12)	66 (12)	Differences in age not statistically significant except *$p < 0.05$
Myocardial infarction	63 (13)	67 (13)*	
Cardiac monitoring	68 (14)	67 (13)	
Cardiac arrest	68 (14)	65 (15)	
Hypertensive crisis	57 (21)	58 (17)	
Acute heart failure	70 (10)	73 (8)	
Acute respiratory insufficiency	63 (14)	67 (13)	
Asthma	45 (18)	36 (14)	
COPD	66 (13)	66 (10) 49 (14)	
ARDS	42 (17)	42 (20)	
Neurological – intoxication	38 (16)	56 (19)	
Neurological – miscellaneous	58 (17)	57 (16)	
Infections	54 (18)	57 (17)	
Other disorders	56 (18)	63 (16)*	
Total patients	62 (16)	66 (12)	

Patient population characteristics: all adult patients admitted to the MICU for more than 48 hours	Baseline: October 1995 to February 1997 (16 months), 2104 patients	Intervention: April to November 1997 (8 months), 1050 patients	Difference between baseline and intervention: total patient-days for baseline and intervention = 13,200
No. mechanically ventilated			
Unstable angina	5 (0.9%)	3 (0.9%)	Differences in number mechanically ventilated not statistically significant except *$p < 0.05$
Myocardial infarction	54 (13%)	15 (7.0%)*	
Cardiac monitoring	7 (3.2%)	1 (0.8%)	
Cardiac arrest	43 (90%)	30 (94%)	
Hypertensive crisis	9 (12%)	3 (12%)	
Acute heart failure	26 (47%)	16 (39%)	
Acute respiratory insufficiency	59 (48%)	28 (38%)	
Asthma	12 (22%)	4 (21%)	
COPD	9 (17%)	2 (13%)	
ARDS	2 (100%)	9 (100%)	
Neurological – intoxication	35 (33%)	17 (31%)	
Neurological – miscellaneous	68 (65%)	25 (60%)	
Infections	59 (60%)	20 (63%)	
Other disorders	33 (18%)	24 (32%)*	
Total patients	439 (21%)	194 (19%)	
Nursing workload: mean (SD; range) monthly Research in Nursing system scores:	188 (66; 152–210)	191 (61; 178–207)	
Device characteristics	A total of 3154 patients in the study (baseline and intervention combined) had at least one intravenous device inserted, 966 (31%) were exposed to arterial lines and 1121 (35%) to CVCs, with similar proportions in the baseline and intervention periods		
Insertion site antisepsis used	Povidone–iodine or chlorhexidine gluconate		
Dressing type and duration/ frequency	Several types according to individual non-standardised criteria. Transparent occlusive dressings or preprepared devices for peripheral lines. Dressing replacement every 24 hours		

Intervention characteristics

Objective	To decrease rates of vascular-access infections using a multimodal, multidisciplinary prevention strategy and to assess the impact of the strategy on the incidence of ICU-acquired infections
Main focus of education	Prevention of ICU acquired infections, including those associated vascular catheter insertion, maintenance and use
Trainers (providers)	Five named study authors carried out the educational intervention
Training of trainers	Not reported directly but the identity of the trainers was reported so their expertise could be checked (three authors wrote and five authors reviewed the guidelines)
Learners (recipients)	All ICU staff received the slide shows and practical demonstrations: 21 fellows or residents, 82 nurses and 15 nursing assistants
Target behaviour change	Behaviours associated with the insertion, maintenance and use of vascular catheters
Development and testing	Not reported
Educational or behavioural theory	Not reported
Educational strategies and topics targeted	30-minute slide shows complemented by individual bedside teaching.* Topics covered were: • *Material preparation*: in advance to avoid any interruption during insertion • *Patient positioning*: followed recommendations to permit optimum access to the insertion site; presence of nurse to assist physician mandatory • *Skin preparation*: hair cutting instead of shaving; use of chlorhexidine gluconate • *Maximal barrier precautions*: sterile gloves, gown, cap, mask, and large sheet used for all but peripheral lines • *Insertion site selection*: subclavian or wrist vein as standard • *Device replacement*: every 72 hours for administration sets and devices; 24 hours for lipid emulsion • *Device removal*: as clinically indicated for central lines, not routinely, with prompt removal of any device not intended for use recommended; peripheral lines after 72 hours systematically • *Hand hygiene*: hand disinfection strongly emphasised before and after any care; hand washing for soiled hands to be followed by hand disinfection • *Dressings*: dry gauze covered by a non-occlusive adhesive band. Replaced every 72 hours except for the first dressing after catheter insertion (*Practical demonstration mentioned but no details reported)
Infection surveillance feedback approach	Not included in intervention
Performance feedback approach	Not included in intervention
Concentration of education	Education comprised 30-minute slide show sessions and unspecified bedside teaching sessions given to all staff. Frequency of slide shows unclear; not stated whether sessions were repeated annually or at other intervals for staff who had already been trained
Non-educational intervention components	None
Costs reported	No

Outcome characteristics

Catheter-BSI definition	The infection was regarded as ICU acquired if it occurred within 48 hours of discharge from the ICU. Primary BSIs were defined as bacteraemia (or fungaemia) for which there was no documented distal source, and included infections resulting from insertion of an intravenous or arterial line. The infection was categorised either as microbiologically documented or as clinical sepsis. CRBSI were those for which the same organism had been isolated from a quantitative culture of the distal catheter segment, and from the blood of a patient with clinical symptoms and no other apparent source of infection. In the absence of catheter culture, defervescence after removal of an implicated catheter from a patient with a BSI was regarded as indirect evidence of infection. Catheter exit site infection, catheter colonisation and clinical sepsis were also defined Infections were defined according to Garner *et al*.[147]
Outcomes reported	Not stated whether primary or secondary: • BSI incidence (defined as microbiologically documented bacteraemia) • LOS • Mortality • Catheter exit site infections* • Bloodstream infections related to clinical sepsis (i.e. other than microbiologically documented)* • Respiratory infections* • Urinary tract infections* • Skin or mucous membrane infections* • Miscellaneous infections* • Total ICU-acquired infections* (*Data not extracted by reviewers)

Results data

Primary outcomes

Outcome		Baseline: October 1995 to February 1997 (16 months), 2104 patients	Intervention: April to November 1997 (8 months), 1050 patients (longer-term data also reported[94])	Difference between baseline and intervention: relative risk (95% CI)
Device duration, days, median		8	7	
Exposure to CVCs, days, median		4	4	
Total device utilisation		Not reported	Not reported	
No. of devices/patient		Not reported	Not reported	
BSI per 1000 CVC-days, mean (95% CI)	(a) Initial data from Eggimann (2000)[94] (b) Longer-term data from Eggimann (2005)[95]	(a) 6.6 (b) 6.3 (4.0 to 9.4)	(a) 2.3 (b) Annual rates: 1997: 2.9 (0.8 to 7.3) 1998: Not reported 1999: 2.4 (1.0 to 4.7) 2000: 2.7 (0.9 to 6.3) 2001: 1.7 (0.5 to 3.9) 2002: 3.4 (1.7 to 6.1)	(a) Not reported (b) Average rate reduction over the study period 56% (range 46% to 63%); no statistical tests of differences reported
[Note: Data for calculating CIs of risk ratios (presented in the main report) were not reported by Eggimann *et al.*[95] but were obtained by contacting the study authors (see *Appendix 7*)]				
BSI incidence per 1000 patient-days		Not reported	Not reported	
LOS, days, mean (SD)				
Unstable angina		2.6 (2.7)	2.7 (1.3)	Differences not statistically significant
Myocardial infarction		3.8 (3.6)	3.6 (2.5)	
Cardiac monitoring		2.1 (1.7)	2.3 (1.6)	
Cardiac arrest		6.0 (5.6)	6.0 (4.8)	
Hypertensive crisis		6.1 (14.0)	2.8 (1.2)	
Acute heart failure		5.4 (5.3)	5.2 (4.4)	
Acute respiratory insufficiency		9.0 (8.2)	8.2 (8.5)	
Asthma		3.9 (3.3)	3.5 (2.0)	
COPD		7.6 (6.0)	6.1 (2.9)	
ARDS		13.6 (12.0)	13.8 (9.7)	
Neurological – intoxication		3.5 (7.1)	2.6 (1.4)	
Neurological – miscellaneous		5.8 (8.2)	5.0 (3.6)	
Infections		5.3 (4.4)	8.3 (8.6)	
Other disorders		4.0 (6.4)	3.8 (3.4)	
Total patients		4.1 (5.8)	3.9 (4.2)	

Outcome	Baseline: October 1995 to February 1997 (16 months), 2104 patients	Intervention: April to November 1997 (8 months), 1050 patients	Difference between baseline and intervention: relative risk (95% CI)
Mortality (no. of ICU deaths)			
Unstable angina	2 (0.4%)	1 (0.3%)	Differences not statistically significant except $*p < 0.05$
Myocardial infarction	31 (7.6%)	9 (4.1%)	
Cardiac monitoring	4 (1.8%)	0	
Cardiac arrest	15 (31%)	19 (59%)*	
Hypertensive crisis	7 (9.2%)	3 (12%)	
Acute heart failure	2 (3.6%)	2 (4.9%)	
Acute respiratory insufficiency	19 (16%)	10 (14%)	
Asthma	0	0	
COPD	3 (5.6%)	0	
ARDS	13 (65%)	5 (56%)	
Neurological – intoxication	2 (1.9%)	0	
Neurological – miscellaneous	16 (15%)	6 (14%)	
Infections	33 (34%)	11 (34%)	
Other disorders	12 (6.5%)	7 (9.2%)	
Total patients	159 (7.6%)	71 (6.8%)	

Secondary outcomes

Reaction to education	Not a study outcome
Attitudes	Not a study outcome
Compliance	Not a study outcome
Knowledge	Not a study outcome
Skills	Not a study outcome
Process evaluation	Not a study outcome

Critical appraisal

Potential for bias

Group selection	Were there systematic differences between the baseline and intervention groups? NO. The groups were similar with respect to number of patients per month, age, number mechanically ventilated, LOS, infection risk factors and mortality If YES, were the differences between the groups adjusted for in statistical analyses (e.g. as covariates or subgroups, or stratification by propensity scores)? NOT APPLICABLE
Intervention administration	Were any confounding variables identified that could influence the effect estimate for the overall intervention? NO. The authors stated that there were no changes in the physicians' profile or in nursing workload. A hospital-wide campaign to improve compliance with hand hygiene practices was introduced before the start of the baseline period. Monitoring infection incidence in a SICU at the same hospital revealed no changes over time in infection incidence rates, suggesting that those observed in the study ICU did not result from external factors Was the effect of educational practice separable from effects of non-educational practice? YES. The intervention was purely educational Were the intervention component(s) implemented as planned? NOT REPORTED
Missing data	Were there systematic differences between the baseline and intervention groups in data availability? NO. The number of patients in the baseline and intervention periods did not differ noticeably (quantitative data reported). Infection surveillance involved all patients (dedicated chart for each patient). Mortality rates were slightly but not statistically significantly lower in the intervention period. Data on the number of devices per patient were not separable by baseline and intervention period
Outcome measurement	Were there systematic differences between the baseline and intervention groups in how outcomes were determined (including differences in how outcomes were defined)? UNCLEAR. The annual incidence rates reported by Eggiman (2005)[95] do not specify which months were used in the measurement ranges: it is unclear whether the 1997 data were adjusted to account for 1997 comprising only 9 months of intervention (since the first 3 months were part of the baseline period) Was any blinding of personnel and/or outcome assessors reported (including assessors of blood cultures)? NO
Other possible sources of bias	No other sources of bias were reported by the authors or identified by the reviewers based on the information presented

SICU, surgical intensive care unit.

Other critical appraisal criteria

Methods	Intervention described in sufficient detail to be replicated? NO. The educational characteristics of the bedside education sessions were not reported. The extent of education reinforcement needed (how often staff were re-educated) to achieve the reported changes in infection rates was not reported. The main components of the slide show were reported but a copy of the slide show was not provided
	Justification given for sample size? NOT REPORTED
	Data collection process reported? PARTIALLY. Surveillance of nosocomial infections was conducted by two named infection control nurses who visited the ICU daily and completed a dedicated surveillance chart for each patient. Surveillance was continued until 5 days after discharge to detect incubating infections attributable to ICU stay. All surveillance records were prospectively reviewed and validated by two named infection control physicians
	If YES or PARTIALLY, was the data collection process shown to be valid? NOT REPORTED
	If YES or PARTIALLY, was the data collection process shown to be reliable? YES. Surveillance methods were pretested and standardised in several pilot phases. Interobserver variability was assessed during three separate periods when the two observers worked simultaneously. Inter-rater reliability was high for all infections (κ = 0.89; range 0.78–1.0)
	Statistical tests described? YES
Results	Educational significance or effect size assessed? NOT REPORTED
	Target behaviour change achieved? UNCLEAR. Information on compliance or other aspects of process was not reported

GALPERN (2008)[97]

Methods

Study characteristics

Lead author, publication year(s) and reference ID(s)	Galpern (2008)[97]
Summary of approach	Single unit central line bundle implementation (proposed by Greater New York Hospital Association) to decrease CLABSIs
Location (country, state/region)	USA, New York
Language	English
Critical care specialty	Mentions SICU, but in discussion of question and answer section states that it included a MICU and a CCU
No. of critical care units	3 (medical–surgical, mixed across three locations; and cardiac) (not reported in the publication – information provided by the author)
No. of hospitals	1
Hospital name (unless multicentre); city	Methodist Hospital, Brooklyn, New York
Study design	Single cohort before-and-after study
Study time periods	Baseline: February to June 2005 (5 months) Intervention: July 2005 to February 2006 (19 months) Infection surveillance: 1 February 2005 to 31 April 2007 (26 months) Follow-up: Unclear (not explicitly stated whether results are for intervention period only (0 months follow up) or for full infection monitoring period (14 months' follow-up)
Funding source	None reported
Conflicts of interest	None reported

CCU, cardiac critical care unit; SICU, surgical intensive care unit.

Population and setting

Critical care unit characteristics	Ranged from 26 to 30 ICU beds The ICUs were in a 628-bed community teaching hospital Stated that there were no changes in materials during the time of the study (catheter kits, drapes, gowns, gloves and caps were all kept the same)
Patient population characteristics	Not reported
Device characteristics	CVCs; avoidance of femoral site; device duration reported. Ultrasonography was used intermittently in the placement of the central lines. Central lines were placed by critical care physicians without assistance, unless requested
Insertion site antisepsis used	Chlorhexidine (ChloraPrep)
Dressing type and duration/frequency	Not reported, but no antibiotic patches were used owing to lack of level 1 evidence

Intervention characteristics

Objective	To determine whether using central line bundles would decrease the incidence of CLABSI
Main focus of education	Catheter insertion
Trainers (providers)	Team to implement bundle: head of SICU as team leader, ICU nurse managers and two infection-control nurses
Training of trainers	Not reported
Learners (recipients)	All ICU staff (physicians and nurses)
Target behaviour change	Nurse to assist with central line insertion, compliance with hand washing, use of full-barrier precautions, appropriate skin preparation, checking and restocking of central cart, avoidance of femoral lines, and early removal of central lines
Development and testing	None reported, but mentions that the bundle protocol was based on the latest evidence-based techniques
Educational or behavioural theory	Not reported
Educational strategies and topics targeted	Education of resident physicians and nurses on BSI control practices. Included: **Discussion of:** proper hand washing, use of full barrier precautions during central line insertion, appropriate skin preparation with chlorhexidine (ChloraPrep), avoiding the femoral site if possible, and early removal of all central lines (justification for continued line use noted on a chart) **Checklist** completed by nurses to ensure compliance with the evidence-based guidelines
Infection surveillance feedback approach	The data (number of critical-care beds used, number of catheters placed, number of days catheters left in place, and number of line-associated infections) were collected by a trained, hospital-based infection-control practitioner. The data were reported to the directors of the surgical and MICUs, which allowed for real-time feedback to the staff on how the intervention was proceeding. Validation and reliability of process was not reported
Process audit feedback approach	Monthly feedback (number of critical care beds used, number of catheters placed, number of days catheters left in place, and number of line-associated infections) to directors of SICU, CCU and MICU, allowing for real-time staff feedback on intervention process
Performance feedback approach	Not included in intervention
Concentration of education	Not reported
Non-educational intervention components	Catheter cart provided Personnel change: A policy was instituted that required nurses to assist in central line insertion
Costs reported	Cost reported as being limited to central line cart cost (reported as around US$500 in the discussion of question and answer section)

CCU, cardiac critical care unit; SICU, surgical intensive care unit.

Outcome characteristics

Catheter-BSI definition	NNIS criteria: presence of a recognised pathogen cultured from one or more blood cultures and the organism cultured from the blood not to be related to infection at another site plus presence of a temperature greater > 38 °C, chills or hypotension, along with signs and symptoms of an infection not related to another site and presence of a common skin contaminant cultured from two or more blood samples on separate occasions, or common skin contaminant cultured from at least one blood sample in a patient with an intravascular catheter, or a positive antigen test on diagnostic phlebotomy
Outcomes reported	Not stated whether primary or secondary: Central line-associated BSI per 1000 catheter-days No. of central lines No. of central line days Development of a line infection

Results data

Primary outcomes

Outcome	Baseline (5 months)	Intervention (19 months)	Difference between baseline and intervention
Device duration (days), average	8.5 ± 1.3	6.8 ± 0.97	$p = 0.17$
Total device utilisation	Not reported	Not reported	(Total for both baseline and intervention: 1395 CVCs; 9938 central line-days)
No. of devices/patient	Not reported	Not reported	
CABSI incidence rate	Not reported	Not reported	
Incidence per 1000 catheter-days – average[a]	5.0 ± 4.3	0.90 ± 1.3	$p < 0.001$
Incidence per 1000 patient-days	Not reported	Not reported	
LOS	Not reported	Not reported	
Mortality	Not reported	Not reported	

a Data for calculating risk ratios with CIs (presented in the main report) were not reported in the primary publication but were obtained by contacting the author.

Secondary outcomes

Reaction to education	Not a study outcome
Attitudes	Not a study outcome
Compliance	Not a study outcome
Knowledge	Not a study outcome
Skills	Not a study outcome
Process evaluation	Stated only that ongoing monitoring kept ICU teams committed to the new protocols (no details given)

Critical appraisal

Potential for bias

Group selection	Were there systematic differences between the baseline and intervention groups? NOT REPORTED If YES, were the differences between the groups adjusted for in statistical analyses (e.g. as covariates or subgroups, or stratification by propensity scores)? NOT APPLICABLE
Intervention administration	Were any confounding variables identified that could influence the effect estimate for the overall intervention? NO. Authors stated that there were no changes in materials and that catheter kits, drapes, gowns, gloves and caps were all kept the same during the study period). However, no information was provided on staffing, infrastructure or policy changes, except for a specific staff role change that occurred within the intervention bundle (policy required nurses to assist critical care physicians, who previously did all insertions) Was the effect of educational practice separable from effects of non-educational practice? NO. Education was part of a bundle: catheter carts were provided and staff changes also occurred Were the intervention component(s) implemented as planned? NOT REPORTED
Missing data	Were there systematic differences between study groups in attrition or exclusions (includes withdrawal due to mortality; missing outcome data)? NOT REPORTED
Outcome measurement	Were there systematic differences between the baseline and intervention groups in how outcomes were determined (including differences in how outcomes were defined)? NOT REPORTED Was any blinding of personnel and/or outcome assessors reported (including assessors of blood cultures)? NO
Other possible sources of bias	Were any other sources of bias present? NO. No other sources of bias were reported by the authors or identified by the reviewers based on the information presented. Authors state that bias of under-reporting infections was controlled by having each patient checked by a qualified trained infection-control nurse on a daily basis

Other critical appraisal criteria

Methods	Intervention described in sufficient detail to be replicated? NO. The duration and number of educational sessions required was not reported, although an overview of the content was given. The checklist was briefly described but was not presented so could not be duplicated or adapted Justification given for sample size? NOT REPORTED Data collection process reported? PARTIALLY. Stated only that data were collected on a monthly basis, which included the number of critical care beds in use at the time, the number of catheters placed, the number of days the catheters were left in place expressed as catheter-days, and the number of line-associated infections. The data were then entered into a spreadsheet and descriptive analysis was performed If YES or PARTIALLY, was the data collection process shown to be valid? NOT REPORTED If YES or PARTIALLY, was the data collection process shown to be reliable? NOT REPORTED Statistical tests described? NO
Results	Educational significance or effect size assessed? NOT REPORTED Target behaviour change achieved? NOT REPORTED

GUERIN (2010)[98]

Methods

Study characteristics

Lead author, publication year(s) and reference ID(s)	Guerin (2010)[98]
Summary of approach	Local addition of a CVC post-insertion care bundle to an existing nationwide CVC insertion bundle as the latter did not prevent CLABSI, despite high compliance
Location (country, state/ region)	USA, Colorado
Language	English
Critical care specialty	MICU and SICU
No. of critical care units	2
No. of hospitals	1
Hospital name (unless multicentre); city	Department of Veterans Affairs Medical Center, Denver
Study design	Single cohort before-and-after study (two ICUs treated as a single group)
Study time periods	Baseline: 1 October 2006 to 30 September 2008 (24 months) Intervention: 1 October 2008 to 30 September 2009 (12 months) Follow-up: None (only intervention monitored) [Note: A nationwide CVC insertion bundle was implemented in April 2006 (i.e. during the baseline period)]
Funding source	None reported
Conflicts of interest	Stated none

SICU, surgical intensive care unit.

Population and setting

Critical care unit characteristics	MICU = 10 beds; SICU = 13 beds Physician staff members were postgraduate residents 1 : 2 nurse to patient ratio University-affiliated acute care teaching hospital **From April 2006 onwards:** Nationwide CVC insertion bundle: hand hygiene: sterile gloves and gown for all in the room prior to procedure; cap and mask for physician inserting the catheter; use of a 2% chlorhexidine gluconate in 70% ethanol scrub for the insertion site; head-to-toe sterile drape of the patient during insertion; time out before performing the procedure; avoidance of the femoral insertion site. Intravenous tubing for parenteral nutrition solutions changed daily, tubing for other intravenous solutions changed every 72 hours **Baseline period (October 2006 onwards):** standard infection control practices as per facility's infection control manual and annual online review training for all nursing staff (required pass rate 80%). Implementation of insertion bundle Training in proper application of the chlorhexidine gluconate-impregnated sponge provided by the manufacturer's representative educator **Staff empowerment:** Nurses monitored compliance of insertion bundle and were empowered to stop procedures breaching sterile technique. Four trained nurses inserted polyurethane peripheral CVCs (PICCs)
Patient population characteristics	Not reported
Device characteristics	96% PICCs (Bard, Murray Hill, NJ, USA) coated in chlorhexidine gluconate and silver sulfadiazine. In patients allergic to coatings, uncoated PICCs (4%) were used – silicone Groshong catheters (Bard). No other concurrent invasive devices were used Insertion sites: subclavian, internal jugular and femoral
Insertion site antisepsis used	Chlorhexidine gluconate-impregnated sponge
Dressing type and duration/frequency	Transparent dressing applied weekly or more frequently if wet or soiled, with a new chlorhexidine gluconate-impregnated sponge applied at each dressing change

SICU, surgical intensive care unit.

Intervention characteristics

Objective	Prevention of post-insertion CLABSI
Main focus of education	Post-insertion care
Trainers (providers)	Line care bundle was implemented by an intravenous champion in each unit (no details reported). Providers of hands-on training not reported
Training of trainers	Not reported
Learners (recipients)	All nursing staff
Target behaviour change	Hand hygiene, insertion and maintenance of PICCs
Development and testing	Stated that the line care bundle was developed by the nursing staff, and that the interventions were developed by frontline nursing staff. A 6-month pilot phase enabled staff to gain experience with device-day monitoring and data collection
Educational or behavioural theory	Not reported

Educational strategies and topics targeted	Hands-on training and competency evaluation: for all nursing staff based on accessing and caring for all intravenous catheters. Insertion site competence covered wearing a mask and sterile gloves for a central line dressing change, scrubbing the site with 2% chlorhexidine gluconate in alcohol for 30 seconds and applying the chlorhexidine gluconate-impregnated sponge properly. Hub care competence included scrubbing the catheter hub for 15 seconds with an alcohol pad at each access and replacing the hub every 72 hours
Infection surveillance feedback approach	Infection surveillance reported but not feedback – except to infection prevention and control (not ICU staff)
Performance feedback approach	Competence evaluation following the hands-on training in which each nurse was required to demonstrate competence in catheter insertion site and hub care
Concentration of education	Four-hour hands-on mandatory training for all nursing staff followed by a competency evaluation (duration not specified). Not stated whether reinforced or re-assessed annually
Other intervention components beyond education	1. An intravenous team provided insertion and site care of PICCs, and monitored site care and dwell time of all intravenous catheters throughout the hospital 2. A line care bundle, developed by the nursing staff and implemented by each unit's intravenous champion: daily inspection of the insertion site; documenting ongoing need for a catheter; proper chlorhexidine gluconate-impregnated sponge application at the insertion site; hand hygiene prior to handling intravenous system; alcohol scrub to the infusion hub for 15 seconds prior to use 3. A nationwide CVC insertion bundle introduced before the baseline period that continued during the intervention period
Device insertion procedure	Continued baseline infection control practices (see pre-intervention baseline control characteristics, clinical practice protocols)
Costs reported	Not reported

Outcome characteristics

Catheter-BSI definition *Reference cited:* Centers for Disease Control and Prevention[198]	*Criterion 1*: Patient has a recognised pathogen cultured from one or more blood cultures and the organism cultured from blood is not related to an infection at another site *Criterion 2*: Patient has at least one of fever (> 38 °C), chills, or hypotension; positive laboratory results are not related to an infection at another site; and common skin contaminant [i.e. diphtheroids (*Corynebacterium* spp.), *Bacillus* (not *B. anthracis*) spp., *Propionibacterium* spp., coagulase-negative staphylococci (including *S. epidermidis*), *viridans*-group streptococci, *Aerococcus* spp., *Micrococcus* spp.] is cultured from two or more blood cultures drawn on separate occasions
Outcomes reported	Not stated whether primary or secondary: • Catheter-days • Catheter dwell time • Catheter utilisation proportion • CLABSI incidence rates • Compliance with insertion bundle (but compliance with line care bundle, which is the main focus of interest, not reported)

Results data

Primary outcomes

Outcome	Baseline	Intervention	Difference between baseline and intervention: relative risk (RR) (95% CI); *p*-value. Except where indicated, statistical comparisons were not reported
Catheter dwell time[a] (no. of days between catheter insertion and onset of CLABSI), days	Mean = 14.5 Median = 12 Range = 0–47[b] IQR = 6–24	Mean = 15 Median = 7 Range = 7–33 IQR not reported	
Total device utilisation, catheter-days	4415	2825	
Total no. of patient-days	11,434	5937	
Catheter utilisation proportion: no. of catheter-days divided by no. of patient-days	0.39	0.48	$p < 0.0001$
No. of devices/patient	Not reported	Not reported	
No. of CLABSI	25	3	
CLABSI incidence per 1000 catheter-days	5.7	1.1	RR = 0.19 (0.06 to 0.63); $p = 0.004$ Adjusted RR[c] = 0.23 (0.07 –0.77); $p = 0.017$
Incidence per 1000 patient-days	Not reported	Not reported	
LOS	Not reported	Not reported	
Mortality	Not reported	Not reported	

a If a patient already had a vascular catheter at admission, the admission date was used for the date of insertion.
b Included two patients with an unexplained dwell time of zero days.
c Adjusted RR assumes constant utilisation proportion in baseline and intervention periods.

Secondary outcomes

Reaction to education	Not a study outcome	
Attitudes	Not a study outcome	
Compliance: CVC insertion bundle	Pre-intervention period: 94%	During intervention period: 93%
Knowledge	Not a study outcome	
Skills	Not reported	
Process evaluation	Brief narrative comment only. The authors stated that their study of local compliance with recommended post-insertion care techniques revealed opportunities for improvement that could possibly lead to reductions in CLABSI. However, the only quantitative compliance data reported were for the CVC insertion bundle, not the post-insertion care bundle	

Critical appraisal

Potential for bias

Group selection	Were there systematic differences between the baseline and intervention groups? NOT REPORTED
	Were any systematic differences between the groups adjusted for in statistical analyses (e.g. as covariates or subgroups, or stratification by propensity scores)? NOT REPORTED
Intervention administration	Were any confounding variables identified that could influence the effect estimate for the overall intervention? NOT REPORTED
	Was the effect of educational practice separable from effects of non-educational practice? NO, part of a bundle
	Were the intervention component(s) implemented as planned? UNCLEAR. The hands-on training and competency evaluation were compulsory. Teaching was given to all ICU nurses and other staff, but implementation of teaching was not reported. Stated that compliance with the CVC insertion bundle was 94% during the pre-intervention period and 93% during the intervention period
Missing data	Were there systematic differences between the baseline and intervention groups in attrition or exclusions (includes withdrawal due to mortality; missing outcome data)? NOT REPORTED
Outcome measurement	Were there systematic differences between the study groups in how outcomes were determined (including differences in how outcomes were defined)? NOT REPORTED
	Was any blinding of personnel and/or outcome assessors reported (including assessors of blood cultures)? NOT REPORTED
Other possible sources of bias	Were any other sources of bias present? NO. No other sources of bias were reported by the authors or identified by the reviewers based on the information presented

Other critical appraisal criteria

Methods	Intervention described in sufficient detail to be replicated? NO. No documentation of the bundle protocol or training sessions was provided. The principles and components of the line care bundle are reasonably clear but it would be difficult to replicate the hands-on training session owing to lack of information on the practical skills components (i.e. which of the line care topics had 'hands-on' activities)
	Justification given for sample size? NOT REPORTED
	Data collection process reported? PARTIALLY. Surveillance was conducted by four certified infection preventionists. They reviewed the medical record of every patient who had a positive blood culture, using a standard data collection form. Each case was then reviewed by the hospital epidemiologist to ensure that it met the case definition. Device-day data collected by ICU nursing staff were compared with data collected daily by the intravenous catheter management team to confirm the accuracy of data collection
	If YES or PARTIALLY, was the data collection process shown to be valid? NOT REPORTED, but stated that it was piloted
	If YES or PARTIALLY, was the data collection process shown to be reliable? UNCLEAR. Stated that device-day data collected by ICU nursing staff were compared with data collected daily by the intravenous catheter management team to confirm the accuracy of data collection, but no data were reported
	Statistical tests described? YES
Results	Educational significance or effect size assessed? NOT REPORTED
	Target behaviour change achieved? NOT REPORTED. No information on compliance with the post-insertion care bundle was reported

HIGUERA (2005)[103]

Methods

Study characteristics

Lead author, publication year(s) and reference(s)	Higuera (2005)[103]
Summary of approach	Single hospital infection control programme comprising 1-hour classes and feedback of compliance with catheter care and hand hygiene, conducted in two ICUs. Focused on CVC-associated BSI but also covered VAP and UTIs Part of an international multicentre project of nosocomial infection surveillance and control called the International Infection Control Consortium (49 ICUs of 39 hospitals in 28 cities of 12 countries)
Location	Mexico
Language	English
Critical care specialties	Medical SICU, neuroSICU
No. of critical care units	2
No. of hospitals	1
Hospital name (unless multicentre); city	General Hospital, Mexico City
Study design	Before-and-after study in two ICUs that were treated mainly as a single cohort; limited outcomes data reported for the ICUs separately
Study time periods	Baseline: June to August 2002 (3 months) Intervention: September 2002 to May 2003 (9 months) Follow-up: none (continuous monitoring of intervention)
Funding source	Supported by a grant from Baxter Health Care International
Conflicts of interest	Not reported

SICU, surgical intensive care unit.

Population and setting

All adult patients admitted to the study ICUs who had a CVC in place for at least 24 hours; patients had undergone neurosurgical, general and orthopaedic surgery or had severe medical illness. Full barrier precautions were used occasionally as resources permitted.

Critical care unit characteristics: two level 3 ICUs in a 1000-bed public university hospital with six ICUs	Baseline: June to August 2003 (3 months)	Intervention: September 2002 to May 2003 (9 months)	Difference between baseline and intervention: relative risk (RR) (95% CI); *p*-value
Mean patients per month	44.0	37.5	Statistics not reported except:
No. of beds per ICU	12	12	Bed occupancy RR = 0.84 (0.69 to 1.02); *p* = 0.08
Total available ICU bed-days	2160	6480	Nurse to patient ratio RR = 1.00 (0.91 to 1.00);[a] *p* = 1.00
Actual bed occupancy, %	45.9	40.1	
Nurses per ICU per work shift	6	6	
Total available nurse days	540	1620	
Nurse to patient ratio	0.54	0.61	
Patient characteristics			
Total no. of patients	132	338	
In medical-surgical ICU[b]	52	170	
In neuroSICU[b]	80	168	
Males, *n* (%)	60 (45.5)	163 (48.2)	*p* = 0.588
Mean ± SD age, years	44.32 ± 18.3	45.91 ± 17.88	*p* = 0.422
Diabetes, *n* (%)	26 (19.7)	72 (21.3)	*p* = 0.700
Cancer, *n* (%)	1 (0.8)	7 (2.1)	*p* = 0.322
Hypertension,[c] *n* (%)	22 (16.7)	75 (22.2)	*p* = 0.183
Cardiac failure, *n* (%)	3 (2.3)	16 (4.7)	*p* = 0.223
Chronic obstructive pulmonary disease, *n* (%)	3 (2.3)	16 (4.7)	*p* = 0.223
Smoker, *n* (%)	17 (12.9)	55 (16.3)	*p* = 0.358
Alcoholism, *n* (%)	24 (18.2)	65 (19.2)	*p* = 0.794
Renal impairment, *n* (%)	3 (2.3)	19 (5.6)	*p* = 0.722

a Confidence interval is from table 3 of the primary publication; reported in the text as (0.91 to 1.10).
b Data are from table 2 of the primary publication; numbers reported in the text of the publication are different and do not sum to the total number of patients reported (Phase 1, 173; Phase 2, 297).
c Systolic blood pressure of > 140 mmHg.

Device characteristics	A semirigid plastic open infusion system was used instead of a collapsible flexible closed infusion system
Insertion site antisepsis used	Povidone–iodine
Dressing type and duration/frequency	If a dressing was used at all, it would be a gauze dressing; no transparent dressings were used

Intervention characteristics

Objective	To ascertain the effect of an infection control programme including process control on ICU rates of intravascular device-associated bloodstream infection (BSI)
Main focus of education	Insertion site dressing, intravenous administration set dating, and hand hygiene
Trainers (providers)	An infection control nurse presented the educational classes
Training of trainers	The project co-ordinator trained the data collectors at each ICU before the start of the study
Learners (recipients)	Health-care workers in the ICU (nurses, ancillary staff and physicians)
Target behaviour change	Insertion site dressing selection and placement, and hand hygiene before patient contact
Development and testing	Not reported
Educational or behavioural theory	Not reported
Educational strategies and topics targeted	**One-hour classes** on epidemiology of nosocomial infections, hand hygiene, disinfection, prevention of intravascular device-associated BSIs, prevention of VAP, and prevention of UTIs **Infection control guidelines:** as published by the CDC. Not reported whether these were disseminated separately or included within the educational classes
Infection surveillance feedback approach	Not included in the intervention (active surveillance for infections took place during both the baseline and intervention periods but feedback to ICU staff was not reported)
Performance feedback approach	Compliance with hand hygiene and catheter care were assessed using a standardised form. Placement of gauze on intravascular device insertion sites, marking the date on the intravascular administration set, condition of the gauze dressing, and hand hygiene with alcohol hand rub or povidone–iodine soap before patient contact were assessed on a standard form by local researchers who observed health-care worker behaviours in the ICUs 5 days a week. The gauze dressing was inspected, and the presence or absence of blood, moisture, and gross soilage, and the appearance of the insertion site were noted. Feedback was provided monthly by a chart with columns representing each month showing rates of compliance with hand hygiene, gauze on CVC insertion sites, dates on intravenous administration sets, and maintenance of gauze dressings on catheter sites. The charts were posted on the walls of the ICU in a visible place in front of the health-care workers (nurses, ancillary staff and physicians). Validity and reliability of the data collection approach not reported
Concentration of education	Classes lasted 1 hour. Number of classes not reported. Classes were given to all the work shifts, with extra classes for new nurses (only few) and new medical residents. Not reported whether staff were re-educated annually
Non-educational intervention components	Alcohol hand rub or hand washing with povidone–iodine soap was started during the intervention period; previously regular non-antiseptic soap had been used
Costs reported	No

Outcome characteristics

Catheter-BSI definition Reference cited**:** Garner *et al.*[147]	*Criterion 1*: Laboratory-confirmed BSI: The patient had a recognised pathogen cultured from one or more percutaneous blood specimens after 48 hours of vascular catheterisation, and the pathogen isolated from the blood was not related to an infection at another site; for common skin commensals (e.g. diphtheroids, *Bacillus* spp., *Propionibacterium* spp., coagulase-negative staphylococci or micrococci), the organism was cultured from two or more blood specimens obtained on separate occasions *Criterion 2*: The patient had fever (temperature > 38 °C), hypotension, (systolic blood pressure < 90 mmHg), and/or oliguria (< 20 ml/hour) with no other recognised cause but blood specimens were not obtained for culture or organisms were not recovered from blood cultures; however, there was not apparent infection at another site, and the physician instituted treatment for sepsis Decisions to remove catheters and obtain blood specimens for culture were made independently by the patient's attending physicians. CVCs were removed aseptically and the last 5 cm of the catheter tip was cultured using a semiquantitative method. All cultures were inoculated within 8 hours of catheter removal. For blood cultures, two blood samples (5–10 ml) were obtained from two separate veins within an interval of 15–20 minutes, inoculated in a 50-ml bottle, and sent to the microbiological laboratory
Outcomes reported	*Primary*: Rate of intravascular device-associated BSI *Secondary*: Hand hygiene Catheter care compliance: dressing use and placement; dating of the catheter administration set Hand hygiene compliance Mortality rate

Results data

Primary outcomes

Outcome		Baseline: June to August 2002 (3 months)	Intervention: September 2002 to May 2003 (9 months)	Difference between baseline and intervention: relative risk (RR) (95% CI); *p*-value
Device duration		Not reported	Not reported	Not reported
Device utilisation, CVC-days		605	2824	Not reported
No. of devices/patient		Not reported	Not reported	Not reported
No. of CVC-associated BSI		28	55	Not reported
CVC-associated BSI incidence/ 1000 CVC-days	Total	46.3	19.5	RR = 0.42 (0.27 to 0.66); $p = 0.0001$
	Medical-surgical ICU	57.4	22.1	RR = 0.38 (0.22 to 0.68); $p = 0.000$
	Neurosurgical ICU	32.8	17.1	RR = 0.52 (0.24 to 1.11); $p = 0.08$
CVC-associated BSI incidence/ 1000 patient-days		Not reported	Not reported	Not reported
LOS		Not reported	Not reported	Not reported
Mortality	Total deaths	64/132	111/338	RR = 0.68 (0.50 to 0.91);[a] $p = 0.01$
	Unadjusted mortality per 100 discharges	48.5%	32.8%	

a From table 4 of the primary publication (three different values of the same CI were reported in the abstract (0.50–0.31), text (0.50–0.79) and table 4 (0.50–0.91) – the values in table 4 are consistent with the calculation method of Kirkwood and Sterne[61] referred to in the main report).

Additional data on central venous catheter-associated BSI incidence/1000 central venous catheter-days[a]

Month	Medical-surgical ICU	Neurosurgical ICU
June 2003	35.7	13.1
July 2003	67.7	36.6
August 2003	43.2	31.3
September 2003	40.8	16.9
October 2003	15.5	24.2
November 2003	16.5	19
December 2003	15.9	6
January 2004	46.2	16.4
February 2004	14.9	18.2
March 2004	15.3	9.4
April 2004	18.3	32.3
May 2004	21.9	13.9

a Data are from figures 1 and 2 in the primary publication and appear to be for an additional 12-month period beyond the specified study duration; unclear whether these data represent follow-up or ongoing monitoring of a continuing intervention or an error (no explanation of figure 2 given in the primary publication).

Secondary outcomes

Outcome	Baseline: June to August 2002 (3 months)	Intervention: September 2002 to May 2003 (9 months)	Difference between baseline and intervention: relative risk (RR) (95% CI); *p*-value
Compliance			
Proper catheter care			
No. of observations	1413	2912	
Gauze presence on insertion site	86.69%	99.24%	RR = 1.14 (1.07 to 1.22); $p = 0.0000$
Proper gauze placement at insertion site	84.21%	97.87%	RR = 1.16 (1.09 to 1.24); $p = 0.0000$
Dating of intravenous administration set	40.69%	93.85%	RR = 2.34 (2.14 to 2.56); $p = 0.0000$
Hand hygiene before patient contact			
No. of observations	584	584	
Hand hygiene practised	62%	62%	RR = 1.37 (1.21 to 1.51); $p = 0.0000$
Reaction to education	Not a study outcome		
Attitudes	Not a study outcome		
Knowledge	Not a study outcome		
Skills	Not a study outcome		
Process evaluation	Not reported other than compliance with catheter care and hand hygiene was assessed and reported back to ICU staff (as summarised above)		

Critical appraisal

Potential for bias

Group selection	Were there systematic differences between the baseline and intervention groups? NO. Patients were similar with regard to sex, age, major disease, smoking and alcoholism. Available beds and nurse to patient ratios were also similar in the baseline and intervention periods. Bed occupancy and mean number of patients per month were slightly lower (more favourable) in the intervention period but the differences were not statistically significant
	If YES, were the differences between the groups adjusted for in statistical analyses (e.g. as covariates or subgroups, or stratification by propensity scores)? NOT APPLICABLE
Intervention administration	Were any confounding variables identified that could influence the effect estimate for the overall intervention? UNCLEAR. The authors stated that a programme to improve hand hygiene was already in place in the neurosurgical ICU but the implementation date was not reported
	Was the effect of educational practice separable from effects of non-educational practice? YES. The intervention was primarily educational (including information provision for compliance). Alcohol hand rub or hand washing with povidone iodine soap was started during the intervention period but although not an educational activity in itself this was a target of the education; no information was reported to suggest that use of the soap was due to non-educational factors (such as changes in availability)
	Were the intervention component(s) implemented as planned? UNCLEAR. Compliance with the educational classes themselves (e.g. whether participation was mandatory for all ICU staff) was not reported and it is unclear whether dissemination of the CDC infection control guidelines was included in the classes or separate (and if the latter, how implementation was achieved). However, compliance with all target behaviours statistically significantly improved (did not reach 100%)
Missing data	Were there systematic differences between the baseline and intervention groups in attrition or exclusions (includes withdrawal due to mortality; missing outcome data)? UNCLEAR. The authors report two different sets of data on the number of patients recruited. Tables 1–4 each agree that the number was 132 in the baseline period and 338 in the intervention period. The text states that the numbers for baseline and intervention periods were, respectively, 173 and 297 (but overall total of 470 patients is the same). Mortality rate was significantly lower in the intervention period; it is unclear whether this was a consequence of the intervention (not discussed by the authors)
Outcome measurement	Were there systematic differences between the baseline and intervention groups in how outcomes were determined (including differences in how outcomes were defined)? UNCLEAR. The definition of infections used appears to be that used within the International Infection Control Consortium; no changes in definition or microbiological culture technique during the study were reported. However, no information about staff diagnosing infections was given
	Was any blinding of personnel and/or outcome assessors reported (including assessors of blood cultures)? NO
Other possible sources of bias	The authors stated that study centre data collection sheets were checked for potential errors and missing items by the project co-ordinator to confirm each diagnosis of intravascular device-associated BSI, but no checking of compliance data was reported

Other critical appraisal criteria

Methods	Intervention described in sufficient detail to be replicated? PARTIALLY. The process feedback approach is reported well enough to be repeated in principle. However, the educational classes are reported superficially and the number of classes required to achieve the observed intervention effect is not clear. The dissemination approach for CDC guidelines is also not clear (whether standalone or included in classes)
	Justification given for sample size? NOT REPORTED
	Data collection process reported? PARTIALLY. A medical doctor at each ICU collected infection data prospectively from patient charts. Compliance data were collected by unspecified local researchers who observed health-care worker behaviours in the ICUs 5 days a week. Not reported how the data were stored after collection
	If YES or PARTIALLY, was the data collection process shown to be valid? NOT REPORTED
	If YES or PARTIALLY, was the data collection process shown to be reliable? NOT REPORTED. However, the authors stated that checks for errors and missing data were conducted for infection surveillance (see above)
	Statistical tests described? YES
Results	Educational significance or effect size assessed? NOT REPORTED
	Target behaviour change achieved? YES. Compliance with the target behaviours (insertion site dressing selection and use; hand hygiene before patient contact) was increased by the intervention (compliance was high but did not reach 100%)

LOBO (2005)[108]

Methods

Study characteristics

Lead author, publication year(s) and reference(s)	Lobo *et al*. (2005)[108]
Summary of approach	Single unit educational programme targeted to specific points observed during CVC care practices on decreasing CVC-blood stream infections (BSI) in a MICU
Location	Brazil
Language	English
Critical care specialty	MICU
No. of critical care units	1
No. of hospitals	1
Hospital name (unless multicentre); city	Hospital das Clinicas of University of São Paulo
Study design	Cohort before-and-after study
Study time periods	Baseline: January 2001 to April 2002 (Phase 1: described as 1-year pre-intervention period and 3 months observation; described as 16 months in Results section) Intervention: May 2002 to December 2002 (Phase 2: 8 months, including an observation period) Follow-up: CVC-BSI were also evaluated during the following year after the educational intervention (Phase 3) (Note: monthly surveillance feedback and prevention guide that was given to all medical residents were continued during follow-up)
Funding source	None reported
Conflicts of interest	Not reported

Population and setting

Critical care unit characteristics: The nursing staff was responsible for the CVC dressing and line care; the medical residents were responsible for CVC insertion and replacement; and CVC manipulation was done by both. ICU staff: five physicians, 36 medical residents, 23 assistant nurses and 10 nurses

Patient population characteristics	All adult patients admitted to the ICU with a CVC for > 24 hours
Device characteristics	Device reported as CVC, no other details reported
Insertion site antisepsis used	Alcohol (chlorhexidine was not available at the hospital)
Dressing type and duration/frequency	Not reported

Intervention characteristics

Objective	Determine the impact of an educational programme targeted to specific points observed during CVC care practices on decreasing CVC-BSI in a MICU
Main focus of education	Hand washing, skin preparation of CVC insertion, pathogenesis of CVC infection and standardisation of CVC manipulation
Trainers (providers)	Not reported (the infection control committee made the posters and set up the hand washing campaign)
Training of trainers	Not reported
Learners (recipients)	The entire unit staff was involved in monthly classes and discussion of infection rates
Target behaviour change	Hand hygiene, sterile catheter insertion procedure and CVC maintenance
Development and testing	The educational programme was developed by a multidisciplinary task force to highlight correct practices for CVC insertion, manipulation, and care. The multidisciplinary task force included three infection control nurses, one physician, and the entire staff of the unit. The educational programme was based on observations by the infection control staff of CVC care practices in the ICU
Educational or behavioural theory	Not reported
Educational strategies and topics targeted The programme consisted of a pre-test and monthly classes, posters, discussions with staff, and a new observation period (Phase 2). The programme was applied for the same people during the study period	*Pre-test*: included 10 questions concerning hand washing, information about when the health-care professional should wash their hands (before and after contact with the patient, before and after CVC insertion, manipulation and dressing) and how (with alcohol povidone–iodine or chlorhexidine), and that the use of glove does not exclude hand washing. The pre-test also covered CVC insertion (skin preparation, CVC site, technique, and the use of maximum barriers), CVC dressing (type, replacement and skin preparation), CVC manipulation (disinfection), hub and line care (replacement) and CVC replacement *Observation Phase 1*: 3 months *Observation checklist*: included hand washing, CVC insertion (skin preparation, site, technique, and use of maximum barriers), CVC dressing (hand washing; type, frequency of replacement, skin care), and CVC manipulation (hand washing, hub disinfecting and line care) **Intervention:** **Classes/discussion:** monthly classes and discussion with staff on infection rates **Hand washing campaign:** use of chlorhexidine and posters with hand washing classes (hand-washing product remained the same pre and post intervention and was not alcohol based) **Colourful stamps:** with tips to remind the unit staff of the importance of hand washing and CVC care were placed on the CVC insertion site or on the CVC lines **Posters:** concerning hand hygiene and pathogenesis of CVC infection **CVC-BSI prevention guide:** the catheter care policy included hand washing with chlorhexidine before and after any patient care and recommendations concerning CVC insertion (skin preparation with povidone–iodine and skin antisepsis with 70% alcohol povidone–iodine and use of maximum barriers; sterile gown and gloves, large sheets, cap and surgical mask, dressing (skin care with alcohol povidone–iodine and dry gauze, replacement every 24 hours and when wet), manipulation (hub disinfection with 70% alcohol), line care (replacement every 72 hours for administration sets, every 24 hours for lipid emulsion, and immediately removed after use for blood products), and CVC replacement (no routine replacement except when clinically indicated, e.g. if unexplained fever) *Observation Phase 2*: **checklist** (not explicitly stated, but presumed to be the same as pre-intervention) on hand washing, CVC insertion (skin preparation, site, technique and use of maximum barriers), CVC dressing (hand washing; type, frequency of replacement, skin care) and CVC manipulation (hand washing, hub disinfecting and line care)

Infection surveillance feedback approach	Monthly feedback on the CVC-BSI rate during the first year after the end of the intervention was given to the unit and the CVC-BSI prevention guide was given to all medical residents. Unclear if feedback was practiced prior to intervention. Validation and reliability of the reporting process not stated
Performance feedback approach	Not reported
Concentration of education	Stated monthly classes, no other details reported
Non-educational intervention components	None (intervention purely educational)
Costs reported	Not reported (stated campaign was done with own resources)

Outcome characteristics

Catheter-BSI definition Reference cited: Garner *et al*.[147]	All patients with CVC for > 24 hours admitted to ICU were included in study. Laboratory-confirmed CVC-BSI was defined according to the Centers for Disease Control and Prevention (CDC). The infection was regarded as ICU acquired if it occurred during ICU stay or within 48 hours of discharge from the MICU. CVC-BSI representing primary bloodstream infection was defined by one of the following clinical signs or symptoms with no other recognised cause: recognised pathogen isolated from blood culture not related to infection at another site; common skin contaminant isolated, such as coagulase-negative *Staphylococcus* from two or more blood cultures drawn on separate occasions, within 24 hours, unrelated to infection at another site; and patients had at least one of the following signs or symptoms – fever of > 37.8 °C, chills or hypotension
Outcomes reported	Primary outcome: rate of CVC-BSI Secondary outcomes: compliance with the CVC-BSI prevention guide

Results data

Primary outcomes

Outcome *n* = no. of patients	Baseline (16 months), *n* = 316	Intervention (8 months), *n* = 190	Follow-up (12 months), *n* = 266	Difference between baseline, intervention and follow-up periods
CVC-days	Not reported	Not reported	Not reported	Not reported
Total device utilisation, days	2450	1481	1701	Not reported
No. of devices/ patient	Not reported	Not reported	Not reported	Not reported
CLAB incidence rate	48	16	22	Not reported
CLAB incidence per 1000 catheter-days	20	11	12	Baseline to post intervention: 40% reduction (no *p*-value reported)[a]
CLAB incidence per 1000 patient-days	Not reported	Not reported	Not reported	Not reported
LOS	Not reported	Not reported	Not reported	Not reported
Mortality	Not reported	Not reported	Not reported	Not reported

a Stated that the rate of CVC-BSI remained almost the same, 22 in 1701 catheter-days (12 per 1000 catheter-days), during the following year after the educational intervention ($p = 0.07$).

Secondary outcomes

Outcome	Baseline (16 months)	Intervention (8 months)	Difference in compliance between baseline and intervention [relative risk (RR) (95% CI); *p*-value][a]
Reaction to education	Not a study outcome		
Attitudes	Not a study outcome		
Compliance*, n *(%)			
CVC insertion (medical residents)	***n* = 22**	***n* = 22**	
Hand washing before (chlorhexidine)	22 (100)	22 (100)	
Maximal barrier (gloves, gown, mask)	20 (91)	22 (100)	0.91 (0.80 to 1.04[a]); $p = 0.147$
Skin antisepsis/alcohol-based povidone–iodine	2 (10)	22 (100)	11.0 (2.93 to 41.2[a]); $p < 0.001$
CVC manipulation (nurses and medical residents)	***n* = 42**	***n* = 46**	
Hand washing before (chlorhexidine)	2 (5)	28 (55)	12.78 (3.24 to 50.42); $p < 0.001$
Glove use	17 (40)	45 (98)[b]	2.36 (1.64 to 3.40[a]); $p < 0.001$
Line protection	29 (69)[b]	45 (98)[b]	1.38 (1.13 to 1.69[a]); $p < 0.001$
Hub disinfection	14 (34)	43 (90)	2.74 (1.78 to 4.22[a]); $p < 0.001$
Hand washing after (chlorhexidine)	16 (38)	20 (43)	1.14 (0.69 to 1.90[a]); $p = 0.6079$
CVC dressing (nurses)	***n* = 31**	***n* = 31**	
Hand washing before (chlorhexidine)	14 (45)	21 (68)	1.50 (0.95 to 2.37); $p = 0.072$
Glove use	30 (97)	30 (97)	1.00 (0.91 to 1.10); $p = 1.00$
Alcohol povidone–iodine antisepsis	1 (3)	31 (100)	31.00 (4.51 to 213.18); $p \leq 0.001$
Hand washing after (chlorhexidine)	8 (26)	18 (58)[b]	2.25 (1.15 to 4.39); $p = 0.010$
Knowledge	Not a study outcome		
Skills	Not a study outcome		
Process evaluation	Not reported other than compliance (above)		

a Reported CIs differ from those that would be calculated using the method of Kirkwood and Sterne.[62]
b Percentage corrected by reviewers.

Critical appraisal

Potential for bias

Group selection	Were there systematic differences between the baseline and intervention groups? NOT REPORTED If YES, were the differences between the groups adjusted for in statistical analyses (e.g. as covariates or subgroups, or stratification by propensity scores)? NOT APPLICABLE
Intervention administration	Were any confounding variables identified that could influence the effect estimate for the overall intervention? NOT REPORTED. However, authors stated that criteria to consider a common skin contaminant as a cause of CVC-BSI were rigid and that the pre- and post-intervention programme was applied to the same people during the study period Was the effect of educational practice separable from effects of non-educational practice? YES. Education-only intervention Were the intervention component(s) implemented as planned? UNCLEAR. Stated in methods section that the entire unit staff was involved in the monthly classes and discussion of infection rates, but implementation was not reported in the results. All staff took part in a pre-test but post-testing was not reported. Authors stated they noticed a profound involvement of the unit staff during the educational period but did not give details
Missing data	Were there systematic differences between the baseline and intervention groups in data availability? UNCLEAR. The combined number of nurses and medical residents differed from pre- (n = 42) to post-intervention (n = 46) for observations on CVC manipulation data. However, the number of medical residents was the same both pre- and post-intervention for observations on CVC insertion, as was the number of nurses' observations on CVC dressing
Outcome measurement	Were there systematic differences between the baseline and intervention groups in how outcomes were determined (including differences in how outcomes were defined)? NOT REPORTED Was any blinding of personnel and/or outcome assessors reported (including assessors of blood cultures)? UNCLEAR. Blinding of assessors reported. Stated that the observation was blinded to following the CVC dressing, manipulation, and care. However, also stated that at times the infection staff was contacted to follow the CVC insertion (mainly during the night)
Other possible sources of bias	No other sources of bias were reported by the authors or identified by the reviewers based on the information presented

Other critical appraisal criteria

Methods	Intervention described in sufficient detail to be replicated? NO. Details about the structure, content and time resources required were not reported Justification given for sample size? NOT REPORTED Data collection process reported? PARTIALLY. Surveillance of nosocomial infections was conducted by 2 infection control nurses, who visited the medical unit daily If YES or PARTIALLY, was the data collection process shown to be valid? NOT REPORTED If YES or PARTIALLY, was the data collection process shown to be reliable? NOT REPORTED Statistical tests described? YES
Results	Educational significance or effect size assessed? NOT REPORTED Target behaviour change achieved? PARTLY. Compliance with hand hygiene did not improve significantly but other behaviours did. Compliance statistically significantly increased in four out of five target behaviour components for CVC manipulation, in one of three target behaviour components for CVC insertion, and one out of four target behaviour components for CVC dressing. Compliance with all target behaviour components increased only for CVC manipulation, but was inconsistent for CVC insertion and CVC dressing

Additional comments

- Device-days not defined (i.e. unclear whether accounts for multiple simultaneous CVCs in a patient).
- Not reported whether participants were aware they were in a study.
- Pre-test and the pre-intervention observation period showed that compliance with the guideline was low, with major problems concerning skin preparation during CVC insertion, disinfection of CVC during manipulation, and non-use of an alcohol-based product during the CVC dressing. Knowledge of CVC insertion procedures and line care were reasonable, but low compliance with disinfection of the CVC hub during manipulation and use of an alcohol-based product during preparation of the CVC dressing because only saline solution was used (data not extracted).
- Authors stated that the distribution of pathogens was different comparing the pre- and post-intervention period. *S. aureus* was the most common pathogen in phase 1 and decreased significantly during the study period ($p = 0.02$).
- Also stated that the adhesion to the overall catheter care policy improved significantly in the post-intervention period ($p = 0.01$).

LOBO (2010)[109]

Methods

Study characteristics

Lead author, publication year(s) and reference(s)	Lobo *et al*. (2010)[109]
Summary of approach	Single centre evaluation of the impact of two models of educational intervention (tailored continuous intervention vs. a single lecture) on the rate of CVC-associated bloodstream infections (CVC-BSI) in 2 MICUs
Location	Brazil
Language	English
Critical care specialty	MICU
No. of critical care units	2
No. of hospitals	1
Hospital name (unless multicentre); city	Hospital das Clinicas, São Paulo, Brazil
Study design	Cohort before-and-after study comprising two separate cohorts with different interventions
Study time periods	*Baseline (surveillance)*: January 2005 to December 2005 (12 months) *Pre-intervention (knowledge assessment and observation of CVC care)*: January 2006 to September 2006 (9 months) *Intervention (differed in the two ICUs)*: October 2006 to June 2007 (9 months) *Follow-up*: None (tailored continuous educational programme) but stated that continued educational intervention resulted in no CVC-BSIs in 2008
Funding source	Main author received a grant from CAPES. (Not defined by the authors; assumed to refer to the CAPES Foundation – a Brazilian government agency awarding scholarship grants to graduate students at universities and research centres)
Conflicts of interest	None stated

Population and setting

Critical care unit characteristics	1000-bed tertiary care teaching hospital attached to the University of São Paulo. Medical residents rotated each 40 days	
	ICU A	ICU B (control)
Beds	5	8
Physician–bed ratio	1 : 5	1 : 8
Medical resident–bed ratio	1 : 1	7 : 8
Registered nurse–bed ratio	1 : 5	3 : 8
Assistant nurse–bed ratio	2 : 5	4 : 8
Sinks–bed ratio	1 : 3	1 : 3
Alcohol-based gel dispensers–bed ratio	1 : 2	1 : 2

Patient population characteristics	ICU A		
	Pre-intervention: *n* = 141	Intervention: *n* = 41	Difference between pre-intervention and intervention
Patient-days	1699	1341	Not reported
CVC days	940	843	Not reported
Age, years: median (range)	51 (8–87)	50 (13–86)	$p = 0.832$
Age, years: mean (SD)	54 (± 21)	53 (± 20)	
Male: *n*, (%)	87 (62)	18 (43)	$p = 0.042$
***Underlying diseases,* n**			$p = 0.890$
Cancer	12	2	
Cardiovascular disease	6	7	
Surgical condition	8	5	
Diabetes mellitus	0	0	
Haematological disease	0	0	
Infectious disease	22	5	
Neurological disease	0	0	
Other diseases	46	12	
Pneumonia	23	5	
Renal failure	11	0	
Respiratory failure	13	5	
Septic shock	0	0	

Patient population characteristics	ICU B		
	Pre-intervention, *n* = 378	Intervention, *n* = 262	Difference between pre-intervention and intervention
Patient-days	3704	2523	Not reported
CVC-days	2175	1694	Not reported
Age, years median (range)	53 (11–97)	50 (14–93)	*p* = 0.045
Age, years mean (± SD)	55 (± 20)	51 (± 19)	
Male, *n* (%)	6 (10)	6 (14)	*p* = 0.815
***Underlying diseases,* n**			*p* = 0.386
Cancer	22	14	
Cardiovascular disease	50	26	
Surgical condition	20	13	
Diabetes mellitus	18	20	
Haematological disease	16	4	
Infectious disease	36	27	
Neurological disease	47	37	
Other diseases	69	40	
Pneumonia	34	23	
Renal failure	14	9	
Respiratory failure	36	30	
Septic shock	16	19	
Device characteristics	Device only described as CVC, no further details reported		
Insertion site antisepsis used	Standardised chlorhexidine gluconate 0.5% alcoholic – remained unchanged during the study		
Dressing type and duration/frequency	Not reported		

Intervention characteristics

Objective	Evaluate the impact of two models of educational intervention on the rate of CVC-BSI
Main focus of education	Hand washing, CVC care and maintenance
Trainers (providers)	Not reported
Training of trainers	Not reported
Learners (recipients)	All staff and medical residents in both ICUs
Target behaviour change	Adherence to CVC practices
Development and testing	The programme in ICU A was based on problems found during an observation phase
Educational or behavioural theory	Not reported
Educational strategies and topics targeted	**Questionnaire pre-intervention period (ICU A and B):** 11-questions questionnaire designed to evaluate health-care workers' knowledge of the Nosocomial Infection Control Committee's recommendations regarding CVC care (adapted from CDC guidelines; reference cited) was applied in both ICUs. The questionnaire covered the following issues: • Hand hygiene (when, how and with which product: chlorhexidine gluconate soap or alcohol-based gel) and the notion that the use of gloves does not preclude the need for hand hygiene • Hand hygiene with alcohol-based gel as an alternative to hand washing • CVC insertion (i.e. preferred CVC site, skin preparation, technique, and the use of maximal barrier precautions) • CVC dressing (i.e. types, changes and skin antisepsis) • CVC handling (e.g. hub disinfection) • CVC replacement sets (e.g. line care) **Second observation period (checklist):** started 1 month after the start of the intervention period in ICU A and 1 month after the lecture in ICU B ***ICU A:*** **Questionnaire** *(same as at pre-intervention)*: administered on a monthly basis as an educational strategy to medical residents **Monthly lectures:** CVC care for all new medical residents **Lectures to small groups:** simple messages, focusing on problems identified in the observation phase **Lectures on hand hygiene practices:** intervention lectures included hand hygiene before and after any CVC care; use of alcohol-based gel or hand hygiene with soap for soiled hands; replacement of intravenous tubing (including add-on devices) no more frequently than at 72-hour intervals; replacement of tubing used to administer blood, blood products or lipid emulsions within 24 hours of initiating infusion; replacement of the extension tubing used for intermittent infusions at every catheter change; use of alcoholic chlorhexidine gluconate 0.5% solution for skin antisepsis during catheter dressing; replacement of gauze dressing every 24 hours or when damp, loose or visibly soiled; replacement of transparent dressings every 7 days or when damp, loose or visibly soiled; protection of the catheter with impermeable material during showering; disinfection of hub and line with 70% alcohol; and protection of line and sets during catheter handling **Posters:** displayed in the unit with stimulating messages in visible places and containing a step-by-step description of hand hygiene **Colourful labels with tips:** reminder to the health-care worker of the importance of CVC care ***ICU B:*** **Lecture:** one lecture on CVC care given to all staff and medical residents who rotated in the unit during this period (immediately after the pre-intervention period) **Observation checklist:** included CVC insertion (hand hygiene, skin antisepsis, and use of maximal barrier precautions); CVC dressing (hand hygiene, glove use, skin antisepsis); CVC handling (hand hygiene, glove use, hub disinfection)

Infection surveillance feedback approach	Surveillance was done by three infection control nurses who visited the ICUs daily. Intervention period: monthly updates of CVC-BSI rates posted in multiple locations in ICU A only. Validation and reliability of the reporting process not stated
Performance feedback approach	Intervention period: Feedback to the entire staff of ICU A regarding problems noted during the observation phase. No further details reported. Validation and reliability of the reporting process not stated
Concentration of education	Monthly lectures and monthly questionnaire in ICU A; single lecture in ICU B. Lengths of lectures not reported
Non-educational intervention components	None (intervention purely educational)
Costs reported	Not reported

Outcome characteristics

Catheter-BSI definition Reference cited: Garner *et al.*[147]	Diagnosis of infection was based on CDC criteria. CVC-BSI was defined as primary BSI in the presence of a CVC. Only laboratory-documented infections were included. Each patient was followed up until 48 hours after discharge from the ICU
Outcomes reported	Not stated whether primary or secondary: • CLAB incidence per 1000 catheter-days • Patient-days • Device utilisation and utilisation rate • Adherence to hand hygiene, maximal barrier precautions, hub disinfection, skin antisepsis during CVC insertion, handling and dressing

Results data

Primary outcomes

Outcome	ICU A			Difference between baseline, pre-intervention and intervention
	Baseline (12 months)	Pre-intervention (9 months)	Intervention (9 months)	
Device duration	Not reported	Not reported	Not reported	Not reported
CVC-days	Not reported	940	843	Not reported
Device utilisation rate[a]	0.72	0.55		Not reported
			Month 1: 0.53	Not reported
			Month 2: 0.65	Not reported
			Month 3: 0.75	Not reported
			Month 4: 0.64	Not reported
			Month 5: 0.62	Not reported
			Month 6: 0.59	Not reported
			Month 7: 0.7	Not reported
			Month 8: Not reported	Not reported
			Month 9: Not reported	Not reported

Outcome	ICU A			Difference between baseline, pre-intervention and intervention
	Baseline (12 months)	Pre-intervention (9 months)	Intervention (9 months)	
Patient-days	1699	1341	Not reported	Not reported
No. of devices/patient	Not reported	Not reported	Not reported	Not reported
CLAB incidence per 1000 catheter-days	Not reported	12	10.6	$p = 0.03$ (pre-intervention vs. intervention) (chi-squared test for trend)
			Month 1: 0	Not reported
			Month 2: 10.3	Not reported
			Month 3: 8.8	Not reported
			Month 4: 0	Not reported
			Month 5: 0	Not reported
			Month 6: 8.8	Not reported
			Month 7: 0	Not reported
			Month 8: 0	Not reported
			Month 9: 0	Not reported
CLAB incidence per 1000 patient-days	Not reported	Not reported	Not reported	Not reported
LOS, days: median (range), mean (SD)	Not reported	7 (1–32), 5 (7)	9 (1–57), 4 (11)	$p = 0.386$
Mortality	Not reported	Not reported	Not reported	Not reported
Primary outcomes	**ICU B**			**Difference between baseline, pre-intervention and intervention**
	Baseline (12 months)	**Pre-intervention (9 months)**	**Intervention (9 months)**	
Device duration	Not reported	Not reported	Not reported	Not reported
CVC-days	Not reported	2175	1694	Not reported
Device utilisation rate[a]	0.61	0.59	Month 1: 0.67[b]	Not reported
			Month 2: 0.68	Not reported
			Month 3: 0.74	Not reported
			Month 4: 0.7	Not reported
			Month 5: 0.69	Not reported
			Month 6: 0.7	Not reported
			Month 7: 0.69	Not reported
			Month 8: 0.63	Not reported
			Month 9: 0.64	Not reported
Patient-days	3704	2523	Not reported	Not reported
No. of devices/patient	Not reported	Not reported	Not reported	Not reported
CLAB incidence rate	Not reported	Not reported	Not reported	Not reported

Outcome	ICU B			Difference between baseline, pre-intervention and intervention
	Baseline (12 months)	Pre-intervention (9 months)	Intervention (9 months)	
CLAB incidence per 1000 catheter-days	Not reported	16.2	Overall: 12.9 Month 1: 0 Month 2: 0 Month 3: 7.41 Month 4: 11.43 Month 5: 0 Month 6: 5.59 Month 7: 4.24 Month 8: 3.44 Month 9: 13.7	Not reported by month $p = 0.41$ (pre-intervention vs. intervention) (chi-squared test for trend)
CLAB incidence per 1000 patient-days	Not reported	Not reported	Not reported	Not reported
LOS, days: median (range), mean (SD)	Not reported	10 (1–99), 6 (10)	11 (1–112), 6 (14)	$p = 0.402$
Mortality	Not reported	Not reported	Not reported	Not reported

a Device utilisation rate, number of central line-days/number of patient-days.
b Obscured in graph and estimated by reviewer.

Secondary outcomes

Reaction to education	Not a study outcome		
Attitudes	Not a study outcome		
Compliance (ICU A) (*n* = no. of observations)	**Pre-intervention (9 months), *n* (%)**	**Intervention (9 months), *n* (%)**	**Difference in compliance between baseline and intervention: relative risk (RR) (95% CI); *p*-value)**
CVC insertion	*n* = 12	*n* = 12	
Hand hygiene before procedure	12 (100)	12 (100)	
Maximal barrier precautions	12 (100)	12 (100)	
Skin antisepsis	11 (100)	12 (100)	
Hand hygiene after procedure	7 (58)	10 (83)	1.43 (0.83 to 2.45); $p = 0.370$
CVC handling	*n* = 63	*n* = 63	
Hand hygiene before procedure	22 (35)	51 (81)	2.32 (1.62 to 3.32); $p < 0.001$
Washing with chlorhexidine soap	18 (29)	26 (41)	Not reported
Alcohol-based gel	4 (6)	25 (40)	Not reported
Use of gloves	63 (100)	63 (100)	

Disinfection of hub	43 (68)	61 (97)	1.42 (1.19 to 1.69); $p < 0.001$
Hand hygiene after procedure	12 (19)	53 (84)	4.42 (2.63 to 7.43), $p < 0.001$
Washing with chlorhexidine soap	6 (9)	27 (43)	Not reported
Alcohol-based gel	6 (9)	26 (41)	Not reported
CVC dressing	*n* = 50	*n* = 50	
Hand hygiene before procedure	14 (28)	49 (98)	3.50 (2.24 to 5.47); $p < 0.001$
Washing with chlorhexidine soap	12 (24)	8 (16)	Not reported
Alcohol-based gel	2 (4)	41 (82)	Not reported
Use of gloves	50 (100)	50 (100)	
Skin antisepsis	27 (54)	50 (100)	1.85 (1.43 to 2.39); $p < 0.001$
Hand hygiene after procedure	17 (34)	48 (96)	2.82 (1.91 to 4.17); $p < 0.001$
Washing with chlorhexidine soap	10 (20)	22 (44)	Not reported
Alcohol-based gel	7 (14)	26 (52)	Not reported
Compliance (ICU B) (*n* = no. of observations)	**Pre-intervention, *n* (%) (9 months)**	**Intervention, *n* (%) (9 months)**	**Difference in compliance between pre-intervention and intervention: relative risk (RR) (95% CI); *p*-value**
CVC insertion	*n* = 12	*n* = 12	
Hand hygiene before procedure	12 (100)	12 (100)	
Maximal barrier precautions	12 (100)	12 (100)	
Skin antisepsis	12 (100)	12 (100)	
Hand hygiene after procedure	8 (67)	8 (67)	
CVC handling	*n* = 34	*n* = 34	
Hand hygiene before procedure	5 (15)	16 (48)	3.20 (1.33 to 7.72); $p = 0.008$
Washing with chlorhexidine soap	3 (9)	15 (45)	Not reported
Alcohol-based gel	2 (6)	1 (3)	Not reported
Use of gloves	34 (100)	34 (100)	
Disinfection of hub	15 (44)[a]	27 (82)	1.80 (1.20 to 2.70; $p < 0.004$
Hand hygiene after procedure	3 (9)	18 (54)	6.00 (1.95 to 18.44), $p < 0.001$
Washing with chlorhexidine soap	3 (9)	13 (39)	Not reported
Alcohol-based gel	0	5 (15)	Not reported

CVC dressing	*n* = 33	*n* = 33	
Hand hygiene before procedure	2 (6)	25 (76)	12.50 (3.22 to 48.56); $p < 0.001$
Washing with chlorhexidine soap	2 (6)	23(70)	Not reported
Alcohol-based gel	0	2 (6)	Not reported
Use of gloves	33 (100)	33 (100)	
Skin antisepsis	9 (27)	32 (97)	3.56 (2.03 to 6.23); $p < 0.001$
Hand hygiene after procedure	9 (27)	21 (64)	2.33 (1.26 to 4.31); $p < 0.006$
Washing with chlorhexidine soap	9 (27)	18 (55)	Not reported
Alcohol-based gel	0	3 (9)	Not reported
Knowledge	Not a study outcome		
Skills	Not a study outcome		
Process evaluation	See above compliance with CVC practices		

a Percentage corrected by reviewer.

Critical appraisal

Potential for bias

Group selection	Were there systematic differences between the baseline and intervention groups? YES. There was no statistical comparison between ICU A and ICU B. Reported data that showed minor differences between the study periods in age, gender, LOS and frequency of underlying diseases. However, in both ICUs the number of patient-days and CVC-days were consistently lower in the intervention period than in the pre-intervention period
	If YES, were the differences between the groups adjusted for in statistical analyses (e.g. as covariates or subgroups or stratification by propensity scores)? NOT REPORTED
Intervention administration	Were any confounding variables identified that could influence the effect estimate for the overall intervention? YES. Authors report that both ICUs were located within the same building, that the chief nurse of ICU A was transferred to ICU B during the study, and that nurses and physicians of all hospital units attended regular general meetings during which the success in ICU A was reported. This could have affected health-care workers' behaviour and had an impact on other units as well, possibly contributing to the initial decreased CVC-BSI rate in ICU B
	Was the effect of educational practice separable from effects of non-educational practice? YES (education alone)
	Were the intervention component(s) implemented as planned? NOT REPORTED. Stated that all staff in both ICUs responded to the questionnaire. However, the percentage of staff observed is unclear and there were a higher number of observations for CVC handling and dressing in ICU A, which had much lower patient numbers than ICU B during the intervention period (*n* = 41 vs. *n* = 262, respectively)
Missing data	Were there systematic differences between the baseline and intervention groups in data availability? UNCLEAR. Patient numbers differed considerably between ICUs, as well as between baseline and intervention

Outcome measurement	Were there systematic differences between the baseline and intervention groups in how outcomes were determined (including differences in how outcomes were defined)? UNCLEAR. Authors implied (not explicitly stated) that the definition of infections and the approach for assessing outcomes would have been the same in both study periods. However, no information was given on the staff diagnosing infections Was any blinding of personnel and/or outcome assessors reported (including assessors of blood cultures)? NO
Other possible sources of bias	Stated that the high compliance with the CVC insertion recommendations observed in the study was likely related to a previous intervention performed in the hospital; however, these recommendations were not stressed in the present educational intervention. CVC-BSI rates already improved in the pre-intervention period prior to the start of the intervention in both ICUs

Other critical appraisal criteria

Methods	Intervention described in sufficient detail to be replicated? PARTIALLY. Good description of the content of the intervention, but no breakdown of the content of each lecture or information about lecture duration Justification given for sample size? NOT REPORTED Data collection process reported? PARTIALLY. Three infection control nurses visited the ICUs daily and each patient was followed until 48 hours after discharge from ICU. However, does not state whether manual or electronic record management was used If YES or PARTIALLY, was the data collection process shown to be valid? NOT REPORTED If YES or PARTIALLY, was the data collection process shown to be reliable? NOT REPORTED Statistical tests described? YES
Results	Educational significance or effect size assessed? NOT REPORTED Target behaviour change achieved? PARTIALLY. Adherence to CVC practice was not 100% in all areas

Additional comments

- Not reported whether the participants knew that they were being observed.
- Device-days not defined (i.e. unclear whether captures multiple simultaneous CVCs/patients).
- Authors were contacted for CVC utilisation rate definition (defined as: number of central line-days/number of patient-days).

LONGMATE (2011)[110]

Methods

Study characteristics

Lead author, publication year(s) and reference(s)	Longmate (2011)[110]
Summary of approach	Single ICU, 4-year QI intervention based on gradual and iterative implementation of bundles, including infection surveillance feedback and performance feedback
Location	Scotland
Language	English
Critical care specialty	MICU and SICU
No. of critical care units	1
No. of hospitals	1
Hospital name (unless multicentre); city	Stirling Royal Infirmary, Stirling
Study design	Single-cohort before-and-after study with phased implementation of interventions
Study time periods	Baseline 1 September 2005 to 31 December 2006: Infection surveillance and interventions aimed at improving hand hygiene practices January 2007: CRBSI bundles and education implemented March 2007 to August 2009: interventions to reduce VAP March 2008: Scottish Patient Safety Programme launched in the ICU [stated this was for the last 16 months of the study (online Appendix 6) or last 18 months (primary publication)] November to December 2008: centralisation of CVC insertion pack March 2009: Three-nurse team assembled to support CVC bundles August 2009: End of monitoring Follow-up: None (continuous monitoring of QI programme)
Funding source	Stated that Health Protection Scotland provided funding for a nurse salary for the second year of the project
Conflicts of interest	Two authors had completed or were taking a SPSP Fellowship; one author was Nursing Lead for the Critical Care work stream of the SPSP at Stirling Royal Infirmary

SICU, surgical intensive care unit; SPSP, Scottish Patient Safety Programme.

Population and setting

Critical care unit characteristics

Nine-bed ICU in a general hospital. Full aseptic technique was not consistently performed at catheter insertion. For established CVCs there was variation in hand hygiene practices, and techniques for commencing injections and infusions. No daily prompt and no consistent approach was used for CVC removal (common practice was routine replacement after 7 days, sometimes over guidewire)

CVC defined as any i.v. catheter ending at or near the heart. Every patient admitted for more than 48 hours who during at least part of their admission had a CVC was assessed daily until discharge for CRBSI occurrence

	Baseline (year 1) (September 2005 to August 2006)[a]	Intervention (January 2007 to 31 August 2009)[b]	Difference between baseline and intervention
Patient population characteristics (all ICU patients)			
No. of patients admitted	439		Not tested statistically
September 2007 to August 2008 (year 3)		465	
September 2008 to August 2009 (year 4)		358	
Patients ventilated, %	69		Not tested statistically
September 2007 to August 2008 (year 3)		74	
September 2008 to August 2009 (year 4)		73	
Mean (SD) APACHE II score	19.8 (8.4)		
September 2007 to August 2008 (year 3)		21.0 (7.3)	Year 3 vs. 1: $p = 0.89$
September 2008 to August 2009 (year 4)		18.7 (8.7)	Year 4 vs. 1: $p = 0.38$
Median LOS, days	2.2		
September 2007 to August 2008 (year 3)		2.5	Year 3 vs. 1: $p = 0.18$
September 2008 to August 2009 (year 4)		2.3	Year 4 vs. 1: $p = 0.72$
ICU mortality rate, %	20		
September 2007 to August 2008 (year 3)		22	Year 3 vs. 1: $p = 0.48$
September 2008 to August 2009 (year 4)		22.6	Year 4 vs. 1: $p = 0.38$
Male gender, *n* (%) for subgroup with CVC and ICU stay > 2 days	143/255 (56.1)		Not tested statistically
September 2007 to August 2008 (year 3)		127/235 (54.0)	
September 2008 to August 2009 (year 4)		125/225 (55.5)	
Device characteristics			
Total no. of CVCs	414		
September 2007 to August 2008 (year 3)		317	Year 3 vs. 1: $p < 0.01$
September 2008 to August 2009 (year 4)		249	Year 4 vs. 1: $p < 0.01$

	Baseline (year 1) (September 2005 to August 2006)[a]	Intervention (January 2007 to 31 August 2009)[b]	Difference between baseline and intervention
Insertion site,* n *(%)			
Internal jugular	332 (80.2)		
September 2007 to August 2008 (year 3)		283 (89.3)	Year 3 vs. 1: $p < 0.01$
September 2008 to August 2009 (year 4)		227 (91.1)	Year 4 vs. 1: $p < 0.01$
Subclavian	63 (15.2)		
September 2007 to August 2008 (year 3)		24 (7.6)	Year 3 vs. 1: $p < 0.01$
September 2008 to August 2009 (year 4)		15 (6.02)	Year 4 vs. 1: $p < 0.01$
Femoral	19 (4.6)		
September 2007 to August 2008 (year 3)		10 (3.1)	Year 3 vs. 1: $p > 0.33$
September 2008 to August 2009 (year 4)		7 (2.81)	Year 4 vs. 1: $p < 0.01$
Insertion site antisepsis used	Default catheters were non-impregnated, four- or five-lumen CVCs. Chlorhexidine antisepsis was not consistently performed at catheter insertion (online appendix 6)		
Dressing type and duration/frequency	IV 3000 semipermeable transparent dressing (Smith and Nephew) (online appendix 6)		

a Baseline period included interventions for hand hygiene.
b Multiple interventions were introduced: CVC bundles from January 2007; VAP intervention from March 2007; Scottish Patient Safety Programme from March 2008.

Intervention characteristics

Objective	To reduce CRBSI in a UK ICU setting
Main focus of education	Catheter insertion and maintenance
Trainers (providers)	Group comprising three consultant clinicians, an infection surveillance nurse and two ICU charge nurses whose stated aim was to reduce CRBSI in the ICU. Two consultants had responsibility for training doctors in anaesthesia and intensive care
Training of trainers	Not reported
Learners (recipients)	ICU nurses and trainee doctors
Target behaviour change	Multiple behaviours associated with catheter insertion and maintenance practices
Development and testing	Not reported other than some changes were made as a result of discussions
Educational or behavioural theory	Not reported
Educational strategies and topics targeted (part from online appendix 6)	**Self-adhesive insertion checklist:** affixed to patients' notes. Highlighted aseptic technique, maximal barrier precautions, chlorhexidine skin antisepsis, preferred insertion site, and whether staff had completed CVC education package **Self-guided education programme** including slide show**:** Information on the insertion and maintenance bundles, and on pathogenesis, recognition and consequences of CRBSI. Completed by nurses and trainee doctors, followed by a brief test involving simple questions, with a record kept of which staff completed the test. Slide show and test mandatory for nurses from late 2008 Regular updates, presentations and tutorials: no details given **Supervision:** trainee doctors had to perform three supervised CVC insertions before working alone **Quarterly compulsory group education** (9–18 per group): Part of ongoing nurse development programmes: covered rates of infections and preventative behaviours (insertion and maintenance bundles) **Transient information provision:** discussion and visual displays **Lasting information provision:** statistical process control charts displayed in the ICU (variables not stated, other than infection incidence) **Promotion of staff engagement:** Initial daytime presence of an infection surveillance and QI nurse to prompt staff to follow bundles; checklist stickers made widely available in the ICU. Interventions publicised through presentations at hospital department meetings and a regional ICU meeting; open discussion and debate about the evidence base and bundles, with some changes made where necessary. Regular meetings with local infection control team and representatives of Health Protection Scotland
Infection surveillance feedback approach	Infection incidence per 1000 device-days and 1000 patient-days was displayed on statistical process control charts. Data were checked against ICU admission records and Ward Watcher database to ensure every patient was captured. Although data in the study were reported monthly and quarterly, it is unclear how often the charts in the ICU were updated. Validity and reliability of data collection not reported
Performance feedback approach (from online Appendix 6)	Hand washing behaviours were audited prior to handling CVCs and results were reported to staff. Details, validity, and reliability of method not stated
Concentration of education	Other than daily checklists and quarterly group sessions, frequency and duration educational approaches not reported
Non-educational intervention components (online Appendix 6)	Self-contained CVC insertion pack (introduced November 2008) Other interventions: • Interventions to reduce VAP/MRSA (March 2007–August 2009) • Scottish Patient Safety Programme (introduced March 2008) • Nurse team to support bundles (introduced March 2009)
Costs reported	Not reported

Outcome characteristics

Catheter-BSI definition (from online appendix 2) *Reference cited:* Hospital In Europe Link for Infection Control through Surveillance (HELICS);[174] supported by flow chart to help classify infection as BSI-A or BSI-B: online appendix 3); supported by flow chart to help diagnose catheter-related infection as CRI 1, CRI 2 or CRI 3: online appendix 4); definitions reported for CRI 1 and CRI 2 (local or general CVC-related infection without a positive blood culture – data not extracted)	**HELICS catheter-related infection (CRI 3) definition (equivalent to CRBSI)** • CVC-related BSI occurring 48 hours before or after catheter removal and positive culture with the same micro-organism of either quantitative CVC culture ≥ 103 CFU/ml or semiquantitative CVC culture > 15 CFU or quantitative blood culture ratio CVC blood sample/peripheral blood sample > 5, or differential delay of positivity of blood cultures or CVC blood sample culture positive ≤ 2 hours before peripheral blood culture (blood samples drawn at the same time) or positive culture with the same micro-organism from pus from insertion site **HELICS BSI classification** *BSI-A*: 1 positive blood culture for a recognised pathogen *or* Patient has at least one of the following signs or symptoms: fever (> 38 °C), chills, or hypotension and two positive blood cultures for a common skin contaminant (from two separate blood cultures drawn within 48 hours) (skin contaminants = coagulase-negative staphylococci, *Micrococcus* spp., *Propionibacterium acnes*, *Bacillus* spp., *Corynebacterium* spp.) *BSI-B*: Patient has at least one of the following signs or symptoms: fever (> 38 °C), chills, or hypotension *and either* One positive blood culture with a skin contaminant in patient with an intravascular line in place and in whom the physician instituted appropriate antimicrobial therapy *or* Positive blood antigen test (e.g. *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Neisseria meningitidis* or group B *Streptococcus*) CVCs removed had their tips routinely sent for Maki roll testing (method reported in online appendix 5)
Outcomes reported	Not stated whether primary or secondary: • All or none insertion bundle reliability • CRBSI annual incidence • CRBSI monthly and quarterly incidence (in statistical process control chart)

CFU, colony-forming units.

Results data

Primary outcomes

Outcome *n* = no. of patients who had a CVC during at least part of ICU stay and ICU stay of > 2 days	Baseline (year 1) (September 2005 to August 2006)[a]	Intervention (January 2007 to 31 August 2009)[b]	Difference between baseline and intervention
Mean (SD) CVC duration, days	4.94 (4.11)		
September 2007 to August 2008 (year 3)		6.11 (3.6)	Year 3 vs. 1: $p < 0.001$
September 2008 to August 2009 (year 4)		9.6 (8.46)	Year 4 vs. 1: $p < 0.001$
Total device utilisation, catheter-days – HELICS definition[c]	2660 (*n* = 255)		Not reported
September 2006 – August 2007 (year 2)		2613 (*n* = 257)	
September 2007 to August 2008 (year 3)		2155 (*n* = 235)	
September 2008 to August 2009 (year 4)		2138 (*n* = 225)	

Outcome			
n = no. of patients who had a CVC during at least part of ICU stay and ICU stay of > 2 days	Baseline (year 1) (September 2005 to August 2006)[a]	Intervention (January 2007 to 31 August 2009)[b]	Difference between baseline and intervention
Patient-days – HELICS definition[d]	1918 (*n* = 255)		Not reported
September 2006 to August 2007 (year 2)		1990 (*n* = 257)	
September 2007 to August 2008 (year 3)		1800 (*n* = 235)	
September 2008 to August 2009 (year 4)		1562 (*n* = 225)	
No. of devices/patient	Not reported	Not reported	Not reported
CRBSI incidence	9 (*n* = 255)		Not reported
September 2006 to August 2007 (year 2)		7 (*n* = 257)	
September 2007 to August 2008 (year 3)		1 (*n* = 235)	
September 2008 to August 2009 (year 4)		0 (*n* = 225)	
CRBSI incidence per 1000 catheter-days: HELICS definition[c]	3.38 (*n* = 255)		Incidence rate ratio (95% CI):
September 2006 to August 2007 (year 2)		2.68 (*n* = 257)	*Year 3 vs. 1*:
September 2007 to August 2008 (year 3)		0.46 (*n* = 235)	0.137 (0.003 to 0.990); *p* = 0.0134
September 2008 to August 2009 (year 4)		0.00 (*n* = 225)	*Year 4 vs. 1*:
			0 (0.0 to 0.63); *p* = 0.0025
CRBSI incidence per 1000 patient-days: HELICS definition[e]	4.69 (*n* = 255)		Not reported
September 2006 to August 2007 (year 2)		3.52 (*n* = 257)	
September 2007 to August 2008 (year 3)		0.56 (*n* = 235)	
September 2008 to August 2009 (year 4)		0.00 (*n* = 225)	
Median (Q1, Q3) LOS, days	9.7 (4, 20)		
September 2007 to August 2008 (year 3)		8.9 (4, 13)	Year 3 vs. 1: *p* = 0.64
September 2008 to August 2009 (year 4)		6.0 (3, 11)	Year 4 vs. 1: *p* = 0.63
Mean (SD) LOS, days	5.4 (3.9)		
September 2007 to August 2008 (year 3)		5.3 (3.7)	Year 3 vs. 1: *p* = 0.65
September 2008 to August 2009 (year 4)		5.9 (3.7)	Year 4 vs. 1: *p* = 0.13
Mortality, *n* (%)	54 (21.2)		
September 2007 to August 2008 (year 3)		49 (20.9)[f]	Year 3 vs. 1: *p* = 0.328
September 2008 to August 2009 (year 4)		36 (16)	Year 4 vs. 1: *p* = 0.013

a Baseline period included interventions for hand hygiene.
b Multiple interventions were introduced: CVC bundles from January 2007; VAP intervention from March 2007; Scottish Patient Safety Programme from March 2008.
c HELICS definition takes into account the number of CVCs per patient – therefore different from the CDC/NNIS definition.
d HELICS definition of patient-days is equivalent to NNIS/CDC definition of device-days.
e HELICS definition of incidence per 1000 patient-days is equivalent to CDC/NNIS definition of incidence per 1000 device-days (as patients and devices are synonymous in the CDC/NNIS definition).
f Incorrect percentage reported (21.7); correct value provided by reviewer (20.9).

Secondary outcomes

Reaction to education	Not a study outcome
Attitudes	Not a study outcome
Compliance	Compliance with CVC insertion bundle reported (chart only) from March 2008 onwards – the time of implementation of Scottish Patient Safety Programme (data not extracted)
Knowledge	Not a study outcome
Skills	Not a study outcome
Process evaluation	Barriers identified (online appendix 6) (no quantitative data reported): 1. Some staff had difficulty seeing the skin area prepared with chlorhexidine, so it was agreed that povidone–iodine could be used to colour the skin, followed by chlorhexidine 2. Two consultant clinicians doubted the need for full aseptic technique for insertion; resolved after evidence sharing 3. Initially unable to reach agreement on a system for collecting process measurements that had full support of both clinicians and data analysts (eventually agreed concurrent with implementation of Scottish Patient Safety Programme)

Critical appraisal

Potential for bias

Group selection	Were there systematic differences between the baseline and intervention groups? UNCLEAR. Gender mix, overall morbidity score, LOS and mortality were broadly similar for years 1, 3 and 4. However, no patient characteristics were reported for year 2. Age not reported If YES, were the differences between the groups adjusted for in statistical analyses? NOT APPLICABLE
Intervention administration	Were any confounding variables identified that could influence the effect estimate for the overall intervention? UNCLEAR. Organisational changes took place during the intervention but were not fully described. The Scottish Patient Safety Programme (a government-supported national initiative) was applied in the ICU during the last 16 months (according to appendix 6) or 18 months (according to main text) of the study, although this was stated as being part of the QI process. Authors stated that this had significant positive implications for leadership, administrative support, prioritisation and infrastructure but details were not reported Was the effect of educational practice separable from effects of non-educational practice? NO. Multicomponent interventions not limited to education Were the intervention component(s) implemented as planned? PARTIALLY. Compliance ('reliability') reported only for the insertion bundle: data showed compliance reached 100% in some but not all months from March 2008 onwards
Missing data	Were there systematic differences between the baseline and intervention groups in data availability? UNCLEAR. Two data sets are reported for the number of patients with CVCs. The data appear to show that the number of patients who had a CVC was smaller than the 'study group' number who had a CVC for at least part of a > 2-day stay in ICU
Outcome measurement	Were there systematic differences between the baseline and intervention groups in how outcomes were determined? NOT REPORTED. The HELICS definition and classification of infections was used throughout the study but no information was given on the staff involved in diagnosing infections Was any blinding of personnel and/or outcome assessors reported (including assessors of blood cultures)? NO. Stated that the data collection and interventions were non-blinded
Other possible sources of bias	Insertion bundle compliance ('reliability') was self-reported by clinicians

Other critical appraisal criteria

Methods	Intervention described in sufficient detail to be replicated? NO. A complex intervention comprising many components, not all of which were clearly reported
	Justification given for sample size? NOT REPORTED
	Data collection process reported? PARTIALLY. Limited information provided. No information on validity and reliability given
	If YES or PARTIALLY, was the data collection process shown to be valid? NO. Authors stated that they did not seek to further enhance validity of the process measurement
	If YES or PARTIALLY, was the data collection process shown to be reliable? NOT REPORTED
	Statistical tests described? YES
Results	Educational significance or effect size assessed? NO
	Target behaviour change achieved? NOT REPORTED

MISSET (2004)[117]

Methods

Study characteristics

Lead author, publication year(s) and reference(s)	Misset *et al*. (2004)[117]
Summary of approach	Single unit continuous quality-improvement programme to reduce nosocomial infection (NI) rates (VAP, UTI and CVC related)
Location	France
Language	English
Critical care specialty	Medical–surgical
No. of critical care units	1
No. of hospitals	1
Hospital name (unless multicentre); city	Saint Joseph Hospital, Paris
Study design	Variation of single-cohort before-and-after study, with trend analysis instead of baseline data
Study time periods	Baseline: none Intervention: 1995–2000 Follow-up: none (continuous quality-improvement programme)
Funding source	None reported
Conflicts of interest	Not reported

Population and setting

Critical care unit characteristics

10-bed ICU in a 450-bed tertiary care centre hospital

Infection control throughout the hospital was co-ordinated by an NI Control Committee and an Operative Infection Control Unit

New nurses received a 2-month training course, during which specific protocols regarding NI prevention were discussed

Nurse to patient ratio: 1 : 2

Nursing assistant to patient ratio: 1 : 10

Universal measures for preventing person-to-person transmission:

- Hand-washing before and after each patient contact
- Wearing gloves for handling secretions or contaminated objects
- Wearing a gown when soiling was anticipated and/or
- When the patient had multiple-drug-resistant bacteria and
- Geographical isolation of all patients

CVCs and arterial catheters were not routinely placed and CVCs were removed when infections was suspected. CVCs inserted before ICU admission were routinely removed or replaced within 48 hours after ICU admission

Patient population characteristics during the 5-year study period (starting/baseline data not reported)[a]	Total patients = 1764 (*n* = no. of patients)
Age (years), mean (± SD)	61 (± 18)
Length of ICU stay, mean days (± SD)	9.7 (± 16.1)
SAPS II[b] score, mean (± SD)	37 (± 21)
Omega score per ICU stay,[c] mean (± SD)	138 (± 256)
In-ICU mortality, %	21
Surgical reasons for admission, *n*	*n* = 529
Scheduled postoperative surveillance, *n*	*n* = 104
Postoperative complications, *n*	*n* = 396
Trauma, *n*	*n* = 29
Medial reasons for admission, *n*	*n* = 1235
Infection as the main diagnosis, *n*	*n* = 553
• Lower respiratory tract, % • Urinary tract,% • Neuromeningeal, % • Endocarditis, % • Cellulitis, %	73 12 6 6 3
Non-infectious disease as the main diagnosis, *n*	*n* = 682
Device characteristics during the 5-year study period (starting/ baseline data not reported)	The site of CVC insertion was at the physician's discretion. Use of single or multiple-lumen catheters as clinically required and use of haemodialysis catheters for fluids or parenteral nutrition only when there was no alternative. CVCs and arterial catheters were not routinely placed and CVCs were removed when infection was suspected. CVCs inserted before ICU admission were routinely removed or replaced within 48 hours after ICU admission

Device characteristics during the 5-year study period (starting/ baseline data not reported)[a]	Total patients = 1764 (*n* = no. of patients)	
CVC (≥ 1), *n* (%)	765 (43)	
CVC used for dialysis, *n*	203	
Arterial catheter (≥ 1), *n* (%)	261 (15)	
Other devices:		
Mechanical ventilation, *n* (%)	976 (55)	
Mechanical ventilation > 48 hours, *n* (%)	682 (39)	
Urinary tract catheter, *n* (%)	960 (55)	
Invasive procedure utilisation rate over the 5-year study period[d]	**Procedure utilisation rate, all patients (%)**	**Duration of procedure use per patient, mean days (± SD)**
Mechanical ventilation	0.74	13.0 (± 18.8)
Urinary tract catheter	0.73	13.1 (± 17.9)
CVC	0.61	13.8 (± 18.3)
Per CVC		6.2 (± 4.4)
Arterial catheter	0.05	3.5 (± 3.2)
Per arterial catheter		3.1 (± 2.3)
Insertion site antisepsis used	Skin disinfection with 10% povidone–iodine solution	
Dressing type and duration/frequency	Replacement of catheter site dressings every 48 hours or at longer intervals when clinically indicated	

a Length of ICU stay, SAPS II and Omega scores also reported per year over the 5-year period but data not extracted by reviewers.
b SAPS II score, Simplified Acute Physiology Score II – used to measure disease severity.
c Omega score used to measure treatment intensity during ICU stay.
d Utilisation rate = procedure days divided by patient-days.

Intervention characteristics

Objective	Maximise compliance of physicians and nurses with infection control practices and assess its long-term impact on the rates of VAP, UTI and vascular catheter-related infection in critically ill patients
Main focus of education	Simultaneous education and training for vascular catheter, VAP and UTI infection prevention and catheter maintenance
Trainers (providers)	Head nurse
Training of trainers	Not reported
Learners (recipients)	All staff (nurses and residents)
Target behaviour change	Compliance with infection control practices
Development and testing	Infection control practices were written by the ICU staff together with the Infection Control Unit and were derived from CDC recommendations
Educational or behavioural theory	Not reported
Educational strategies and topics targeted	**Guidelines** or their modifications were explained and given to all the staff during a **yearly unit meeting** and to the new nurses and residents by the head nurse. They were continuously available in a specific written form located in the unit Infection prevention and catheter maintenance, including daily examination of catheter sites, skin disinfection with 10% povidone–iodine, use of surgical drapes and of a gown for the operator, use of single- or multiple-lumen catheters as clinically required, use of haemodialysis catheters for fluids or parenteral nutrition only when there was no alternative, replacement of catheter site dressings every 48 hours or at longer intervals when clinically indicated. Measures for preventing person-to-person transmission included hand washing before and after each patient contact, wearing gloves for handling secretions or contaminated objects, and wearing a gown when soiling was anticipated and/or when the patient had multiple-drug resistant bacteria, and geographical isolation of all patients. The site of the CVC insertion was at the physician's discretion. The programme was updated regularly according to infection and colonisation rates and reports in the literature (no further details reported)
Infection surveillance feedback approach	All the patients referred to the ICU were included in the nosocomial infection surveillance programme. Microbiological specimens were collected when the attending physician suspected infection based on systemic signs (unexplained fever, chills, hypotension) and/or local signs (pus or pain at a vascular catheter insertion site), consisting of the catheter tip for vascular catheter colonisation (details for VAP/UTI procedure not data extracted). All CVCs and arterial catheters were cultured at removal, regardless of whether or not infection was suspected. ICU-acquired infection was defined as infection documented after at least 48 hours in the ICU Monitoring of trends in vascular catheter colonisation and related bacteraemia rates: programme on microbial resistance containment (policy for containing antibiotic resistance included collection of microbiological specimens from suspected infection sites if at all possible and starting broad-spectrum antibiotic therapy early, then changing to narrow-spectrum therapy as soon as the organism was identified and its antimicrobial susceptibility profile established. Selective digestive decontamination was used in 15 patients (0.8%) as an adjunctive technique to control outbreaks of multiple-drug-resistant bacteria) Descriptive statistics of nosocomial infection rates were communicated to the ICU staff every 6 months (no further details reported). Validity and reliability of the assessment approach were not reported
Performance feedback approach	Not included in the study
Concentration of education	Not reported, other than yearly unit meetings
Non-educational intervention components	Catheter tunnelling was required for internal jugular and femoral sites from 1996 and 1999, respectively; use of povidone–iodine
Costs reported	Not reported

Outcome characteristics

Catheter-BSI definition *Reference cited*: Centers for Disease Control and Prevention[199]	All patients in ICU were included. All CVCs and arterial catheters were cultured at removal, regardless of whether infection was suspected. ICU-acquired infection was defined as infection documented after at least 48 hours in the ICU Microbiological specimens were collected as recommended by the CDC. For CVCs and arterial catheters. Colonisation was assessed by quantitatively culturing CVC/arterial catheter tips. CVC and arterial catheter infection was considered when bacteraemia due to a micro-organism simultaneously colonising the catheter (at least two positive blood cultures in the case of *Staphylococcus* spp. other than *S. aureus*) was present. Thresholds above which cultures were considered positive were 10^3 CFU/ml for CVC or arterial catheter colonisation
Outcomes reported	Not stated whether primary or secondary: • CVC colonisation • CVC bacteraemia per 1000 procedure-days • Patient device-days • Device utilisation Surveillance data also reported for VAP and UTI, but data not extracted by reviewers

Results data

Primary outcomes

Outcome		1995–6	1996–7	1997–8	1998–9	1999–2000	Changes in incidence rates over the 5-year study period (chi-squared test for tendency)
Device duration		Not reported					Not reported
Total device utilisation[a]	**CVC**	0.65	0.76	0.56	0.58	0.57	5-year rate not significant (no *p*-value reported)
	Arterial catheter	0.07	0.07	0.05	0.05	0.04	
CVC-BSI/CVC patients		7/117	6/154	6/178	2/147	0/153	$p = 0.001$
CLAB incidence rate		7	6	6	2	0	Not reported
CVC-BSI incidence per 1000 CVC-days		3.5	2.4	2.9	0.9	0.0	Not reported
Mean length of ICU stay per year[a]		9.52	10.67	9.52	9.14	8.76	Not reported
Mortality		Not reported other than 5-year rate					Not reported

a Data extracted from graph using Engauge software.

Secondary outcomes

Reaction to education	Not a study outcome
Attitudes	Not a study outcome
Compliance:	Compliance with hand washing guidelines was only assessed in the first year of the project
Knowledge	Not a study outcome
Skills	Not a study outcome
Process evaluation	Not a study outcome

Critical appraisal

Potential for bias

Group selection	Were there systematic differences between the baseline and intervention groups? NOT REPORTED. However, states that there were no significant changes in disease severity (SAPS II score), mean length of ICU stay, and treatment intensity (Omega score) (graph provided), regardless of invasive device utilisation rates (no *p*-value reported)
	If YES, were the differences between the groups adjusted for in statistical analyses (e.g. as covariates or subgroups, or stratification by propensity scores)? NOT APPLICABLE
Intervention administration	Were any confounding variables identified that could influence the effect estimate for the overall intervention? NOT REPORTED. However, stated that there were no changes in the structure or staffing of the unit during the study
	Was the effect of educational practice separable from effects of non-educational practice? NO
	Were the intervention component(s) implemented as planned? NOT REPORTED. However, states that 6% of items in an audit were considered insufficiently respected and the results allowed the continuous reinforcement of the observance of procedures of hand washing and surfaces cleaning and implementing formation sessions about cross-transmission
Missing data	Were there systematic differences between the baseline and intervention groups in data availability? NOT REPORTED
Outcome measurement	Were there systematic differences between the baseline and intervention groups in how outcomes were determined (including differences in how outcomes were defined)? NOT REPORTED
	Was any blinding of personnel and/or outcome assessors reported (including assessors of blood cultures)? NO
Other possible sources of bias	No other sources of bias were reported by the authors or identified by the reviewers based on the information presented

Other critical appraisal criteria

Methods	Intervention described in sufficient detail to be replicated? NO. No details of education and training provided
	Justification given for sample size? NOT REPORTED
	Data collection process reported? PARTIALLY. Nurses collected the specimens and documented the dates of insertion and removal of devices. The physicians collected all other data. Format of data collection (e.g. electronic, hard copy) and nature of archiving not reported
	If YES or PARTIALLY, was the data collection process shown to be valid? NOT REPORTED
	If YES or PARTIALLY, was the data collection process shown to be reliable? NOT REPORTED
	Statistical tests described? YES
Results	Educational significance or effect size assessed? NOT REPORTED
	Target behaviour change achieved? UNCLEAR. Compliance assessment was made by the Infection Control Unit only twice during the first year of study and hand washing compliance was assessed only during the first year, but compliance data were not reported

Additional comments

- Assessment of the quality of hand washing and invasive devices management was made each time a patient was colonised with MRSA among the nurses and physicians in charge of the colonised patient (136 audits assessing 26 items). No further details reported.
- Hand washing compliance was assessed during the first year of the study only, with a global score built from the quality of washing, rinsing, soap or antiseptic utilisation, drying and duration. The results were based on 46 samples of hands before and after washing from 12 nurses and 8 physicians/residents [first 6 months of study: mean score 88 (± 5%); second 6 months of study: mean score 93 (± 4%)].
- CVC colonisation data reported (not extracted).
- Data were compared between first 2.5 years and last 2.5 years but these periods appear arbitrary (no justification was provided in relation to the timing of intervention components).

PALOMAR MARTINEZ (2010)[68]

Methods

Study characteristics

Lead author, publication year(s) and reference(s)	Palomar Martinez (2010)[68]
Summary of approach	A multicentre regional-scale pilot study to test the feasibility of applying the Michigan approach for preventing CRBSI in Spanish critical care units. Catheter maintenance practice was included in addition to the five-catheter insertion bundle components used in the Michigan study
Location	Spain (three separate regions: Castilla-León, Cataluña, Andalucía)
Language	Spanish
Critical care specialty	Not reported (list of participating hospitals included cardiac surgery and general ICUs but specialties not mentioned for most hospitals)
No. of critical care units	17 (nine intervention, eight control) in study period; varied in baseline period
No. of hospitals	16
Hospital name (unless multicentre); city	Hospital names are listed in the publication
Study design	Non-randomised parallel group study with nine intervention and nine control ICUs, distributed evenly among three separate autonomous regions of Spain
Study time periods	Baseline: 2004, 2005, 2006 (3 years, with separate historical data for each) (note: no baseline data immediately preceding the intervention, i.e. during January to September 2007) Intervention: 1 October to 31 December 2007 (3 months) Follow-up: None reported
Funding source	Spanish Ministry of Health and Social Policy
Conflicts of interest	Not reported

Population and setting

Critical care unit characteristics	Not reported
Patient population characteristics	Not reported
Device characteristics	Described only as CVCs; stated that the use of catheters impregnated with antiseptic or antibiotics was not monitored
Insertion site antisepsis used	Not reported
Dressing type and duration/frequency	Not reported

Intervention characteristics

Objective	To assess the applicability on a national level in Spain of the interventions proposed by Pronovost and colleagues in Michigan, USA, for the prevention of central vascular catheter-related bacteraemia in patients admitted to the ICU
Main focus of education	Catheter insertion and maintenance
Trainers (providers)	Not explicitly reported. Authors stated that a responsible physician and a nurse were identified (in each intervention ICU) to ensure compliance with the intervention
Training of trainers	Not reported
Learners (recipients)	ICU doctors and nurses
Target behaviour change	Not stated explicitly but compliance was assessed for skin preparation with chlorhexidine, hand hygiene, preparation and maintenance of the sterile field, and the use of barrier precautions (gloves, masks, gowns)
Development and testing	A pilot study – no prior development or testing reported other than that the study was based on the Michigan intervention in the USA
Educational or behavioural theory	Not reported
Educational strategies and topics targeted	**Meetings:** Briefing meeting: Held in September, 2007, attended by two representatives (physician and nurse) from each participating ICU. At this meeting, materials to be used were distributed, including an electronic version of the programme/intervention. To assess compliance with the recommendations and the degree of acceptance of the project, a meeting was held at the end of the study period, in which each of the leaders explained their experiences and reported especially on the worst aspects of compliance **Daily goals sheet** (no details provided) **Catheter insertion** checklist (no details provided) **Safety rounds** (no details provided) **Online 2-hour course:** For all ICU staff, synthesising the key points of catheter-related infections, particularly clinical impact and prevention measures **Poster(s):** Covered the five proposed procedures to reduce bloodstream infections (hand hygiene, maximum use of aseptic barriers during insertion, asepsis of the skin at the insertion site with chlorhexidine, avoiding the femoral access route and removing all unnecessary CVCs). Posted in all intervention ICUs in joint meetings between the medical and nursing staff **Teams:** Trained in each hospital or working group to ensure the implementation of interventions and safety of hospitalised patients (no further details given) **Supporting document(s):** Available in graphical format recalling the points of intervention (no details provided)
Infection surveillance feedback approach	Stated that to be eligible in the project the ICUs should have experience in nosocomial infection surveillance, although not itself part of the intervention
Performance feedback approach	Not explicitly stated as being part of the intervention; unclear whether performance feedback might have occurred in specific ICUs. A standardised questionnaire [the Spanish version of the Hospital Survey on Patient Safety of the Agency for Healthcare Research and Quality (AHRQ)] was used to assess the safety culture, but it was not stated whether the results were known by ICU staff
Concentration of education	Unclear whether all the meetings that took place are described. The main training component appeared to be an online study module with 2-hour duration
Non-educational intervention components	Chlorhexidine skin antisepsis used. Note that, although a catheter insertion cart was also planned, this was not actually implemented
Costs reported	No

Outcome characteristics

CVC-related bacteraemia infection definition	Infections meeting the following definitions were accepted as CVC-related bacteraemia: CVC-related bacteraemia (after withdrawal of the CVC): • Isolation of the same micro-organism (gender and species and identical antibiogram) in blood extracted from a peripheral vein and quantitative culture or respectively from tip of the catheter in a patient with clinical sepsis and without another apparent focus of infection. In the case of coagulase-negative staphylococci it is necessary to isolate the same micro-organism (gender, species and antibiogram) in at least two blood cultures CVC-related bacteraemia (without removal of the CVC): • Clinical picture of sepsis, no other apparent source of infection, in which the same organism is isolated in quantitative simultaneous blood cultures at a rate ≥ 5 : 1 in samples extracted through catheter compared with those obtained by venepuncture Bacteraemia probably related to CVC, in absence of catheter culture: • Clinical picture of sepsis but no other apparent source of infection, with blood culture positive and symptoms disappearing within 48 hours of withdrawal of the venous line. In case of coagulase-negative staphylococci isolation of the same organism is required (genus, species and sensitivity) in at least two blood cultures. This clinical situation is known as primary bacteraemia
Outcomes reported	Catheter-related bacteraemia incidence and incidence density per 1000 CVC-days Secondary bacteraemia incidence and incidence density per 1000 patient-days No. of CVC-days No. of patient-days Compliance with evidence-based practices (most data reported for only six ICUs that submitted data)

Results data

Primary outcomes

Outcome *n* = no. of ICUs	Intervention ICUs	Control ICUs	Difference between baseline and post intervention
Device duration	Not reported	Not reported	Not reported
Total device utilisation, CVC-days			
(a) Baseline: 2004	(a) 6434 (*n* = 5)	(a) 2600 (*n* = 5)	Statistical significance not reported
(b) Baseline: 2005	(b) 7960 (*n* = 7)	(b) 3260 (*n* = 6)	
(c) Baseline: 2006	(c) 9164 (*n* = 8)	(c) 4644 (*n* = 8)	
(d) Intervention (2007; 3 months)	(d) 11,432 (*n* = 9)	(d) 8453 (*n* = 8)	
No. of devices/patient	Not reported	Not reported	Not reported
CVC-related bacteraemia incidence			
(a) Baseline: 2004	(a) 39 (*n* = 5)	(a) 32 (*n* = 5)	Statistical significance not reported
(b) Baseline: 2005	(b) 60 (*n* = 7)	(b) 47 (*n* = 6)	
(c) Baseline: 2006	(c) 59 (*n* = 8)	(c) 59 (*n* = 8)	
(d) Intervention (2007; 3 months)	(d) 44 (*n* = 9)	(d) 28 (*n* = 8)	
CVC-related bacteraemia incidence density per 1000 catheter-days			
All three regions*			
(a) Baseline: 2004	(a) 6.06 (*n* = 5)	(a) 12.31 (*n* = 5)	Differences among all four study dates: Intervention: $p < 0.0032$ Control: $p < 0.0001$
(b) Baseline: 2005	(b) 7.54 (*n* = 7)	(b) 14.4 (*n* = 6)	
(c) Baseline: 2006	(c) 6.44 (*n* = 8)	(c) 12.7 (*n* = 8)	
(d) Intervention (2007; 3 months)	(d) 3.85 (*n* = 9)	(d) 3.31 (*n* = 8)	
CVC-related bacteraemia incidence per 1000 patient-days	Not reported	Not reported	Not reported
LOS	Not reported	Not reported	Not reported
Mortality	Not reported	Not reported	Not reported

*Data were also reported separately for Castilla-León, Andalucía and Cataluña but the numbers of ICUs contributing data for these regions in each year were not specified (data not extracted by reviewers)

Secondary outcomes

Reaction to education	Not a study outcome
Attitudes	Not a study outcome
Compliance	No compliance data were reported for the baseline years. For the study period, compliance with insertion checklists was reported narratively to be around 90%. No hospitals created a catheter insertion cart (i.e. 0% compliance). Removal of unnecessary catheters was not quantified. Femoral insertions were 18% of the total CVC insertions. Further data on compliance with the following practices were reported only for six ICUs that submitted data: skin preparation with chlorhexidine, hand hygiene, preparation and maintenance of the sterile field, and the use of barrier precautions (gloves, masks, gowns). Compliance was high in all six ICUs except for chlorhexidine use in one ICU (approximately 17%) owing to lack of availability. The above data are assumed to be for intervention ICUs, although this was not stated explicitly
Knowledge	Not a study outcome
Skills	Not a study outcome
Process evaluation	Formal process evaluation was not reported, although the following potential barriers and other factors were mentioned narratively **Variable implementation:** • A daily goals sheet was used 'unevenly' across the ICUs • Only one unit developed a registry of problems related to CVCs • In the 'Clean Hands Campaign' one hospital provided bedside alcohol hand wash • Variation in the choice of insertion site was 'very high' across the ICUs • Some of the units formed working groups identifying specific mistakes and improvement targets but others did not **Potential barriers:** • Stated that the heads of each unit, doctor and nurse, did not have the extra time resource for implementation of the programme as opposed to what happened in Michigan; more than half of the staff surveyed considered there were not enough staff to cope with the care load • Initially, some practitioners expressed doubts about the effectiveness of chlorhexidine; it was difficult to obtain from some pharmacies • Only one-third of the respondents considered themselves informed of the problems occurring in their unit/service; and < 40% said that in their work unit errors were discussed and corrective measures sought • Only 40% of respondents considered that there was good cooperation between units/services • In one ICU a presentation was delivered only to doctors, not nurses, and in this ICU CVC-bacteraemia rates rose; in two other ICUs there were delays in presentations for various reasons • Stated that the posters used were small in size and over time they failed to attract attention

Critical appraisal

Potential for bias

Group selection	Were there systematic differences between the baseline and intervention groups? YES. Stated that the improvement (in CVC-bacteraemia rates) was more pronounced in those units that had the highest starting rates, which generally occurred more in the control ICUs
	If YES, were the differences between the groups adjusted for in statistical analyses? NO
Intervention administration	Were any confounding variables identified that could influence the effect estimate for the overall intervention? UNCLEAR. Limited detail reported. Stated that the use of antiseptic or antibiotic impregnated catheters was not monitored
	Was the effect of educational practice separable from effects of non-educational practice? UNCLEAR. No information provided about other practices such as use of antibiotics or impregnated catheters
	Were the intervention component(s) implemented as planned? NO. None of the hospitals implemented a catheter insertion cart. Chlorhexidine was difficult to obtain in one ICU
Missing data	Were there systematic differences between the baseline and intervention groups in data availability? NOT REPORTED. No information given on the patient population
Outcome measurement	Were there systematic differences between the baseline and intervention groups in how outcomes were determined (including differences in how outcomes were defined)? UNCLEAR. Standard infection definitions appear to have been used, although it was not stated explicitly that these were always applied in all ICUs in all project years
	Was any blinding of personnel and/or outcome assessors reported (including assessors of blood cultures)? NO
Other possible sources of bias	The authors acknowledged that participants in control interventions were able to attend the initial intervention briefing meetings and would have been aware of the published Michigan study so may have independently implemented some aspects of clinical practice that formed the basis of the intervention. This could lead to performance bias

Other critical appraisal criteria

Methods	Intervention described in sufficient detail to be replicated? PARTIALLY. The objectives and the evidence-based practices included in the intervention are clear but details of how they were implemented are lacking, so the general principles could be reproduced but not the specific approaches used
	Justification given for sample size? NOT REPORTED
	Data collection process reported? NOT REPORTED
	If YES or PARTIALLY, was the data collection process shown to be valid? NOT APPLICABLE
	If YES or PARTIALLY, was the data collection process shown to be reliable? NOT APPLICABLE
	Statistical tests described? YES
Results	Educational significance or effect size assessed? NO
	Target behaviour change achieved? UNCLEAR. Formal behaviour change targets were not explicitly specified. Compliance with some evidence-based practices was high but the data appear to be only from intervention ICUs (no baseline or control ICU data appear to have been presented for compliance)

PEREZ PARRA (2010)[122]

Methods

Study characteristics

Lead author, publication year(s) and reference(s)	Perez Parra (2010)[122]
Summary of approach	Single hospital intervention based on short (15-minute) lecture on evidence-based approaches for catheter insertion and maintenance, with pre- and post-tests in three ICUs (no reinforcement of education)
Location	Spain
Language	English
Critical care specialty	Medical, general post-surgery, cardiac post-surgery
No. of critical care units	3
No. of hospitals	1
Hospital name (unless multicentre); city	Hospital General Universitario Gregorio Maragñón, Madrid
Study design	Cohort before-and-after study, with outcomes data for three ICUs grouped as a single cohort and also presented as three separate cohorts
Study time periods	Baseline: February to October 2006 (9 months) Intervention: November 2006 (15–20 minutes) Follow-up: December 2006 to August 2007 (9 months) Post-intervention test: May 2007 (6 months after intervention)
Funding source	La Investigación Biomédica del Hospital General Universitario Gregorio Maragñón and Fondo de Investigación Sanitaria (funding to lead author)
Conflicts of interest	Stated no conflicts of interest

Population and setting

Critical care unit characteristics	Three critical care units with a joint total of 60 beds in a tertiary university hospital. CVCs were routinely inserted by physicians and managed by nurses Mean (95% CI) duration of work experience for the ICU staff: • Nurses 8.9 (7.8–10.1) years • Physicians: 8.1 (5.3–10.8) years
Patient population characteristics	Not reported
Device characteristics	Described only as CVCs; stated that the type of CVC did not change during the study
Insertion site antisepsis used	Not reported, but stated that there were no changes in antiseptics during the study
Dressing type and duration/ frequency	Not reported, but stated there were no changes in supplies used in CVC insertion and care during the study

Intervention characteristics

Objective	To analyse the effect of a single evidence-based educational intervention on the incidence of CLABSI in ICUs with acceptable baseline incidences and to assess the knowledge standards for CLABSI prevention among health-care workers in a large teaching hospital
Main focus of education	Catheter insertion and maintenance
Trainers (providers)	Not stated explicitly but the study authors implied that they gave the lectures
Training of trainers	Not reported
Learners (recipients)	The same lecture was given to all ICU workers (physicians, residents, nurses and students) on all shifts
Target behaviour change	Compliance with IDSA-CDC guidelines for preventing intravascular catheter-related infections (10-point list as below)
Development and testing	Not reported
Educational or behavioural theory	Not reported
Educational strategies and topics targeted	**Short lecture (15 minutes):** On the 10 main points of the IDSA-CDC guidelines for prevention of intravascular catheter-related infections: 1. Use of a sterile sheet when preparing CVC insertion site 2. Choice of subclavian vein as preferred insertion site 3. Use of closed needleless catheter connection systems 4. Chlorhexidine skin disinfection before CVC insertion 5. CVC site dressing regimens 6. Aseptic technique during CVC care and maintenance (hand washing and use of gloves) 7. Optimal frequency of CVC dressing replacement 8. Use of parenteral nutrition through a multilumen CVC 9. Management of suspected CLABSI (avoiding guidewire exchange of CVC) 10. Replacement of administration sets, needleless systems and parenteral fluids
Infection surveillance feedback approach	Not included in intervention
Performance feedback approach	Multiple-choice questionnaire conducted a few minutes before and 6 months after the lecture. Covered the 10 points specified in the lecture (see above). Validity and reliability of questionnaire not reported
Concentration of education	Each questionnaire test took 15–20 minutes to complete. Total time to complete a 15-minute lecture and two tests would be 45–55 minutes. In total, 30 lectures were given to cover all shifts in the three ICUs. Six months between education and post-education test
Non-educational intervention components	None (intervention purely educational)
Costs reported	No

Outcome characteristics

Catheter-BSI definition Reference cited: O'Grady NP *et al.*[196]	Followed definitions and recommendations of the IDSA-CDC guidelines (reference cited). A CVC-related bloodstream infection was considered to be ICU-related if it occurred at least 48 hours after admission to or up to 48 hours after discharge from the ICU. Catheter tips were cultured using the roll plate method (references and equipment for catheter tip and blood cultures cited)
Outcomes reported	Not stated whether primary or secondary: CLABSI incidence Device utilisation (catheter-days) Knowledge

IDSA, Infectious Diseases Society of America.

Results data

Primary outcomes

Outcome	Baseline (9 months)	Post intervention (9 months)	Difference between baseline and post intervention
Device duration	Not reported	Not reported	Not reported
Total device utilisation, catheter-days			
All three ICUs	10,661	11,582	Not reported
General post-surgery ICU	3,403	4,064	
Cardiac post-surgery ICU	2,842	2,981	
MICU	4,416	4,537	
No. of devices/patient	Not reported	Not reported	Not reported
CLABSI incidence			
All three ICUs	45	34	Relative risk[a] = 0.69 (95%CI 0.44 to 1.08); $p = 0.11$
General post-surgery ICU	18	14	
Cardiac post-surgery ICU	12	8	
MICU	15	12	
CLABSI incidence per 1000 catheter-days			
All three ICUs	4.22	2.94	30.3%;[b] $p = 0.03$
General post-surgery ICU	5.3	3.4	35.8%; $p = 0.05$
Cardiac post-surgery ICU	4.2	2.7	35.7%; $p = 0.12$
MICU	3.4	2.6	23.5%; $p = 0.31$
CLABSI incidence per 1000 patient-days	Not reported	Not reported	Not reported
LOS	Not reported	Not reported	Not reported
Mortality	Not reported	Not reported	Not reported

a Based on Poisson regression for overall CLABSI incidence.
b Reported by authors as 30.9%.

Additional monthly CLABSI data extracted from graph (figure 1)[122] using Engauge software	Baseline	Post intervention
January 2006	2.5	
February 2006	5.9	
March 2006	4.8	
April 2006	3.8	
May 2006	4.4	
June 2006	4.6	
July 2006	4.2	
August 2006	3.3	
September 2006	4.4	
October 2006	3.2	
November 2006	3.0	
December 2006		2.9
January 2007		3.5
February 2007		3.8
March 2007		0
April 2007		3.6
May 2007		1.7
June 2007		3.6
July 2007		4.2
August 2007		2.7
September 2007		3.1
October 2007		2.3
November 2007		0.9
December 2007		2.9
January 2008		5.7
February 2008		2.2
March 2008		1.8
April 2008		2.5
May 2008		0.9
June 2008		6.9
July 2008		2.5
August 2008		4.6
September 2008		5.6
October 2008		2.3
November 2008		3.8
December 2008		2.5

Secondary outcomes

Reaction to education	Not a study outcome
Attitudes	Not a study outcome
Compliance	Number receiving the pre-test and intervention: Nurses: 125 (including 22 students) Physicians: 30 (including 10 residents) Total health-care workers: 155 No. completing the post-intervention test (% of those who received the intervention): • Nurses: 64 (51%) • Physicians: 10 (33%) • Total health-care workers: 74 (48%) The proportion of the total ICU staff that participated in the intervention was not reported
Knowledge	Mean (95% CI) percentage of correctly answered questions among all health-care workers who took the intervention: Baseline: 59.7% (39.9% to 78.4%) Post intervention: 73.4% (58.1% to 88.6%) Difference: 13.7%; $p = 0.01$
Skills	Not a study outcome
Process evaluation	The authors noted that the test questions that received the greatest number of incorrect responses (< 50% correct responses) were those on the use of full sterile barriers during CVC insertion and on the choice of antiseptic for skin disinfection. Small drapes were incorrectly assumed sufficient for CLABSI prevention and the 2002 IDSA-CDC guidelines indicated (incorrectly) that tincture of iodine could still be used, although Chlorhexidine was the current recommendation

IDSA, Infectious Diseases Society of America.

Critical appraisal

Potential for bias

Group selection	Were there systematic differences between the baseline and intervention groups? NOT REPORTED. Authors stated that there were no changes in hospital policy on prevention of CLABSI or in the availability of supplies used (type of CVC, connectors, antiseptics or other supplies used in CVC insertion and care) but no data reported; no information at all provided on the patient population If YES, were the differences between the groups adjusted for in statistical analyses (e.g. as covariates or subgroups, or stratification by propensity scores)? NOT APPLICABLE
Intervention administration	Were any confounding variables identified that could influence the effect estimate for the overall intervention? NO. The authors stated no other interventions potentially affecting the incidence of CLABSI were performed. However, they also stated that to control for the confounding effects of secular trends and external events that occurred during the study period a Poisson regression technique was used. The potential confounding variables in question were not reported Was the effect of educational practice separable from effects of non-educational practice? YES (education alone) Were the intervention component(s) implemented as planned? UNCLEAR. Not reported what proportion of the ICU staff participated in the intervention. Of those that participated, approximately half completed the post test
Missing data	Were there systematic differences between the baseline and intervention groups in data availability? NOT REPORTED. No information given on the patient population

Outcome measurement	Were there systematic differences between the baseline and intervention groups in how outcomes were determined (including differences in how outcomes were defined)? NO. The authors stated that there were no changes in CLABSI diagnosis procedures in the microbiology laboratory and the staff members responsible for data collection did not change during the study period
	Was any blinding of personnel and/or outcome assessors reported (including assessors of blood cultures)? NO
Other possible sources of bias	No other sources of bias were reported by the authors or identified by the reviewers based on the information presented

Other critical appraisal criteria

Methods	Intervention described in sufficient detail to be replicated? YES. A short 15-minute lecture and tests, for which the component 10 topics were specified in a table; the number of lectures required was also reported
	Justification given for sample size? NOT REPORTED
	Data collection process reported? NOT REPORTED
	If YES or PARTIALLY, was the data collection process shown to be valid? NOT APPLICABLE
	If YES or PARTIALLY, was the data collection process shown to be reliable? NOT APPLICABLE
	Statistical tests described? YES
Results	Educational significance or effect size assessed? NO
	Target behaviour change achieved? NOT REPORTED

Additional comments

- The proportion of the patients monitored for CLABSI was not reported.
- Not reported whether the participants knew they were involved in a research study.

PRONOVOST (2006–10)[34,123,124]

Methods

Study characteristics

Lead author, publication year(s) and reference ID(s)	Pronovost 2006,[34] 2008,[124] 2010[123] (data are from Pronovost 2006[34] unless specified)
Summary of approach	State-wide safety initiative regarding patients in ICUs known as the MHA Keystone Center for Patient safety and Quality Keystone ICU project; set predominantly in Michigan
Location	USA, Michigan (plus five out-of-state hospitals)
Language	English
Critical care specialty	ICUs for adults: included medical, surgical, cardiac medical, cardiac surgical, neurological, surgical trauma and one paediatric unit
No. of critical care units	103 (originally 108: two merged, four reported no data) participated in monitoring up to 18 months.[34] Ninety participated in monitoring up to 36 months; of which 43 reported data continuously for 0–36 months[123]
No. of hospitals	Sixty-seven participated in monitoring up to 18 months (34 hospitals in Michigan did not participate).[34] Sixty-one participated in monitoring up to 36 months[123]
Hospital name (unless multicentre); city	Ninety-three hospital units listed in an appendix to the paper (unclear how these relate to the number of ICUs included in the different study periods)
Study design	Cohort before-and-after study
Study time periods	Baseline: Not reported (varied by ICU) [a]Implementation period: The first 3 months of intervention[123] Intervention period: March 2004 to September 2005 (18 months) (starting time varied by ICU: 40/103 ICUs started intervention immediately, i.e. had no baseline period) Sustainability period: 19 to 36 months after implementation (continuation of same intervention but with slightly different eligibility criteria: participation fee)[123] Follow-up: None (continuous monitoring of ongoing intervention) Note: Staggered implementation: Two cultural interventions, followed by two interventions targeting patients' safety (in any order), were each implemented at 3-month intervals
Funding source	Funded predominantly by the AHRQ and the MHA, plus congressional funding to develop and maintain the NNIS and a staff of hospital-based infection control practitioners. Stated there was no influence of the sponsors on study design, conduct, interpretation or publication
Conflicts of interest	Reported in detail

AHRQ, Agency for Healthcare Research and Quality; MHA, Michigan Health and Hospital Association.
a Implied this was from June to August 2004.[34] It was also implied[34] that four intervention components each took 3 months to implement, in sequence (i.e. implementation would have taken 12 months overall – if so, this 3-month-period would have only captured the initial stages of implementation).

Population and setting in the baseline (control) group

Critical care unit characteristics	1625 beds in total (103 ICUs); 15.8 beds/ICU on average; represented 85% of all ICU beds in Michigan 52% of the hospitals were teaching facilities
Patient population characteristics	Not reported
Device characteristics	Central catheters (defined) including PICCs (no further details reported). Average duration of catheter use in individual patients was not monitored
Insertion site antisepsis used	13/93 hospitals (19%) included chlorhexidine in the central-line kits used in the ICUs
Dressing type and duration/frequency	Not reported

Intervention characteristics

Objective	Reduction of CRBSIs
Main focus of education	Catheter insertion
Trainers (providers)	Team leaders: At least one physician and one nurse designated per ICU, dedicating 20% of their effort to project activities (at a minimum, a team consisted of senior executive, the ICU director and nurse manager, plus a designated physician and nurse team leader)
Training of trainers	Instructed in the science of safety and in the interventions then disseminated this information among their colleagues. Training received through conference calls every other week, coaching by research staff and state-wide meetings twice a year. Team leaders were partnered with their local hospital-based infection-control practitioners to assist implementation of the intervention and to obtain data on CRBSI
Learners (recipients)	ICU colleagues (no further details)
Target behaviour change	Hand washing, use of full-barrier precautions during insertion of CVC, skin cleaning with chlorhexidine, avoidance of femoral site and removal of unnecessary catheters
Development and testing	Based on evidence-based procedures recommended by the CDC and identified as having the greatest effect on the rate of CRBSI and the lowest barriers to implementation (reference cited). No other details of development/testing reported. Conceptual model for large-scale knowledge translation[123]
Educational or behavioural theory	Not reported. However, the authors refer to the '4E' framework proposed by Heifetz for distinguishing technical and adaptive aspects of the intervention; technical aspects are education and evaluation; adaptive aspects are engagement and execution

Educational strategies and topics targeted	Education was one of five interventions to reduce CRBSI by targeting awareness of evidence-based infection control practices (hand hygiene, chlorhexidine skin preparation, full-barrier precautions during CVC insertion, subclavian vein placement as the preferred site, and CVC maintenance). Stated that clinicians were educated about practices to control infection and harm resulting from CRBSI – cited Berenholtz *et al*.[77] but no other details given. Strategies included: **Checklist:** To monitor adherence to infection control practice/CVC maintenance. Details not reported. Staff were empowered to halt breaches of evidence-based practice **Discussion:** about removal of catheters at daily rounds **One-page fact sheet:** Available in an online appendix.[34] Lists evidence sources for evidence-based practices (hand hygiene, skin preparation with chlorhexidine, maximal barrier precautions, and avoidance of the femoral site). Provided to participants to share with their staff **Daily goals sheet:** to improve clinician-to-clinician communication within the ICU. No other details reported (classified by the authors as separate from the educational intervention) **PowerPoint presentation:** Provided to participants to share with their staff. Content not reported Also stated that participants were provided with articles – but no details of which ones and whether reading was voluntary or mandatory and how encouraged or enforced
Infection surveillance feedback approach	Number and rates of CRBSI were provided to staff at monthly and quarterly meetings respectively. Infection rates were collected and reported according to the guidelines of the NNIS by trained hospital-based infection-control practitioners who were independent of the ICU staff implementing the intervention. Validity and reliability not reported. Stated that infection control staff at the hospitals adjudicated cultures before submitting data for the study but no details reported
Performance feedback approach	Not reported
Concentration of education	Not reported
Non-educational intervention components	Catheter insertion cart; chlorhexidine for skin antisepsis
Costs reported	No. The authors stated that the intervention was implemented without the use of expensive technology or additional ICU staffing. Funding was from the AHRQ and MHA and staffing was provided by the participating hospitals. However, resources were insufficient to enable evaluation of compliance with the study intervention. After the first 18 months of intervention ICUs were required to pay a MHA fee for continued participation (amount not specified)[124]

MHA, Michigan Health and Hospital Association.

Outcome characteristics

Catheter-BSI definition Defined according to the National Nosocomial Infections Surveillance System	Presence of a recognised pathogen cultured from one or more blood cultures, and organism cultured from blood not related to infection at another site *or* Presence of one or more of the following: fever (temperature > 38 °C), chills, hypotension, and: Signs and symptoms and positive results not related to infection at another site, and: Presence of one or more of the following: Common skin contaminant (e.g. diphtheroids, *Bacillus* spp., *Propionibacterium* spp., coagulase-negative staphylococci or micrococci) cultured from two or more blood samples drawn on separate occasions Common skin contaminant cultured from at least one blood culture in a sample from a patient with an intravascular catheter Positive antigen test on blood (e.g. *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Neisseria meningitidis* or group B streptococcus)
Outcomes reported	Not stated whether primary or secondary: • Quarterly rate of CRBSI per 1000 catheter-days, catheter-days per month and incidence rate ratios

Results data

Primary outcomes

The 0- to 18-month data are from Pronovost *et al.*,[34] and 19- to 36-month data are from Pronovost *et al.*,[124] except where stated otherwise.

Outcome *n* = no. of ICUs	Baseline	Intervention: (a) implementation period; (b) months 0–18; (c) months 19–36; and (d) individual quarters	Difference between baseline and intervention
Device duration (months)	Not reported	Not reported	Not reported
	551 (220–1091) (*n* = 55)	(a): 57,033 (*n* = 96)	Not reported
		(b): 300,175 (*n* = 103)	
		(c): 300,310 (*n* = 90)	
		(d)	
0–3 (*n* = 95)		436 (246–771) [4779[a]]*	
4–6 (*n* = 95)		460 (228–743) [4757]	
7–9 (*n* = 96)		467 (252–725)	
10–12 (*n* = 95)		431 (249–743)[55,70]	
13–15 (*n* = 95)		404 (158–695)	
16–18 (*n* = 95)		367 (177–682)	
19–21 (*n* = 89)		399 (230–680)	
22–24 (*n* = 89)		450 (254–817)	
25–27 (*n* = 88)		481 (266–769)	
28–30 (*n* = 90)		479 (253–846)	
31–33 (*n* = 88)		495 (265–779)	
34–36 (*n* = 85)		456 (235–787)	

*Total device-days, median (IQR) [monthly mean]; *n* = no. of ICUs

Outcome *n* = no. of ICUs	Baseline	Intervention: (a) implementation period; (b) months 0–18; (c) months 19–36; and (d) individual quarters	Difference between baseline and intervention
No. of devices/patient	Not reported	Not reported	Not reported
	2 (1–3)	(a): 1 (0–2)*	Not reported
		(b), (c): not reported	
		(d)	
0– 3 (*n* = 95)		0 (0–2)	
4–6 (*n* = 95)		0 (0–1)	
7–9 (*n* = 96)		0 (0–1)	
10–12 (*n* = 95)		0 (0–1)	
13–15 (*n* = 95)		0 (0–1)	
16–18 (*n* = 95)		0 (0–1)	
19–21 (*n* = 89)		0 (0–1)	
22–24 (*n* = 89)		0 (0–1)	
25–27 (*n* = 88)		0 (0–1)	
28–30 (*n* = 90)		0 (0–1)	
31–33 (*n* = 88)		0 (0–1)	
34–36 (*n* = 85)		0 (0–1)	
*No. of CRBSI, median (IQR)			
CRBSI incidence per 1000 catheter-days	2.7 (0.6–4.8); 7.7 ± 28.9 (*n* = 55)	(a): 1.6 (0–4.4); 2.8 ± 4.0*	
		(b), (c): Not reported	
		(d)	
0–3 (*n* = 96)		0 (0–3.0); 2.3 ± 4.0	$p \leq 0.002$
4–6 (*n* = 96)		0 (0–2.7); 1.8 ± 3.2	$p \leq 0.002$
7–9 (*n* = 95)		0 (0–2.1[b]); 1.4 ± 2.8	$p \leq 0.002$
10–12 (*n* = 90)		0 (0–1.9[b]); 1.2 ± 1.9	$p \leq 0.002$
13–15 (*n* = 85)		0 (0–1.6[b]); 1.5 ± 4.0	$p \leq 0.002$
16–18 (*n* = 70)		0 (0–2.4); 1.3 ± 2.4	$p \leq 0.002$
19–21 (*n* = 89)		0 (0–1.4); 1.8 ± 5.2	Not reported
22–24 (*n* = 89)		0 (0–1.6); 1.4 ± 3.5	Not reported
25–27 (*n* = 88)		0 (0–2.1); 1.6 ± 3.9	Not reported
28–30 (*n* = 90)		0 (0–1.6); 1.3 ± 3.7	Not reported
31–33 (*n* = 88)		0 (0–1.1); 0.9 ± 1.9	Not reported
34–36 (*n* = 85)		0 (0–1.2); 1.1 ± 2.7	Not reported
*Median (IQR); mean ± SD			

Outcome *n* = no. of ICUs		Baseline	Intervention: (a) implementation period; (b) months 0–18; (c) months 19–36; and (d) individual quarters	Difference between baseline and intervention
CRBSI incidence per 1000 patient-days		Not reported	Not reported	
		1.00*	(a): 0.81 (0.61 to 1.08)*	
			(b), (c): Not reported	
			(d)	
0–3 months			0.62 (0.47 to 0.81[b])	$p = 0.001$
4–6 months			0.56 (0.38 to 0.84[b])	$p = 0.005$
7–9 months			0.47 (0.34 to 0.65[b])	$p < 0.001$
10–12 months			0.42 (0.28 to 0.63[b])	$p < 0.001$
13–15 months			0.37 (0.20 to 0.68[b])	$p = 0.001$
16–18 months			0.34 (0.23 to 0.50[b])	$p < 0.001$
19–21 (*n* = 89)			0.34 (0.23 to 0.50)	Not reported
22–24 (*n* = 89)			0.33 (0.23 to 0.48)	Not reported
25–27 (*n* = 88)			0.44 (0.34 to 0.57)	Not reported
28–30 (*n* = 90)			0.40 (0.30 to 0.53)	Not reported
31–33 (*n* = 88)			0.31 (0.21 to 0.45)	Not reported
34–36 (*n* = 85)			0.34 (0.24 to 0.48)	Not reported
*Incidence rate ratio (95% CI)[c]				
Mean per quarter change in rate of CRBSI (95% CI)				
All ICUs (*n* not reported):	0–18 months		12% (9% to 15%)	Not reported
	19–36 months		–1% (–9% to 7%)	
ICUs with continuous data (*n* = 43)	0–18 months		13% (9% to 16%)	
	19–36 months		–1% (–4% to 5%)	
LOS		Not reported	Not reported	Not reported
Mortality		Not reported	Not reported	Not reported

a Stated this is for ICUs that implemented interventions in the first 3 months after baseline; however, the number of ICUs it relates to is unclear.
b Different data for the same outcome were reported by Pronovost[34] and Pronovost;[124] the data presented here are from Pronovost [34] as they correspond to the reported *p*-values.
c Adjusted for the hospital's teaching status and number of beds.

Secondary outcomes

Reaction to education	Not assessed as an outcome
Attitudes	Not assessed as an outcome
Compliance	Not assessed as an outcome
Knowledge	Not assessed as an outcome
Skills	Not assessed as an outcome
Process Evaluation	Effectiveness of intervention was found to be modestly higher in small hospitals, with an incidence rate ratio of 0.97 (95% CI 0.96 to 0.99; $p < 0.001$) for each 100-bed decrease in the size of the hospital, but it is unclear if the study was powered for this type of analysis. The stocking of chlorhexidine was also monitored and, 6 weeks following a letter to hospital CEOs to provide it, 56/67 (84%) stocked chlorhexidine, 46/67 (69%) stocked the agent in the ICU and 43/67 (64%) stocked it in central-line carts (1/67; 19% at baseline)

CEO, Chief Executive Officer.

Critical appraisal

Potential for bias

Group selection	Were there systematic differences between the baseline and intervention groups? NOT REPORTED. No information was presented on patient demographics or health status other than that patients were mostly adult If YES, were the differences between the groups adjusted for in statistical analyses (e.g. as covariates or subgroups, or stratification by propensity scores)? UNCLEAR. Analyses were conducted to account for nested clustering within the data; analyses also adjusted for hospitals' teaching status and bed size. However, no population variables were included in the analyses. A sensitivity analysis of results was conducted, which included only ICUs with continuous data, including baseline data. During months 19–36 after intervention implementation (the 'sustainability period'), 13 hospitals dropped out because they chose not to pay the MHA fee for continued participation).[124] These 13 hospitals were more likely to be a teaching hospital (93% vs. 65%), $p = 0.04$, but they did not vary in median number of hospital beds (383 vs. 338) or in CRBSI incidence rates during the first and final quarters of the preceding 18-month intervention period[123]
Intervention administration	Were any confounding variables identified that could influence the effect estimate for the overall intervention? NOT REPORTED, but ICUs could implement two interventions in any order. Authors stated that according to their knowledge, no other infection-reducing practices were implemented during the study. They also stated that they did not evaluate the use of new technologies such as impregnated dressings or catheters and chlorhexidine baths, on rates of infection[124] Was the effect of educational practice separable from effects of non-educational practice? NO. Change in supplies (central line cart and chlorhexidine). Also introduced new QI initiative unrelated to CRBSI,[124] including an intervention to reduce the incidence of VAP Were the intervention component(s) implemented as planned? NOT REPORTED
Missing data	Were there systematic differences between the baseline and intervention groups in data availability? UNCLEAR. Only 53 ICUs reported data continuously from baseline to 18 months[124] and 43 reported data continuously to 36 months.[124] Sensitivity analysis (up to 18 months) showed little change in the association between the intervention and outcomes when only ICUs for which complete data (including baseline data) were available were included. However, data availability from 19–36 months may be related to hospital teaching status (see above). Stated[124] that missing data were very high and lowered to about 12% by sending letters to CEOs of the hospitals informing them of the per cent of missing data for their hospital; CEOs were requested to submit the required data or advised they would have to be dropped from the collaborative. Also stated[123] that roughly 5% of data were lost when the 13 units left the collaboration, and roughly 5% of CRBSI were missing for the remaining units

Outcome measurement	Were there systematic differences between the baseline and intervention groups in how outcomes were determined (including differences in how outcomes were defined)? UNCLEAR. Three ICUs changed the CRBSI definition used from their own to that of the NNIS but these were not included in a sensitivity analysis. Authors stated that medians were used to summarise the data as the data were non-normal.[34] However, means were also reported[123,124] and in some cases were markedly different to median values – but no guidance on interpretation was given Was any blinding of personnel and/or outcome assessors reported (including assessors of blood cultures)? NOT REPORTED
Other possible sources of bias	Were any other sources of bias present? UNCLEAR. Despite conducting a sensitivity analysis, authors refer to the possibility of measurement bias, which can if present exaggerate results

CEO, Chief Executive Officer; MHA, Michigan Health and Hospital Association.

Other critical appraisal criteria

Methods	Intervention described in sufficient detail to be replicated? PARTIALLY. The principles of the intervention are described well enough to be replicated, but not the specific content. A copy of the fact sheet was provided in a supplementary appendix. However, this was a very small component of the overall intervention and its effectiveness in isolation is not known. An underlying principle of the intervention is that it should be adaptable according to local circumstances: an independent post hoc analysis[149] revealed that the intervention evolved beyond what was initially stated in the protocol Justification given for sample size? NOT REPORTED Data collection process reported? PARTIALLY. Stated only that throughout the study, data on the number of CRBSIs and catheter-days were collected monthly from a trained, hospital-based infection-control practitioner. Potential underreporting of catheter-related bloodstream infections and the lack of baseline data from ICUs that immediately implemented the intervention when the project was launched could have created a measurement bias that exaggerated the results If YES or PARTIALLY, was the data collection process shown to be valid? NOT REPORTED If YES or PARTIALLY, was the data collection process shown to be reliable? NOT REPORTED Statistical tests described? YES Educational significance or effect size assessed? NO Target behaviour change achieved? NOT REPORTED (behavioural outcomes not reported)

Additional comments

- A programme evaluation of the Michigan study by Dixon-Woods and colleagues[149] highlighted the fact that the intervention evolved over time. Later innovations included a networking section at residential project workshops, as well as project tokens, all not part of the original protocol.
- The authors stated that random assignment of the intervention and the time of implementation was not feasible because all of the ICU teams wanted to implement the intervention and to decide for themselves when to do so. Some ICUs immediately implemented the intervention without collecting any baseline data but were included in sensitivity analyses.
- The authors stated that they did not monitor catheter duration to simplify data collection, and they did not collect data on who inserted the central catheters.
- Not reported why 67 hospitals participated, whereas 34 hospitals in Michigan did not (stated that hospitals were not asked to provide reasons). Mean number of beds per participating ICU was 1625/103 = 15.8; mean number of beds per non-participating ICU was 268/34 = 7.9. Suggests study specifically excluded smaller ICUs but reason not given. The authors included hospital bed numbers as a variable and found the intervention appeared to be more effective in smaller hospitals but this analysis appears not to consider the size of the ICUs so its interpretation is unclear.

- Statistical analyses accounted for clustering of infections/ICUs/hospitals but did not account for any population variables.
- Stated that inclusion of clustering effects in the statistical analysis (CRBSIs within ICUs, ICUs within hospitals, and hospitals within geographical regions) did not change the results.
- The authors noted that similar large decreases in infection rates were not observed outside Michigan during the study period; however, CRBSI data were not collected from the non-participating ICUs.
- Not reported whether participating staff were aware that they were part of a study.
- Stated[125] that Rhode Island implemented a similar programme, with every hospital in the state participating and reported similar results as Michigan.
- The AHRQ has awarded a grant to the Health Research and Educational Trust and Quality and Safety Research Group (QSRG) researchers at Johns Hopkins to replicate the Michigan study in 10 states and the QSRG has received 'philanthropic support' to implement the collaborative in another 20 states.[124]
- A graph[123] shows that in some cases the 3-monthly infection incidence per 1000 catheter-days in 50 randomly selected ICUs equalled or exceeded that in the baseline and implementation phases, but the graph does not distinguish the individual ICU data within this subgroup of 50. Not reported whether the graph presents mean, median or total values.

RENDER (2006)[126,200]

Methods

Study characteristics

Lead author, publication year(s) and reference(s)	Render (2006);[126,200] Elder (2008)[201]
Summary of approach	Regional collaborative based on work/learning/reporting cycles, including performance feedback and infection surveillance feedback
Location	USA
Language	English
Critical care specialty	Not reported, but stated that intervention was in a MICU if more than one ICU was present at a given hospital
No. of critical care units	8
No. of hospitals	4
Hospital name (unless multicentre); city	Multicentre
Study design	Single cohort before-and-after study (results from eight critical care units pooled). Hospitals were randomised to CRBSI prevention in critical care units or surgical site prevention in operating rooms – only results for four hospitals that were randomised to CRBSI prevention are reported
Study time periods	Baseline: 2003 (months not specified) Intervention: Not explicitly stated. intervention period appears to be January 2004 to December 2006 (data reported for 2004) Follow-up: None (continuous monitoring of ongoing QI intervention during 2004)
Funding source	50% funded by the health-care systems to which the hospitals belonged. No other funding sources reported
Conflicts of interest	Not reported

Population and setting

Critical care unit characteristics	Eight units in four hospitals (two urban referral and two suburban; one affiliated with a national health-care organisation) Total critical care unit beds = 104 Total central line days per year = 7714 Total patients in the four hospitals in first year = 686 No other information on critical care units reported (Also included a control group: five hospitals with 13 ICUs, no data reported)
Patient population characteristics	Not reported; author contacted by reviewer and confirmed that patients were adult (author's reply would indicate that the included children's hospital is part of the control group)
Device characteristics	Central lines, defined as any intravenous catheter whose distal end was in a central vein During first year: • Total central line-days = 742 • Urgent lines = 27% • Multilumen catheters = 60% • Placed in femoral vein = 25% No other details reported
Insertion site antisepsis used	Not stated explicitly; implied that betadine was used
Dressing type and duration/ frequency	Not reported

Intervention characteristics

Objective	To implement evidence-based patient safety practices that reduce CRBSI (chlorhexidine and maximal sterile barriers) in a regional group of hospitals, and train hospital staff in methods to successfully create and sustain change. Four hospitals that started the project set a goal to reduce their CRBSI rates by 50%
Main focus of education	Catheter insertion, focusing on use of maximal sterile barriers and skin antisepsis
Trainers (providers)	Experts in organisational change (two named co-authors) facilitated practice change strategies. At project initiation each hospital's CEO and other hospital leaders identified the project leader and team members. Project leaders, often the infection control professionals, led the team, which consisted of the nurse manager of the intervention unit, two or more staff nurses, a physician champion, and the supply manager. Teams implemented the evidence based practices using a collaborative approach. Stated that all team members were invited but the number participating varied from only the team leader (the infection control practitioner) to eight or more team members
Training of trainers	Not reported. However, stated that the leadership role of the infection control practitioner proved important because he/she already knew and believed the literature, had previously collaborated outside the confines of their own hospital, and understood the data collection issues. Stated[200] that the infection control practitioners who were the project leaders had previous experience working together
Learners (recipients)	ICU nurses and physicians
Target behaviour change	Not explicitly stated but focused on use of skin antisepsis and large drapes during catheter insertion
Development and testing	Stated that the project was developed by a patient safety researcher (the lead author). No other information provided
Educational or behavioural theory	None reported

Educational strategies and topics targeted	**Joint 1.5-day kick-off session:** National experts presented evidence for practices; experts in organisational change presented the methods for change and mentored teams' implementation planning. Teams were requested to provide: a 'SMART' aim (specific, measurable, actionable, reliable, and time driven); a 90-day goal, with communication strategy, measurement, and tests of change; and a 3-day itemised action plan addressing recruitment of additional team members, the first test of change, and roles **Work/learning/reporting cycles:** Organised by project leaders at each site. Involved at minimum one (initially very small) test of change each month **Monthly small group meetings** (< 10 people) between project leaders and leadership: to present experience in a standard format (6 presentation slides) to share effective strategies, solve joint problems together, reinforce the change theory (not specified) and methodology, and develop consistent data collection strategies and definitions **Checklist** (provided in paper)**:** Completed by ICU nurses as the physician prepared the catheter insertion. Nurses recorded binary choices (yes/no) for hand washing; chlorhexidine use; bed-sized sterile drape; and use of cap, mask, sterile gown, and sterile gloves during insertion; and the catheter date and insertion site. Stated[200] that personnel were encouraged to use the checklist to identify the earliest possible moment when the central line could be removed; however, line need review was not a specific item on the checklist **Written policies:** approved by the clinical executive board to match the best practices to codify practice changes Stated[200] that preferred insertion site was head or neck, with femoral lines to be removed within 48 hours, and all clinical lines were prepped with chlorhexidine rather than betadine. However, the specific educational approaches used to convey these policies were not reported
Infection surveillance feedback approach	Each patient record was reviewed by the infection control nurses and compliance and infection rates were reported to the ICU clinical collaborative committee and posted in the unit monthly.[200] Validity and reliability of data collection and reporting methods not reported
Performance feedback approach	Unit level: Team leaders entered information from checklists in a secure de-identified web-based database. Each project leader reported processes and outcomes to the unit staff, usually posting the monthly project meeting slides on a bulletin board throughout the unit. Results also reported through existing hospital committees' structure (e.g. infection control and critical care committees) and to the wider hospital through its newsletter Community level: Project leadership reported outcomes to Greater Cincinnati Health Council (GCHC) infection control and patient safety committees. Twice yearly, hospital CEOs were informed of results by project leadership. Validity and reliability of data collection and reporting methods not reported. Stated that to ascertain capture of all central lines, nurse managers each month sampled the lines in place in the ICU against the forms (not described)
Concentration of education	Not reported, other than kick-off meeting had duration of 1.5 days, checklists were used daily, and feedback was monthly. Unclear whether newly recruited staff received the intervention. Stated in a commentary paper[200] that data continued to be posted quarterly but unclear when the switch from monthly to quarterly reporting occurred
Non-educational intervention components	In collaboration with two manufacturers, team leaders modified pre-packaged insertion trays, removing the betadine (in most units) and small drape and developed an accessory pack that bundled the large drape, sterile gown, cap and mask. The insertion tray, accessory pack and sterile gloves were kept on a central line cart
Costs reported	Not reported; stated that the drapes and new kits added some cost to the procedure, which had to be justified to leadership[200]

CEO, Chief Executive Officer.

Outcome characteristics

CLBSI infection definition	A hospital-acquired infection is one that occurs 48 hours after admission to the hospital and < 72 hours following discharge
Reference cited: Raad and Bodey[201]	A CRBSI is defined as a positive blood culture with clinical or microbiological evidence that strongly implicates the catheter as the source of infection (reference cited, left). It is distinguished from local infection (evidence of purulence at the site of insertion) and catheter colonisation (growth of greater than 15 CFUs of an organism from the tip or subcutaneous portion of the catheter using the semiquantitative roll-plate culture technique) (reference cited)
Outcomes reported	Not stated whether primary or secondary: • Pre- and post-line-days • CRBSI incidence density/1000 line-days • Adherence to chlorhexidine and large drape

CFU, colony-forming unit.

Results data

Primary outcomes

Outcome For eight critical care units	Baseline (2003)	Intervention (2004)	Difference between baseline and intervention
Mean (± SD) line duration, days	7.0 (± 6.2)	Not reported	Not reported
Total device utilisation	Not reported	Not reported	Not reported
No. of devices/patient (not reported; data e-mailed by the author)	7593 (in three quarters of 2003)	7830 (in three quarters of 2004)	Not reported
CRBSI incidence rate (not reported; data e-mailed by the author)	11 (in three quarters of 2003)	5 (in three quarters of 2004)	Not reported
CRBSI incidence per 1000 line-days[a] **(a) reported (period unclear)**	(a) 1.7	(a) 0.4	(a) $p < 0.05$
(b) calculated from data e-mailed by the author (three-quarter period)	(b) 1.4	(b) 0.6	
CRBSI incidence per 1000 patient-days	Not reported	Not reported	Not reported
LOS	Not reported	Not reported	Not reported
Mortality	Not reported	Not reported	Not reported

a Data for calculating risk ratios with CIs (presented in the main report) were not reported in the primary publication but were obtained by contacting the author.

Secondary outcomes

Reaction to education	Not a study outcome
Attitudes	Not a study outcome
Compliance	The data presented indicate that an improvement in compliance occurred both for chlorhexidine and large drape use, but it is not clear from the information provided how the data relate to the timing of intervention implementation. Stated that four of the health-care systems implemented chlorhexidine and maximal sterile barriers in the first year and timing of antibiotics in the operating room or consistent use of maximal sterile barriers during the second year[200] Adherence to evidence-based practices was reported to have increased from 30% to 95% at the project midpoint (three quarters of 2004)

Project year[a]	**Adherence to chlorhexidine, %**	**Adherence to large drape, %**
Month 1	42	0
Month 2	45	39
Month 3	49	47
Month 4	72	67
Month 5	86	82
Month 6	90	82
Month 7	72	95
Month 8	73	62
Month 9	73	87
Month 10	92	68
Month 11	94	83
Month 12	82	83

Knowledge	Not a study outcome
Skills	Not a study outcome
Process evaluation	A table (table 2) of facilitators and barriers is provided, but it is unclear whether this is based on quantitative evidence. Authors reported that after 6 months, the project leader and project co-ordinator (named authors) reviewed their detailed notes from the monthly reporting meetings to independently identify themes contributing to or delaying project success. The list of barriers and facilitators was then validated by the project leaders. However, the validation process was not explained. Some aspects of the reported information are unclear – for example, building on a prior pilot was rated as a facilitator but no prior pilot was reported elsewhere in the publications

a Data extracted by reviewer from graph using Engauge software. 'Project year' is taken to mean 12 months and not 12 years, but graph label is unclear.

Critical appraisal

Potential for bias

Group selection	Were there systematic differences between the baseline and intervention groups? UNCLEAR. Population characteristics not reported
	If YES, were the differences between the groups adjusted for in statistical analyses (e.g. as covariates or subgroups, or stratification by propensity scores)? NOT APPLICABLE
Intervention administration	Were any confounding variables identified that could influence the effect estimate for the overall intervention? NOT REPORTED. Not mentioned whether any changes in staffing occurred or whether any interventions were introduced in parallel at any of the ICUs. Stated that all commercially available central line trays included a small drape and both chlorhexidine and betadine, allowing practitioners to easily avoid practice change (meaning unclear)
	Was the effect of educational practice separable from effects of non-educational practice? NO. In addition to educational activities, the insertion site antisepsis was changed from betadine to chlorhexidine and catheter insertion kits were re-organised, which may have influenced infection incidence
	Were the intervention component(s) implemented as planned? NOT REPORTED
Missing data	Were there systematic differences between the baseline and intervention groups in data availability? NOT REPORTED
Outcome measurement	Were there systematic differences between the baseline and intervention groups in how outcomes were determined (including differences in how outcomes were defined)? UNCLEAR. Stated that hospitals were already collecting CRBSI data using the CDC definitions at the project's inception. However, also stated that collection of line days was more accurate after intervention
	Was any blinding of personnel and/or outcome assessors reported (including assessors of blood cultures)? NO
Other possible sources of bias	Stated in a subsequent publication[201] that the four participating hospitals were more willing than others to participate in the study – suggesting that the management at these ICUs may possess different qualities than non-participating ICUs

Other critical appraisal criteria

Methods	Intervention described in sufficient detail to be replicated? NO. The general intervention approach is described and the key topics are reported but it is unclear which parts of the approach were used to support each topic. The checklist is reproducible but is a rudimentary list mainly of binary (yes/no) responses that would be difficult to implement effectively without additional instructions
	Justification given for sample size? NOT REPORTED
	Data collection process reported? NOT REPORTED
	If YES or PARTIALLY, was the data collection process shown to be valid? NOT REPORTED
	If YES or PARTIALLY, was the data collection process shown to be reliable? NOT REPORTED
	Statistical tests described? YES. Line days were stratified by ICU
Results	Educational significance or effect size assessed? NOT REPORTED
	Target behaviour change achieved? PARTIALLY. Improvements in adherence to chlorhexidine and large drapes were reported but remained below 100% for both

Additional comments

- Stated that infection rates were zero in three of four hospitals for four quarters.
- Lead author was contacted to clarify whether the population included children. She confirmed that the population was entirely adult.
- A line-day was not defined – it is unclear whether the data reflect all the vascular catheters used or the number of days on which patients had at least one vascular catheter.
- Not reported whether participants were aware they were being studied.

ROSENTHAL (2003)[129]

Methods

Study characteristics

Lead author, publication year(s) and reference(s)	Rosenthal (2003)[129]
Summary of approach	Infection control intervention in four ICUs, comprising education followed by performance feedback; the performance feedback focused on compliance with the management of catheter dressings and dating of intravenous tubing sets
Location	Argentina
Language	English
Critical care specialty	Cardiac, medical/surgical
No. of critical care units	4
No. of hospitals	2
Hospital name (unless multicentre); city	Bernal Medical Center and Colegiales Medical Center, Buenos Aires
Study design	Single cohort before-and-after study, with data from four ICUs pooled into single cohort
Study time periods Note that a hand washing programme (not described) was implemented concurrently during the same time periods as the education and performance feedback intervention at Bernal Medical Center (total duration 12 months) but implementation times varied or differed in all phases at Colegiales Medical Center (total duration 11 months)	*Phase 1, baseline (infection surveillance)* Bernal Medical Center: April to May 1999 (2 months) Colegiales Medical Center: September to November 2000 (3 months) Intervention: *Phase 2, education*:[a] Bernal Medical Center: June to July 1999 (2 months) Colegiales Medical Center: December 2000 (1 month) *Phase 3, performance feedback* Bernal Medical Center: August 1999 to March 2001 (8 months) Colegiales Medical Center: January to July 2001 (7 months) *Follow-up*: None (monitoring only during intervention implementation phases)
Funding source	Supported in part by a grant from Baxter Healthcare
Conflicts of interest	Not reported

a Data are from table 1; text also stated that education was 1 month at Bernal and 3 months at Colegiales (appears contradictory).

Population and setting

Critical care unit characteristics	Four level III cardiac and MICUs/SICUs in two hospitals Bernal Medical Center: Private hospital, 150 beds 1 medical–surgical ICU (17 beds) 1 coronary ICU (15 beds) Colegiales Medical Center: Private hospital, 180 beds 1 medical–surgical ICU (10 beds) 1 coronary ICU (10 beds) Each hospital had an infection control team that comprised a medical doctor (with formal education and medical background in internal medicine, infectious diseases, and hospital epidemiology) and an infection control nurse		
Patient population characteristics[a] All admitted adult patients with a CVC in place for at least 24 hours (840 patients) were included	Baseline (2 or 3 months) (172 patients [b])	Intervention (8 or 10 months) (668 patients [b])	Difference between baseline and intervention
Male sex, *n* (%)	84 (48.8)	358 (53.6)	$p = 0.265$
Mean ± SD age, years	71.98 ± 13.45	71.91 ± 12.19	$p = 0.944$
Diabetes, *n* (%)	32 (18.6)	103 (15.4)	$p = 0.314$
Cancer, *n* (%)	9 (4.8)	33 (4.9)	$p = 0.925$
HIV, *n* (%)	1 (0.6)	0 (0)	$p = 0.205$
Device characteristics	Not reported	Not reported	Not reported
Insertion site antisepsis used	Not reported	Not reported	Not reported
Dressing type and duration/ frequency	Not reported	Not reported	Not reported

SICU, surgical intensive care unit.
a Patients had undergone open heart, neurosurgical or orthopaedic operation, or had severe medical illness.
b Not reported; number estimated by reviewers from the percentage data given.

Intervention characteristics

Objective	To ascertain the effect of an infection control programme, using education and performance feedback, on intravascular device-associated BSI
Main focus of education	Unclear – appears to be catheter care in general (guidelines cited but unclear whether education was based on part or all of the guidelines) – but management and care of dressings and dating of intravascular administration sets were the areas for which compliance was assessed
Trainers (providers)	Not reported
Training of trainers	The principal investigator (lead author) trained the data collectors at each centre before in initiation of the trial, but the training of education providers was not reported
Learners (recipients)	Not specified other than health-care workers from the ICUs
Target behaviour change	Not explicitly stated in education, but target behaviours for which compliance was assessed were: placement of gauze on intravascular device insertion sites; marking of the date on the intravascular administration set; and checking/ensuring appropriate condition of the gauze dressing
Development and testing	Not reported
Educational or behavioural theory	Not reported
Educational strategies and topics targeted	Health-care workers from the ICUs underwent education and training for CVC care based on infection control practices published by the CDC and Hospital Infection Control Practices Advisory Committee (reference cited). This occurred during 1 month (Bernal Medical Center) or 3 months (Colegiales Medical Center). However, table 1 shows the duration of this phase as two months for Bernal Medical Center and 1 month for Colegiales Medical Center
Infection surveillance feedback approach	Not included in the intervention
Performance feedback approach	A research nurse observed health-care worker behaviour in the ICUs twice a week, and assessed and entered the following into a standard form: placement of gauze on intravascular device insertion sites; marking of the date on the intravascular administration set; and condition of the gauze dressing. Performance feedback was provided at monthly infection control meetings using bar charts documenting rates of compliance with hand washing, gauze on CVC insertion sites, dates on intravascular administration sets, and maintaining the condition of catheter gauze dressings. Also, a formal report of compliance rates was provided to administrators in each ICU. Validity and reliability of the method not reported
Concentration of education	Not reported – no information was given on the number and duration of sessions, other than that performance feedback occurred monthly
Non-educational intervention components	A study to improve health-care worker compliance with hand washing was undertaken at each institution and overlapped in time with the current trial. However, no details were reported
Costs reported	Not reported

Outcome characteristics

Catheter-BSI definition Reference cited: Garner *et al.*[147]	There were two criteria for 'laboratory-confirmed BSI': 1. A recognised pathogen cultured from one or more percutaneous blood cultures, after 48 hours of vascular catheterisation, and the pathogen cultured from the blood was not related to an infection at another site. With common skin commensals (e.g. diphtheroids, *Bacillus* spp., *Propionibacterium* spp., coagulase-negative staphylococci or micrococci), the organism was cultured from two or more blood cultures drawn on separate occasions; *and* 2. Patient had at least one of the following signs or symptoms that were not considered to be related to an infection at another site: fever (> 100.4 °F), chills or hypotension Blood and catheter tip culture techniques were briefly described (references cited)
Outcomes reported	Primary outcome: The combined rate of intravascular device-related BSI in Phases 2 and 3 of the study (education and performance feedback) compared with the rate in Phase 1 (baseline infection surveillance) Secondary outcomes: Rate of intravascular device-related BSI in phase 2 vs. Phase 1 Rate of intravascular device-related BSI in phase 3 vs. Phase 2

Results data

Primary outcomes

Outcome	Phase 1 (baseline)	Phase 2 (education)	Phase 3 (performance feedback)	Phase 2 + Phase 3 (overall intervention)	Difference (relative risk (RR) (95% CI); *p*-value)
Device duration	Not reported	Not reported	Not reported	Not reported	Not reported
Total device utilisation, intravascular device-days	1219	586	4140	4726	Not reported
No. of devices/patient	Not reported	Not reported	Not reported	Not reported	Not reported
Intravascular device-related BSI incidence rate	56	10	41	51	Not reported
Intravascular device-related BSI incidence per 1000 catheter-days	45.94	17.06	9.90	11.10	Phase 2 vs. 1: RR = 0.37 (0.19 to 0.73), $p < 0.001$ Phase 3 vs. 2: RR = 0.58 (0.29 to 1.18), $p = 0.11$ Phase 2 + 3 vs. 1: RR = 0.25 (0.17 to 0.36), $p < 0.001$
Intravascular device-related BSI incidence per 1000 patient-days	Not reported	Not reported	Not reported	Not reported	Not reported
LOS	Not reported	Not reported	Not reported	Not reported	Not reported
Mortality	Not reported	Not reported	Not reported	Not reported	Not reported

Secondary outcomes

Compliance (*n* = no. of observations)	Baseline (Phase 1) (*n* = 347)	Education (Phase 2) (*n* = 169)	Performance feedback (Phase 3) (*n* = 5165)	Difference (relative risk (RR) (95% CI); *p*-value)
Presence of gauze on intravascular device site	53.02% (184/347)	56.21% (95/169)	96.53% (4986/5165)	Phase 2 vs. Phase 1: RR = 1.06 (0.86 to 1.30); $p = 0.64$ Phase 3 vs. Phase 2: RR = 1.72 (1.40 to 2.10); $p < 0.001$
Date on intravascular administration set	0.57% (2/347)	0% (0/169)	74.00% (3839/5165)	Phase 2 vs. Phase 1: $p = 0.32$ Phase 3 vs. Phase 2: $p < 0.001$
Good gauze condition	48.70% (169/347)	43.19% (73/169)	89.56% (4626/5165)	Phase 2 vs. Phase 1: RR = 0.89 (0.67 to 1.17); $p = 0.39$ Phase 3 vs. Phase 2: RR = 2.07 (1.65 to 2.62); $p < 0.001$
Outcome				
Reaction to education	Not a study outcome			
Attitudes	Not a study outcome			
Knowledge	Not a study outcome			
Skills	Not a study outcome			
Process evaluation	Not included in the study			

Critical appraisal

Potential for bias

Group selection	Were there systematic differences between the baseline and intervention groups? UNCLEAR. Patients were similar in the baseline and intervention periods for gender, age, and proportion with diabetes, cancer or HIV. However, no other aspects of patients' health status were reported
	If YES, were the differences between the groups adjusted for in statistical analyses (e.g. as covariates or subgroups, or stratification by propensity scores)? NOT APPLICABLE
Intervention administration	Were any confounding variables identified that could influence the effect estimate for the overall intervention? YES. Stated that a similar study to improve health-care worker compliance with hand washing was undertaken at each institution resulting in overlap with the current trial. However, no information on the hand washing programme was reported
	Was the effect of educational practice separable from effects of non-educational practice? YES. Education-only intervention with effects of education per se and performance feedback separable
	Were the intervention component(s) implemented as planned? NOT REPORTED. The educational approach was not described

Missing data	Were there systematic differences between the baseline and intervention groups in data availability? NOT REPORTED. The sample sizes for the different study periods were not explicitly stated
Outcome measurement	Were there systematic differences between the baseline and intervention groups in how outcomes were determined (including differences in how outcomes were defined)? NOT REPORTED Was any blinding of personnel and/or outcome assessors reported (including assessors of blood cultures)? NO
Other possible sources of bias	YES. Study centre data collection sheets were checked for potential errors and missing items by one person – the study co-ordinator – to confirm each diagnosis of intravascular device-associated BSI. The study co-ordinator might have a vested interest in a successful outcome The authors mentioned that the parallel implementation of a hand washing programme probably had an impact on the results of this study. They stated that in particular, it is possible that the earlier implementation of a hand washing programme at both institutions enhanced the impact of the educational phase of this study, potentially reducing the overall impact of performance feedback. However, this potential effect is speculative

Other critical appraisal criteria

Methods	Intervention described in sufficient detail to be replicated? NO. The educational approach was not reported. Justification given for sample size? NOT REPORTED Data collection process reported? PARTIALLY. An infection control nurse at each study centre extracted data prospectively from charts. Study centre data collection sheets were checked for potential errors and missing items by the study co-ordinator to confirm each diagnosis of intravascular device-associated BSI If YES or PARTIALLY, was the data collection process shown to be valid? NOT REPORTED If YES or PARTIALLY, was the data collection process shown to be reliable? NOT REPORTED Statistical tests described? YES
Results	Educational significance or effect size assessed? NO Target behaviour change achieved? UNCLEAR. The target behaviours addressed by the education were not reported. Compliance with three reported behaviours ranged from 0% to 56.21% after education alone and from 74.00 to 96.53% after both education and performance feedback

Additional comments

- The authors commented that most health-care institutions in Latin America lack the resources to prevent intravascular device-related BSI and many hospitals lack basic infection control programmes. In this context the high baseline incidence is notable.
- It was not reported whether the participants were aware they were being studied.

ROSENTHAL (2005)[130]

Methods

Study characteristics

Lead author, publication year(s) and reference(s)	Rosenthal (2005)[130]
Summary of approach	Education and performance feedback intervention to improve hand hygiene practices in two ICUs
Location	Argentina
Language	English
Critical care specialty	Coronary, medical surgical
No. of critical care units	2
No. of hospitals	1
Hospital name (unless multicentre); city	Colegiales Medical Center, Buenos Aires
Study design	Single cohort before-and-after study, which pooled data from two ICUs
Study time periods	Baseline (Phase 1): September to December 2000 (4 months) Intervention (Phase 2): January 2001 to May 2002 (17 months) Follow-up: None. The specified follow-up period from January 2001 to May 2002 included the implementation of education in January 2001 and implementation of performance feedback in May 2001 (although education sessions appear to have been 1 week long, performance feedback appears to have been continuous during the monitoring period – but precise details of timing were not reported)
Funding source	Stated no external funding was provided; the human resources for the intervention were those of the infection control programme
Conflicts of interest	Not reported

Population and setting

Critical care unit characteristics	Private hospital, 180 beds: 1 medical–surgical ICU (12 beds) 1 coronary ICU (12 beds) Infection control team composed of a medical doctor (with formal education and medical background in internal medicine, infectious diseases and hospital epidemiology), an infection control nurse, and personnel support Stated that soap and antibiotic use were not changed No other information reported
Patient population characteristics	Not reported
Device characteristics	Mentioned only that devices were centrally inserted and peripherally inserted CVCs
Insertion site antisepsis used	Not reported other than that soap and antibiotic use were not changed
Dressing type and duration/ frequency	Not reported

Intervention characteristics

Objective	To enhance compliance with hand hygiene by implementing education, training and performance feedback
Main focus of education	Hand hygiene
Trainers (providers)	Education providers were not reported. One nurse was trained to detect hand washing compliance and record it on a form designed for the study. A trained infection control nurse identified nosocomial infections. Senior hospital management provided full administrative support for the study
Training of trainers	Not reported
Learners (recipients)	Health-care workers in the ICU (nurses, physicians, ancillary staff)
Target behaviour change	Hand hygiene
Development and testing	Not reported
Educational or behavioural theory	Not reported
Educational strategies and topics targeted	Focused education of all health-care workers: **One-hour group session educational classes:** For all shifts every day for 1 week. All health-care workers were given a comprehensive infection control manual, and the Association for Professionals in Infection Control (APIC) hand hygiene guideline was used as an educational tool to reinforce classroom teaching. Attendance was voluntary and monitored; each health-care worker could attend the course as many times as desired. Theoretical and practical indications for the use of hand hygiene were reviewed. The guidelines were also posted at a strategic location in each ICU (display format and location not specified) **Post tests:** To evaluate retention of educational material – were given 1 month later **Routine infection control review classes:** Held by the primary investigator to provide an opportunity for infection control questions and sharing of infection and compliance surveillance data

Infection surveillance feedback approach	Not part of the intervention: standardised NNIS data collection methods (reference cited) were used during baseline as well as intervention periods. Surveillance data were shared via: routine infection control review classes; reports to the ICU manager and administrator; and feedback data posted in the ICUs (no details of format given). Stated that feedback was 'frequent' but the timing was not specified. Validity and reliability of the data collection were not reported
Performance feedback approach	Pre- and post-intervention data on compliance of health-care workers with hand hygiene before contact with patients were collected in the ICUs by a trained infection control practitioner, who covertly observed the hand washing techniques of the health-care workers (physicians, nursing staff, and technicians) at random times twice a week, including all shifts, for 30-minute intervals. Data were recorded on a specially designed form and shared via routine infection control review classes; graphic presentations of hand hygiene rates in the form of bar charts were displayed in monthly meetings; reports to the ICU manager and administrator; and feedback data in the form of bar charts were posted in the ICUs. Validity and reliability of the data collection method were not reported. Health-care workers were informed that their hand hygiene practices were being monitored but were not aware of precisely when these observations were being made
Concentration of education	Timing of group sessions was one hour per day for 1 week for all shifts. Timing of infection review classes not reported. Performance feedback on compliance was monthly. Timing and duration of post tests not reported
Non-educational intervention components	Interventions for reducing CVC-associated BSI and for reducing urinary catheter-associated UTIs overlapped with the current intervention by 7 of 21 months and 17 of 21 months, respectively
Costs reported	Not reported, but described as 'relatively low-cost approach'

Outcome characteristics

Catheter-BSI definition Reference cited: Garner *et al*.[147]	Laboratory-confirmed CABSI A patient with a CVC has a recognised pathogen cultured from one or more percutaneous blood cultures, after 48 hours of vascular catheterisation, and the pathogen cultured from the blood is not related to an infection at another site and patient has at least one of the following signs or symptoms: fever (≥ 38 °C), chills or hypotension. With common skin commensals (e.g. diphtheroids, *Bacillus* spp., *Propionibacterium* spp., coagulase-negative staphylococci or micrococci), the organism is cultured from two or more blood cultures drawn on separate occasions
Outcomes reported	Not stated explicitly as primary or secondary Focus of a priori hypothesis: • Compliance with hand hygiene • Reduction in overall nosocomial infection incidence Other outcomes: • Incidence of nosocomial infections by type • Central vascular catheter-associated BSI • Peripheral vascular catheter-associated BSI Also included, but not data extracted: • Central vascular catheter-suspected BSI (clinical sepsis) • Peripheral vascular-suspected BSI (clinical sepsis) • VAP • Non-ventilator pneumonia • Catheter-associated UTI • Non-catheter UTI

Results data

Primary outcomes

Outcome	Baseline (4 months; 2000) (2187 bed-days)	Intervention (17 months; 2001–2) (7409 bed-days)	Difference in compliance between baseline and intervention
Device duration	Not reported	Not reported	Statistical comparison (relative risk) reported only for the total nosocomial infections per 1000 bed-days; number of catheters not reported
Total device utilisation	Not reported	Not reported	
No. of devices/patient	Not reported	Not reported	
Central catheter-associated laboratory-confirmed BSI incidence rate	15 (3.75 per month[a])	12 (0.71 per month[a])	
Peripheral catheter-associated laboratory-confirmed BSI incidence rate	3 (0.75 per month[a])	4 (0.24 per month[a])	
Total CABSI incidence[a]	18 (4.5 per month)	16 (0.94 per month)	
CABSI incidence per 1000 catheter-days	Not reported	Not reported	
CABSI incidence per 1000 patient-days	Not reported	Not reported	
LOS	Not reported	Not reported	
Mortality	Not reported	Not reported	

a Not reported; estimated by reviewers.

Secondary outcomes

Compliance with hand hygiene	Baseline (4 months; 2000) (*n* = 1160)	Intervention (17 months; 2001–2) (*n* = 3187)	Difference in compliance between baseline and intervention [relative risk (RR) (95% CI); *p*-value]
Total observed hand washing episodes, number (%)	268 (23.1)	2056 (64.5)	RR = 2.79 (2.46 to 3.17); $p < 0.0001$
Observed hand washing episodes by post-intervention study period (baseline = period 1),[a] number (%)	1. 268 (23.1)		
2. January to June 2001		724 (53.5) (*n* = 1353)[b]	Period 2 vs. period 1: RR = 2.32 (2.01 to 2.66); $p = 0.0001$
3. July to December 2001		828 (72.1) (*n* = 1148)[b]	Period 3 vs. period 2: RR = 1.35 (1.22 to 1.49); $p = 0.0001$
4. January to May 2002		518 (73.8) (*n* = 701)[b]	Period 4 vs. period 3: RR = 1.02 (0.92 to 1.14); $p = 0.665$

n, number of opportunities for hand hygiene.

Further information on compliance. Compliance was assessed and compared for different subgroups of health-care workers (nurses, physicians, ancillary staff), men and women, different types of procedures (superficial, invasive), times of shift work (morning, afternoon, night), and the different ICUs (medical surgical, coronary). Data on per cent adherence to hand hygiene are presented but it is unclear to which study periods they refer (in table 3 the data for each subgroup sum to 2564 (in one case 2563) opportunities for hand hygiene, which is less than the 3187 post-intervention opportunities reported in table 2). Compliance data ranged from a minimum of 30.8% adherence (physicians subgroup) to a maximum of 66.0% adherence (night period subgroup). It is unclear if the study was powered for this type of comparison (statistics were reported only for comparisons within subgroups (e.g. men vs. women), not for pre- versus post-intervention implementation)

Reaction to education	Not a study outcome
Attitudes	Not a study outcome
Knowledge	Not a study outcome
Skills	Not a study outcome
Process evaluation	Not reported other than compliance as detailed above

a The post-intervention study periods appear arbitrary as they do not coincide with the implementation of specific intervention components (education in January 2001 and performance feedback in May 2001).
b The number of hand washing opportunities in separate study periods sums to 3202, which is a discrepancy of 15 compared with the reported total number of opportunities (3187); the number of observed hand washing episodes in separate study periods sum to 2070, which is a discrepancy of 14 compared with the reported total number of observed episodes (2056).

Critical appraisal

Potential for bias

Group selection	Were there systematic differences between the baseline and intervention groups? NOT REPORTED – no data reported on the population and only limited information given on the critical care characteristics and devices
	If YES, were the differences between the groups adjusted for in statistical analyses (e.g. as covariates or subgroups, or stratification by propensity scores)? NOT APPLICABLE
Intervention administration	Were any confounding variables identified that could influence the effect estimate for the overall intervention? YES. Reported that interventions for reducing CVC-associated BSI and for reducing urinary catheter-associated UTIs overlapped with the current intervention by 7 of 21 months and 17 of 21 months, respectively
	Was the effect of educational practice separable from effects of non-educational practice? UNCLEAR. Possible confounding owing to two other overlapping interventions
	Were the intervention component(s) implemented as planned? UNCLEAR. Stated that attendance at education sessions while voluntary was monitored, but no attendance data were reported. Post-evaluation test results also not reported (education was aimed at enhancing compliance with hand hygiene, which statically significantly increased but did not reach 100%)
Missing data	Were there systematic differences between the baseline and intervention groups in data availability? UNCLEAR. There are discrepancies in both the data for the number of hand washing opportunities and the number of observed hand washing episodes. Numbers of patients and catheters were not reported
Outcome measurement	Were there systematic differences between the baseline and intervention groups in how outcomes were determined (including differences in how outcomes were defined)? NOT REPORTED
	Was any blinding of personnel and/or outcome assessors reported (including assessors of blood cultures)? UNCLEAR. Observations of hand washing were done covertly but blinding of data collection for infection surveillance was not reported
Other possible sources of bias	The authors acknowledged that the Hawthorne effect must be taken into account – i.e. observed effects may have resulted from the ICU staff being observed (staff were aware they were being monitored but not precisely when)

Other critical appraisal criteria

Methods	Intervention described in sufficient detail to be replicated? PARTIALLY. The nature of the education sessions was poorly described. However, the educational material is available as published guidelines which could be reproduced, disseminated and discussed
	Justification given for sample size? NOT REPORTED
	Data collection process reported? PARTIALLY. Compliance data were collected by a trained infection control practitioner and data were recorded on a specially designed form (no further details provided)
	If YES or PARTIALLY, was the data collection process shown to be valid? NOT REPORTED
	If YES or PARTIALLY, was the data collection process shown to be reliable? NOT REPORTED
	Statistical tests described? YES
Results	Educational significance or effect size assessed? NO
	Target behaviour change achieved? PARTIALLY. The authors hypothesised that they could increase hand hygiene compliance to 70% with a reduction in nosocomial infection of 30%. Compliance with hand hygiene did not reach this target when the overall 17 months of intervention were taken together but did reach the target for arbitrary time periods covering the last 11 months of the intervention period (possibly selective definition of monitoring periods?). Compliance with hand hygiene was significantly increased from 23.1% to 64.5%. Nosocomial infection reductions exceeded the target reduction but this outcome does not capture device-related infections

SHERERTZ (2000)[135]

Methods

Study characteristics

Lead author, publication year(s) and reference(s)	Sherertz (2000)[135]
Summary of approach	Single hospital, multiple-unit, 1-day hands-on course on infection control practices and procedures given in June 1996 and June 1997 for third-year medical students and physicians completing their first postgraduate year
Location	USA, North Carolina
Language	English
Critical care specialty	General MICUs/SICUs and associated step-down unit
No. of critical care units	Six ICUs and one step-down unit (data pooled)
No. of hospitals	1
Hospital name (unless multicentre); city	Wake Forest University Baptist Medical Center, Winston-Salem
Study design	Single-cohort before-and-after study
Study time periods	Baseline: July 1995 to June 1996 Intervention, course 1: 3 days in June 1996 Intervention, course 2: 3 days in June 1997 Follow-up: June 1997 to December 1997
Funding source	Not reported
Conflicts of interest	Not reported

SICU, surgical intensive care unit.

Population and setting

Critical care unit characteristics	CVC and arterial catheter insertions were performed by physicians in training The hospital's infection control policy on vascular catheters did not change substantially during the study period, with the exception of the educational intervention Stated that the seven study units did not differ between the baseline and post-intervention periods in number of admissions or severity of illness (data not shown) No other information provided
Patient population characteristics	None reported
Device characteristics	Included CVCs, PICCs and arterial catheters. Antibiotic-coated catheters were not used. No other details reported
Insertion site antisepsis used	Povidone–iodine; avoidance of antibiotic ointment
Dressing type and duration/frequency	Clear plastic dressing

Intervention characteristics

Objective	To improve standardisation of infection control practices and techniques during invasive procedures
Main focus of education	CVC insertion, specifically the use of full sterile drapes and other barrier precautions
Trainers (providers)	Infection control practitioners and a hospital epidemiologist taught 1 hour of basic infection control principles One to three faculty members oversaw training at hands-on rotation stations. Staff teaching the hands-on sessions were: Oncology catheter care nurses: Blood draws through vascular lines Respiratory therapists: Arterial puncture for analysis of blood gas Critical care medicine faculty and fellows and trauma faculty: Insertion of arterial catheters and CVCs Nurse instructors: Urinary catheter insertion and peripheral venous catheter insertion (PICC) Oncologist: Lumbar puncture Faculty from the School of Medical Technology: Phlebotomy
Training of trainers	Not reported
Learners (recipients)	Third-year medical students and physicians completing their PGY-1
Target behaviour change	Principal focus was to determine whether the intervention could increase the use of full-size sterile drapes for CVC insertion
Development and testing	Not reported. Informal surveys indicated physicians in training at the study hospital had poor compliance with maximal barrier precautions when inserting CVCs, despite conventional bedside and didactic instruction by critical care medicine faculty over 2 years. Unpublished observations also suggested CVC insertion practices varied widely
Educational or behavioural theory	Not reported
Educational strategies and topics targeted	**1-hour session on basic infection control principles:** Content included hand washing, isolation, appropriate use of barrier garments, handling of patients with resistant organisms and varicella **1-hour session** on Occupational Safety and Health Administration (OSHA) considerations for blood and body fluids and tuberculosis – taught on a different day **7 × 1-hour rotation stations (7–16 participants per group):** Each had 5–15 minutes of **didactic instruction** (in year 2 this was done mostly by videotape), followed by hands-on **skills practice** overseen by one to three faculty members. The hands-on sessions were delivered by various trainers (see above): (1) blood draws through vascular lines; (2) arterial puncture for obtaining arterial blood gas; (3) insertion of arterial catheters and CVCs; (4) urinary catheter insertion; (5) lumbar puncture; (6) PICC insertion; and (7) phlebotomy **Simulation** with mannequins was used in all hands-on sessions for skills practice. Phlebotomy skills were practised on fellow students. PICCs were started first on a mannequin and later on a fellow student A member of the infection control department reviewed the content of each didactic session to ensure consistency with existing infection control policies. To ensure appropriate content delivery, the course director observed each rotation station instructor for an entire session Courses on vascular catheters covered: use of povidone–iodine for skin preparation; avoidance of antibiotic ointment at the insertion site; use of clear plastic dressings; regular changes of intravenous tubing every 3 days; and instruction not to adhere to fixed schedules for changing CVCs
Infection surveillance feedback approach	Not included in the intervention
Performance feedback approach	Not included in the intervention

Concentration of education	A 1-day course run on 3 days in June in 1996 and on 3 days in June 1997 (different participants each year). In each year the course was for medical students (1 day) and for two groups of PGY-1 physicians (1 day each, with about 50 physicians per group). The physician education was part of the orientation for new interns. The course comprised 7 × 1-hour hands-on sessions, with 15-minute morning and afternoon breaks and a 1-hour lunch break. Two 1-hour sessions on basic infection control principles and OSHA were also reported but it is unclear how they relate to the 1-day course (stated that the OSHA session was on a different day). Authors mention when considering costs that there were eight hands-on stations, not seven (see below) No. of participants was: • 1996: 110 PGY-1 physicians, 107 medical students • 1997: 95 PGY-1 physicians, 94 medical students, 46 physician assistant students
Non-educational intervention components	None: educational intervention only
Costs reported	During year 1, supplies cost approximately US$25,000, largely because of the mannequins and CVC kits. Year 2 supplies cost approximately US$12,000. Almost all physicians teaching the course were fellows; most other faculty were nurses or had salaries equivalent to those of nurses. Using a yearly salary plus benefits (US$50,000) as an average cost for the participating faculty, it was estimated that each day of participation time cost approximately US$200 (excluding faculty preparation time or lost opportunity). Assuming eight stations with two faculty each for three different course days, the total cost for faculty time was approximately US$9600 per year (total for 2 years US$19,200). The 2021 full-size drapes used cost US$9.28 each (total US$18,755). In the baseline year the sterile sheets cost approximately US$874 (US$1.00 per reprocessed drape for 874 drapes). The overall course cost was therefore US$74,081 [= US$25,000 + US$12,000 + US$19,200 + (US$18,755 to US$874)]

PGY-1, first postgraduate year.

Outcome characteristics

Catheter-BSI definition	Primary bloodstream infections: a pathogen is isolated from one or more blood cultures and is not related to an infection at another site, unless that site is a catheter
Reference cited: Garner *et al.*[147]	Catheter-related infections were defined as meeting definition 3 of the CDC Cardiovascular System Infection Criteria for arterial or venous infection (reference, left). Fulfilment of this definition required the presence of fever (temperature > 38 °C), pain, erythema or heat at the catheter site plus the presence of a negative blood culture or absence of any blood cultures and the presence of a positive roll-plate culture of the catheter (method reported). Blood cultures (method reported) were predominantly drawn through only a peripheral vein, or as paired cultures through a peripheral vein and through a catheter
Outcomes reported	Not stated whether primary or secondary: • Physician perceptions of need for full drapes, towels, povidone–iodine, gowns, gloves, masks • Frequency of use of full sterile drapes • CRBSI incidence

Results data

Primary outcomes

Outcome	Baseline (12 months)	Post–intervention (18 months)	Difference between baseline and post intervention
Device duration	Not reported	Not reported	Not reported
Total device utilisation	Not reported	Not reported	Not reported
Total no. of CVCs inserted	2009	3090	
CRBSI incidence rate (CVCs and arterial catheters):[a]			
July to December 1995	19		Not tested statistically
January to June 1996	13		
July to December 1996		14	
January to June 1997		8	
July to December 1997		8	
CRBSI incidence per 1000 catheter-days	Not reported	Not reported	Not reported
CRBSI incidence per 1000 patient-days:[b]			Baseline vs. time after first course:
July to December 1995	1.4 (3.0)		CRBSI not tested statistically
January to June 1996	0.9 (3.5)		
July to December 1996		1.0 (2.4)	Total number of infections (CRBSI + primary BSI); $p = 0.01$
January to June 1997		0.6 (2.6)	
July to December 1997		1.3 (1.6)	
LOS	Not reported	Not reported	Not reported
Mortality	Not reported	Not reported	Not reported

a Stated that blood cultures were negative or were not done; definition appears to be for CABSI, not CRBSI as stated.
b Data extracted from graph by reviewer using Engauge software.

Secondary outcomes

Outcome [in relation to first (June 1996) training course only]	Immediately before course (baseline)	Immediately after course	Six months after course	Difference relative to baseline
Reaction to education	Not assessed as an outcome			
Attitudes: % of physicians (*n* = 109) who perceived a need for				
Full drapes	33	99	73	$p < 0.01$[a,b]
Towels	88	25	53	$p < 0.01$[a,b]
Povidone–iodine	97	99	96	Not significant
Gowns	80	98	82	Not significant
Gloves	96	99	98	Not significant
Masks	82	98	91	$p < 0.01$[a]
Compliance: % of CVC insertions for which sterile drapes used	44	65		$p < 0.001$
Knowledge	Not assessed as an outcome			
Skills	Not assessed as an outcome			
Process evaluation	At the end of each 1-day course participants were asked to rate various factors, including each instructor on a scale of 1 (poor) to 5 (excellent). In both years, all mean evaluation scores for course instructors ranged from 4.4 to 4.8 (no further data provided)			

a Footnote for *Table 2* stated that the difference between pre-course and post-course scores was significant: $p < 0.01$ immediately post intervention.
b For 6 months' follow up, $p < 0.001$.

Critical appraisal

Potential for bias

Group selection	Were there systematic differences between the baseline and intervention groups? NOT REPORTED If YES, were the differences between the groups adjusted for in statistical analyses (e.g. as covariates or subgroups, or stratification by propensity scores)? NOT APPLICABLE
Intervention administration	Were any confounding variables identified that could influence the effect estimate for the overall intervention? UNCLEAR. Stated that hospital's infection control policy on vascular catheters did not change substantially during the study period, and the seven study units did not differ between the baseline and post-intervention periods in number of admissions or severity of illness. However, no quantitative data were provided and no information at all was given about the patient population Was the effect of educational practice separable from effects of non-educational practice? YES. Education-only intervention (although catheter kits and drapes were provided, these were standard hospital practice) Were the intervention component(s) implemented as planned? PARTIALLY. The number of staff who took the intervention was reported for each year, but it was not reported whether all staff in the ICU took all components of the intervention
Missing data	Were there systematic differences between the baseline and intervention groups in data availability? UNCLEAR. For attitudes, the same sample size was reported for pre-intervention and post-intervention results. For other outcomes, it was not indicated or discernible whether there were any missing data

Outcome measurement	Were there systematic differences between the baseline and intervention groups in how outcomes were determined (including differences in how outcomes were defined)? UNCLEAR. The definition and microbiological culture approach for infections were the same pre-and post-intervention, but no information was provided on the staff diagnosing infections. Information on sterile drape and CVC use was provided by the purchasing department, but the person(s) responsible for transcribing and analysing this information were not reported Was any blinding of personnel and/or outcome assessors reported (including assessors of blood cultures)? NO
Other possible sources of bias	The authors acknowledged that other unmeasured effects may have affected outcomes, and because faculty participated in the course, they may have changed their approach to care of patients and subsequent supervision of physicians-in-training. Only processes that are routinely performed by physicians were monitored (i.e. excluding arterial punctures, urinary catheter insertions, blood draws through lines, peripheral line insertions, and phlebotomy)

Other critical appraisal criteria

Methods	Intervention described in sufficient detail to be replicated? YES. The numbers, duration, content, and cost of sessions were reported, although it is unclear whether the training course comprised 7- or 8-hour-long sessions and whether a session on OSHA was included Justification given for sample size? NO Data collection process reported? NOT REPORTED. Methods for assessing outcomes were reported but no information was provided on who collected the outcomes data or how the data were managed If YES or PARTIALLY, was the data collection process shown to be valid? NOT APPLICABLE If YES or PARTIALLY, was the data collection process shown to be reliable? NOT APPLICABLE Statistical tests described? YES
Results	Educational significance or effect size assessed? NO. Significance discussed but no effect size provided Target behaviour change achieved? PARTIALLY. Reported briefly the proportion of CVC insertions for which sterile drapes were used immediately before and in the 6 months after an education course. There was a statistically significant increase in compliance with the use of drapes; before and after the education course compliance was 44% and 65% respectively ($p < 0.001$)

Additional comments

- Stated that use of CVCs in the seven study units was high (central-line days/patient-days × 100 = 73%). Because of this, the authors concluded that patient-days could serve as a surrogate of device-days (even though the latter would probably be more accurate under other circumstances).
- Authors refer to catheter related infections inconsistently in the text, in some cases to describe the total number of (catheter related + primary BSI) infections. The definition of 'catheter related' infections given is consistent with catheter-associated infections (blood cultures negative or not done).
- Surveys (data reported but not extracted) showed that most physicians had little experience performing procedures during medical school (1 of 3 PGY-1 physicians had never inserted a CVC during medical school).

SPEROFF (2011)[136]

Methods

Study characteristics

Lead author, publication year(s) and reference(s)	Speroff (2011)[136]
Summary of approach	Multicentre, cluster RCT in ≥ 60 ICUs (number not stated) comparing virtual collaborative and toolkit QI approaches for preventing CLABSI and VAP
Location	USA, multistate (primarily southern states)
Language	English
Critical care specialty	Not reported (multiple ICUs)
No. of critical care units	Not reported (≥ 60 assuming at least one per hospital)
No. of hospitals	60 in total (29 and 31 per group)
Hospital name (unless multicentre); city	Multicentre (hospital names not reported)
Study design	Cluster RCT (Clinicaltrials.gov registration number NCT 00975923)
Study time periods	**Baseline surveys:** July to November 2005 **Randomised** December 2005 **Intervention:** January 2006 to September 2007 (18 months) **Follow-up:** September 2007 to January 2008; outcomes survey January to April 2008 (data not reported) **Note:** Reported that study was 18 months with follow-up thereafter: unclear whether any embedding of QI practices continued into the follow-up period
Funding source	Supported by a grant from the Partnerships in Implementing Patient Safety (PIPS) from the Agency for Healthcare Research and Quality (AHRQ)
Conflicts of interest	Stated no disclosure to report: AHRQ provided funding only

Population and setting

Median hospital size = 117 beds; median ICU size = 16 beds; medical centres: rural (11%), inner city (28%) and suburban (61%). At baseline 45% of the facilities reported having a CLABSI programme and 62% a VAP programme (not stated whether facilities refer to hospitals or ICUs; number of ICUs per hospital not reported).

Baseline data Critical care unit characteristics	Group 1: Toolkit (29 hospitals)	Group 2: Virtual collaborative (31 hospitals)	Difference Group 1 vs. Group 2
Median (IQR) ICU patient volume per year	578 (244–1077)	568 (294–904)	$p = 0.93$
Median (IQR) ICU LOS, days	4228 (1645–6725)[a]	3882 (1758–5718)[a]	$p = 0.95$
Mean (SD)% ICU mortality rate[b]	7.1 (3.6)	5.7 (3.1)	$p = 0.13$
Mean (SD)% patients admitted to ICU from emergency department[b]	67 (20)	71 (15)	$p = 0.27$
Mean (SD)% Medicare/ Medicaid[b]	68.5 (10.1)	68.6 (9.5)	$p = 0.95$
% hospitalist ICU management	40	47	$p = 0.61$
Patient population characteristics			
Mean (SD)% female[b]	50.3 (7.7)	49.7 (5.7)	$p = 0.79$
Age, ethnicity, health status, socioeconomic status, oral or i.v. antimicrobial use	Not reported	Not reported	Not reported
Device characteristics	None reported	None reported	Not reported
Insertion site antisepsis used	Not reported	Not reported	Not reported
Dressing type and duration/ frequency	Not reported	Not reported	Not reported

a Interpretation unclear: reported LOS appears excessive; time period of data not stated.
b Not explicitly stated, but presumed to be mean (as SD reported).

Intervention characteristics

Objective	To determine if a QI virtual collaborative intervention would perform better than a toolkit-only approach at preventing CLABSI and VAP
Main focus of education	Not explicitly stated, but the key interventions for preventing CLABSI were routine hand hygiene, site selection, barrier precautions, chlorhexidine skin preparation, and catheter need review. Education also covered epidemiology and prevention of infections, teamwork and QI approaches. Education also included in intervention for preventing VAP
Trainers (providers)	Not reported; appears to be ICU nurse and quality managers
Training of trainers	Not reported; appears to be co-ordinated by the Hospital Corporation of America (HCA) corporate office of Quality, Safety, and Performance Improvement
Learners (recipients)	ICU teams; no details reported
Target behaviour change	Not explicitly stated: interventions address multiple possible behaviours associated with prevention of CLABSI and VAP
Development and testing	Drew upon existing research in QI approaches; intervention components were iteratively developed by teams based on plan-do-study-act cycles
Educational or behavioural theory	Not reported
Educational strategies and topics targeted For the hospitals owned and operated by the HCA, stated[203] that 130/133 infection control programmes (97.7%) conducted surveillance in accordance with the CDC definitions for BSI	**Both groups:** Both groups were offered **interactive web seminars**: five were on clinical subject matter, and five were on patient safety, charting use of statistical process control and QI methods (total number of seminars not stated) **Group 1 (toolkit)** Hospitals received a toolkit containing a set of evidence based **guidelines** and **fact sheets** for preventing CLABSI and VAP, a review of QI and teamwork methods, and standardised data collection and charting tools. HCA **website** provided nurse and quality managers with access to all educational seminars, clinical and QI tools. Education was provided to standardise outcome measurement (online tutorial, Talbot TR, November 2005). Other aspects of QI for preventing CLABSI and VAP were left to the discretion of the ICU to develop and implement **Group 2 (virtual collaborative)** Teams attended web seminars and teleconferences for reporting back to the larger group. Supported by monthly educational and troubleshooting conference calls, individual coaching co-ordinated by the HCA corporate office of quality, safety and performance improvement, and an e-mail Listserv designed to stimulate interaction among teams Intervention components reportedly used in both interventions included **BSI checklists**; **daily catheter review**; **seminars; continuing education** classes for BSI; **written education**; BSI **surveillance guide**; **QI efforts** to prevent CLABSI; and statistical process control

Infection surveillance feedback approach	Self-reported. Stated that data collection and surveillance methods varied across hospitals (reference cited[203]). Survey[203] indicated that hospital acquired infection (HAI) reports were routinely provided to ICU staff and other stakeholders during the baseline period (September 2005). Web application data registry created and infection data reporting by the infection control personnel mandated from first quarter of 2006. To verify electronic data and correct missing information, infection control personnel were requested to complete a retrospective data collection sheet providing quarterly reports from January 2005 to December 2007 (i.e. part baseline, part intervention period). Validity and reliability of data collection not reported. Stated 'Nearly all ICPs provided HAI reports to senior hospital leaders, nurse management of the ICU, and institutional committees. Feedback of data was less frequent for front-line health-care workers, such as nurses, physicians, respiratory therapists, and support staff
Performance feedback approach	Self-reported. Referred to as provider performance feedback for BSI and VAP but method of feedback not reported. Stated that validity of data collection method was not assessed
Concentration of education	Not reported and not discernible owing to the large-scale nature of the intervention with multiple educational activities, site-to-site variation and iterative implementation.
Non-educational intervention components	Infrastructural changes (team development); IHI care bundles for CLABSI and VAP (not described but reference cited); Concurrent intervention to prevent VAP
Costs reported	Not reported

Outcome characteristics

Catheter-BSI definition From online HCA webcast at Vanderbilt Medical School (TR Talbot, 2005) Stated that although most hospitals defined CLABSI using CDC definitions, data collection and surveillance methods varied across hospitals (reference cited[203])	CDC NNIS laboratory-confirmed CVC-related bloodstream infection. Must meet at least one of the following criteria: *Criterion 1*: Patient with CVC has a recognised pathogen cultured from one or more blood cultures *and* organism cultured from blood is not related to an infection at another site *Criterion 2*: Patient with CVC has at least one of the following signs or symptoms: fever, chills, or hypotension, and at least one of the following: (a) common skin contaminant (e.g. coagulase-negative staphylococci) is cultured from two or more blood cultures drawn on separate occasions; (b) common skin contaminant is cultured from at least one blood culture from a patient with CVC, and the physician institutes appropriate antimicrobial therapy; *and* signs and symptoms and positive laboratory results are not related to an infection at another site
Outcomes reported	Not stated whether primary or secondary (study power based on hospital-acquired infections, not specifically mentioned whether CLABSI or VAP): CLABSI per 1000 catheter-days; VAP per 1000 ventilator days (data not extracted); Process implementation

Results data

Primary outcomes

Outcome Hospital-wide outcomes data (data pooled per hospital; not reported for separate ICUs)	Group 1: Toolkit (29 hospitals)	Group 2: Virtual collaborative (31 hospitals)	Difference between Groups 1 and 2
Device duration	Not reported	Not reported	Not reported
Device-days (not reported; e-mailed by the author)			
Baseline	26,599	22,172	Not reported
3 months	25,257	22,202	
6 months	24,618	22,951	
9 months	27,821	23,268	
12 months	29,066	26,211	
15 months	29,818	25,646	
18 months	24,245	19,276	
No. of devices/patient	Not reported	Not reported	Not reported
CLAB incidence rate (not reported; e-mailed by the author)			
Baseline	81	37	Not reported
3 months	72	52	
6 months	76	54	
9 months	72	53	
12 months	75	45	
15 months	62	65	
18 months	66	53	
Median (IQR) CLABSI incidence per 1000 catheter-days per hospital			
Baseline	2.42 (0.65–6.80)	1.18 (0.00–3.83) 2.24 (0.54–4.69)	Baseline: $p = 0.24$ Baseline vs. 12 months: $p = 0.13$ Baseline vs. 18 months: $p = 0.95$ Overall trend: $p = 0.71$[a]
3 months	2.47 (1.48–5.35)	2.28 (0.00–3.73)	
6 months	2.54 (0.00–4.98)	1.76 (0.00–3.74)	
9 months	1.23 (0.00–3.93)	1.18 (0.00–2.71)	
12 months	1.17 (0.00–3.61)	2.04 (0.00–4.91)	
15 months	1.77 (0.00–3.30)	2.76 (0.00–4.67)	
18 months	1.16 (0.00–5.46)	1.18 (0.00–3.83) 2.24 (0.54–4.69)	

Outcome Hospital-wide outcomes data (data pooled per hospital; not reported for separate ICUs)	Group 1: Toolkit (29 hospitals)	Group 2: Virtual collaborative (31 hospitals)	Difference between Groups 1 and 2
CLABSI incidence per 1000 catheter-days per hospital calculated by reviewers from authors' device-days and incidence data[b]			
Baseline	3.0	1.7	
3 months	2.9	2.3	
6 months	3.1	2.4	
9 months	2.6	2.3	
12 months	2.6	1.7	
15 months	2.1	2.5	
18 months	2.7	2.7	
CLAB incidence per 1000 patient-days	Not reported	Not reported	Not reported
LOS	Not reported	Not reported	Not reported
Mortality	Not reported	Not reported	Not reported

a Hierarchical negative binomial regression modelling of change in CLABSI rate over time.
b Data for calculating risk ratios with CIs (presented in the main report) were not reported in the primary publication but were obtained by contacting the author.

Secondary outcomes

Reaction to education	Not a study outcome
Attitudes	Not a study outcome
Compliance	Not a study outcome
Knowledge	Not a study outcome
Skills	Not a study outcome

Process evaluation	Group 1: Toolkit (29 hospitals)	Group 2: Virtual collaborative (31 hospitals)	Difference between Groups 1 and 2
No. (%) of hospitals responding to survey	19 (66)	27 (87)	
No. of ICUs responding to survey	25	36	
Clinical tool use[a]	**49%**	**61%**	***p* = 0.23**
BSI surveillance guide	13/25 (52%)	22/36 (61%)	$p = 0.60$
BSI checklist	16/25 (64%)	31/36 (86%)	$p = 0.06$
Data tool use[a]	**30%**	**56%**	***p* = 0.004**
QI implementation tools	6/25 (24%)	19/36 (53%)	$p = 0.03$
BSI statistical process control	5/25 (20%)	23/36 (64%)	$p = 0.001$

Process evaluation	Group 1: Toolkit (29 hospitals)	Group 2: Virtual collaborative (31 hospitals)	Difference between Groups 1 and 2
All tools used			
Median no. of tools downloaded	7	10	$p = 0.051$
Strategy use[a]	**54%**	**69%**	***p* = 0.017**
Protocols for BSI	19/25 (76%)	24/36 (67%)	$p = 0.57$
Computer documentation for BSI	13/25 (52%)	24/36 (67%)	$p = 0.29$
Increased staffing	0/25 (0%)	3/36 (8%)	$p = 0.26$
Written education for BSI	19/25 (76%)	31/36 (86%)	$p = 0.33$
Continuing education classes for BSI	16/25 (64%)	28/36 (78%)	$p = 0.26$
QI teams	14/25 (56%)	27/36 (75%)	$p = 0.16$
Provider performance feedback for BSI	11/25 (44%)	23/36 (64%)	$p = 0.18$
Implementation			
QI efforts to prevent CLABSI	88%	97%	$p = 0.99$
Implemented hand hygiene[b]	93%	100%	Not reported
Implemented site selection[b]	72%	86%	Not reported
Implemented barrier precautions[b]	97%	100%	Not reported
Implemented chlorhexidine[b]	100%	100%	Not reported
Implemented daily assessment[b,c]	68%	92%	Not reported
Implemented daily catheter review[c]	Less often (no data)	More often (no data)	$p = 0.04$
Implemented all components of BSI interventions	64%	100%	$p = 0.13$
Implemented BSI checklist	15/25 (60%)	28/36 (78%)	$p = 0.16$
Participation in education			
Participated in seminars	39%	57%	$p = 0.014$
Attended the clinical topics	56%	64%	$p = 0.37$
Participated in data and method topics	22%	50%	$p < 0.001$
Other			
Hospitals found seminars useful to QI efforts	30%	49%	$p = 0.017$

a Tools and strategies reported for CLABSI (extracted) and VAP (not extracted).
b Data extracted by reviewers from graph (figure 1) using Engauge software.
c Unclear whether 'daily assessment' refers to 'catheter need review' or whether these are distinct variables.

Critical appraisal

Potential for bias

Group selection[a]	Were there systematic differences between the study groups? UNCLEAR. Very limited demographic information reported; unable to rule out selective presentation of data, as no justification provided for the focus on those variables presented If YES, were the differences between the groups adjusted for in statistical analyses (e.g. as covariates or subgroups, or stratification by propensity scores)? NOT APPLICABLE (note that part of analysis included adjustment for covariates, but the covariates were not specified)
Intervention administration	Were any confounding variables identified that could influence the effect estimate for the overall intervention? UNCLEAR. Limited information on staffing, infrastructure and care policy reported (staffing of infection control programmes varied among hospitals[203]). The study authors noted that the study was implemented during the IHI's 100,000 Lives Campaign, which may have influenced regional infection rates (baseline incidence rate was noted to be low) Was the effect of educational practice separable from effects of non-educational practice? NO. Although many aspects of the interventions were educational, there were other non-educational components, e.g. provision of QI teams Were the intervention component(s) implemented as planned? PARTIALLY. The intervention components varied across hospitals but implementation was reported only for hospitals who responded to surveys (see *Process Evaluation* section for details)
Missing data[a]	Were there systematic differences between the study groups in data availability? NOT REPORTED. The number of hospitals was specified for each study group but no indication was given of whether any hospitals did not provide follow-up data. The number of ICUs was given only for those reporting follow-up data; the number of ICUs in each study group was not stated
Outcome measurement[a]	Were there systematic differences between the baseline and intervention groups in how outcomes were determined (including differences in how outcomes were defined)? UNCLEAR. Stated that data collection and surveillance methods varied across hospitals in the baseline period. Education aimed to improve standardisation of outcome definitions but it appears that same education may have been common to both study groups Was any blinding of personnel and/or outcome assessors reported (including assessors of blood cultures)? NO
Other possible sources of bias	1. Data were dependent on self-reports and were not verified by independent assessment 2. Implementation was at the level of ICUs, but the number of ICUs in the study was not reported, and only hospital-wide outcomes data were provided 3. Parts of the educational interventions appear to have been shared by both study groups but it is not possible to identify which intervention components were unique to the study groups

Risk of selection bias in randomised studies	Risk of bias: reviewer judgement (low/high/unclear)	Support for judgement
Random sequence generation	UNCLEAR	No information given. Stated that hospitals willing to participate were matched on geographic location and ICU volume and then randomised but method of achieving this randomisation approach not stated
Allocation concealment	UNCLEAR	No information given

a Assessment criteria for this RCT differ slightly from assessment criteria used for single-cohort studies (differences are compared between parallel study groups rather than sequential before-and-after groups).

Other critical appraisal criteria

Methods	Intervention described in sufficient detail to be replicated? NO. A large-scale study that did not mandate fixed specific intervention components, with each centre free to tailor its use of tools and change ideas. Many education components appear to have been common to both study groups, but this was not clearly reported, hence although numerous online supporting resources were provided, it is difficult to establish which are relevant to each study group. Although implementation was at the level of ICUs, the number of ICUs in the study, the number per hospital, and their specialties were not reported
	Justification given for sample size? YES. Power of 82–91% for testing group differences calculated a priori with one-tailed $\alpha = 0.05$ and group size of 30, assuming a 50% decrease in hospital-associated infection rates for the collaborative group vs. a 10–15% decrease for the toolkit group
	Data collection process reported? PARTIALLY. Limited information given on infection surveillance feedback; no information given on performance feedback methods
	If YES or PARTIALLY, was the data collection process shown to be valid? NO. Stated that data were not verified by independent assessment
	If YES or PARTIALLY, was the data collection process shown to be reliable? NO. Stated that data were not verified by independent assessment
	Statistical tests described? PARTIALLY. Stated that trend analysis was adjusted for clustering of ICUs within hospitals and adjusted for covariates but no intraclass correlation coefficient to account for clustering was reported. The covariates were not specified (limited baseline variables reported). Not stated whether analysis was by intention to treat (missing data not reported)
Results	Educational significance or effect size assessed? NO
	Target behaviour change achieved? NOT REPORTED. Implementation of infection-prevention practices is reported through a post-study survey but unclear whether these practices had changed relative to baseline

Additional comments

- Medical centres included were those of the HCA, a network of hospitals located primarily in the southern USA. Stated that to minimise contamination bias between study groups within the same facility, the unit of randomisation was the hospital and implementation was at the level of the ICU.
- Stated that outcomes were reported hospital-wide, but appears to present data from ICUs.
- A related paper by Talbot and colleagues[203] (cited) indicated that nearly half of 126 hospitals in the HCA system surveyed from September 2005 reported difficulty in obtaining denominator data needed to determine BSI rates, with nearly one-quarter of the 126 hospitals unable to provide BSI rates for some months. Unclear whether these figures are representative for the 60 hospitals included in the present study.
- Speroff and colleagues[136] stated that data collection and surveillance methods varied across hospitals, citing evidence from Talbot and colleagues[203] but unclear how representative the latter data from 162 hospitals are for the 60 hospitals included in the present study.
- Stated that the 60 participating sites did not differ from 113 non-participating sites (data not shown).
- The study population consisted of hospitals that were part of a larger health-care system owned by a specific corporation. This may influence generalisability.
- Correspondence with the main author confirmed that, while the majority of ICUs were adult based, there were two paediatric ICUs per study arm.

WALL (2005)[138]

Methods

Study characteristics

Lead author, publication year(s) and reference(s)	Wall (2005)[138]
Summary of approach	Single-unit, continuous QI programme involving real-time feedback of CRBSI rates and compliance with insertion practice, based on data collected by nurses using a standard checklist
Location	USA: Tennessee
Language	English
Critical care specialty	Adult MICU
No. of critical care units	1
No. of hospitals	1
Hospital name (unless multicentre); city	Vanderbilt University Medical Center, Nashville
Study design	Single cohort before-and-after study
Study time periods	**Baseline:** January 2000 to October 2002 (CRBSI data reported for November 2000 to October 2002) (2 years) **Intervention:** November 2002 to October 2004 (2 years) **Follow-up:** None (continuous QI programme)
Funding source	Lead author (Wall) was supported by the Office of Academic affiliations, Department of Veterans Affairs, VA National Quality Scholars Program, and with resources at the VA Tennessee Valley Healthcare System, Nashville, TN. Co-author (Ely) received the Paul Beeson Faculty Scholar Award from the Alliance for Aging Research and received a K23 from the National Institute of Health
Conflicts of interest	Stated no competing interests declared

Population and setting

Critical care unit characteristics	14 MICU beds in a 640-bed tertiary teaching hospital Approximately 600 MICU admissions per year Most CVCs in the medical MICU were inserted by trainees (house staff). Details of the staff who inserted catheters were reported only for the intervention period: Medical student = 19 (3%) Intern (postgraduate year 1) = 357 (57%) Resident (postgraduate year 2) = 176 (28%) Fellow/attending = 78 (12%) Total insertions = 630 (100%)
Patient population characteristics	Patients with conditions including acute respiratory distress syndrome, asthma, chronic obstructive pulmonary disease, respiratory failure, pneumonia, sepsis, poisoning, drug overdose and gastrointestinal bleeding. Also critically ill solid organ and bone marrow transplant patients
Device characteristics	Only devices placed by MICU staff were included (the authors implied that dialysis catheters were excluded but the numbers given below for the 630 catheters inserted by MICU staff during the intervention period include dialysis catheters). Catheter types and insertion sites were reported only for the intervention period: Catheter type (total = 630): • Triple lumen = 372 (59%) • Introducer = 191 (30%) • Dialysis catheter = 38 (6%) • Swan–Ganz = 21 (3%) • Other = 8 (1%) Venous insertion site (total = 630): • Internal jugular = 180 (29%) • Subclavian = 245 (39%) • Femoral = 171 (27%) • Other = 34 (5%) Insertion circumstances (total = 630): • Non-emergency = 481 (76%) • Emergency = 149 (24%) Not reported whether antiseptic or antimicrobial coated catheters were used.
Insertion site antisepsis used	Not reported
Dressing type and duration/ frequency	Not reported

Intervention characteristics

Objective	The primary goal was to show that real-time measurement of CVC care was feasible in the MICU and that process measurements would guide continuous QI and thereby lead to a reduced CRBSI rate
Main focus of education	Catheter insertion. Real-time feedback of compliance with insertion practices and data on infections based on checklists completed by nurses
Trainers (providers)	Voluntary interdisciplinary team
Training of trainers	Not reported
Learners (recipients)	MICU house staff (proceduralists) and MICU nursing staff (as observers of procedures)
Target behaviour change	Sterile catheter insertion procedure
Development and testing	A voluntary interdisciplinary team of leaders (nurse manager, MICU director), front-line staff (MICU nurses and physicians), infectious diseases experts (chief hospital epidemiologist, infection control practitioners) and improvement experts developed a system for measuring the process of CVC care in real time based on review of the published literature and observation of MICU practice to identify risk factors during catheter insertion and maintenance Priority areas for measurement established by the multidisciplinary team included provider education, trainee supervision, insertion site, hand hygiene, skin antisepsis, and use of maximal sterile barriers. Nursing checklist for CVC insertion was pilot tested for 1 week with two MICU nurses and revised before being implemented across the MICU
Educational or behavioural theory	Not reported
Educational strategies and topics targeted	**Nursing checklist for CVC insertion.** The checklist recorded through check boxes whether providers used hand hygiene; used barrier precautions (gloves, gown, mask, patient drape; using all four together being defined as maximal barrier precautions); maintained a sterile field; used chlorhexidine skin antisepsis; and were properly supervised. '**Supervision**' was defined as the proceduralist having successfully completed five CVC insertions or if another provider with experience of at least five CVC insertions supervised them during the procedure. Nurses obtained this information for the checklist but had the option of recording 'didn't ask'. Providers were not obliged to follow infection reducing steps if a life-threatening situation mandated immediate CVC insertion **Web-based tutorial**. This discussed catheter-related infections, described the checklist and explained the evidence base. House staff were requested by letter to complete the tutorial before their rotation. Nursing staff were requested by letter to complete the tutorial as part of their annual competencies curriculum. The website recorded whether each provider completed a self-assessment examination. Reminder letters were re-sent after 3 months if necessary, and MICU leadership personally approached non-compliers
Infection surveillance feedback approach	*Pre-intervention*: Monthly infection incidence reports were provided by infection control practitioners to the MICU staff *Intervention period*: To better account for the rarity of infections, infection surveillance data were fed back to MICUs as the time interval between infections rather than as incidence rates. This approach followed the principles of statistical process control, with g-charts displaying the time interval between infections. Formal validity and reliability analyses for data capture using the checklist were not undertaken
Performance feedback approach	Completed checklists were dropped in a secure lock box then collected daily by infection control practitioners who scanned the de-identified information into a spreadsheet database using automatic scanning software. Data were held on a central computer at the Centre for Clinical Improvement. Process measurements obtained from the checklists were 'bundled' with the monthly infection surveillance reports and fed back to front-line MICU staff (feedback presentation method not reported). Formal validity and reliability analyses for data capture using the checklist were not undertaken. Competence in completing the online tutorial (*knowledge*) was assessed but the method of feeding back the results to staff (e.g. identifying learning goals) was not reported

Concentration of education	Checklist was applied daily and could be completed in 1 minute Feedback on infections and compliance with insertion practice was reported as in 'real time' but the way MICU staff accessed the information was not reported. The time required for training and assessment was not reported
Non-educational intervention components	None (all components including checklist, infection surveillance feedback and performance feedback are considered educational for the purposes of this systematic review)
Costs reported	No

Outcome characteristics

Catheter-BSI definition Reference cited: O'Grady *et al.*[196]	NNIS definition (reference cited). Laboratory-confirmed bacteraemia (or fungaemia) is attributed to a patient with a CVC if they have been in the MICU for at least 48 hours, provided that the infection is not related to another distal source. Patients with a CVC who develop a BSI within 48 hours of MICU discharge also have CR-BSI
Outcomes reported	Not referred to as primary or secondary: CRBSI rate and the time between CRBSI events Compliance with CVC insertion practices

Results data

Primary outcomes

Outcome	Baseline: 24 months (November 2000 to October 2002)	Intervention: 24 months (November 2002 to October 2004)	Difference between baseline and intervention
Device duration	Not reported	Not reported	
Total device-days (not reported; e-mailed by the author)	3571 during 24 months	1132 during 24 months	
No. of devices/patient	Not reported	Not reported	
CRBSI number	25 during 24 months	6 during 24 months	76% reduction
CRBSI incidence per 1000 catheter-days (a) reported and also confirmed by the author; (b) not reported; e-mailed by the author	(a) 7.0 during 24 months	(a) 3.8 during final 6 months (b) 5.3 during 24 months	No statistical comparison reported
CRBSI incidence per 1000 patient-days	Not reported	Not reported	
LOS	Not reported	Not reported	
Mortality	Not reported	Not reported	

Secondary outcomes

Reaction to education	Not a study outcome
Attitudes	Not a study outcome
Knowledge	Not a study outcome
Skills	Not a study outcome

Compliance: Percentage of insertions compliant. Data extracted by reviewer from line graph using Engauge software

Month of intervention	Hand hygiene	Chlorhexidine skin preparation	Maximal barriers	Guidewire exchange
1–3	73	57	68	18
4–6	87	76	49	13
7–9	91	88	62	15
10–12	92	95	70	16
13–15	95	91	75	18
16–18	91	96	69	25
19–21	94	96	70	13
22–24	89	100	86	20

Process evaluation

The checklist generated real-time measurements for the CVC insertion process. These data were used for cycles of continuous QI in which the reasons for certain provider behaviours were explored

A decline in adherence to maximal barrier precautions during December 2002 to February 2003 was found to have been caused by lack of use of patient drapes (data presented but not extracted by reviewers). Adherence to maximal barrier precautions improved after the team purchased new sterile kits pre-packaged with drapes, and confirmed providers had completed the tutorial

Use of the femoral insertion site compared with other insertion sites was associated with statistically significantly lower adherence to hand washing, chlorhexidine skin preparation and maximal sterile barriers (data presented but not extracted by reviewers)

Critical appraisal

Potential for bias

Group selection	Were there systematic differences between the baseline and intervention groups? UNCLEAR. The authors stated that mortality rates, admission diagnoses, ventilator days, and lengths of stay were similar for patients admitted during the pre-intervention and intervention periods. However, other patient characteristics (e.g. age, gender, health acuity) were not reported If YES, were the differences between the groups adjusted for in statistical analyses (e.g. as covariates or subgroups, or stratification by propensity scores)? NOT APPLICABLE
Intervention administration	Were any confounding variables identified that could influence the effect estimate for the overall intervention? UNCLEAR. The authors acknowledged that it is possible that some undetected case mix variable or change in catheter duration may have contributed to the decreased CRBSI rate and that while the checklist specifically targeted catheter insertion, unmeasured improvements during catheter maintenance may also have contributed to the reduced CRBSI rate Was the effect of educational practice separable from effects of non-educational practice? YES. All components of this intervention (checklist, infection surveillance feedback and process feedback) are classed as educational Were the intervention component(s) implemented as planned? PARTIALLY. Stated in the methods section that the checklist was introduced to all nursing staff and implemented throughout the entire MICU. Letters were sent requesting ICU staff to complete the tutorial. If individuals still did not complete the tutorial, the MICU leadership approached them privately. Stated that a total of 630 CVCs were inserted using the new checklist
Missing data	Were there systematic differences between the baseline and intervention groups in attrition or exclusions (includes withdrawal due to mortality; missing outcome data)? UNCLEAR. The authors stated that admissions, admission diagnoses, and mortality did not differ between the baseline and intervention groups; however, no quantitative data were reported
Outcome measurement	Were there systematic differences between the baseline and intervention groups in how outcomes were determined (including differences in how outcomes were defined)? UNCLEAR. The MICU used a standard definition of CRBSI which appears to have applied both in the baseline and intervention periods. However, no information was given on the staff diagnosing infections Was any blinding of personnel and/or outcome assessors reported (including assessors of blood cultures)? NO
Other possible sources of bias	No other sources of bias were reported by the authors or identified by the reviewers based on the information presented

Other critical appraisal criteria

Methods	Intervention described in sufficient detail to be replicated? NO. Although the principles and practices are mostly well described, only a summary of the checklist content is reported. The training module is general and covers topics relevant to infection prevention beyond those described by the authors; the scope of the knowledge assessment based on the tutorial is not reported Justification given for sample size? NOT REPORTED Data collection process reported? PARTIALLY. Stated that upon completing the checklist, a nurse detached the top page (with all items readable) and dropped it in a secure lockbox. The second page remained on the patient's chart with the sensitive items blacked out. The infection control practitioners collected the checklists daily and scanned the de-identified forms into a pre-established computerised database using scanning software which scanned pre-established fields on the checklist and imported the information into a spreadsheet database. These data were stored on a secure computer at the Center for Clinical Improvement for future statistical analyses If YES or PARTIALLY, was the data collection process shown to be valid? NO. Formal validity and reliability analyses for data capture using the checklist were not undertaken If YES or PARTIALLY, was the data collection process shown to be reliable? NO. Formal validity and reliability analyses for data capture using the checklist were not undertaken Statistical tests described? YES. Statistical process control approach
Results	Educational significance or effect size assessed? NOT REPORTED Target behaviour change achieved? PARTIALLY. Some aspects of catheter insertion procedure were complied with more extensively than others. Failure to use patient drapes was identified as a problem and steps were taken to improve compliance

Additional comments

The data reported above are from the primary research publication[138] and web-based tutorial available at www.mc.vanderbilt.edu/cvctutorial.

WARREN (2003)[139]

Methods

Study characteristics

Lead author, publication year(s) and reference(s)	Warren (2003)[139]
Summary of approach	Ten-page self-study module, lectures and posters on the prevention of CABSIs given in two ICUs during 3 months in a non-teaching hospital
Location	USA, Missouri
Language	English
Critical care specialty	Medical and SICU
No. of critical care units	2
No. of hospitals	1
Hospital name (unless multicentre); city	Missouri Baptist Medical Center, St Louis
Study design	Single-cohort before-and-after study combining data from two ICUs
Study time periods	**Baseline:** 1 March 1998 to 30 June 1999 (16 months) **Intervention:** 1 July to 30 September 1999 (3 months) **Follow-up:** 1 October 1999 to 31 July 2000 (10 months) Data on anatomical insertion site of CVCs were collected from 1 August 1998
Funding source	Supported in part by a CDC Cooperative Agreement and the National Foundation for Infectious Diseases (NFID) postdoctoral fellowship in Nosocomial Infection Research and Training (to lead author)
Conflicts of interest	Not reported

SICU, surgical intensive care unit.

Population and setting

Critical care unit characteristics:

500-bed non-teaching private community hospital affiliated to a 13-hospital integrated health-care system

Each ICU: 10 beds (total 20 beds); combined admission approximately 150 patients per month

No medical students or house staff; only registered nurses provided patient care

Four hospital-employed, board-certified critical care physicians staffed both ICUs and were responsible for central catheter insertion and critical care management

Patient population characteristics: 1215 of 3943 of patients admitted to the ICU during the study (30%) had a CVC	**Baseline (16 months)**	**Post intervention (10 months)**	**Difference between baseline and post intervention**
Total no. of patients	674	541	Not reported
No. (%) in MICU	310 (46)	239 (44)	$p = 0.56$
No. (%) in SICU	364 (54)	302 (56%)	Not reported
Male gender, *n* (%)	351 (52)	280 (52)	$p = 0.91$
Median age, years	71	71	$p = 0.62$
Caucasian, *n* (%)	630 (94)	499 (92)	$p = 0.65$
Congestive heart failure, *n* (%)	280 (42)	248 (46)	$p = 0.13$
COPD, *n* (%)	226 (34)	180 (33)	$p = 0.92$
Malignancy, *n* (%)	113 (17)	106 (20)	$p = 0.20$
Diabetes mellitus, *n* (%)	200 (30)	170 (31)	$p = 0.51$
HIV infection, *n* (%)	1 (0.1)	0 (0)	$p = 1.0$
Mean APACHE II score	25.2	25.1	$p = 0.86$
Haemodialysis, *n* (%)	91 (14)	69 (13)	$p = 0.70$
Corticosteroid use, *n* (%)	231 (34)	197 (36)	$p = 0.44$
Immunocompromised, *n* (%)	84 (13)	51 (9)	$p = 0.09$
Mechanically ventilated, *n* (%)	389 (58)	305 (56)	$p = 0.64$
Mean no. of ventilator days	9.1	9.0	$p = 0.28$
Tracheostomy, *n* (%)	49 (7)	45 (8)	$p = 0.50$
Re-intubation, *n* (%)	70 (10)[a]	64 (12)	$p = 0.95$
Device characteristics	Antimicrobial (chlorhexidine and silver sulfadiazine)-coated CVCs were used routinely during the entire study period CVC supplies were kept in a supply room within the unit; no changes in the accessibility of supplies were made during the intervention Insertion site data were available for 651 of the patients (54%) who had 941 non-tunnelled CVCs: Proportion inserted in subclavian vein: Baseline: 124 (25%) of 487 CVCs (in 318 patients) Intervention: 188 (41%) of 454 CVCs (in 333 patients) Difference: $p < 0.001$		
Insertion site antisepsis used	Not reported		
Dressing type and duration/frequency	Not reported		

SICU, surgical intensive care unit.
a Authors reported 12%.

Intervention characteristics

Objective	To evaluate the effectiveness of an evidence-based intervention to prevent CABSIs among intensive care unit patients at a non-teaching, community hospital
Main focus of education	Covered catheter insertion and maintenance and the collection of blood cultures, also infection epidemiology
Trainers (providers)	Not explicitly stated. Mentioned in the acknowledgements section that two registered nurses from the Department of Infection Control and one from the Department of Nursing implemented the educational programme among the ICU staff
Training of trainers	Not reported
Learners (recipients)	Nurses and physicians in the ICUs
Target behaviour change	Education appears to target multiple behaviours, including aseptic technique; use of maximal barrier precautions during CVC insertion; selection of the subclavian vein as an insertion site; routine CVC site care; proper technique for obtaining blood cultures; and changing intravenous tubing and administration sets
Development and testing	Not reported
Educational or behavioural theory	Not reported
Educational strategies and topics targeted	**10-page self-study module:** Based on 1996 Hospital Infection Control Practices Advisory Committee guidelines (reference cited). Required to be completed by all ICU nurses and physicians. After the intervention period the self-study module was mandatory for all newly-hired ICU nurses **45 minute lectures:** given to nursing and medical personnel **Grand rounds:** Presented to hospital staff on the prevention of CABSI **Posters:** distributed around the ICUs **Fact sheets:** distributed around the ICUs **Topics** in the teaching module included: the epidemiology of CABSI; aseptic technique and the use of maximal barrier precautions during CVC insertion; preference for the subclavian vein as an insertion site; routine CVC site care; proper technique for obtaining blood cultures; and guidelines for changing intravenous tubing and administration sets Not reported how the topics were allocated among the educational strategies
Infection surveillance feedback approach	Stated that all the ICU staff received reports of CABSI rates as part of the intervention. However, this process was already in place before the intervention. The time of initiation of the feedback and methodological details were not reported. While it appears that infection surveillance feedback was an ongoing activity, authors specifically stated that it was part of the intervention and it is unclear if the existing process was modified as part of the educational intervention
Performance feedback approach	A 20-question pre-test was given before receiving the study module; the same questions were given as a post-test at the end of the module. The post-test was mandatory for all ICU nurses; the pre-test was optional. However, it was not reported whether staff were aware of their test results, i.e. unclear whether performance feedback occurred
Concentration of education	The module with pre- and post-tests took an average of 1 hour to complete. After the intervention period, the module was mandatory for all newly hired ICU nurses. However, it is unclear whether all nurses were recruited solely during the specified intervention period or whether some recruitment – and hence education – continued in the follow-up period
Non-educational intervention components	None (purely educational intervention)
Costs reported	Authors estimated that the intervention cost US$3500 in personnel time and US$500 in printed material to implement in the two study ICUs. Cost-effectiveness was not investigated

Outcome characteristics

Catheter-BSI infection definition Reference cited: National Nosocomial Infections Surveillance [186]	CABSI was defined by using National Nosocomial Infections Surveillance (NNIS) system criteria. CABSI defined as concordant growth between cultures obtained from the catheter tip; hub, infusate, or insertion site exudate and percutaneously drawn blood cultures; or a recognised pathogen isolated from blood culture that is not related to infection at another site. A CABSI was considered ICU related if it occurred > 24 hours after admission to the ICU. For low-virulence organisms, two or more positive blood cultures obtained on separate occasions had to be noted for the isolate to be considered a true pathogen, and at least one of the blood cultures had to be from a peripheral venepuncture
Outcomes reported	Not stated whether primary or secondary: CABSI incidence and incidence density Time to infection LOS Mortality Completion of pre- and post-intervention tests

Results data

Primary outcomes

Outcome		Baseline (16 months, 674 patients)	Post intervention (10 months, 541 patients)	Difference between baseline and post intervention
Device duration		Not reported	Not reported	Not reported
Total device utilisation, catheter-days	Total	6110	5210	$p = 0.46$
	Mean per patient	9.1	9.6	
No. of devices/patient		Not reported	Not reported	Not reported
CABSI incidence, *n* (% of patients)				
(a) Overall		30 (4)	11 (2)	$p = 0.02$
(b) For specific post-intervention time periods				
1 July to 30 September 1999			1	
1 October to 31 December 1999			4	
1 January to 31 March 2000			4	
1 April to 31 July 2000			2	

Outcome		Baseline (16 months, 674 patients)	Post intervention (10 months, 541 patients)	Difference between baseline and post intervention
CABSI incidence per 1000 catheter-days			0	
(a) Overall		4.9	2.1	Relative risk = 0.43 (95% CI 0.22 to 0.84) (57% decrease)
(b) For specific post-intervention time periods				
1 July to 30 September 1999			0.9	
1 October to 31 December 1999			3.1	
1 January to 31 March 2000			2.7	
1 April to 31 July 2000			1.6	
CABSI incidence per 1000 patient-days		Not reported	Not reported	Not reported
Median time to infection among patients with CABSI, days		9	6	$p = 0.70$
Mean LOS, days	ICU	7.8	8.0	$p = 0.09$
	Hospital	19.0	19.3	$p = 0.37$
Mortality, *n* (%)		182 (27)	128 (24)	$p = 0.18$

Secondary outcomes

Reaction to education	Not a study outcome
Attitudes	Not a study outcome
Compliance with pre-and post-tests:	
Total no. of nurses staffing both ICUs	110
Were distributed the pre-test, *n* (%)	71 (65%)
Completed the pre-test, *n* (%)	64 (58%)
Completed the post-test, *n* (%)	103 (94%)
Total no. of physicians staffing both ICUs	4
Completed the pre-test, *n* (%)	4 (100)
Completed the post-test, *n* (%)	4 (100)
Knowledge	Not a study outcome
Skills	Not a study outcome
Process evaluation	Not included in the study, other than compliance with tests noted above

Critical appraisal

Potential for bias

Group selection	Were there systematic differences between the baseline and intervention groups? NO. Data showed that the study periods were similar in terms of patients' gender, age, ethnicity, major disease, APACHE score, frequency of haemodialysis, immune incompetence, corticosteroid use, mechanical ventilation, ventilator days, tracheostomy and re-intubation
	If YES, were the differences between the groups adjusted for in statistical analyses (e.g. as covariates or subgroups, or stratification by propensity scores)? NOT APPLICABLE
Intervention administration	Were any confounding variables identified that could influence the effect estimate for the overall intervention? UNCLEAR. Stated that antimicrobial catheters and CVC supplies did not differ between the baseline and intervention periods and that no formal education programme was in place before or after the adoption of the antimicrobial catheters hospital-wide in the early 1990s. However, data on markers of changes in processes of care (i.e. systematic observations of CVC insertion and care techniques, and appearances of insertion site dressing) were not collected, apart from the insertion site
	Was the effect of educational practice separable from effects of non-educational practice? YES. Education-only intervention
	Were the intervention component(s) implemented as planned? PARTIALLY. Exposure to education was not explicitly reported and it is unclear whether test participation is reflective of education exposure. However, post-tests described as mandatory were completed by 94% of nurses and 100% of physicians, exposing nearly all the staff to part of the intervention
Missing data	Were there systematic differences between the baseline and intervention groups in data availability? UNCLEAR. For most outcomes, data were for all patients who had a CVC. However, data for insertion site were reported to be available for 381 patients (47%) in the baseline period and 333 patients (62%) in the intervention period (reason for the missing data not reported)
Outcome measurement	Were there systematic differences between the baseline and intervention groups in how outcomes were determined (including differences in how outcomes were defined)? NOT REPORTED
	Was any blinding of personnel and/or outcome assessors reported (including assessors of blood cultures)? NO
Other possible sources of bias	The authors acknowledged that staff behaviour might have changed as a result of observation alone, independent of the intervention; this can neither be ruled out nor confirmed

Other critical appraisal criteria

Methods	Intervention described in sufficient detail to be replicated? NO. The educational topics were described superficially and it was not reported how the topics were allocated among the educational strategies. The test questions were not reported
	Justification given for sample size? NO. Authors commented that the study was not powered to determine the impact of the intervention on lengths of stay, but they did not comment on whether it was powered to detect differences in infection incidence rates
	Data collection process reported? PARTIALLY. Stated only that trained data collectors, including infection control and research nurses, collected data prospectively on all admissions to both ICUs
	If YES or PARTIALLY, was the data collection process shown to be valid? NOT REPORTED
	If YES or PARTIALLY, was the data collection process shown to be reliable? NOT REPORTED
	Statistical tests described? YES. Data were initially analysed separately for each ICU and found to be homogeneous (Breslow–Day test), so were pooled in the final analysis
Results	Educational significance or effect size assessed? NO
	Target behaviour change achieved? NOT REPORTED

Additional comments

- Stated that the intervention was similar to that reported by Coopersmith (2002).[50]
- In this hospital a dedicated team of intensivists performed catheter insertion in the ICUs. This may not reflect practice in other hospitals.

WARREN (2004)[51]

Methods

Study characteristics

Lead author, publication year(s) and reference(s)	Warren (2004)[51]
Summary of approach	10-page self-study module on the prevention of CABSIs, lectures and posters and an awareness campaign given during 1 month in one ICU in a teaching hospital
Location	USA, Missouri
Language	English
Critical care specialty	MICU
No. of critical care units	1
No. of hospitals	1
Hospital name (unless multicentre); city	Barnes-Jewish Hospital, St Louis
Study design	Single-cohort before-and-after study
Study time periods	**Baseline:** January 2000 to December 2001 (24 months) **Intervention:** January 2002 **Follow-up:** January 2002 to December 2003 (23 months) Authors reported data for 2002 and 2003 (24 months) as post intervention, although this period included the intervention itself (January 2002). Newly hired nurses received education but it was not reported when or how many nurses were hired during the study period
Funding source	Work supported by funding from a Centers for Disease Control and Prevention Cooperative Agreement and the Barnes-Jewish Hospital Foundation
Conflicts of interest	Not reported

Population and setting

Critical care unit characteristics	ICU had 19 beds; located in a 1400-bed university-affiliated teaching hospital Patient care was provided by a multidisciplinary team directed by attending physicians who were board certified in critical care medicine Nurse to patient ratio 1 : 2. CVCs were usually inserted by resident physicians (i.e. physicians in training) Stated that patient care policies and protocols in the MICU remained unchanged during the study period, except for a new policy for prevention of VAP (introduced October 2000 during the baseline period)
Patient population characteristics	No details of the patients were provided. All patients admitted to the MICU during the study period were prospectively followed up by members of the hospital infection control team and surveyed for occurrence of CVC-associated bloodstream infection

Device characteristics	Included CVCs, dialysis catheters, pulmonary artery catheters but excluded arterial catheters All were standard catheters without antimicrobial or antiseptic coatings Mean ± SD monthly % of CVCs placed in the femoral vein: Baseline: 26.3 ± 5.8% Post-intervention: 20.4 ± 6.6% Difference: $p = 0.002$
Insertion site antisepsis used	Not reported
Dressing type and duration/frequency	Not reported

Intervention characteristics

Objective	To determine whether an educational programme could decrease the rate of catheter-associated bloodstream infection in the MICU of a teaching hospital
Main focus of education	Covered catheter insertion and maintenance and the collection of blood cultures, also infection epidemiology
Trainers (providers)	Not explicitly reported; probably provided by registered infection control nurses (as in Warren 2003[138]) who were among the study authors and contributed to programme development
Training of trainers	Development and testing (see below) involved information exchange among infection control professionals
Learners (recipients)	All nurses in the ICU received the intervention by the end of January 2002. Newly-hired nurses were required to complete the education module as part of their job orientation. Physicians (interns, residents, fellows, attending physicians) completed the module during the first 3 days of their ICU rotation
Target behaviour change	Education appears to target multiple behaviours, including: aseptic technique; use of maximal barrier precautions during CVC insertion; selection of the subclavian vein as an insertion site; routine CVC site care; proper technique for obtaining blood cultures; and changing intravenous tubing and administration sets
Development and testing	The education programme was developed by a multidisciplinary task force in 1998 by infection control practitioners representing nine hospitals in the Barnes-Jewish-Christian Health System (Coopersmith (2002)[50] cited). The local implementation plan was developed during monthly meetings of the MICU infection control community from July to December 2001. The committee comprised two ICU infection control nurses, two medical directors of the hospital infection control group, two physicians from the ICU, the unit clinical nurse specialist (all named authors), and members of the nursing staff. Objectives of the meetings were: educate the ICU leadership on the problem of CABSI; review in detail the optimal practices for catheter insertion and maintenance in the ICU; describe components of the education programme and their local implementation; foster team building; develop a strategy for educating resident and attending physicians; and have a feedback mechanism for reporting problems during implementation. Additional meetings were held by members of the ICU infection control committee to revise CVC insertion and maintenance policies and procedures. Flow charts for all aspects of CVC care were developed and approved by the committee

Educational or behavioural theory	Not reported
Educational strategies and topics targeted	Approach was similar to that of Warren (2003)[139] **10-page self-study module:** Based on guidelines of the Hospital Infection Control Practices Advisory Committee as updated in 2002 (reference cited). Five major sections: (1) Goal of the Self-study Module; (2) Risk Factors; (3) Causes of CABSI; (4) Definition of CABSI; and (5) How to Decrease CABSI Risk **In-services at scheduled staff meetings:** No details provided (mentioned only in the abstract) **45-minute lectures:** No details provided **Group discussions:** No details provided, but implied that group discussions occurred between taking the self-study module and post-test **Posters and fact sheets**: Distributed at each patient computer terminal located directly outside of the patient room (unclear whether these were the same posters and fact sheets referred to in the promotional campaign) Promotional campaign: Involved regular administration of lapel buttons to a staff member promoting the education programme, fact sheets and posters displayed throughout the ICU describing the programme, and photographic guidelines at each bedside computer station illustrating correct CVC insertion and maintenance, including dressing of the insertion site Topics in the education module and tests: The epidemiology of CABSI; aseptic technique and the use of maximal barrier precautions during CVC insertion; preference for the subclavian vein as an insertion site; routine CVC site care; proper technique for obtaining blood cultures; and guidelines for changing intravenous tubing and administration sets. Specific topics listed were: (1) hand hygiene before and after patient contact; (2) sterile gloves when changing dressing; (3) avoidance of femoral insertion site where possible; (4) wear sterile gown, gloves, mask and cap when inserting a catheter; (5) remove hair around insertion site only with scissors or clippers; (6) use appropriate insertion site antiseptic; (7) use full sterile drape; (8) use sterile technique to apply transparent dressing; (9) do not use antimicrobial ointment at insertion site except for dialysis catheters; (10) avoid catheter changes over a guidewire; (11) change dressing only when necessary; and (12) follow hospital protocol for changing i.v. fluid administration and cleaning of injection ports
Infection surveillance feedback approach	A monthly update of the CABSI was posted in the ICU in multiple locations for feedback to ICU staff. Not reported whether this system was already in place before the educational intervention
Performance feedback approach	Tests were based on the same guidelines as used in the self-study module The same 20-question test was conducted before and after implementation of the self-study module and group discussion. Score required to pass the test was 85%; if necessary the self-study module and post-test were repeated until a pass score was achieved Validity and reliability of the assessment approach were not reported
Concentration of education	Not reported other than that the lecture was 45 minutes. More detailed information on the time and staff resources required for a similar intervention were reported by Warren (2003)[139] but unclear whether they are applicable to this intervention
Non-educational intervention components	A new policy for prevention of VAP was introduced in October 2000 (during the baseline period) and was in place for > 1 year before the educational intervention started
Costs reported	Not reported (crude estimate of cost savings presented based on assumed infection incidence)

Outcome characteristics

Catheter-BSI definition Reference cited: National Nosocomial Infections Surveillance[186]	Bloodstream infections were classified as primary or secondary according to CDC NNIS surveillance definitions. Primary BSI (bacteraemia) was defined employing either of the following two criteria: (a) Isolation of a recognised pathogen from blood culture (*Staphylococcus aureus*, *Enterococcus* spp., *Candida* spp.) not related to infection at another site; and [sic] (b) Fever of ≥ 38.0 °C, chills, or hypotension, and either of the following: – common skin contaminant (e.g. diphtheroids, *Bacillus* spp, *Propionibacterium* spp, coagulase-negative staphylococci, or micrococci) isolated from two blood cultures drawn on separate occasions, within 24 hours, unrelated to infection at another site; – common skin contaminant isolated from a blood culture from a patient with an intravascular device and the physician institutes appropriate antimicrobial therapy Specifically, requirements for a definition of CABSI were given in the education programme as: 1. Presence of a vascular catheter within the last 48 hours; 2. Either of criteria (a) or (b) above Details of the technique for collecting and culturing blood samples were reported (not extracted by reviewers)
Outcomes reported	Specified as the main outcome measure: CABSI incidence and incidence per 1000 catheter-days

Results data

Primary outcomes

Outcome	Baseline (24 months)	Post intervention (23 months)	Difference between baseline and post intervention – only reported for incidence per 1000 CVC-days
Device duration	Not reported	Not reported	
Total device utilisation, catheter-days	7876[a]	7455	
No. of devices/patient	Not reported	Not reported	
CABSI incidence rate, *n*	74	41	
CABSI incidence per 1000 catheter-days	9.4	5.5	3.9 (95% CI 1.2 to 6.6); 41.5% decrease; $p = 0.019$ (risk ratio not reported)
CABSI incidence per 1000 patient-days	Not reported	Not reported	
LOS	Not reported	Not reported	
Mortality	Not reported	Not reported	

a Data from the results section; reported in the abstract as 7879 catheter-days.

Additional CVC incidence density data per month (data extracted from graph by reviewer using Engauge software)

	Baseline		Post intervention	
Monthly CVC rate per 1000 CVC-days	2000	2001	2002	2003
January	5.3	7.5	0	0
February	18.5	18.9	3.9	0
March	7.8	12.1	18.6	3.4
April	14.2	15.6	4.3	3.3
May	11.6	2.8	8.4	9.6
June	6.4	0	13.3	0
July	12.6	6.8	14.3	5.7
August	12.7	16.6	0	7.8
September	15.4	0	9.0	5.3
October[a]	6.0	12.6	3.3	5.0
November	6.9	0	5.9	10.6
December	5.7	6.6	0	0

a Intervention for prevention of VAP introduced in October 2000.

Secondary outcomes

Reaction to education	Not a study outcome
Attitudes	Not a study outcome
Compliance	Not a study outcome
Knowledge	Not a study outcome
Skills	Not a study outcome
Process evaluation	Not included in the study other than recording the frequency of insertions in the femoral vein (noted above)

Critical appraisal

Potential for bias

Group selection	Were there systematic differences between the baseline and intervention groups? NOT REPORTED. No data were given on the patient population
	If YES, were the differences between the groups adjusted for in statistical analyses (e.g. as covariates or subgroups, or stratification by propensity scores)? NOT REPORTED
Intervention administration	Were any confounding variables identified that could influence the effect estimate for the overall intervention? UNCLEAR. Stated that patient care policies and protocols in the MICU remained unchanged during the study period, except for a new policy for prevention of VAP (introduced October 2000 – during the baseline period). However, data on markers of changes in processes of care (i.e. systematic observations of CVC insertion and care techniques, device duration, and appearances of insertion site dressing) were not collected, apart from the insertion site
	Was the effect of educational practice separable from effects of non-educational practice? YES. Education-only intervention
	Were the intervention component(s) implemented as planned? NOT REPORTED
Missing data	Were there systematic differences between the baseline and intervention groups in data availability? NOT REPORTED. The number of patients in the ICU and the proportion of those that had a CVC were not specified
Outcome measurement	Were there systematic differences between the baseline and intervention groups in how outcomes were determined (including differences in how outcomes were defined)? NOT REPORTED
	Was any blinding of personnel and/or outcome assessors reported (including assessors of blood cultures)? NO. The authors stated that the ICU staff was not blinded to either the presence of or the recipients of the education intervention
Other possible sources of bias	The authors acknowledged that other sources of potential bias may have influenced their results. These would include unrecognised differences in ascertainment or reporting of CABSI between the two study periods

Other critical appraisal criteria

Methods	Intervention described in sufficient detail to be replicated? PARTIALLY. The self-study module was described well enough for the main educational topics to be reproduced in a similar strategy. However, the test questions were not reported and the nature of other educational elements (lectures, in-service and group discussions) was not reported
	Justification given for sample size? NOT REPORTED
	Data collection process reported? NOT REPORTED
	If YES or PARTIALLY, was the data collection process shown to be valid? NOT APPLICABLE
	If YES or PARTIALLY, was the data collection process shown to be reliable? NOT APPLICABLE
	Statistical tests described? YES
Results	Educational significance or effect size assessed? NO
	Target behaviour change achieved? NOT REPORTED

Additional comments

- Unclear whether infection surveillance feedback approach changed during the study period.
- The majority of CVCs in this ICU were placed by physicians in training.
- Related studies: Coopersmith (2002)[50] study was in the SICU of the same hospital; Warren (2003)[139] applied a nearly identical programme within two ICUs of a community hospital.
- Stated that the 20-question post test at the end of the module was to reinforce the topic and group discussion; the authors planned to reinforce the education by repeating the programme at 2-year intervals.

ZINGG (2009)[144]

Methods

Study characteristics

Lead author, publication year(s) and reference(s)	Zingg (2009)[144]
Summary of approach	Educational programme targeting hand hygiene and catheter care in five ICUs at a single hospital
Location	Switzerland
Language	English
Critical care specialty	Medical, cardiovascular, trauma, general surgery and neurosurgery ICUs
No. of critical care units	5
No. of hospitals	1
Hospital name (unless multicentre); city	University Hospital, Zurich
Study design	Single-cohort before-and-after study that combined data from five ICUs into a single cohort (data also presented also separately for two of the five ICUs)
Study time periods	**Baseline:** September to December 2003 (4 months) **Intervention:** March to July 2004 (5 months) **Follow-up:** None (monitoring during intervention only)
Funding source	Not reported
Conflicts of interest	Authors disclosed no potential conflicts of interest

Population and setting

Critical care unit characteristics

Total for the five ICUs:

- Beds = 52, sited in a 960-bed tertiary referral centre
- Nursing staff = 395 (head nurses, teaching nurses, assistant nurses, trainee nurses)
- Medical staff = 34

Internal guidelines recommended the use of maximal barrier precautions – but not stated whether the guidelines applied equally to baseline and intervention periods

Patient population characteristics: all adult patients hospitalised in any of the ICUs and with one or more CVCs in place were eligible for study entry; there were no exclusion criteria	**Baseline (4 months)**	**Intervention (5 months)**	**Difference between baseline and intervention**
Total no. of patients	499	500	
Cumulative no. of ICU-days	2944	3705	Not reported
Median (IQR) age, years	62 (49–71)	61 (48–73)	$p = 0.75$
Male sex, *n* (%)	320 (64)	334 (67)	$p = 0.35$
McCabe fatality score < 6 months, *n* (%)	187 (37)	223 (45)	$p = 0.01$
Median (IQR) SAPS[a] II score	23 (16–31)	24 (18–34)	$p = 0.11$
Charlson score > 3, *n* (%)	67 (13)	63 (13)	$p = 0.73$
Cardiovascular surgery, *n*	208	196	$p = 0.42$
Diabetes, *n*	71	60	$p = 0.30$
Trauma, *n* (%)	10 (2)	55 (11)	$p < 0.001$
Stay on MICU, *n* (%)	62 (12)	74 (15)	$p = 0.26$
Intubation, *n* (%)	130 (26)	131 (26)	$p = 0.96$
Non-CRBSI nosocomial infections, *n* (%)	129 (26)	131 (26)	$p = 0.90$

Device characteristics	Baseline (4 months)	Intervention (5 months)	Difference between baseline and intervention
Insertion vein			
Subclavian	494	477	$p = 0.10$
Jugular	370	398	$p = 0.56$
Femoral	110	139	$p = 0.10$
		(1 missing data)	
Catheter type			
CVC	626	673	$p = 0.34$
Pulmonary CVC	211	175	$p = 0.01$
Other	137	167	$p = 0.14$
Lumens			
Single lumen	100	121	$p = 0.21$
Multi (> 1) lumen	868	878	$p = 0.21$
	(6 missing data)	(16 missing data)	

Device characteristics	Baseline (4 months)	Intervention (5 months)	Difference between baseline and intervention
Insertion venue:			
Emergency room	39	31	$p = 0.25$
Operating room	644	636	$p = 0.11$
ICU	290	347	$p = 0.03$
	(1 missing data)	(1 missing data)	
Insertion site antisepsis used	Povidone-iodine (three SICUs) and octenidine (medical and neurosurgical ICUs)	Same as baseline practice	Quantitative data not reported
Dressing type and duration/frequency	Not reported	Not reported	Not reported

SICU, surgical intensive care unit.
a Simplified Acute Physiology Score.

Intervention characteristics

Objective	To study the impact of a teaching intervention on the rate of central venous CRBSIs in intensive care patients
Main focus of education	Hand hygiene, dressing of the insertion site, manipulation of tubing and stopcocks, and aseptic preparation of infusates; explicitly stated that CVC insertion was not the focus of the intervention and was not observed
Trainers (providers)	Two infection control nurses were responsible for teaching phases 1 and 2 (details of phases below). Two additional infection control nurses from the infection control unit participated in the bedside teaching sessions of phase 3. An infection control physician and an infection control nurse conducted teaching phase 4. (Note that the authors described teaching phases and content modules but mixed up the terminology – the above interpretation provided by the reviewers)
Training of trainers	Not stated explicitly but appears that phase 1 (training of nurses) was conducted by two infection control nurses.
Learners (recipients)	Nurses and physicians in the ICU (different emphasis of education for each group)
Target behaviour change	Hand hygiene, dressing of the insertion site, manipulation of tubing and stopcocks, and aseptic preparation of infusates
Development and testing	Not reported, except that teaching phase 1 was very helpful to build trust and learn from nurses' (i.e. the learners') experiences, and that procedure proposals were adapted to everyday situations which changed the modules significantly
Educational or behavioural theory	Not reported

Educational strategies and topics targeted	Four sequential teaching phases within each of which four sequential content modules were provided (in the order below) Teaching phases: 1. **Training of head nurses and nurse instructors:** A total of 12 interactive training sessions, organised to discuss discrepancies in existing CVC practice, evidence-based CVC care procedures, and feasibility in the units, and to achieve agreement for uniform hospital-wide procedures 2. **General teaching sessions to all ICU nurses:** Five 45-minute ex cathedra teaching interventions in the auditorium that comprised a short review of the literature, followed by practical demonstrations onsite and by video 3. **Small group bedside teaching sessions for nurses:** A total of 80 sessions of 15 minutes each, referred to as practical teaching workshops; stratified into the four modules, with only one module discussed per session 4. **Teaching of medical staff:** Physicians participated in a separate teaching programme focusing mainly on hand hygiene, although information about the content of the other modules was provided as well. Compared with the nurses' teaching the theoretical background was more detailed, with a thorough discussion of the literature. Furthermore, they were confronted with findings on perceptions and beliefs of health-care workers about hand hygiene in the literature (references cited) Content modules: 1. Hand hygiene 2. Dressing of the insertion site 3. Manipulation of tubing and stopcocks 4. Aseptic preparation of infusates Detailed specification of the topic content for each module is reported in a table (data not extracted by reviewers)
Infection surveillance feedback approach	Not included in the intervention
Performance feedback approach	Not included in the intervention
Concentration of education	The intervention comprised 47 hours of teaching by two infection control nurses (total 94 staff working hours), divided as follows: • Phase 1: 18 hours (three courses of 90 minutes for each of the four modules) • Phase 2: Five 45-minute ex cathedra teachings; total 3 hours and 45 minutes • Phase 3: Eighty 15-minute bedside sessions; total 20 hours • Phase 4: Five 1-hour interactive sessions with physicians; total 5 hours
Non-educational intervention components	None (intervention purely educational)
Costs reported	Not reported

Outcome characteristics

Catheter-BSI definition Reference cited: Garner *et al.*[147]	Primary bloodstream infection was defined as bacteraemia (or fungaemia) without any other documented source. For coagulase-negative staphylococci, two positive blood cultures or a complete antibiotic therapy adjusted for susceptibility testing was required. All patients were monitored for the development of CRBSI until 48 hours after ICU discharge. CRBSI was considered as ICU acquired if diagnosed ≥ 48 hours after admission or within 48 hours after discharge from the ICU. Patients with CRBSI > 48 hours after discharge were excluded from the risk analysis
Outcomes reported	*Primary (study powered to detect 2% change)*: CRBSI incidence and incidence density *Secondary*: Compliance with hand hygiene *Other outcomes*: Device duration Time to CRBSI LOS Mortality

Results data

Primary outcomes

	Baseline (4 months) (974 CVCs) (499 patients) (2944 ICU-days)	Intervention (5 months) (1015 CVCs) (500 patients) (3705 ICU-days)	Difference between baseline and intervention
Median (range) device duration, catheter-days	5 (1–39)	6 (1–44)	$p < 0.001$
Total device utilisation, catheter-days	6200	7279	Not reported
No. of devices/patient	Not reported	Not reported	Not reported
Median (IQR) and [mean] catheter-days per patient	5 (3–8) [6.4]	6 (3–9) [7.2]	$p < 0.001$
CRBSI incidence rate	24	7	$p < 0.001$
CRBSI incidence per 1000 catheter-days			
Overall (5 ICUs)	3.9	1.0	$p < 0.001$
MICU	9.0[a]	3.9[a]	Not reported
SICU	3.0[a]	0.2[a]	Not reported
Other 3 ICUs	Not reported	Not reported	Not reported

	Baseline (4 months) (974 CVCs) (499 patients) (2944 ICU-days)	Intervention (5 months) (1015 CVCs) (500 patients) (3705 ICU-days)	Difference between baseline and intervention
Median (IQR) time to CRBSI, days	6.5 (3–19)	9 (7–16)	$p = 0.02$
No. of blood cultures obtained per 1000 catheter-days	190	225	Not reported
CRBSI incidence per 1000 patient-days	Not reported	Not reported	Not reported
Median (IQR) and [mean] length of ICU stay, days[b]	3 (2–7) [5.9]	4 (2–9) [7.5]	$p < 0.001$
Mortality	44	44	$p = 0.99$

SICU, surgical intensive care unit.
a Difference between MICU and SICU statistically significant ($p < 0.001$); differences between other ICUs not reported.
b Median (IQR) LOS was 15.5 (10–25) days in patients with CRBSI and 5 (3–12) days in patients without CRBSI (difference reported as 10.5 days).

Secondary outcomes

Reaction to education	Not a study outcome
Attitudes	Not a study outcome
Compliance	Overall compliance with hand hygiene: • Baseline 59.1%; intervention 65% (difference: $p = 0.466$) Rate of correctly performed hand disinfection procedures: • Baseline 22.5%; intervention 42.6% (difference: $p = 0.003$) Hand hygiene performed before patient contact: • Baseline 26%; intervention 45% (difference: $p = 0.007$) Hand hygiene performed after patient contact: • Baseline 21%; intervention 56% (difference: $p < 0.001$)
Knowledge	Not a study outcome
Skills	Not a study outcome
Process evaluation	Not included in the study, apart from the observations on compliance noted above

Critical appraisal

Potential for bias

Group selection	Were there systematic differences between the baseline and intervention groups? YES. The number of ICU-days, McCabe rapid fatality score, number of trauma patients and number who had a CVC inserted in the ICU were statistically significantly higher in the intervention than the baseline period. LOS in the MICU was also significantly longer in the intervention period, by around 10 days. The converse applied to the number of patients with pulmonary CVCs. Significantly fewer patients had pulmonary CVCs in the intervention period. The data suggest that patients in the intervention period were sicker than in the baseline period but data for non-CRBSI infections and mortality were identical for both periods
	If YES, were the differences between the groups adjusted for in statistical analyses? NO
Intervention administration	Were any confounding variables identified that could influence the effect estimate for the overall intervention? NOT REPORTED. The staffing and staff to patient ratios were not reported separately for baseline and intervention periods. It was not reported whether any care policies other than those in the intervention changed during the study period
	Was the effect of educational practice separable from effects of non-educational practice? YES. Education-only intervention
	Were the intervention component(s) implemented as planned? UNCLEAR. All of the teaching models appear to have been implemented, but it is unclear if participation was mandatory or how many staff took part in all or some of the modules (compliance for hand hygiene statistically significantly increased, but did not reach 100%)
Missing data	Were there systematic differences between the baseline and intervention groups in data availability? NO. Missing data were reported and appear to represent a small proportion of the total data for the outcomes in question (insertion vein, lumen number, and insertion venue). Specified that the population was all patients in the ICUs who had a CVC
Outcome measurement	Were there systematic differences between the baseline and intervention groups in how outcomes were determined (including differences in how outcomes were defined)? NOT REPORTED
	Was any blinding of personnel and/or outcome assessors reported (including assessors of blood cultures)? NO
Other possible sources of bias	No other sources of bias were reported by the authors or identified by the reviewers based on the information presented

Other critical appraisal criteria

Methods	Intervention described in sufficient detail to be replicated? YES. The structure, content and time resources required were reported in detail
	Justification given for sample size? YES. Stated that a minimum of 870 catheters was needed to prove a significant CRBSI reduction from 3% (baseline) to 1% (intervention) (80% power, 0.05 significance level)
	Data collection process reported? PARTIALLY. CVC surveillance was conducted by a trained infection control nurse who visited all ICUs daily and recorded relevant information in a surveillance protocol for each patient. All protocols were reviewed and checked for completeness and plausibility by two study physicians
	If YES or PARTIALLY, was the data collection process shown to be valid? NOT REPORTED
	If YES or PARTIALLY, was the data collection process shown to be reliable? NOT REPORTED
	Statistical tests described? YES
Results	Educational significance or effect size assessed? NO
	Target behaviour change achieved? PARTIALLY. Compliance was only reported for one of the behaviour changes (hand hygiene); compliance with hand hygiene was not 100%, although there were improvements

Additional comments

- Not reported whether the participants were aware that they were being studied.

Appendix 6 Lists of records not included in the data syntheses

Conference abstracts (*n* = 67) excluded from the evidence map

These abstracts either met the inclusion criteria or were of unclear relevance at the title and abstract screening step but were excluded as they provided insufficient information for inclusion in the keyword mapping exercise.

Abrusci TA, Bion JF, Richardson A. Central venous catheter blood-stream infections (CVC-BSIs) in ICUs in England: Phase 1 pilot study. *Intensive Care Med* 2010:S90.

Adams T, Williams M, Brown V, Troxler H, Wood S, Tate A, *et al.* Using lean/Six sigma quality improvement methodologies to reduce central line-associated bloodstream infections (CLABSI) in a pediatric hospital. *Am J Infect Control* 2010;**38**(5):E112.

Almeida M, Ferreira A, Reis P, Alves V, Dias C, Granja C. Reducing catheter-related bloodstream infections (CRBSI) in the ICU with an evidence-based intervention. *Intensive Care Med* 2009:S271.

Alvarez C, Pisapia J, Rosello C, Lira M, Curone M, Vidiella G. Implementation of a central line bundle to reduce central line associated bacteremia at the intensive care unit. *Int J Infect Dis* 2010; Conference (ICID):ASM.

Andion E, Bologna R, Battistezza J, Carbonaro M, Sasbon J, Weller G, *et al.* Control program for central line associated bloodstream infections in two pediatric intensive care units. *Infect Control Hosp Epidemiol* 2000;**21**:93.

Armstrong P, Alfieri N, Clowser M, Steinberg R, Spornitz M, Runge W, *et al.* Central line-associated (CLA) surveillance and continuing quality improvement in an intensive care unit (ICU). *J Hosp Infect* 1998;**40**(Suppl. 1):45.

Atherton SL, Tjoelker RC. Evidence based fact sheet: An effective method for implementing change. *Am J Infect Control* 2006;**34**:E51.

Balkhy HH, Alsaif S, El-Saed A, Dichinee R, Memish Z. Approaching zero rates bloodstream infections in a tertiary care neonatal intensive care unit: a multifaceted approach. *Clin Microbiol Infect* 2009;**15**(Suppl. S4):S322.

Beckett P, Jerrett H, Pain T, Hermon A, Szakmany T. Effect of care bundle implementation on catheter related bloodstream infection on the intensive care unit. *Intensive Care Med* 2010:S126.

Benjamin-Phillips S, Nelson E. Keeping the bugs out: strategies to reduce central line bloodstream infections. *J Pediatr Nurs* 2007;**22**:143.

Bhattacharyya M, Bhakta A, Todi S. Impact of quality improvement process on healthcare-associated infection in the ICU in a tertiary care hospital in India. *Crit Care* 2010:S154.

Brennan PJ, Hoegg C, Samel C, Skalina D, Barbagallo S, Shulkin D. Performance improvement in a medical intensive care unit (MICU) resulting from device based surveillance (DBS) from central venous catheter related bloodstream infections (CVC-BSI). *Infect Control Hosp Epidemiol* 1997;**18**:20.

Cherry-Bukowiec JR, Denchev KL, Dickinson S, Chenoweth C, Zalewski C, Meldrum C, *et al.* Prevention of catheter-related BSIs: back to basics? *Surg Infect* 2009;**10**(2).

Conceicao F, Wey S, Amaral J, Medeiros E. Blood stream infection associated with central venous catheter in an intensive care unit. *Abstr Intersci Conf Antimicrob Agents Chemother* 1997;**37**.

Eggimann P, Hugonnet S, Harbarth S, Chraiti M, Touveneau S, Chevrolet J, *et al.* Reduction of bloodstream infection 2 years following a global prevention strategy targeted at vascular access in ICU. *Abstr Intersci Conf Antimicrob Agents Chemother* 2001;**41**.

Eggimann P, Hugonnet S, Harbarth S, Sax H, Chevrolet J, Pittet D. Long-term reduction of vascular access-associated bloodstream infection (BSI) 6 years after a global prevention strategy. *Abstr Intersci Conf Antimicrob Agents Chemother* 2004;**44**.

Ellis D, Brungs S, Burns P, Render M, Nicholson M. Implementing evidence-based practices to reduce catheter-related bloodstream infections in the intensive care unit. *Am J Infect Control* 2005:**33**:e61–e62.

Elsayed A, Mahanes D, Nathan B, Gress D. Prevention of catheter-related blood stream infection in the neurointensive care unit. *Neurocrit Care* 2010;S140.

Fauerbach LL, Gross MA, Ruse C, Kelly R. The quest for the irreducible minimum: 8 years of performance improvement in preventing central line-associated infections in a surgical intensive care unit. *Am J Infect Control* 2005;**33**:e60–1.

Flinchum A, Harris C, Swiderski P, Conigliaro J, Chang P. A novel five-tier approach to reduce central line-associated blood stream infections in an academic medical center. *Am J Infect Control* 2010;**38**:E24–5.

Fontcuberta A, Chacon E, Valente A, Alcaraz D, Pedragosa R, Turegano C, *et al.* Do nurse consultant teams prevent mechanical ventilation associated pneumonia and catheter-related bloodstream infection in the ICU? The Sabadell experience. *Intensive Care Med* 2010:S330.

Frankel H, Rabinovici R, Crede W, Roumanis S, Topal J, Devlin M, *et al.* The use of corporate Six Sigma performance improvement strategies to reduce the incidence of catheter-related bloodstream infections (CR-BSI) in a surgical intensive care unit (SICU) of a tertiary referral university hospital. *Crit Care Medicine* 2003;**31**:436.

Gómez WV, Vergara GR, Pertuz AM, Rosenthal VD. Education and performance feedback effect on rates of central vascular catheter-associated bloodstream infections in newborn intensive care units in a private hospital in Colombia. *Am J Infect Control* 2005;**33**:E76–7.

Gowell J, Marrorana K, Gregory ML, Natale K, Nickerson C, Carter J, *et al.* Re-education initiative to reduce central line associated blood stream infections in the neonatal intensive care unit. *Crit Care Med* 2009;**37**(12)(Suppl.):A279.

Gross I. *Effect of an intervention on rate of central vascular catheter-related bloodstream infection, in intensive care units at Hadassah Medical Center*. Sourced from Israel Medical Convention website. Date unknown.

Hansen S, Schwab F, Schneider S, Sohr D, Geffers C, Gastmeier P. Significant decrease of CVC-associated BSI rates in 38 German ICUs. *Int J Med Microbiol* 2008;**298**(Suppl. 45):35–6.

Honeycutt M, Curry S, Goins G, Fugitt D, Marotti T, Gilliam C. Implementing a catheter-associated blood stream infection prevention bundle in the neonatal intensive care unit – Will it reduce methicillin resistant staphylococcus aureus? *Am J Infect Control* 2009;**37**(5):E146.

Hujcs M, Eckhradt D, Danielle M. Clinical nurse champions improve patient outcome: sustaining catheter-related BSI reduction in neurocritical care. *Crit Care Nurse* 2009;**29**:e5–6.

Karali V, Stefanopoulou P, Bitzani M, Ambatzidou F, Vassiliadou G, Riggos D. Effects of an education: prevention strategy on decreasing catheter-related infections in intensive care. *Crit Care* 2003; **7**(Suppl. 2)S60.

Kawagoe JY, Dal Forno CB, Dornaus MF, Cunha LB, Santos MFC, Martins RAL, *et al.* Cultural and clinical changes in the NICU: Impact of a multi-faceted program on reduction of CVC associated BSI. *Am J Infect Control* 2009;**37**(5):E123.

Khouli HI, Jahnes K, Mathew J, Gohil A, Shapiro J, Rose K, *et al.* Medical residents performance in maximum barrier precautions during central venous catheter placement: Effect of simulation-based training. *Chest* 2009;**136**(4 meeting abstracts):12S.

Koch D, Sykora C, Ferrara L, Griesbaum R, Cruz O. An effective intervention program that resulted in a sustained significant reduction in catheter-associated bloodstream infections in three intensive care units (ICUs). *Am J Infect Control* 2005;**33**(5):E26.

Kovari F. The elimination of central line related bloodstream infection (CRBSI) on the intensive care unit. *Intensive Care Med* 2009:S269.

Kurachek S, Rusakov A, Thornton A, Kuelbs M, Sturtevant B, Finkelstein M. Reducing central line entries (CLEs): an adjunctive maneuver to reduce catheter associated blood stream infections (CABSIS). *Crit Care Med* 2009;**37**(12)(Suppl.):A322.

Loh-Trivedi M, Croley W, Goudzwaard C. Impact of multidisciplinary team training in a surgical intensive care unit. 9th Critical Care and Emergency Medicine Meeting of the Greek Armed Forces Medical Corps, Athens, 27–28 May 2011.

Longo A, Hensley B, Schilling S. Striving for excellence in central venous catheter care: Applying a blended learning approach to nursing staff education on CVC bundle care practices aimed at reducing catheter-associated blood stream infection. *J Pediatr Nurs* 2008;**23**:e18–e19.

Madrid PA, Berkowitz K, Farber M, Weldon S, Bachmeier L. Nosocomial infections? Get a CAT! *Crit Care Nurse* 2009;**29**:e18.

Magerl MA, Madalone J, Gwardschaladse C, Longo K, Hemmer D, Haas J, *et al.* A regional trauma intensive care unit (ICU) thirty-one month experience in decreasing central venous catheter-bloodstream infections (CVC-BSI). *Am J Infect Control* 2009;**37**(5):E39.

McCalla S, Downing-Janos T, Ellsworth K, Allinger P, Kirkpatrick K, Zaicek S. Central line-associated blood-stream infections in the ICU: the struggle to achieve and the effort to maintain zero. *Am J Infect Control* 2009;**37**(5):E41.

Melamed R, Zmora E, Peled N, Schlaeffer P, Gilad J, Eskira S, *et al.* Control of bloodstream infection (BSI) in a neonatal intensive-care unit (NICU). *Abstr Intersci Conf Antimicrob Agents Chemother* 2002;**42**.

Miller M, Brilli R, Moss M. *Elimination of Pediatric CA-BSI*. URL: http://aap.confex.com/aap/2009/webprogram/Paper5966.html 2009 (accessed May 2012).

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Full-text records (*n* = 62) excluded from the evidence map

Note that for most records only the most apparent exclusion criteria agreed by the reviewers are listed. Records may have also failed to meet other criteria that are not listed below.

Reference	Reason for exclusion			
	Population criteria not met	Design criteria not met	Intervention criteria not met	Relevant outcomes not reported
Agra Varela (2009)[63]				✗
Agvald-Ohman (2010)[74]			✗	
Berg (1995)[204]				✗
Bezzio (2009)[205]	✗	✗	✗	
Bijma (1999)[206]			✗	
Chien (2001)[207]		✗		
Clancy (2009)[208]			✗	
Collignon (1985)[209]	✗			
Cooley (2009)[210]		✗		
DuBose (2010)[211]				✗
Eggimann (2004)[212]		✗		
Elder (2008)[201]				✗
Gnass (2004)[213]		✗		
Goeschel (2010)[214]		✗		
Goeschel (2011)[215]		✗		
Gurskis (2009)[216]				✗
Halton (2010)[151]		✗		
Harnage (2008)[217]		✗		
Jeffries (2009)[218]			✗	
Joshi (2005)[219]				✗
Kilbride (2003)[220]				✗
Kilbride (2003)[221]		✗		
Lindsey (2007)[222]		✗		
Lisboa (2008)[66]		✗		
Lolom (2009)[72]	✗			
Meier (1998)[223]	✗			✗

Reference	Reason for exclusion			
	Population criteria not met	Design criteria not met	Intervention criteria not met	Relevant outcomes not reported
Moureau (2005)[224]		✗		
Moureau (2009)[225]	✗	✗		
Nelson (2005)[226]		✗		
Northway (2005)[227]		✗		
O'Grady (2007)[228]		✗		
Palomar (2010)[67]				✗
Papadimos (2008)[229]			✗	
Penne (2002)[4]	✗			
Plouffe (2010)[230]		✗		
Pronovost (2005)[231]				✗
Render (2006)[200]		✗		
Riel-Roberge (2010)[71]		✗		
Rizzo (2005)[232]		✗		
Rodriguez-Paz (2008)[233]		✗		
Rosenthal (2008)[234]		✗		
Rosenthal (2010)[235]		✗		
Scales (2011)[181]				✗
Schelonka (2006)[236]				✗
Schindler (2007)[73]		✗		
Schuerer (2007)[237]			✗	
Schulman (2009)[238]		✗		
Seguin (2010)[239]			✗	
Sherertz (2004)[240]		✗		
Sherman (1988)[241]				✗
Smith (2006)[242]		✗		
Smith (2007)[243]				✗
Stewart (2008)[244]		✗		
Tsuchida (2007)[245]		✗		
Vandijck (2009)[246]		✗		
Verdier (2006)[247]			✗	
Warye (2009)[248]		✗		✗
Watson (2009)[249]		✗		
Weber (2010)[250]		✗		
Yilmaz (2007)[251]	✗			
Young (2006)[252]			✗	
Zack (2009)[253]		✗		

Studies (*n* = 50) excluded from the clinical effectiveness systematic review

Study	Reason for exclusion from systematic review		
	Population not adult	Design unclear or not prospective	Catheter-BSI definition not reported
Anguera Saperas[64]			✗
Barsuk[75]/Cohen[76]			✗
Berenholtz[77]			✗
Berriel-Cass[79]			✗
Bhutta[78]	✗		✗
Bishop-Kurylo[80]	✗	✗	✗
Bizzarro[81]	✗	✗	
Bonello[82]		✗	✗
Buttes[84]			✗
CDC[85]			✗
Chua[86]			✗
Costello[88]	✗		
Curchoe[89]			✗
Curry[90]	✗	✗	✗
DePalo[91]			✗
Duane[92]			✗
Esteve[65]			✗
Frankel[96]		✗	
Harnage[100]		✗	
Harrigan[101]			✗
Hatler[102]		✗	✗
Jain[104]			✗
Joy-Joseph[105]	✗	✗	✗
Khouli[145]			✗
Koll[106]		✗	✗
Koll[107]			✗
Leboucher[70]	✗		✗
Maas[111]	✗	✗	
Marra[112]			✗
McKee[113]	✗	✗	✗
Miller[114]			✗
Miller[115]	✗		✗
Miller-Hoover[116]	✗	✗	✗

Study	Reason for exclusion from systematic review		
	Population not adult	Design unclear or not prospective	Catheter-BSI definition not reported
Moreira[118]			✗
Northway[119]	✗		✗
Orsi[120]			✗
Peredo[121]		✗	
Racco[125]		✗	✗
Rey[127]	✗		
Rogers[128]	✗		
Sannoh[131]	✗		
Santana[132]			✗
Schulman[133]	✗		
Shannon[134]		✗	✗
Urrea Ayala[69]	✗		✗
Venkatram[137]		✗	✗
Warren[140]			✗
Wirtschafter[141]	✗	✗	✗
Yoo[142]		✗	
Zack[143]			✗

Excluded studies from the systematic review of cost-effectiveness

Study	Reason for exclusion
Moureau NL. Reducing the cost of catheter-related bloodstream infections. *Nursing* 2009;**39**:14–15	Not cost-effectiveness study (review)
Young EM, Commiskey ML, Wilson SJ. Translating evidence into practice to prevent central venous catheter-associated bloodstream infections: a systems-based intervention. *Am J Infect Control* 2006;**34**:503–6	Not economic analysis (not full-cost study)
Warren DK, Quadir WW, Hollenbeak CS, Elward AM, Cox MJ, Fraser VJ. Attributable cost of catheter-associated bloodstream infections among intensive care patients in a non-teaching hospital. *Crit Care Med* 2006;**34**:2084–9	Not economic analysis (not full-cost study)
Coopersmith CM, Rebmann TL, Zack JE, Ward MR, Corcoran RM, Schallom ME, *et al*. Effect of an education program on decreasing catheter-related bloodstream infections in the surgical intensive care unit. *Crit Care Med* 2002;**30**:59–64	Not economic analysis (not full-cost study)
Kim JS, Holtom P, Vigen C. Reduction of catheter-related bloodstream infections through the use of a central venous line bundle: epidemiologic and economic consequences. *Am J Infect Control* 2011;**39**:640–6	Not economic analysis (not full-cost study)

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Jacob J, Sims D, Van de Rostyne C, Schmidt G, O'Leary K. Toward the elimination of catheter-related bloodstream infections in a newborn intensive care unit (NICU). *Jt Comm J Qual Patient Saf* 2011;**37**:211–16.

Kim JS, Holtom P, Vigen C. Reduction of catheter-related bloodstream infections through the use of a central venous line bundle: epidemiologic and economic consequences. *Am J Infect Control* 2011;**39**(8):640–6.

Kime T, Mohsini K, Nwankwo MU, Turner B. Central line 'attention' is their best prevention. *Adv Neonatal Care* 2011;**11**:242–8.

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Perez AJ, Monge FJC, Vivas AM. Effect of a program to improve prevention measures of catheter-related bloodstream infections in a medical ICU. *Intensive Care Med* 2011;**37**(1)(Suppl.):S172.

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Appendix 7 Data for clinical effectiveness forest plots

Data for forest plot: regional-scale interventions (see *Figure 4*)

Study	Comparison	Intervention incidence	Intervention device-days	Baseline incidence	Baseline device-days
Burrell 2011[83]	INT months 4–6 vs. INT months 1–3	(20)	(7684)	(28)	(9308)
	INT months 7–9 vs. INT months 1–3	(13)	(9634)	(28)	(9308)
	INT months 10–12 vs. INT months 1–3	(18)	(9725)	(28)	(9308)
	INT months 13–15 vs. INT months 1–3	(10)	(9589)	(28)	(9308)
	INT months 16–18 vs. INT months 1–3	(11)	(8773)	(28)	(9308)
Palomar Martinez 2010[68]	INT (3 months) vs. B (2006 data)	44	11432	59	9164
	Control (3 months) vs. B (2006 data)	28	8453	59	4644
Pronovost 2006, 2008, 2010[34,123,124]	INT months 0–3 vs. B	Reported as summary statistics and ranges (see data extraction form)			
	INT months 4–6 vs. B	Reported as summary statistics and ranges (see data extraction form)			
	INT months 7–9 vs. B	Reported as summary statistics and ranges (see data extraction form)			
	INT months 10–12 vs. B	Reported as summary statistics and ranges (see data extraction form)			
	INT months 13–15 vs. B	Reported as summary statistics and ranges (see data extraction form)			
	INT months 16–18 vs. B	Reported as summary statistics and ranges (see data extraction form)			
	INT months 19–21 vs. B	Reported as summary statistics and ranges (see data extraction form)			
	INT months 22–24 vs. B	Reported as summary statistics and ranges (see data extraction form)			
	INT months 25–27 vs. B	Reported as summary statistics and ranges (see data extraction form)			
	INT months 28–30 vs. B	Reported as summary statistics and ranges (see data extraction form)			
	INT months 31–33 vs. B	Reported as summary statistics and ranges (see data extraction form)			
	INT months 34–36 vs. B	Reported as summary statistics and ranges (see data extraction form)			
Render 2006[126]	INT vs. B (timing unclear)	Not reported	Not reported	Not reported	Not reported
	INT (9 months) vs. B	(5)	(7830)	(11)	(7593)
Speroff 2011[136]	Toolkit months 1–3 vs. B	(72)	(25257)	(81)	(26599)
	Toolkit months 4–6 vs. B	(76)	(24618)	(81)	(26599)
	Toolkit months 7–9 vs. B	(72)	(27821)	(81)	(26599)
	Toolkit months 10–12 vs. B	(75)	(29066)	(81)	(26599)
	Toolkit months 13–15 vs. B	(62)	(29818)	(81)	(26599)
	Toolkit months 16–18 vs. B	(66)	(24245)	(81)	(26599)
	Virtual collab. months 1–3 vs. B	(52)	(22202)	(37)	(22172)
	Virtual collab. months 4–6 vs. B	(54)	(22951)	(37)	(22172)
	Virtual collab. months 7–9 vs. B	(53)	(23268)	(37)	(22172)
	Virtual collab. months 10–12 vs. B	(45)	(26211)	(37)	(22172)
	Virtual collab. months 13–15 vs. B	(65)	(25646)	(37)	(22172)
	Virtual collab. months 16–18 vs. B	(53)	(19276)	(37)	(22172)

B, baseline; INT, intervention.
Note: Data in parentheses were obtained from primary study authors (not reported in the publications); data in square brackets were calculated by reviewers.

Intervention incidence density	Baseline incidence density	RR	SE of log RR	95% confidence limits of RR	
				Lower	Upper
[2.6]	[3.0]	[0.87]	[0.293]	[0.49]	[1.54]
[1.3]	[3.0]	[0.45]	[0.336]	[0.23]	[0.87]
[1.9]	[3.0]	[0.63]	[0.302]	[0.34]	[1.11]
[1.0]	[3.0]	[0.33]	[0.368]	[0.17]	[0.71]
[1.3]	[3.0]	[0.43]	[0.356]	[0.21]	[0.84]
3.85	6.44	[0.60]	[0.199]	[0.41]	[0.89]
3.31	12.70	[0.26]	[0.229]	[0.17]	[0.41]
Reported as summary statistics and ranges (see data extraction form)		0.62	Not reported	0.47	0.81
Reported as summary statistics and ranges (see data extraction form)		0.56	Not reported	0.38	0.84
Reported as summary statistics and ranges (see data extraction form)		0.47	Not reported	0.34	0.65
Reported as summary statistics and ranges (see data extraction form)		0.42	Not reported	0.28	0.63
Reported as summary statistics and ranges (see data extraction form)		0.37	Not reported	0.20	0.68
Reported as summary statistics and ranges (see data extraction form)		0.34	Not reported	0.23	0.50
Reported as summary statistics and ranges (see data extraction form)		0.34	Not reported	0.23	0.50
Reported as summary statistics and ranges (see data extraction form)		0.33	Not reported	0.23	0.48
Reported as summary statistics and ranges (see data extraction form)		0.44	Not reported	0.34	0.57
Reported as summary statistics and ranges (see data extraction form)		0.40	Not reported	0.30	0.53
Reported as summary statistics and ranges (see data extraction form)		0.31	Not reported	0.21	0.45
Reported as summary statistics and ranges (see data extraction form)		0.34	Not reported	0.24	0.48
0.4	1.7	0.24	Not reported (not calculable)		
[0.6]	[1.4]	[0.44]	[0.539]	[0.15]	[1.27]
[2.9]	[3.0]	[0.97]	[0.162]	[0.68]	[1.29]
[3.1]	[3.0]	[1.03]	[0.160]	[0.74]	[1.39]
[2.6]	[3.0]	[0.87]	[0.162]	[0.62]	[1.17]
[2.6]	[3.0]	[0.87]	[0.160]	[0.62]	[1.16]
[2.1]	[3.0]	[0.7]	[0.169]	[0.49]	[0.95]
[2.7]	[3.0]	[0.9]	[0.166]	[0.65]	[1.24]
[2.3]	[1.7]	[1.35]	[0.215]	[0.92]	[2.14]
[2.4]	[1.7]	[1.41]	[0.213]	[0.93]	[2.14]
[2.3]	[1.7]	[1.36]	[0.214]	[0.90]	[2.08]
[1.7]	[1.7]	[1.0]	[0.222]	[0.67]	[1.59]
[2.5]	[1.7]	[1.47]	[0.206]	[1.01]	[2.27]
[2.7]	[1.7]	[1.59]	[0.214]	[1.08]	[2.51]

Data for forest plot: local-scale interventions of duration up to 12 months (see *Figure 5*)

Study	Comparison	Intervention incidence	Intervention device-days	Baseline incidence
Coopersmith 2002[50]	INT (6 months) vs. B	26	7044	74
DuBose 2008[93]	INT (1 month) vs. B	Not reported	Not reported	Not reported
Guerin 2010[98]	INT (12 months) vs. B	3	2825	25
Higuera 2005[103]	Total, INT (9 months) vs. B	55	2824	28
	Medical-surgical ICU, INT vs. B	Not reported	Not reported	Not reported
	Neurosurgical ICU, INT vs. B	Not reported	Not reported	Not reported
Lobo 2005[108]	INT (8 months) vs. B	16	1481	48
	F (12 months) vs. B	22	1701	48
	F vs. INT	22	1701	16
Lobo 2010[109]	ICU 'A,' INT (9 months) vs. B	8.94	843	11.28
	ICU 'B', INT (9 months) vs. B	21.85	1694	35.24
Perez Parra 2010[122]	Total (three ICUs), INT (9 months) vs. B	34	11582	45
	General ICU, INT (9 months) vs. B	14	4064	18
	Cardiac ICU, INT (9 months) vs. B	8	2981	12
	MICU, INT (9 months) vs. B	12	4537	15
Rosenthal 2003[129]	Education (1–2 months) vs. B	10	586	56
	PF (7–8 months) vs. education	41	4140	10
	PF + education (8–10 months) vs. B	51	4726	56
Sherertz 2000[135]	F (18 months) vs. B (12 months)	30	Not reported[a]	32
Warren 2003[139]	INT (10 months) vs. B	11	5210	30
Warren 2004[51]	INT (1 month) + F (23 months) vs. B	41	7455	74
Zingg 2009[144]	Total (5 ICUs), INT (5 months) vs. B	7	7279	24
	MICU, INT (5 months) vs. B	Not reported	Not reported	24
	SICU, INT (5 months) vs. B	Not reported	Not reported	24

B, baseline; F, follow-up; INT, intervention; PF, performance feedback; SICU, surgical intensive care unit.
a The author confirmed these data were not recorded during the study.
Data in square brackets were calculated by reviewers.

Baseline device-days	Intervention incidence density	Baseline incidence density	RR	SE of log risk ratio	95% confidence limits of RR	
					Lower	Upper
6874	3.7	10.8	[0.34]	[0.228]	[0.22]	[0.54]
Not reported	5.8	Unclear	Not reported (not calculable)		Not reported (not calculable)	
4415	1.1	5.7	0.19	[0.611]	0.06	0.63
605	19.5	46.3	0.42	[0.232]	0.27	0.66
Not reported	22.1	57.4	0.38	Not reported	0.22	0.68
Not reported	17.1	32.8	0.52	Not reported	0.24	1.11
2450	10.8	19.6	[0.55]	[0.289]	[0.31]	[0.97]
2450	12.9	19.6	[0.66]	[0.257]	[0.40]	[1.09]
1481	12.9	10.8	[1.19]	[0.329]	[0.63]	[2.28]
940	10.6	12.0	[0.88]	[0.448]	[0.37]	[2.13]
2175	12.9	16.2	[0.80]	[0.272]	[0.47]	[1.36]
10661	2.9	4.2	[0.70]	[0.227]	[0.45]	[1.09]
3403	3.4	5.3	[0.65]	[0.356]	[0.32]	[1.31]
2842	2.7	4.2	[0.64]	[0.456]	[0.26]	[1.55]
4416	2.6	3.4	[0.76]	[0.387]	[0.36]	[1.66]
1219	17.1	45.9	0.37	[0.343]	0.19	0.73
586	9.9	17.1	0.58	[0.353]	0.29	1.18
1219	10.8	45.9	0.24	[0.194]	0.17	0.36
Not reported[a]	Not reported	Not reported	Not reported (not calculable)		Not reported (not calculable)	
6110	2.1	4.9	0.43	[0.352]	0.22	0.84
7879	5.5	9.4	[0.59]	[0.195]	[0.40]	[0.86]
6200	1.0	3.9	[0.26]	[0.430]	[0.11]	[0.58]
6200	3.9	9	[0.43]	Not reported (not calculable)	Not reported (not calculable)	
6200	0.2	3	[0.07]	Not reported (not calculable)	Not reported (not calculable)	

Data for forest plot: local-scale interventions of duration of > 12 months (see *Figure 6*)

Study	Comparison	Intervention incidence	Intervention device-days	Baseline incidence
Coopersmith 2004[87]	INT (15 months) vs. B	17	6152	32
Eggimann 2000;[94] 2005[95]	INT months 1–8 vs. B	(5)	(2174)	(28)
	INT months 1–8 vs. B[a]	Not reported	Not reported	Not reported
	INT months 24–36 vs. B	(8)	(3333)	(28)
	INT months 37–41 vs. B	(4)	(1481)	(28)
	INT months 51–60 vs. B	(5)	(2941)	(28)
	INT months 61–72 vs. B	(11)	(3235)	(28)
Galpern 2008[97]	INT (19 months) vs. B	(7)	(7345)	(12)
Longmate 2011[110]	INT months 1–12 vs. B	7	1981	9
	INT months 12–24 vs. B	1	1786	9
	INT months 24–36 vs. B	0	Not reported	9
	INT months 1–12 vs. B[a]	7	2613	9
	INT months 12–24 vs. B[a]	1	2155	9
	INT months 24–36 vs. B[a]	0	2138	9
Misset 2004[117]	INT years 2–5 vs. INT year 1	14	Not reported	7
Rosenthal 2005[130]	INT (17 months) vs. B (4 months)	[18]	Not reported	[16]
Wall 2005[138]	INT (24 months) vs. B	6	[1132]	25
	INT (last 6 months) vs. B	Not reported	Not reported	25

a Multiple concurrent vascular catheters per patient counted separately in the calculation of device-days.
Data in parentheses were obtained from primary study authors (not reported in the publications); data in square brackets were calculated by reviewers.

Baseline device-days	Intervention incidence density	Baseline incidence density	RR	SE of log risk ratio	95% confidence limits of RR	
					Lower	Upper
9353	2.8	3.4	[0.82]	[0.300]	[0.45]	[1.45]
(4243)	(2.3)	(6.6)	[0.35]	[0.486]	[0.13]	[0.90]
Not reported	0.8	2.4	0.31	Not reported	0.09	0.53
(4243)	(2.4)	(6.6)	[0.36]	[0.401]	[0.17]	[0.80]
(4243)	(2.7)	(6.6)	[0.41]	[0.535]	[0.14]	[1.17]
(4243)	(1.7)	(6.6)	[0.26]	[0.486]	[0.10]	[0.67]
(4243)	(3.4)	(6.6)	[0.52]	[0.356]	[0.26]	[1.03]
(2593)	[1.0]	[4.6]	[0.22]	[0.476]	[0.08]	[0.52]
1918	3.5	4.7	[0.74]	[0.504]	[0.28]	[2.02]
1918	0.6	4.7	[0.1]	[1.054]	[0.02]	[0.94]
1918	0.0	4.7	0.00	Not reported (not calculable)	Not reported (not calculable)	
2660	2.7	3.4	0.79	0.504	0.29	2.13
2660	0.5	3.4	0.14	1.054	0.02	1.08
2660	0.0	3.4	0.00	Not reported	0.00	0.63
Not reported	0–2.9	3.5	Not reported (not calculable)		Not reported (not calculable)	
Not reported	Not reported	Not reported	Not reported (not calculable)		Not reported (not calculable)	
[3571]	(5.3)	7.0	[0.76]	[0.455]	[0.31]	[1.85]
[3571]	(3.8)	7.0	[0.54]	Not reported (not calculable)	Not reported (not calculable)	

Appendix 8 Data extraction forms for cost-effectiveness analyses

Cohen and colleagues

This record was compiled by the Southampton Health Technology Assessments Centre (SHTAC) following the format used by the NHS CRD Economic Evaluation Database.

Study characteristics

Reference
Cohen *et al.* (2010).[76]

Health technology
Simulation-based education for prevention of CRBSIs in an ICU.

Interventions and comparators
Simulation-based education training in CVC insertion versus no training.

Was a no-treatment/supportive care strategy included?
Yes.

Describe interventions/strategies
Simulation-based education with training in CVC insertion. The training consisted of two 2-hour educational sessions of a lecture, ultrasound training, and deliberate practice with the CVC simulator and instructor feedback. The CVC simulator features a realistic tissue with ultrasound compatibility, an arterial tube, and self-sealing veins and skins.

Research question
To estimate cost savings related to a reduction in CRBSI after simulation training.

Study type
Cost–consequence analysis.

Study population
A total of 477 patients had a CVC inserted in the MICU during the study period.

Institutional setting
Intensive Care Unit.

Country/currency
United States of America; US dollars 2008.

Funding source
Not stated.

Analytical perspective
United States health-care payer.

Effectiveness
Before simulation-based intervention, the average infection rate was 4.2/100 (11 infections in 239 CVC patients). After the intervention, the infection rate was reduced to 0.42/100 admission (one infection in 238 CVC patients). Thus, preventing an estimated 9.95 CRBSI cases.

Intervention costs
Intervention costs stated in the analysis includes hospital costs, obtained from the hospital finance department. The stated costs included both direct and indirect costs estimates and are listed as follows.

Item	Units	Cost (US$)/unit	Total cost (US$)
Ultrasound[a]	1	19,475.07	19,475.07
Central line simulator[a]	1	1353.40	1353.40
CVC kits	210	35.73	7429.80
Simulator supplies	16	439.35	6960.00
Ultrasound cover probes	90	14.10	1256.40
Sterile gowns	150	2.98	442.50
Sterile drapes	15	50.08	743.70
Supply cart[a]	1	1633.20	1633.20
Supplies total			39,294.07
Other expenses	Hour	Cost/hour	Total cost
Simulator facility rental	330	45.00	14,850.00
Salary support			
Instructor			50,500.00
Research assistant			7272.00
Total costs			111,916.07

a One-time cost.

Indirect costs
Were indirect costs included?

No.

Health-state valuations/utilities
None included.

List the utility values used in the evaluation
None.

Modelling
The study developed a trial-based economic model based on a non-randomised trial for the intervention. Two statistical methods were used: the propensity score match case–control comparison method and linear regression models. The trial data were analysed and regression models were used to derive estimates of cost and LOS for the intervention and control group, controlling for age, sex and Charlson score (an indicator of the severity of the disease). In order to give the intervention and the control group the same infection risk, a regression-based propensity score was used. Estimates of cost differences between the matched cases and controls were then derived.

Extract transition probabilities for the model and show sources

The model does not use transition probabilities but reported propensity score quartiles based on predicted probabilities of infection in relation to LOS in the hospital and MICU.

What is the model time horizon?

12 months.

What, if any, discount rates have been applied in the model? Same rate for costs and outcomes?

Not applicable.

Results/analysis

What measure(s) of benefit were reported in the evaluation?

Average LOS:

		Hospital MICU					
Quartile	No. non–CRBSI patients	Non-CRBSI patients	CRBSI patients	Difference	Non-CRBSI patients	CRBSI patients	Difference
1.2–1.4	42	12.98	25.67	12.69	6.39	23.00	16.61
1.5–3.4	267	16.18	38.67	22.49	7.69	27.33	19.64
3.5–4.2	39	18.21	34.00	15.79	8.79	13.33	4.54
> 4.2	49	16.33	22.00	5.67	8.43	16.00	7.57
Average total	397	15.93	30.09	14.16	7.83	19.92	12.09

Comparison between MICU patients with CVCs with and without a CRBSI.

Provide a summary of the costs estimated for each intervention/strategy assessed in the evaluation

Quartile	No. of non-CRBSI patients	Non-CRBSI patients (US$)	CRBSI patients (US$)	Difference (US$)
1.2–1.4	42	51,829	152,678	100,849
1.5–3.4	267	58,335	155,878	97,543
3.5–4.2	39	63,057	108,581	45,524
> 4.2	49	57,465	144,468	87,003
Average total	397	57,671	140,401	82,730

Comparison between MICU patients with CVCs with and without a CRBSI.

Synthesis of costs and benefits: are the costs and outcomes reported together? If so, provide a summary of the results

9.95 CRBSI prevented, total annual savings were US$704,034 and US$711,248 and 137 patients hospital days and 120 and 121 MICU days.

Give results of any statistical analysis of the results of the evaluation
Not applicable.

Was any sensitivity analysis performed?
No.

What scenarios were tested in the sensitivity analysis?
None.

Give a summary of the results of the sensitivity analysis
None.

Conclusions/implications

Give a brief summary of the author's conclusions from their analysis
The results of the analyses show that simulation-based educational intervention is highly cost-effective.

Southampton Health Technology Assessments Centre Commentary

Selection of comparators
Appropriate.

Validity of estimate of measure of benefit
Appropriate.

Validity of estimate of costs
Acceptable.

Halton and colleagues

This record was compiled by SHTAC following the format used by the NHS CRD Economic Evaluation Database.

Study characteristics

Reference
Halton *et al*. (2010).[151]

Health technology
Central venous catheter care bundle.

Interventions and comparators
A bundle approach to CVC care compared with non-bundled approach.

Was a no-treatment/supportive care strategy included?
Yes.

Describe interventions/strategies
Intervention: optimal hand hygiene, chlorhexidine skin antiseptic, maximal barrier precautions for catheter insertion, choice of optimal insertion site and prompt catheter removal.

Research question
To estimate cost-effectiveness of catheter care bundle in the prevention of CRBSIs in intensive care.

Study type
Cost-effectiveness and cost–utility.

Study population
Patients aged 50–80+ years in ICUs.

Institutional setting
ICU.

Country/currency
2006 Australian dollars (A$).

Funding source
Medical Research Council.

Analytical perspective
Australian health-care payer perspective.

Effectiveness
The effectiveness data were derived from the study by Pronovost *et al*.[34] The bundle was comprised five elements. The intervention reduced the rate of CRBSI from 7.7 to 1.4 per 1000 line-days over a 18-month period, a reduction in the relative risk of 0.34 (95% CI 0.23 to 0.5). Effect estimates for each type of commercially available antimicrobial central venous catheter, relative to uncoated catheters, were taken from the results of a meta-analysis: chlorhexidine/silver sulfadiazine (CH/SSD)-coated catheters (RR = 0.66) and minocycline and rifampicin (MR)-coated catheters (RR = 0.39).

Intervention costs
The costs for the intervention were unknown.

List the direct intervention costs and other direct costs used in the evaluation.

Parameters	Estimate	Source	Ref.	Level of evidence
ICU bed-days (2006 A$)	3021	Costing study	161	4
Hospital bed-day (2006 A$)	843	Prior economic evaluation	162	3
Diagnostics CRBSI (2006 A$)	101.7	Health system database	–	1
Treatment CRBSI (2006 A$)	591.3			

Were the methods for deriving these data adequately described?
Yes.

Indirect costs
No.

Health state valuations/utilities
Preference-based utility weights were taken from a study with participant demographics similar to the modelled cohort. These weights were assigned to patients in ICU and 6 months post discharge. Australian population QoL norms were used for long-term survival.

Were the methods for deriving these data adequately described?
Yes

List the utility values used in the evaluation:

The utilities are as follows:

Parameters	Age, years	Estimate
ICU		0.66
Population norms	50–59	0.80
	60–69	0.79
	70–79	0.75
	80+	0.66

Modelling
A Markov state transition model was used. The model was adapted from a previously reported model.[155] Patients were assumed to receive a CVC on entry to the ICU. Over subsequent cycles the catheter was either removed as no longer necessary, or retained owing to the patient developing CRBSI. The model consists of six health states as follows: ICU patient with CVC; ICU patient recently infected with CRBSI; ICU patient without CRBSI and with CVC being removed; hospital ward patient with previous history of CRBSI; remaining ward patient without CRBSI; and recently discharged patient with or without previous history of CRBSI.

What was the purpose of the model?
To evaluate the cost-effectiveness of CVC care bundle.

What are the main components of the model (e.g. health states within a Markov model)?

The main components are as follows:

Patients were assumed to receive a CVC on entry to ICU, and over subsequent daily cycles either retained their catheter, had it removed, or developed a CRBSI. Patient faced an underlying risk of mortality while in the ICU and a further risk if they developed CRBSI. The surviving cohorts were modelled for the remainder of their life time in monthly cycles. The estimated risk of mortality due to hospital acquired CRBSI was 1.06.

Extract transition probabilities for [natural history/disease progression] model and show sources (or refer to table in text).

Parameters		Estimates	Sources
Daily probabilities of CRBSI	Day 1–5	0.4%	Table 1
	Day 6–15	0.9%	
	Day 16–30	2%	
Daily probability of catheter removal		Not stated (varied)	
Baseline mortality (probabilities)			
ICU		0.098	
Hospital		0.069	

Parameters		Estimates	Sources
Annual post discharge	Year 1	0.050	
	Year 2–3	0.027	
	Year 4–5	0.028	
	Year 6–10	0.037	
	Year 11–15	0.042	
Underlying annual mortality	45–64 years	0.004	
	65–84 years	0.030	
	85+ years	0.140	

What is the model time horizon?

The patients were followed for the remaining part of their lifetime in monthly cycles.

What, if any, discount rates have been applied in the model?

Three per cent applied to both costs and outcomes

Results/analysis

What measure(s) of benefit were reported in the evaluation?

The measure of benefit reported was QALYs and number of bed-days gained for the catheter care bundle relative to current practice.

Provide a summary of the costs estimated for each intervention/strategy assessed in the evaluation
Not applicable.

Synthesis of costs and benefits
As the cost of implementing a bundle in Australia was unknown, deterministic threshold analyses were conducted. The maximum cost for the bundle was identified at which it would remain cost-effective (i.e. if the cost per QALY was less than A$64,000) assuming it would reduce the risk of CRBSI by 0.34. The baseline analyses show the benefits for the bundle or standard practice under different scenarios. The bundle at an implementation cost of A$4,349,730 was shown to be cost-effective for the whole 18-month period compared with current practice alone. For the strategy that includes CH/SSD catheters, the implementation cost over the same period was estimated to be A$2,287,400. MR catheter would result in a total implementation cost of A$1,144,465.

Halton and colleagues[151] also estimated the maximum cost for the bundle at which it would remain cost-effective assuming it would effectively eliminate infection (RR CRBSI = 0.001). According to this assumption, the maximum nationwide implementation cost would be below A$6.6M if the A-CVCs are not considered a good alternative.

Give results of any statistical analysis of the results of the evaluation.
Not applicable.

Was any sensitivity analysis performed? If yes, what type(s)?
Yes, deterministic (one-way).

What scenarios were tested in the sensitivity analysis?
Threshold analyses were used to determine the effectiveness and implementation cost of different types of bundle that would be more cost-effective relative to the current practice. The analyses were undertaken in three different ways; where three separate comparisons were made one after the other. An initial comparison was between the current practice and the bundle. A subsequent comparison includes a three-way comparison; where current practice was compared with the bundle and then with CH/SSD catheters. The final stage of the analysis, involved a four-way comparison of current practice against the bundle, CH/SSD catheters and MR catheters.

Give a summary of the results of the sensitivity analysis.
See above.

Conclusions/implications

Give a brief summary of the author's conclusions from their analysis
Implementation of catheter care bundles is cost-effective in the intensive care setting, if the decision-makers are willing to spend more on infection intervention control.

Southampton Health Technology Assessments Centre commentary

Selection of comparators
Comparator selection is adequate.

Validity of estimate of measure of benefit
Valid.

Validity of estimate of costs
Reasonable but no costs estimated for the intervention.

Bond and King

This record was compiled by SHTAC following the format used by the NHS CRD Economic Evaluation Database.

Study characteristics

Reference
Bond and King (2011).[152]

Health technology
Educational intervention to improve the safety of CVC insertion.

Interventions and comparators
Educational intervention vs. no educational intervention.

Was a no treatment/supportive care strategy included?
Yes.

Describe interventions/strategies
The educational intervention consists of a CVC education course. It is a day-long programme with brief introductory lectures followed by hands-on procedural simulation in CVC insertion, using training mannequins, appropriate sterile procedures, ultrasound imaging and receiving feedback from instructors. In addition, residents and nurses are taught the Institute for Healthcare bundle of barrier precautions and new processes to encourage, ensure and track compliance.

Research question
To model the cost and mortality outcomes of CVC placement with respect to an educational intervention that attempts to reduce both infectious and mechanical complications.

Study type
Cost-effectiveness analysis.

Study population
Baseline cohort was 600 patients who had CVCs placed outside the operating room setting in the hospital setting each year. The proposed setting was described as a health-care system that includes a tertiary care center, a community hospital, and a free-standing emergency department. There are three emergency departments and 12 ICUs in the system.

Institutional setting
ICU.

Country/currency
United States of America; US dollars. Cost year not stated.

Funding source
None.

Analytical perspective
Not stated.

Effectiveness

The evaluation assumes that the educational intervention would reduce the rate of the infectious complication CLAB by 50% and reduce the rate of the mechanical complications by 25%. The study does not discuss the sources that these are based upon nor the rationale behind their use.

Intervention costs

The intervention costs are detailed although it is not stated where these costs were collected.

Item	No. item/ hours per year	Cost per item/hour	Programme Year 1	Programme Year 2–5
Acquisition of training mannequins	5	US$2000	US$10,000	US$0
Acquisition of ultrasound technology	3	US$18,000	US$54,000	US$0
Trainer time	10	US$150	US$1500	US$1500
Trainee time (nurses)	1900	US$25	US$47,500	US$4750
Trainee time EM residents (14/year)	112	US$20	US$2240	US$2240
Transitional interns (12/year)	96	US$20	US$1920	US$1920
Trainee time IM residents (16/year)	128	US$20	US$2560	US$2560
Trainee time surgery residents (4/year)	32	US$20	US$640	US$640
Chart review 0.5 FTE	2000		US$30,000	US$30,000
Data analysis	40	US$100	US$4000	US$4000
Programme oversight	400	US$40	US$16,000	US$16,000
Total per programme year			US$170,360	US$63,610[a]

EM, emergency medicine; FTE, full-time equivalent; IM, internal medicine.
a Total cost for years 2–5 is US$254,440.

The cost per CLAB case was US$16,350 based upon those reported by Institute of Healthcare (full reference not supplied). The mean excess cost of mechanical complication was US$17,312.

Indirect costs

None included.

Health-state valuations/utilities

None included.

List the utility values used in the evaluation

None.

Modelling
A decision-analytic model was compiled in TreeAge. The model began with the need for a CVC, with a focus on non-emergent cases, defines as those where there was sufficient time to follow sterile precautions in CVC insertion. One cohort of patients received the education intervention and the other did not. In each cohort, a proportion received the CVC in the internal jugular, subclavian and femoral. Patients then either had no complications, mechanical complication or CLAB. Patients who suffered a CLAB or a mechanical complication had corresponding higher costs and mortality than those without.

Extract transition probabilities for the model and show sources:

- Location of CVC: internal jugular 0.35; subclavian 0.6, femoral 0.05.
- Probability of CLAB line infection 0.7%.
- Baseline mortality risk for an ICU patient: 10.
- Mortality risk for patients with CLAB: 12.
- Excess mortality of mechanical complications associated with iatrogenic pneumothorax: 7.

What is the model time horizon?
The duration of the hospital stay.

What, if any, discount rates have been applied in the model?
None applied.

Results/analysis

What measure(s) of benefit were reported in the evaluation?
Survival with education (per patient) 0.899; survival without education 0.898.

Provide a summary of the costs estimated for each intervention/strategy assessed in the evaluation
Cost with education (per patient) US$546; cost without education US$392. Additional cost of education intervention US$154. Using programme cost of US$170,360 per year.

Synthesis of costs and benefits: are the costs and outcomes reported together? If so, provide a summary of the results
Yearly annual additional cost of US$92,400 to a large health-care system is the cost to reduce the number of CLAB infections from 4 to 2. (No discussion in the text on the reduction in mortality.)

Give results of any statistical analysis of the results of the evaluation
Not applicable.

Was any sensitivity analysis performed? If yes, what type(s)? [i.e. deterministic (one-way, two-way, etc.) or probabilistic]
One-way sensitivity analyses.

What scenarios were tested in the sensitivity analysis?
The programme cost, CLAB baseline rate, intervention effectiveness on CLAB rate were varied.

Give a summary of the results of the sensitivity analysis
For lower programme cost of US$63,610 per year, additional cost of education intervention (per patient) US$44*. Raising CLAB infection rate to 5%* gives a net monetary benefit of US$158 (i.e. cost saving) with an additional survival of 0.003.

(*Note that neither of the sensitivity analyses had a reduction in mechanical complications).

Conclusions/implications

Give a brief summary of the author's conclusions from their analysis

If the educational intervention is effective, a small increase in costs can reduce complications.

Southampton Health Technology Assessments Centre commentary

Selection of comparators

Appropriate.

Validity of estimate of measure of benefit

Appropriate, although rationale for selection not given.

Validity of estimate of costs

Uncertain. Derivation of cost associated with CLAB is unclear.

Appendix 9 The model parameters and their distributions included in the probabilistic sensitivity analysis

Name	Base case	Upper value	Lower value	SE	Distribution	Alpha	Beta
Catheter-BSI incidence rate, per 1000 catheter-days	3.7	5.0	1.3	1.22	Log-normal	1.6	0.3
Critical care mortality, no catheter-BSI	0.169	0.203	0.135	0.02	Beta	79.6	391.6
RR for critical care mortality due to catheter-BSI	3.25	3.6	2.7	0.28	Log-normal	1.3	1.0
Catheter utilisation	0.71	0.96	0.49	0.13	Beta	8.3	3.4
Costs							
Ward bed-day, £	246	295.2	196.8	25.10	Gamma	96.0	2.6
Critical care bed-day, £	1440	1171	1657	–110.93	Gamma	168.5	8.5
Treatment for catheter-BSI	518	622	415	52.89	Gamma	96.0	5.4
Standard care (per patient in critical care)	0						
Bundle (per patient in critical care)	15.48	20.13	10.84	2.37	Gamma	42.7	0.4
Clinical effectiveness							
Bundle effectiveness	0.4	0.67	0.22	0.10	Log-normal	–0.5	–1.6
Additional LOS for catheter-BSI, critical care	1.5	2.5	0.0	0.30	Triangle	2.0	0.5
Additional LOS for catheter-BSI, ward	5.13	8.68	1.58	1.81	Log-normal	2.2	0.5

Appendix 10 Calculating the cost of the central venous catheter care bundle

The cost of the bundle consists of the national programme and local implementation costs. The programme grant for implementing Matching Michigan in England was £1,750,000 for a 2-year period. Thus the annual cost would be £875,000 per annum.

The local training costs were calculated based on advice on implementation of Matching Michigan in one local centre. In this centre, one Band 6 nurse trained and monitored critical care staff in three critical care units and this took 20% whole time equivalent (WTE).

Using the assumptions above, the costs were estimated per patient attending ICU and these are shown in the table below.

Parameter	Value	Source
National ICU data		
No. of patients attending critical care per year in England	89,618	ICNARC[163]
No. of critical care units	188	ICNARC[163]
Average no. of patients per critical care unit	477	ICNARC[163]
National programme costs		
National programme costs/year	£875,000	Matching Michigan[162]
National programme costs per patient in critical care	£9.76	Matching Michigan[162]
Local unit costs		
Annual salary of a band 6 nurse	£40,917	Agenda for Change[a]
Proportion of time allocated to staff training	20%	Assumption
No. of critical care units covered	3	Assumption
No. of patients admitted to critical care	1431	ICNARC
Local training costs per patient in critical care (expert opinion, Matching Michigan[162])	£5.72	
Total cost of bundle	**£15.48**	

ICNARC, Intensive Care National Audit & Research Centre.
a See: www.nhscareers.nhs.uk/working-in-the-nhs/pay-and-benefits/agenda-for-change-pay-rates/ (accessed October 2012).

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