

Cost Effectiveness Analysis of Bundle versus No Bundle Strategy during Central Venous Catheter Insertion on Reduction of Central Line-Associated Bloodstream Infections in Abu El Reesh Hospital, Egypt.

¹Amal S. Sedrak, ²Sally Kamal Ibrahim, ²Hanaa Rady, ²Tamer A. Abdel Hamid

¹Public Health Department, ²Pediatric Department Faculty of Medicine, Cairo University.

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Abstract:

Background: Central line-associated bloodstream infections (CLABSI) are frequent, costly to payers and patients, and potentially fatal. This paper aims to appraise the cost-effectiveness of implementing "Bundle precautions" during Central Venous Catheter (CVC) insertion, focusing on reducing CLABSI infections from the hospital perspective.

Objective: To determine cost-effectiveness of using bundle versus non-bundle application in term of nosocomial infection rate. **Method:** Economic evaluation sub-study, parallel to a non-randomized controlled trial comparing "Bundle precautions" to non-Bundle precautions applied to patients with CVC insertion. The study was conducted in intensive care units, teaching pediatric hospital. Pediatric patients in 2 months to age of 18 years age interval, requiring CVC insertion were recruited following ICU admission and classified into 2 groups with one group receiving bundle precautions and one not. Economic costs of "Bundle precautions" versus "No Bundle precautions" of central line-associated bloodstream infections were estimated from the perspective of the hospital in 2015 Egyptian pounds. Primary main outcome measure is Central line-associated bloodstream infections prevented. Cost-effectiveness ratios were estimated. One way sensitivity analysis was performed. **Results:** Weighed against the current practice, the "Bundle precautions" is strongly dominant; approx. 482.95 LE were saved, and about 9.8 episodes of CLABSI/1000 CVL were avoided. In One-way sensitivity analysis, Bundle precautions continued to be a dominant strategy. **Conclusions:** Use of "Bundle precautions" during CVC insertion lowers medical costs and decreases the incidence of Central line-associated bloodstream infections. Cost savings were found over a range of clinical and economic assumptions, suggesting that "Bundle precautions" should be routinely used during CVCs insertion at Abu-El Reesh Hospital' Pediatric Intensive Care Unit.

Keywords: Cost-effectiveness, Bundle precautions, Central Line-Associated Bloodstream Infections

Corresponding Author : Amal Samir Sedrak E-mail address:amalnewlife82@gmail.com

Introduction

Central venous catheters (CVCs) represent a vital procedure for intravenous therapy for intensive care units (ICU) patients and for ambulatory patients needing long-term intravenous access.¹

Central line-associated bloodstream infections (CLABSIs) are among the most frequent health care-associated

infections (HAIs). The Joint Commission defines CLABSI as "a primary blood stream infection (that is, there is no apparent infection at another site) that develops in a patient with a central line in place within the 48-hour period before onset of the bloodstream infection that is not related to infection at another site".² CLABSI is associated with prolonged

ICU stay and increased morbidity and mortality.³⁻⁵

A study in the United states showed that each year, nearly 80 000 Americans develop CLABSIs in intensive care units (ICU), and more than 31.25% of these patients die.⁶

WHO estimated HAI Prevalence in some developing countries, to be 13.9% in Malaysia, 17.8% in Morocco and Tunisia.⁷ Mortality rates caused by CLABSI was estimated to be as high as 50%.⁸

The National Surveillance Systems used to estimate the incidence rates of HAIs, including CLABSI, is almost defective in resource limited countries, being relatively expensive and time consuming methods.⁹

However it was highlighted that prevalence surveys may propose an alternative to conventional surveillance methods as a way to identify the most common HAIs, including CLABSI, particularly in resource-limited countries.^{10, 11}

In a recent prospective surveillance for Health care Associated Infections (HAIs), performed in 46 ICUs in 11 Egyptian hospitals, conducted from April 2011 through March 2012, it was highlighted that the highest central line-associated blood infection (CLABSI) rates were reported in neonatal intensive care unit (NICUs) (5.1 CLABSI/1,000 central line-days).¹²

The incurred costs due to CLABSI include those costs related to diagnosis and treatment, and prolonged hospital stays that might extend up to three weeks, leading to significant escalation of the financial burden to hospitals and patients.¹³⁻¹⁶ Despite these findings, CLABSIs are potentially preventable through the use of evidence-based practices.¹⁷

Several studies documented that implementing evidence-based practices, including combining several measures into a CVC insertion “prevention

bundle,” has resulted in improved CLABSI rates.¹⁸⁻²⁰

A central line prevention bundle consists of five key components: hand hygiene, maximum sterile barrier precautions (which include use of cap, mask, sterile gown, gloves and full sterile body drape for insertion), chlorhexidine skin antisepsis, optimal catheter insertion site selection and daily review of line necessity with prompt removal of unnecessary lines.²¹

The bundle is currently being endorsed for use in several countries. Ten studies in pediatric intensive care unit PICU patients demonstrated a significant decrease in the CLABSI rate after implementation of the bundle.²² There is growing interest for applying evidence based decision making due to the wide spread concern about increasing healthcare costs all over the world and the fundamental need for effective health measures and efficient resource allocation.²³

Nevertheless, the cost-effectiveness of the bundle compared to the standard infection control interventions is currently not assessed in Egypt. Each individual component of the bundle has relatively low cost to implement. Our main question in this study is whether or not this “bundle precaution approach” is cost effective to implement compared to current practice, from Cairo University Pediatric Teaching hospital (Abou Elreesh Hospital) perspective. We have chosen to analyze costs from the hospital perspective because hospitals bear the greatest burden of nosocomial infection costs.

Method

The main study was a prospective, non-randomized, controlled trial, performed on 300 beds, at Abou Elreesh Children Hospital, Cairo University, at the 7th floor pediatric intensive care unit (PICU). One hundred patients with different organ involvement who fulfill

Table (1): Baseline Clinical characteristics:

		No Bundle Group (N= 50)		Bundle Group (N= 50)		P value
		N	%	N	%	
Sex	Male	24	48.0	27	54.0	
	Female	26	52.0	23	46.0	
Diagnosis	Respiratory disorders	14	28.0	19	38.0	0.377
	Cardiac disorders	9	18.0	11	22.0	
	Neurologic disorders	8	16.0	12	24.0	
	Hepatic disorders	4	8.0	1	2.0	
	Renal disorders	3	6.0	2	4.0	
	Metabolic disorders	3	6.0	1	2.0	
	Others*	9	18.0	4	8.0	
Mechanical ventilation	Yes	41	82.0	45	90.0	0.249
Previous hospitalization	Yes	30	60.0	29	58.0	0.839
Previous antibiotic therapy	Yes	30	60.0	35	70.0	0.295
Urinary catheter	Yes	46	92.0	37	74.0	0.031
Outcome	Discharged	40	80.0	43	86.0	0.424
	Died	10	20.0	7	14.0	

the inclusion criteria: age between 2 months old and 18 years, and need for central line insertion according to the PICU indications, were recruited for both groups. Exclusion criteria included children with immunodeficiency, expected length of stay in the PICU less than 48 hrs, CVL had been placed outside the pediatric intensive care unit (PICU) in Abou Elreesh Children Hospital).

The study was conducted during the period from October 2014 to October 2015. This economic evaluation was conducted simultaneously with the non-randomized Controlled trial and costs was calculated for all recruited patients. Patients were assigned and equally classified between two groups, group I of 50 patients receiving the standard

Table (2): CLABSI Rate per 1000 catheter days and per 1000 ICU days

	No Bundle Group (N= 50)	Bundle Group (N= 50)	P value
CLABSI Rate per 1000 catheter days	19.6	9.8	0.114

CLABSI Rate per 1000 catheter days = (Total no. of CLABSI cases / No. of catheter days) × 1000

practice for infection control, and Group II of 50 receiving the bundle precaution approach during CVC placement. Subjects were allocated into either groups according to their serial order of admission (e.g. the 1st admitted patient allocated to group I, then the 2nd allocated to group 2 and so on).

Table (3): Resource Utilization and Cost for the Bundle Specific Activities

Bundle specific activities	Resource used / unit		Total Cost for Bundle group
	Unit	Frequency	
Catheter care component			
Appropriate hygiene (Routine CVL care)	hand 25 sec Soap, alcohol	Per catheter insertion	39.85±23.76
Maximal barrier precautions			
Mask, gloves, gown, cap, large drape	1 set	Per catheter insertion	35.91 ± 20.51
Chlorhexidine preparation	skin 3 days' supply	Per catheter insertion	20.26 ± 11.57
Mentoring and leadership activities in the study			
<i>Assistant professors</i>	1.5 H	Per week	13.73 ± 8.27
<i>lecturers</i>	3 H	Per week	21.57 ± 17.65
<i>Ass. lecturers</i>	6 H	Per week	32.96 ± 19.86
<i>Consultant</i>	1.5 H	Per week	15.20 ± 9.16
TOTAL Mentoring activities			83.47 ± 50.3

Bundle application for CVL insertion is a dominant strategy i.e. cost saving with CLABSI reduction by 50%

Demographic data (age, gender), history of previous hospitalization or antibiotic therapy, history of blood transfusion, admission diagnosis, clinical examination had been carried out for every case. For signs suggestive of infection presence of mechanical ventilation, presence of urinary catheter, and the following labs were ordered.

Primary outcome (CLABSI) was defined as laboratory-confirmed BSIs in patients who did not have a central vascular access device in use within the 48-hour period before the development of the BSI. Secondary BSIs were defined as laboratory confirmed BSIs in patients who also met NHSN criteria for infection at another site (e.g. urinary tract infection, pneumonia, or surgical site infection). A positive blood culture was determined to be contaminated if a common skin contaminant (e.g., diphtheroids, *Bacillus* spp, *Propionibacterium* spp, coagulase-negative staphylococci, or micrococci) grew in a single blood culture and the physician did not institute appropriate

antimicrobial therapy. This proxy outcome is reasonable because numerous studies have shown that, (CLABSI) are deadly hospital acquired infections with a reported mortality rate of 12-25%.

The number of days between CLABs was recorded throughout the study period. A base line central venous line assessment for detection signs of infection was done for all patients in control and study groups on admission after insertion. Axillaries body temperature, WBCs, blood culture was recorded for all patients in control and study groups after 48 hours of line insertions. All blood cultures obtained from patients admitted to the ICU were reviewed by the General lab at Abou Elreesh children hospital Cairo University and all suspected CLABSI.

Determination of medical care costs for patients: Costs measured were direct medical cost, where the consumption was entirely attributable to the patient's hospital stay, including direct labor costs, direct medical supplies cost and direct equipment cost; other non- medical costs,

(e.g. utility costs, laundry, sterilization and housekeeping) related to the overall Table (4) Application of Bundle Precautions compared to No Bundle Precautions; resources and costs

	Bundle (n=50)	Use	No Bundle use (n=50)	Bundle use- no bundle use (95% CI)	P-value
	Mean ± SD		Mean ± SD		
Non physician fees	283.93 ± 171.1		354.02 ± 306.7	-70.09(-168.67 to 28.48)	0.16
Physician fees	1136.42 ± 684.87		1416.97 ± 1227.75	-280.55 (-675.09 to 113.99)	0.16
Routine CVL care	39.85 ± 23.76		43.98 ± 30.88	- 4.13 (-15.06 to 6.8)	0.45
Supplies	223.44 ± 14.12		91.62 ± 69.22	-68.18 (-88.01 to -48.35)	<0.001
Medications and blood products	2901.28 ± 6310.6		3120.79 ± 6450.8	-219.51 (-2752.14 to -2313.12)	0.86
Total investigation costs	1087.50 ± 433.97		1094.04 ± 394.3	-6.5 (-171.1 to 158.02)	0.93
Antibiotics	703.2 ± 423.7		876.8 ± 759.7	-173.6 (-417.7 to 70.5)	0.16
	Bundle (n=50)	Use	No Bundle use (n=50)	Bundle use- no bundle use (95% CI)	P-value
	Mean ± SD		Mean ± SD		
Bundle specific activities					
• Maximal barrier precautions	35.91 ± 20.51		-		
• Chlorhexidine skin preparation	20.26 ± 15		-		
• Mentoring , training and maintenance care	83.47 ± 50.30		-		

costs incurred by the hospital as well as overhead costs were not included. These costs were assumed to be equally allocated among the two groups and were not measured in this study. The vast majority of economic and cost analyses of CVL insertion and followed CLABSI focus primarily on direct medical costs as these costs directly impact hospital finances.

Direct Medical care costs items were assessed from the hospital perspective using combination of micro-costing technique (resource based accounting method) and hospital list data (according to the 2015 user Fees Schedule) and were

reported in 2015 Egyptian pounds. Measuring cost of stay within the department was done using Bottom-Up micro-costing approach.

Costs of application of bundle procedure(appropriate hand hygiene; maximal barrier precautions for insertion; chlorhexidine skin antiseptic and the required major disposable items (sterile gown, gloves, cap, masks, Dressings) in addition to time of the staff allocated for training and mentoring activities were calculated for patients in the bundle group. Also cost for all resources used in the non-bundle group was calculated.

Central Venous Line insertion procedure' costs for each patient in the trial were tracked through estimating the unit costs **Table (5): Comparison of costs and outcomes between Bundle and no-Bundle precautions for CVL insertion:**

	Mean	SD
NO Bundle		
Costs	6998.24**	8059.27
CLABSI Rate per 1000 catheter days	19.6	3.45
Bundle		
Costs	6515.284 *	7368.88
CLABSI Rate per 1000 catheter days	9.8	0.019
Benefit of the Bundle		
Net Costs	-482.956	11148.5
CLABSI Rate per 1000 catheter days prevented	-9.8	0.01

* Is the result of summation of all cost items of the Bundle precautions used in table (4)

** Is the result of summation of all cost items of the non Bundle precautions in table (4)

of the medical supplies and the disposable items, the time allocated by nurses for providing such services and allocated for each patient according to the utilization rate during the PICU stay. Lab investigations costs (as CBC, blood culture, CRP, CSF analysis, hepatitis markers) and radiological imaging costs (included X- ray, US, Echocardiogram, ECG, Doppler, MRI) were estimated using unit costs for each investigation derived from 2015 User Fee schedule of Kasr Al Aini Hospitals and allocated to the patients according to the utilization rate during their length of stay.

Treatment costs' of the primary indications for CVL insertion, including drug acquisition, dosing, administration, in addition to total parental nutrition, blood and blood products were also estimated based on the unit cost and multiplied by the utilization rate. Resource utilized were recorded on a

standardized data form for each procedure, where quantities and unit costs were first estimated and then multiplied, aggregated to cost per procedure during the specified length of stay for each individual patient Also cost of CLABSI complicating CVL insertion was calculated in terms of pharmaceuticals used, dosing, acquisition, monitoring (Lab. investigation). Professional fees: Associate professors, consultants, lectures, residents and nursing staff' fees for inpatients services were derived from 2015 Cairo University Medical Staff Fee Schedule. These data were obtained from the financial affairs unit where the basic salary (of physicians with different staff levels together with nurses); call duty allowance, hazard allowance and housing allowance were allocated to patients based on the average time allocated by medical staff per patient, for providing health care services.

Discounting: All Costs and outcomes were evaluated during one year period, hence no discounting was performed.

Time horizon: Costs and outcomes were tracked during the patients stay in the PICU till discharge whether cured, referred or dead.

Statistical Analysis:

Data were collected, revised, entered to SPSS statistical package (version 18). Continuous, normally distributed data were presented as mean \pm 2 SD and were compared using Student t-test. Cost data were described as both mean and median and were compared using Student t-test. Even though not all cost estimates were generally normally distributed, however inquiring whether mean cost were significantly different or not, commonly addresses the health system perspective. A two-tailed $P < 0.05$ was considered statistically significant.

Sensitivity analysis: Variability of the cost effectiveness estimates within the trial was assessed using one way sensitivity analysis. Distributions were

created for several parameters including total costs, total benefits and probability of developing a CLABSI with and without the bundle intervention.

Cost-effectiveness analysis: The outcome of interest was the number of CLABSIs prevented. It was calculated as (number of CLABSI per 1000 central line days) associated with CVL insertion in the PICU.²⁴ The reference of the cost data collection tool. Average cost effectiveness ratio was calculated to compare the average cost of each CVL insertion technique (using bundle versus no bundle technique) with the clinical benefit of reducing CLABSI rate. For each comparison we assessed average cost effectiveness ratio in terms of cost per CLABSI rate averted.

Ethical consideration:

Each patient in the control group was offered more meticulous observation and covered by broad spectrum antibiotics to guard against hypotheses of increased CLABSI probability. An informed consent was obtained from every care giver for each child before enrollment, including express permission for the collection and analysis of economic data. The ethical approval was obtained from the ethics committee at Kasr Al Aini according to the Ministry of Health demands compliance with the Helsinki Declaration. All procedures done in the current study were reviewed and approved by Infection Prevention and Control Committee of the Hospital. The general patient consent for any procedure in ICU was taken upon admission as per hospital policy and documented on each patient's medical record.

However, more observation and coverage with broad spectrum antibiotics was provided to those patients not having Bundle precautions in CVL insertion, so as to compensate for the increased CLABSI probability.

Results

Baseline patient characteristics before randomization are shown in table 1. The two groups were well matched concerning; age, different diagnoses, Mechanical ventilation, previous hospitalization and previous antibiotic therapy.

However, as regards urinary catheterization; 92% of the non-bundle group had urinary catheter compared to 74% of the bundle. Resource Utilization and Cost for the Bundle Specific Activities (Table 2): Details resource use and costs for the bundle precautions' activities. Whereas Table 4 illustrates resources utilized and their costs compared between the 2 groups. Although costs of supplies consumed were significantly higher among the bundle group (223.44 ± 14.12 vs 91.62 ± 69.22 , $p < 0.001$) however this cost rising was counter balanced by lower physician, non-physician fees, medications, blood products, total investigation costs which were much lower in the bundle group compared with the no bundle group. This finding may be attributed to the lower length of stay and days of catheter insertion (17.58 ± 10.59 , 15.2 ± 8.6 respectively) in the bundle group compared to (21.92 ± 18.99 , 16.3 ± 10.34 respectively) in the no- bundle group.

Cost-effectiveness analysis

The expected clinical and economic outcomes are shown in table 3. In the base-case analysis, implementation of bundle precautions resulted in fewer infections and lower costs. Use of bundle precautions decreased the incidence of CLABSI 9.8% (from 19.6%- 9.8%) and decreased the mean cost incurred by the hospital for treating 50 patients from 6998.24LE to 6515.284LE. Thus the present study emphasized that the bundle precaution was economically dominant strategy, both more effective and cost saving of approximately 482.95 LE for the 50 included patients.

Sensitivity analysis

Application of bundle precautions remained a dominant strategy throughout 1-way sensitivity analyses. The effect of the only influential parameter on the incremental cost estimate in the 1-way sensitivity analyses is shown in figure 1. Varying the incidence of CLABSI between 23.05/1000 catheter day and 16.15/1000 CVL days altered the ICER from 76.05 to 36.44. Cost variables were set at their highest probable level to demonstrate the worst-case scenario analysis, however application of bundle precautions continued to decrease the incidence of CLABSI by 0.56/1000 CVL days. This was associated with cost saving of approximately 482 LE for the 50 patients.

Discussion:

The current economic sub-study represents the initial cost-effectiveness analysis. For the implementation of Central Venous Catheter (CVC) bundles of care in Pediatric ICU at Abou Elreesh Hospital, Egypt, to reduce the CLABSI rate among Pediatric patients undergoing CVC insertion.

Owed to the improved proxy outcome in the form of CLABSI rate reduction and the allied cost saving compared to no bundle precautions, it is advocated as an economically attractive infection control strategy for pediatric patients undergoing CVC insertion in Abou Elreesh Hospital. It was proven during this study, to be a dominant strategy satisfying the increasing need for implementing cost effective infection prevention and control programs.

Numerous studies have documented that use of such bundles is effective, sustainable, and cost-effective in both adults and children.²⁵⁻²⁸ Moreover, after catheter insertion, maintenance bundles have been proposed to ensure optimal catheter care.²⁹

In the present study despite the additional cost of the bundle group of (139.65 ± 82.39), attributed to the implementation

of maximal barrier precautions, skin antisepsis with chlorhexidine gluconate solution in addition to mentoring and

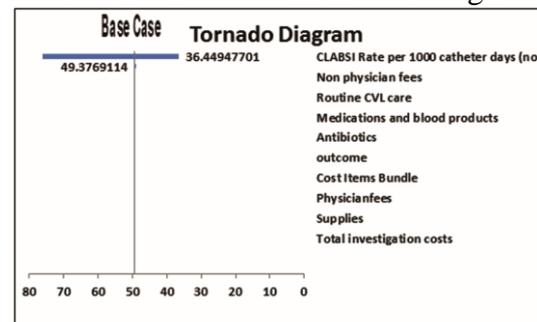


Figure (1): Incremental Cost Effectiveness Ratio Deterministic Sensitivity Analysis

training activities for the nursing staff. As well as the cost of consumed supplies was significantly higher among the bundle group (223.44 ± 14.12 vs 91.62 ± 69.22, $p < 0.001$). This extra cost was more or less counterbalanced by lower physician, non-physician fees, medications, blood products, total investigation costs which were much lower in the bundle group compared with the no bundle group. This findings might be attributed to the lower length of stay and days of catheter insertion (17.58 ± 10.59, 15.2 ± 8.6 respectively) in the bundle group compared to (21.92 ± 18.99, 16.3 ± 10.34 respectively) in the non-bundle group.

In agreement with our results, a study performed at the USA in 2004, emphasized that implementation of MSBs resulted in fewer infections and lower costs. Use of MSBs decreased the incidence of CR-BSI by 2.5%, decreased the incidence of catheter colonization with local infection by 2.6%, decreased the incidence of death by 0.4% (from 0.8% to 0.4%), and decreased costs by \$252 per catheter (30).

Also, a recent study conducted in a pediatric intensive care unit in Turkey illustrated that implementation of CVL program lowered central line-associated bloodstream infection rates by 0.4%, together with reduction in the daily cost of the patients by \$60.5, mainly by

decreasing the antimicrobial and antifungal drug costs by increasing infection-free catheter days.³¹

Consistent with these findings a study conducted in an intensive care unit in Kuwait, for an incidence density of CLABSI reduced from 14.9 to 11.08 per 1000 catheter days after implementation of CVL insertion bundle

Despite some discrepancies, where a review of 11 randomized controlled trials, included a control group with non-impregnated CVCs. This review failed to display any significant clinical benefit associated with the use of antimicrobial-impregnated CVCs for the purpose of reducing CLABSI or improving patient outcomes.³²

On the contrary, many studies have shown that use of antimicrobial-coated catheters and skin antiseptic with chlorhexidine gluconate solution each decrease the incidence of infectious complications and provide cost savings.^{33,34}

Making Health Care Safer accentuated that certain practices (e.g. the use of maximal sterile precautions) were associated with both a decrease in CLABSI risk and reduced cost, whereas others (e.g. intravenous antimicrobial prophylaxis) added expense without clear benefit.³⁵

This economic evaluation study highlighted that, approx. 64.4 LE consumed in the Bundle group to prevent an episode of CLABSI/1000 CVL compared to approx. 76.14 LE consumed in the Non- Bundle group. Moreover, throughout this study it was highlighted that approx. 482.95LE would be saved, and about 9.8 episodes of CLABSI/1000 CVL would be avoided.

Study Limitation:

First of all, owing to data limitations we were unable to assess the impact of patient heterogeneity, such as demographics and clinical diagnoses, on baseline risk, treatment effect or resource

utilization, that were not fully investigated.

Second, it should be emphasized that this analysis is based on the estimated number of infections and direct medical cost incurred during the non-randomized control trial conducted at the PICU of Abou Elreesh Hospital during the time interval 2014-2015 and may not be representative for all pediatric hospitals nationwide. Direct non-medical cost, overhead utilities were not calculated. This was based on the assumption that direct non-medical, overhead, utilities costs are almost equally allocated among both groups. The study also focused on the financial rather than the economic costs of CLABSIs, where rehabilitation costs and productivity loss (of the care givers) were not assessed.

Furthermore, the particular indication for CVCs insertion may fluctuate between different settings that might impact the rate of developing CLABSI. Generalizing these conclusions to individual hospitals should be done cautiously. For instance, hospitals with lower CLABSI rates of catheter-related infection than our estimates were to adopt use of bundle precautions, their potential cost savings and infections avoided would be less than described in this analysis.

Conclusion and Recommendations

Results of this study powerfully advocate for the use of bundle precautions during CVC insertion in hospitalized children admitted to Abou Elreesh Hospital. Economic Evaluation based on randomized Controlled Trail conducted on larger sample size is strongly recommended, followed by identifying and overcoming barriers to using bundle precautions during CVL insertion. Also, persuading physicians and hospital managers of the extra safety and economic benefits of bundle precautions

is influential to increasing their use in clinical practice. Thus, in view of, how commonly CVCs are used in hospitals, the potential reductions in morbidity, mortality, and cost could be considerable.

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