



INICC Bundle to Prevent Ventilator-Associated Pneumonia in Intensive Care Units: An International Perspective.

Purpose

Previously published guidelines are available that provide comprehensive recommendations for detecting and preventing healthcare-associated infections, especially in the USA. The intent of this document is to highlight practical recommendations in a concise format designed to assist acute care hospitals worldwide in implementing and prioritizing their ventilator-associated pneumonia (VAP) prevention efforts.

VAP Background

VAP Rates Internationally.

Ventilator-associated pneumonia (VAP) has been considered to be the most serious healthcare-associated infection (HAI), and it was reported to be the leading cause of morbidity and mortality for device-associated infections (DAI), particularly, in the adult intensive care unit (AICU) setting.^{1,2} Additionally, in a large body of scientific literature, VAPs are among the commonest type of DAI, resulting in a substantial increase in hospital costs and length of stay (LOS).¹⁻³

The scope of the burden posed by VAP internationally, however, has not been systematically addressed.¹ Although surveillance has been reported as an effective tool for the reduction of VAP in the USA,⁴ the importance of surveillance for measuring AICU patient infection risks, outcomes and processes internationally remains many times under-recognized.^{1,5} As a countervailing strategy, in 2002 the International Nosocomial Infection Control Consortium (INICC) developed an outcome and process surveillance program specifically designed for ICUs internationally.⁶⁻⁸

Through the implementation of the INICC program, it was demonstrated that there was a notable difference in the VAP rates between the ICUs of hospitals from the industrialized world and those internationally, with rates ranging from 3 to 5 times higher in the latter ones.⁹⁻¹⁸

The prevalence of HAI internationally was found to be at least double the rates published by the European Centre for Disease Prevention and Control,¹⁹ and triple those found in the USA.²⁰

In the case of DA-HAIs, the rate of device use was found to be analogous or even lower to the one reported of U.S. ICUs by the National Nosocomial Infection Surveillance System (NNIS)/ National Healthcare Safety Network (NHSN) System;^{21,22} however, pooled mean rates identified in intensive care units (ICUs) internationally by the International Nosocomial Infection Control Consortium (INICC) were found to be exceedingly higher than those reported from U.S.'s ICUs by the National Healthcare Safety Network (NHSN).^{5,17,22}

Meta-analyses and systematic reviews on HAI have been scant internationally. Furthermore, such analyzes could not retrieve enough data from some regions and many countries were not even represented.²³ The systematic review and meta-analysis on the burden of endemic HAI internationally by Allegranzi *et al* concluded that HAI prevalence was significantly higher in low and middle low-income countries compared to USA and Germany. The incidence density of DAI in critically ill patients was found to be from two- to 19-fold higher than those reported from the USA and Germany.²³ In a systematic review by Arabi *et al* on VAP in adults internationally, from 1966 to 2007, the rates of VAP were higher overall than NHSN benchmark rates, and ranged from 10 to 41.7 per 1000 ventilator-days. The review found that the crude mortality attributable to VAP ranged from 16% to 94%.¹

Applying INICC methodology the following VAP rates per 1000 mechanical ventilator days were collected and found: in Argentina is 46.3;²⁴ in Brazil is 20.9;²⁵ in China is 20.8;²⁶ in Colombia is 10.1;²⁷ in Cuba is 52.5;²⁸ in Egypt is 73.4;²⁹ in El Salvador is 12.1 in PICU,³⁰ and 9.9 in NICU;³⁰ in India is 10.4;³¹ in Mexico is 21.8;³² in Morocco is 43.2;³³ in Peru is 31.3;³⁴ in Philippines is 16.7 in adult ICU,³⁵ and is 12.8 in Pediatric ICU;³⁵ in Poland is 18.2;³⁶ in Turkey is 26.5;³⁷ in Lebanon is 8.1;³⁸ in the INICC international report from 8 countries is 24.1;³⁹ in the INICC international report from 18 countries is 19.5;⁴⁰ in the INICC international report from 25 countries is 13.6;⁴¹ in the INICC international report from 36 countries is 15.8;⁴² in the INICC report of Neonatal ICUs of 15 countries is 9.7.⁴³

VAP Mortality, Extra Length of Stay, and Extra Cost Internationally.

From the available literature, it is highly visible that the adverse consequences of device-associated HAIs (DA-HAI) internationally —that is, attributable mortality,^{2,3,6,9,10,12,13,17,33,44-54} prolonged length of stay,^{2,3,6,9,10,12,36,44-49,51-54} extra hospital costs,^{3,44,47} and increased bacterial resistance^{25,27,31,33,34,36,40,41,55-58} — are more far-reaching in terms of severity than in the USA and Germany.

In order to calculate the cost of nosocomial pneumonia in intensive care units, a 5-year matched cohort study was undertaken at 6 ICUs of three hospitals in Argentina members of INICC. Three hundred and seven patients with VAP (exposed) and 307 patients without VAP (unexposed) were matched for hospital, ICU, period, LOS more than seven days, gender, age, and average severity of illness score (ASIS). The mean extra LOS for 307 cases (compared to the controls) was 8.95 days, the mean extra antibiotic defined daily doses (DDD) was 15, the mean extra antibiotic cost was \$996, the mean extra total cost was \$2,255, and the extra mortality was 30.3%.⁵⁹ Nevertheless, the extended suffering of patients and their relatives cannot be estimated in terms of economic costs only. Mortality due to ventilator-associated pneumonia (VAP) has been found by Rosenthal to be as high as 56.7%.³³

In a study performed in hospitals member of INICC in 10 developing countries to estimate extra LOS and mortality in an intensive care unit (ICU) due to a VAP, a cohort of 69,248 admissions were followed for 283,069 days in ICUs. Data were arranged according to a multi-state format. Extra LOS and increased risk of death were estimated independently in each country, and their results were combined using a random effects meta-analysis. The findings of the analysis showed that a VAP prolonged LOS by an average of 2.03 days (95% CI: 1.52, 2.54 days), and increased the risk of death by 14% (95% CI: 2, 27%).⁶⁰

Antibiotic Usage and Bacterial Resistance Internationally.

The relationship of antibiotic use and the emergence of antibiotic-resistant HAI is an issue that epidemiologists and hospital authorities internationally must be aware of. In INICC's ICUs, antimicrobial resistance rates found for *Staphylococcus aureus* isolates as resistant to methicillin (MRSA), *enterobacteria* resistant to ceftazidime (extended-spectrum beta-lactamase producers), and *Pseudomonas aeruginosa* as resistant to fluoroquinolones, were far higher than NHSN ICUs' rates.⁶¹ Nonetheless, the rates found in the INICC's ICUs for *enterococcal* isolates as resistant to vancomycin were much lower than NHSN ICUs' rates.^{33,55,61}

VAP Rates in Neonatal ICUs Internationally.

In several studies, researchers have highlighted the extreme vulnerability of neonates hospitalized in neonatal intensive care units (NICUs) to mortality attributable to DA-HAI, with rates ranging from 24% in the pre-surfactant era to 11% in the post-surfactant era in the developed countries.⁶²⁻⁶⁵ However, within the context of developing countries, access to knowledge regarding DA-HAI is scarce, and there is an insufficient recognition of the importance of surveillance for measuring the infection risks, outcomes and processes concerning the neonatal patient hospitalized in the NICU.^{30,66-68} In this respect, a recent study was performed to evaluate the impact of country socioeconomic status and hospital type on device-associated healthcare-associated infections (DA-HAIs) in 30 neonatal

intensive care units (NICUs), from hospitals members of INICC in 15 developing countries. Its findings revealed that ventilator-associated-pneumonia (VAP) rates in patients hospitalized in NICUs from academic hospitals were significantly higher than rates found in private or public hospitals.⁵²

Strategies for VAP Rate Reduction Internationally.

According to a review by Arabi *et al* on VAP in adults internationally, a small number of VAP intervention studies were performed, which found that staff education programs, implementation of hand hygiene, and VAP prevention guidelines, and implementation of sedation protocol were related to a significant reduction in VAP rates.¹

Since 1998, INICC has conducted several studies internationally, in order to reduce VAP rates, applying similar methodology. The aim of these studies was to analyze the effect of the INICC multidimensional infection prevention model on the reduction of VAP in hospitalized patients. It was a prospective active surveillance before-after study to assess the impact of a multi-dimensional prevention model on the VAP rate. The study was divided into two phases. During phase 1, the infection control team at each ICU conducted active prospective surveillance of VAP by applying the definitions of the Centers for Disease Control and Prevention (CDC) National Health Safety Network (NHSN), and the methodology of INICC. During phase 2, the prevention model for VAP was implemented at each ICU, in addition to the active surveillance. The INICC VAP prevention model included the following measures: 1- bundle of infection control interventions, 2- education, 3- outcome surveillance, 4- process surveillance, 5- feedback of VAP rates, and 6- performance feedback of infection control practices. The VAP rates obtained in phase 1 were compared to the rates obtained in phase 2.

The one conducted by INICC in China,⁶⁹ from January 2005 to July 2009, recorded data from 16,429 patients hospitalized in 3 ICUs, for a total of 74,116 ICU bed days. The VAP baseline rate was 24.1 per 1000 ventilator-days. During phase 2, the VAP rate significantly decreased to 5.7 per 1000 ventilator-days in 2009 (2009 vs 2005: relative risk, 0.31; 95% confidence interval, 0.16-0.36; P = .0001), amounting to a 79% cumulative VAP rate reduction.⁶⁹

The one conducted by INICC in Adult ICUs,⁷⁰ showed that in 44 AICUs, from 38 hospitals members of the International Nosocomial Infection Control Consortium (INICC), from 31 cities of the following 14 developing countries: Argentina, Brazil, China, Colombia, Costa Rica, Cuba, India, Lebanon, Macedonia, Mexico, Morocco, Panama, Peru, and Turkey. During Phase 1, we recorded 10,292 mechanical ventilator (MV) days, and during Phase 2, with the implementation of the multifaceted prevention model, we recorded 127,374 MV days. The rate of VAP was 22.0 per 1000 MV days during Phase 1, and 17.2 per 1000 MV days during Phase 2. The adjusted model of linear trend shows a 55.83% reduction of the rate of VAP at the end of

the study period; that is, the VAP rate is 55.83% lower than it was at the beginning of the study.⁷⁰

The one conducted by INICC in Pediatric ICUs,⁷¹ showed that during the baseline period, we recorded 5,212 mechanical ventilator (MV) days, and during the implementation of the bundle of interventions, we recorded 9,894 MV days. VAP rate during baseline period was 11.7, and during intervention period, it was 8.1 per 1000 MV days (RR; 0.69; 95% CI 0.5-0.96; P 0.02), which showed a 31% VAP rate reduction.⁷¹

The one conducted by INICC in Neonatal ICUs,⁷² showed that during Phase 1, we recorded 3,153 mechanical ventilator (MV) days, and during Phase 2, with the implementation of the bundle of interventions, we recorded 15,981 MV days. VAP rate during Phase 1 period was 17.8, and during Phase 2 period was 12.0 per 1000 MV days (RR; 0.67; 95% CI 0.50-0.91; P 0.001), showing a 33% VAP rate reduction.⁷²

Our results demonstrate that the implementation of the INICC multidimensional infection control program was associated with a significant VAP rate reduction in adult, pediatric and neonatal ICUs internationally.⁶⁹⁻⁷²

Conclusion

These findings are a clear indication of the influence that economics, as a surrogate of available medical supplies, outdated technology, and scarce human resources availability, have on developing countries, and of the close relation between hospital type and limited access to health care resources. In public and academic hospitals, the limited resources in terms of adequate number of trained and specialized staff, budget, medical supplies and hospital administrative support is markedly more serious than in private hospitals, as the public hospital are more dependent on the socio-economic category of the country concerning the budget allocation. Limited-resource countries are confronted with aspects that transcend clinical findings and good delivery of healthcare practices; the harsher reality suffered by patients hospitalized in the ICUs of developing countries lies outside the scope of the hospital itself, and reflects the country's social and political situation, poor living conditions, difficult or differentiated access to labor market and precarious labor conditions, diversity of cultural values, unequal allocation of assets among population resulting in unsatisfied basic needs, including sanitary infrastructure and limited access to the education and health system. As long as these conditions prevail, healthcare workers from developing countries are urged to focus their best efforts on improving healthcare and clinical practices, and disseminating their successful achievements, so as to be able to counteract the many social factors that cannot be directly controlled by clinical practices alone.⁷³ Also the findings of these reviews and meta-analyses evidence the urgent need to improve surveillance, infection control practices, update outdated technology, and to increase the number of intervention studies to reduce these high DA-HAI rates internationally. Therefore, additional epidemiological studies are to be performed to develop more definitive approaches for DA-HAI

prevention in the form of practical, cost-effective technological measures that are feasible to implement internationally. Finally, INICC results demonstrate that the implementation of the INICC multidimensional infection control program was associated with a significant VAP rate reduction in adult, pediatric and neonatal ICUs internationally.

INICC Methodology

The INICC Surveillance Program includes two components: outcome surveillance (VAP rates and consequences) and process surveillance (adherence to hand hygiene and other basic preventive infection control practices).⁷

The investigators at the participating hospitals were required to perform outcome and process surveillance by completing forms, which were then sent for their monthly analysis to the INICC office in Buenos Aires.⁷

Outcome Surveillance

The INICC Surveillance Program is focused on the methods and definitions for DAI developed by the U.S. Centers for Disease Control and Prevention (CDC) for the National Nosocomial Infection Surveillance System (NNIS)/ National Health Safety Network (NHSN) program.^{74,75} However, the INICC methods have taken into consideration the different socioeconomic status and specific limitations of limited-resource countries, and were adapted for their application in this setting.⁷ Outcome surveillance includes rates VAP per 1000 device-days; microorganism profile, bacterial resistance, length of stay, and mortality in their ICUs.

Process surveillance

Preventive strategies in INICC member hospitals are based on simple, inexpensive, evidence-based measures, which include outcome surveillance, process surveillance, education and performance feedback of outcome surveillance and process surveillance.⁷

Process surveillance is designed to monitor compliance with easily measurable, key infection control measures. It includes the surveillance of compliance rates for hand hygiene practices and some specific infection control measures for the prevention of VAP.^{73,76-78}

Hand-hygiene (HH) compliance by healthcare workers (HCWs) is determined by measuring the frequency of HH performances when clearly indicated, and such practices are monitored by the hospital's ICP during randomly selected 1-hour observation periods, 3 times a week. Although HCWs know that HH practices are regularly monitored, they are not actually aware of the precise moment in which observations are taking place.⁷

ICPs were trained to detect HH compliance and record HH opportunities and compliance through direct observation. The INICC direct observation comprises the "Five Moments for Hand Hygiene," as recommended by the World Health Organization (WHO). The "Five Moments" were designed on the basis of the evidence concerning DAI prevention and control, and include the monitoring of the following moments: (1) before patient contact, (2)

before an aseptic task, (3) after body fluid exposure risk, (4) after patient contact, and (5) after contact with patient surroundings.⁷⁹

Training and Validation

Investigators are self-trained by means of a manual and training tool that describe how to perform surveillance and complete surveillance forms. Investigators have continuous e-mail and telephone access to a support team at the INICC Central Office in Buenos Aires, Argentina, which is in charge of responding to all queries within 24 hours. The INICC Chairman further reviews all queries and responses.

Surveillance forms for individual patients allow internal and external validation, because they include every clinical and microbiological criterion for each type of DAI, such as temperature, blood pressure, use of invasive devices, cultures taken, culture results, antibiotic use. Surveillance also includes a form where positive cultures are registered and matched with patients' forms.

On a monthly basis, participating hospitals submit the completed surveillance forms to the INICC Central Office, where the validity of each case was checked and the recorded signs and symptoms of infection and the results of laboratory studies, radiographic studies, and cultures were scrutinized to assure that the NNIS System criteria for device-associated infection were fulfilled.

The ICT member who reviewed the forms completed at the participating AICU was able to

verify that criteria for infection had been met accurately in each case. Additionally, the original patient data forms were further validated at the INICC Central Office, before data on the reported infection were entered into the INICC's database. To that end, queries were submitted from INICC office in Buenos Aires to the ICT teams at each hospital, challenging those cases with suspected VAP, and data were uploaded after receiving the reply from hospital teams. Finally, the INICC team performed consistency analyses of database, such as age, gender, dates, among other data, and reviews of medical records that compared data registered in forms and data in medical records.

Performance Feedback

The concept of using performance feedback of outcome surveillance and process surveillance as a valuable control measure in limited-resource hospitals was based on its effectiveness as proved in previous INICC studies.^{73,76-78,80,81}

The INICC Central Office team prepared and sent monthly chart reports to each participating hospital that detailed their rates of VAP, microbiology profile, and rates of adherence to hand hygiene, among other infection related data. The participating ICU staff received feedback on their performance at monthly meetings, by means of the review of said charts, which were posted in a prominent location in the ICU.

Bundle Background

Within the INICC program, the infection prevention bundle was based on the guidelines published by the Society for Health Care Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA), which describe evidence-based interventions and recommendations for VAP prevention in the ICU.⁸² In addition, the INICC prevention bundle also followed the recommendation by the Institute of Healthcare Improvement (IHI) that a ventilator bundle be implemented at every ICU to reduce the incidence of VAP to zero, which was part of the 5 Million Lives campaign, endorsed by leading US agencies and professional societies.⁸³ Within the international context, outcome and process surveillance, integrated in an intervention bundle with performance feedback of infection control practices, has been shown to successfully reduce and control DAIs in different studies conducted in INICC member hospitals.^{69-73,76,77,80,81}

These bundle provide feasible and cost-effective infection control measures, applicable internationally.

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2. Core Strategies to prevent VAP

i. Prevent Aspiration of Secretions

- Maintain patients in a semi-recumbent position.
- Avoid gastric overdistention.
- Avoid unplanned extubation and reintubation.
- Use a cuffed endotracheal tube with in-line or subglottic suctioning.
- Maintain an endotracheal cuff pressure of at least 20 cm H₂O.

ii. Prevent Colonization of the Aerodigestive Tract

- Orotracheal intubation.
- Perform comprehensive oral care.

iii. Prevent Use of Contaminated Equipment.

- Remove condensate from ventilatory circuits. Keep the ventilatory circuit closed during condensate removal.
- Change the ventilatory circuit only when visibly soiled or malfunctioning.
- Store and disinfect respiratory therapy equipment properly.
- Use sterile water to rinse reusable respirator equipment.

1. General Strategies to prevent VAP

i. Conduct active surveillance for VAP.⁸⁴

Perform ongoing surveillance of the incidence density of VAP on units that care for patients undergoing mechanical ventilation who are known or suspected to be at high risk for VAP, to permit longitudinal assessment of process of care.

Incidence density of VAP, reported as the number of episodes of VAP per 1,000 ventilator-days.

Preferred measure of VAP incidence density: 1- Numerator: number of patients undergoing mechanical ventilation who have VAP, defined using National Healthcare Safety Network definitions; 2- Denominator: number of ventilator-

days; 3- Multiply by 1,000 so that the measure is expressed as cases per 1,000 ventilator-days.

ii. Educate healthcare personnel who care for patients undergoing ventilation about VAP.¹⁻⁴

1. Educate healthcare personnel who care for patients undergoing ventilation about VAP, including information about the following: a. Local epidemiology; b. Risk factors; c. Patient outcomes.
2. Educate clinicians who care for patients undergoing ventilation about noninvasive ventilatory strategies.

iii. Adhere to Hand-Hygiene Guidelines

Published by the Centers for Disease Control and Prevention or the World Health Organization.^{84,85}

Collect data on a sample of healthcare personnel from all disciplines who provide hands-on care to patients undergoing ventilation, including physicians, nurses, respiratory therapists, and radiology technicians. Perform observations at regular intervals (e.g., 1 set of measurements per week). The frequency of observations can be adjusted on the basis of compliance rates (e.g., as compliance improves, less frequent observations may be needed).

iv. Limit the use of mechanical ventilation: Use noninvasive ventilation whenever possible.⁸⁶⁻⁹³

Noninvasive ventilation (NIV) refers to the administration of ventilatory support without using an invasive artificial airway (endotracheal tube or tracheostomy tube). NIV has been used primarily for patients with acute hypercapnic ventilatory failure, and especially for acute exacerbation of chronic obstructive pulmonary disease. In this population, the use of NIV is associated with a marked reduction in the need for endotracheal intubation, a decrease in complication rate, a reduced duration of hospital stay and a substantial reduction in hospital mortality. Similar benefits have also been demonstrated in patients with asphyxial forms of acute cardiogenic pulmonary edema. Major benefits have also been demonstrated in selected populations with no contraindications such as multiple organ failure, loss of consciousness or haemodynamic instability. One important factor in success seems to be the early delivery of noninvasive ventilation during the course of respiratory failure. Noninvasive ventilation allows many of the complications associated with

mechanical ventilation to be avoided, especially the occurrence of nosocomial infections.

**iv. Limit the use of mechanical ventilation:
Minimize the duration of ventilation.**^{89,94-100}

Daily interruption of sedation followed by a readiness to wean assessment and readiness for a spontaneous breathing trial. Around the clock sedation assessment using a reliable and valid tool.

**iv. Limit the use of mechanical ventilation:
Perform daily assessments of readiness to wean.**^{84,96} **Use weaning protocols.**^{101,102}

Hospital teams across the United States have developed and tested process and system changes that allowed them to improve performance on daily sedation vacations and daily assessment of readiness to extubate. These measures, taken together, support the implementation of the ventilator bundle. Some of these changes are:

- 1- Implement a protocol to lighten sedation daily at an appropriate time to assess for neurological readiness to extubate. Include precautions to prevent self-extubation such as increased monitoring and vigilance during the trial.
- 2- Include a sedation vacation strategy in your overall plan to wean the patient from the ventilator; if you have a weaning protocol, add sedation vacation to that strategy.
- 3- Assess compliance each day on multidisciplinary rounds.
- 4- Consider implementation of a sedation scale such as the Riker scale to avoid over-sedation.
- 5- Post compliance with the intervention in a prominent place in your ICU to encourage change and motivate staff.

v. Implement a multidimensional approach.⁶⁹⁻⁷²

Apply a multidimensional approach for VAP prevention including the following measures:

- 1- Bundle of infection control interventions,
- 2- Education,
- 3- Outcome surveillance,
- 4- Process surveillance,
- 5- Feedback of VAP rates, and
- 6- Performance feedback of infection control practices.

2. Core Strategies to Prevent VAP

i. Prevent Aspiration of Secretions

Maintain patients in a semi-recumbent position (30-45 elevation of the head of the bed) unless there are contraindications.¹⁰⁰

Head of the bed elevated for the majority of the day (unless medically contraindicated). It is understood that patients might be cared for at different bed angles during different times of the day, and that continuous monitoring of bed angles is impossible. Therefore, to implement this measure, the ventilator patient in the intensive care unit must be monitored at least two times in a 24-hour period to see if the head of the bed is elevated to 30 degrees or greater. The observations should coincide with the structure of the ICU shifts and one observation should be

made on at least two different shifts within the 24 hour period. It is recommended that there be a minimum of 8 hours between observations. In order to achieve the most valid results, it is suggested that a pre-determined schedule be devised. The schedule may or may not be random, but should ensure that equal numbers of observations are made during each day of the week.

Consider progressive mobility: continuous lateral rotation therapy or at least early mobility.

(a) Experimental trials have demonstrated that backrest elevation is associated with a reduced risk of pulmonary aspiration.¹⁰³¹⁻²

(b) Multivariable analysis of risk factors associated with VAP found up to a 67% reduction in VAP among patients maintained in semi-recumbency during the first 24 hours of mechanical ventilation.¹⁰⁴

(c) The impact of semi-recumbency was confirmed in an observational study,⁹⁸ and a randomized trial.¹⁰⁵

(d) However, recent studies indicate that semi-recumbent positioning is rarely maintained,¹⁰⁶ and may not be associated with a reduced rate of tracheal colonization¹⁰⁶ or VAP.¹⁰⁷

Avoid gastric overdistention.^{89,108-112}

According with Heyland study, patients fed into the stomach had more episodes of gastroesophageal regurgitation (39.8% vs. 24.9%, $p = .04$) and trended toward more microaspiration (7.5% vs. 3.9%, $p = .22$) compared with patients fed beyond the pylorus.

Avoid unplanned extubation and reintubation.^{84,96,113,114}

Perhaps the most risky aspect of lightening the sedation that the patient is receiving daily is the chance that patients might self-extubate. This risk can be diminished by ensuring that the process is adequately supervised and that appropriate restraints are applied to the patient's arms in a comfortable fashion.

Use a cuffed endotracheal tube with in-line or subglottic suctioning.

Subglottic secretion drainage is associated with a decreased incidence of VAP. To increase their utility and cost-effectiveness, these tubes should only be placed in patients expected to require prolonged mechanical ventilation.

(a) Meta-analysis demonstrated that subglottic secretion drainage was effective in preventing early-on set VAP.¹¹⁵

Maintain an endotracheal cuff pressure of at least 20 cm H₂O.¹

Cuff pressure must be monitored frequently.¹¹⁶

ii. Strategies to reduce colonization of the aerodigestive tract

Orotracheal intubation is preferable to nasotracheal intubation.

Oral endotracheal intubation is associated with a trend toward a reduction in VAP compared to

nasotracheal intubation and with a decreased incidence of sinusitis (the incidence of VAP is lower in patients who do not develop sinusitis). Reintubation should be avoided if possible. (a) Nasotracheal intubation increases the risk of sinusitis,^{117,118} which may increase the risk for VAP.^{111,119}

Perform comprehensive oral care,^{89,120-124} with an antiseptic solution.¹²⁵⁻¹²⁸

- 1- Perform tooth brushing, oral cleansing with antiseptic solution (e.g. Chlorhexidine 0.12%) and suctioning, twice daily.
- 2- Antiseptic oral rinse with Chlorhexidine after brushing.
- 3- In between tooth brushing, debride biofilm with swab impregnated with an oral solution (e.g. hydrogen peroxide) and suctioning simultaneously, every 4 hours.
- 4- Apply a mouth moisturizer to the oral mucosa and lips to keep tissue moist as needed.

Oral Care Rationale and Other Considerations:

(a) Oropharyngeal cleaning and decontamination with an antiseptic agent; develop and implement a comprehensive oral-hygiene program (that might include the use of an antiseptic agent) for patients in acute-care settings or residents in long-term care facilities who are at risk for healthcare associated pneumonia (II).^{120,129}

(b) Use of Chlorhexidine Gluconate (0.12%) oral rinse during the perioperative period on adult patients who undergo cardiac surgery (II).¹²³

(c) Antiseptic oral rinses (Chlorhexidine Gluconate, Cetylpyridinium Chloride [CPC]), added after brushing or done in conjunction with comprehensive oral care did achieve elimination of VAP.⁴¹³⁰

iii. Strategies to minimize contamination of equipment used to care for patients receiving mechanical ventilation

Remove condensate from ventilatory circuits. Keep the ventilatory circuit closed during condensate removal.^{84,89,96,131}

Periodically drain and discard any condensate that collects in the tubing of a mechanical ventilator, taking precautions not to allow condensate to drain toward the patient.

Change the ventilatory circuit only when visibly soiled or malfunctioning.^{84,132-137}

Do not, on the basis of duration of use, routinely change the breathing circuit (ie, ventilator tubing and ex- halation valve and the attached humidifier) that is in use by an individual patient. Change the circuit when it is visibly soiled or mechanically malfunctioning.

Store and disinfect respiratory therapy equipment properly.⁸⁴

Thoroughly clean all respiratory equipment to be sterilized or disinfected. Whenever possible, use steam sterilization or high- level disinfection by wet heat pasteurization at temperatures higher than 70C (158F) for 30 minutes for reprocessing semicritical equipment or devices (ie, items that come into direct or indirect contact with mucous membranes of the lower respiratory tract). Use low-temperature sterilization methods (as approved by the Office of Device Evaluation, Center for Devices and Radiologic Health, US Food and Drug Administration) for equipment or devices that are heat or moisture sensitive. After disinfection, proceed with appropriate rinsing, drying, and packaging, taking care not to contaminate the disinfected items.

Use sterile water to rinse reusable respirator equipment.⁸⁴

Preferentially use sterile water to rinse reusable semicritical respiratory equipment and devices when rinsing is needed after chemical disinfection. If this is not feasible, rinse the device with filtered water (ie, water that has been through a 0.2-mm filter) or tap water, and then rinse with isopropyl alcohol and dry with forced air or in a drying cabinet.

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INICC Bundle to Prevent Central Line Associated Bloodstream Infections in Intensive Care Units: An International Perspective.

Purpose

Previously published guidelines are available that provide comprehensive recommendations for detecting and preventing healthcare-associated infections, especially in the USA. The intent of this document is to highlight practical recommendations in a concise format designed to assist acute care hospitals worldwide in implementing and prioritizing their Central Line Associated Bloodstream Infections (CLAB) prevention efforts.

Introduction

One of the central premises of healthcare-acquired infection (HAI) control is that thorough surveillance knowledge of the occurrence of infections is essential to effectively address this public health burden. Such accurate knowledge is many times underestimated, and the actual, critical impact that HAI internationally is difficult to assess.¹⁻³

From the available literature, it is highly visible that the adverse consequences of HAI in the developing world—that is, attributable mortality,^{4,23} prolonged length of stay,^{4,5,7-10,12-14,17-24} extra hospital costs,^{4,10,21} and increased bacterial resistance^{11,24-34}—are more far-reaching in terms of severity than in the developed world. The prevalence of HAI internationally was found to be at least double the rates published by the European Centre for Disease Prevention and Control,³⁵ and triple those found in the USA.³⁶

CLAB Rates

In the case of DA-HAIs, the rate of device use internationally was found to be analogous or even lower to the one reported of U.S. ICUs by the National Nosocomial Infection Surveillance System (NNIS)/ National Healthcare Safety Network (NHSN) System;^{37,38} however, pooled mean rates identified in intensive care units (ICUs) internationally by the International Nosocomial Infection Control Consortium (INICC) were found to be exceedingly higher than those reported from U.S.'s ICUs by the National Healthcare Safety Network (NHSN).^{15,38,39}

The systematic review and meta-analysis on the burden of endemic HAI in developing countries by Allegranzi *et al* concluded that HAI prevalence was significantly higher in low and middle low-income countries compared to high-income countries. The density of DAI in critically ill patients was found to be from two- to 19-fold higher than those reported from developed countries.⁴⁰

In a review on incidence of CLABs in limited-resource countries by Rosenthal *et al.* in 2009, it was reported that the CLAB rate ranged from 1.6 to 44.6 cases per 1000 central line days in adult and pediatric intensive care units (ICUs) and from 2.6 to 60.0 cases per 1000 central line days in neonatal

ICUs, and was associated with significant extra mortality.⁴¹

Extra Mortality of CLAB

As regards mortality attributable to HAI internationally, it has been showed in different publications that it can range from 3 to 75.1%.^{11,5,9-14} In this respect, Rosenthal *et al* have shown mortality due to central line-associated bloodstream infections (CLABs) has rates that ranged from 4 to 75.1%.^{9,11} In a review, it was demonstrated that the CLAB rate was associated with significant extra mortality, with an odds ratio ranging from 2.8 to 9.5.⁴¹

Extra LOS and Cost of CLAB

Within the adverse consequences of HAI, prolonged length of stay (LOS) and the correlated extra hospital costs have been shown to cause a high impact at hospital and national levels. In order to calculate the cost of CLAB in intensive care units, a 5-year prospective nested case-control study was undertaken in 6 adult ICUs from 3 hospitals of Argentina, members of INICC. One hundred and forty-two patients with CLAB (cases) and 142 patients without CLAB (controls) were matched for hospital, type of ICU, year of admission, length of stay, gender, age, and average severity of illness score. The mean extra LOS for cases (compared to the controls) was 11.90 days, the mean extra antibiotic defined daily doses was 22.6, the mean extra antibiotic cost was \$1,913, the mean extra cost was \$4,888.42, and the excess mortality was 24.6%.⁴²

An 18-month prospective nested case-control study was undertaken at three hospitals in Mexico City, members of INICC, in four ICUs. Fifty-five patients with CLAB (cases) and 55 patients without CLAB (controls) were compared by analyzing hospital, type of ICU, year of admission, length of stay, gender, age, and average severity of illness score. The results indicated that extra LOS of patients with CLAB was 6.05 days. The mean extra cost of antibiotics amounted to \$598, the mean extra cost of other drugs was \$25.77, and the mean extra cost of hospitalization was \$8,326. The mean extra cost for cases (compared to the controls) amounted to \$11,591. Finally, the extra mortality attributable to BSI was 20%.⁴³

A study to estimate the excess LOS in an intensive care unit (ICU) due to CLAB was performed in hospitals members of INICC in three Latin American countries (Argentina, Brazil and Mexico). An analysis was made by means of a statistical model that accounted for the timing of infection. A cohort of 3,560 patients hospitalized in 11 ICUs was followed for 36,806 days. The average excess LOS due to a CLAB increased and varied between -1.23 days to 4.69 days.⁴⁴

CLAB Impact in Neonatal ICUs

In several studies, researchers have highlighted the extreme vulnerability of neonates hospitalized in neonatal intensive care units (NICUs) to mortality attributable to DA-HAI, with rates ranging from 24% in the pre-surfactant era to 11% in the post-surfactant era in the developed countries.⁴⁵⁻⁴⁸ The burden of CLAB in the NICU is not limited to mortality, and newborn sepsis was associated with adverse consequences in the central nervous system, longer duration of mechanical ventilation, and hepatic fibrosis and chronic lung disease higher incidence.^{47,49-52} However, internationally, access to knowledge regarding DA-HAI is scarce, and there is an insufficient recognition of the importance of surveillance for measuring the infection risks, outcomes and processes concerning the neonatal patient hospitalized in the NICU.⁵³⁻⁵⁶ In this respect, a recent study was performed to evaluate the impact of country socioeconomic status and hospital type on device-associated healthcare-associated infections (DA-HAIs) in 30 neonatal intensive care units (NICUs), from hospitals members of INICC in 15 countries. Its findings revealed that DA-HAIs were significantly lower in private than academic hospitals (10.8 vs. 14.3 CLAB per 1,000 catheter-days [p<0.03]), but not different in public and academic hospitals (14.6 vs. 14.3 CLAB per 1,000 catheter-days [p.0.86]).¹⁹ Furthermore, CLAB rates found in NICUs enrolled from low-income countries were significantly higher than in lower middle-income countries or upper middle-income countries.¹⁹

CLAB Risk factors

In a review about CLAB in developing countries, published by Rosenthal in 2009, a number of structural and behavior reasons were associated with higher rates of CLAB, and among their most common observations were overcrowded ICUs, insufficient rooms for isolation, lack of sinks, lack of medical supplies in general, including but not limited to alcohol hand rub, antiseptic soap, and paper towels. In addition, a lack of supplies for the wearing of maximal barriers during catheter insertion, a lack of chlorhexidine (and thus the use of povidone iodine), a lack of needleless connectors (and the subsequent use of three ways stopcocks), the use of vented IV containers instead of closed IV systems, a lack of ready to use drugs (and the subsequent reliance on manual admixture for all drugs) were noted. Moreover, poor performances in infection control practices, such as the case of using cotton balls already impregnated with antiseptic contained in a contaminated container, not covering insertion site with sterile dressing, storing drugs in

already open single use vials, reusing single use vials, leaving needles inserted in multiple use vials, taking fluids from 1000 cc container for dilution of parenteral solutions, and using tacky mats were paramount.⁴¹

In a study published by INICC in 2010, applying process surveillance a number of measures were found as associated with increased risk of CLAB, and they are the following: lack of hand hygiene, hand washing with non antiseptic soap, insufficient skin antisepsis with chlorhexidine, lack of sterile gauze or transparent dressing for catheter care, keep the central line in place beyond the needs, use of three ways stop cock, use of open infusion containers, among others.⁵⁷

CLAB Prevention

There are several measures to be considered as basic recommendations for the implementation of an infection control program, which should be consistent with the actual capabilities of the healthcare facility and personnel. The logical initial step is the organization of a surveillance system, as it permits the identification of local problems, distinctively specific to a particular institution, and will thus serve as guide for subsequent changes. Targeted surveillance and calculation of device-associated infection rates per 1000 device-days also allows benchmarking with other similar institutions. In this respect, "Outcome Surveillance" developed by INICC includes the systematic standardized measurement of DA-HAI rates and their associated effects: mortality, morbidity, extra length of stay, extra hospital costs, and bacterial resistance.⁵⁸ Surveillance data are essential to have an accurate knowledge of the burden of HAI and focus efforts on the areas that need more attention.^{29,34} Hospitals internationally need to start surveillance of critical areas, such as intensive care units, where DA-HAI pose the most threatening risks for patient safety. This first approach needs to be followed by the surveillance and monitoring of processes. Process Surveillance is necessary to monitor compliance with infection control prevention guidelines and basic measures, such as hand hygiene, vascular catheter care, urinary catheter care, and measures to prevent VAP. Thirdly, a continuing education program on HAI control and prevention must be addressed to healthcare-workers, particularly nurses, who have the greatest risk of transmission of organisms, and are essential to interrupt the transmission of HAI.^{30,41,57,59-65}

In this respect, the recommendations described in the guidelines published by the Society for Health Care Epidemiology of America (SHEA) the Infectious Diseases Society of America (IDSA), Center for disease control and prevention, and World Health Organization provide cost-effective preventative measures, feasibly applicable to infection control programs in developing countries.⁶⁶⁻⁷¹

It is to be noted that a reduction in DA-HAI rates cannot be expected to derive from surveillance by itself, and such educational efforts may be short-lived if regular reinforcement is absent. For this reason, in a context where there is lack of financial resources, it is compelling to find and show the

information on the incidence and magnitude of the burden of HAI at the hospital level. The collection of this data must be used for improvement of patient care practices, higher adherence to published infection control guidelines, and performance feedback.^{4,57,72-76} As reported in different studies internationally, disseminating data on morbidity and mortality due to HAI, and avoidable patient suffering and economic impact, is a necessary approach to move the hospital administration and healthcare workers into supporting the infection control program.⁶⁰

In a time-sequence analysis of the effectiveness of a multi-dimensional approach in reducing rates of central line-associated bloodstream infection (CLAB) in 15 countries from INICC, it was concluded that after implementing the infection control program, adherence to infection control compliance significantly improved, the CLAB incidence was reduced by 54% (16.0 to 7.4 CLABs per 1000 CL-days; RR 0.46, 95% CI 0.33 - 0.63, P< 0.001) and the number of CLAB-associated deaths decreased by 58%.⁵⁷

A recent study was performed by INICC on pediatric intensive care units (PICUs) of 6 developing countries to analyze the impact of a multidimensional infection control approach on CLAB rates. The approach included (1) a bundle of infection control interventions, (2) education, (3) outcome surveillance, (4) process surveillance, (5) feedback of CLAB rates, and (6) performance feedback of infection control practices. After intervention, the CLAB was reduced from baseline by 47% (13.0 to 6.9 CLABs per 1000 CL-days; RR 0.53, 95% CI 0.29 - 0.94, P 0.0271).⁷⁷ A similar multidimensional approach for CLAB reduction was adopted in another study conducted by INICC in NICUs of 11 developing countries. During baseline, the CLAB rate was 18.1 per 1000 CL days, and after intervention, the CLAB rate decreased to 12.1 per 1000 CL days [RR 0.67 (95% CI 0.51 - 0.8)], showing a 33% CLAB rate reduction.⁷⁸

The extracted findings from the available trials are representative and consistent evidence of the effectiveness that multi-faceted infection control strategies can have internationally. Within the broad spectrum of infection control, to successfully address the burden of HAI internationally, it has been key to implement surveillance of DA-HAI rates and of processes related to appropriate use and care of devices, educate healthcare workers, assess their practices, and provide them with feedback of observed processes, and ensure adequate observations of the recommendations set forth in published guidelines. These findings reveal that the reduction of DA-HAIs is feasible and cost-effective internationally; therefore, this valid evidence should lead to the mandatory organization of multi-dimensional infection control programs at every hospital.

Conclusion

To conclude, it is necessary to highlight that in order to reduce the hospitalized patients' risk of infection internationally, a multidimensional approach is primary and essential. As a first step it is necessary to include the implementation of DA-

HAI surveillance, because it effectively describes and addresses the importance and characteristics of the threatening situation created by HAIs. Additionally, surveillance of DA-HAI has played a fundamental role, not only in increasing the awareness of DAI risks, but also providing an exemplary basis for the institution of infection control practices. It is key that surveillance is implemented along with the monitoring of practices of infection control (process surveillance), education, presence of practice bundles, performance feedback, and feedback of DA-HAI rates and consequences. The high incidence of DA-HAI and mortality has been reduced by carrying out a multidimensional approach, with targeted performance feedback programs for hand hygiene and central line, ventilator, and urinary catheter care.^{55,72,73,76,79,80} Finally, it is of utmost importance to restrict the administration of anti-infective in order to effectively control of antibiotic resistance; however, this subject exceeds the scope of this bundle.

INICC Methodology

The INICC Surveillance Program includes two components: outcome surveillance (CLAB rates and consequences) and process surveillance (adherence to hand hygiene and other basic preventive infection control practices).⁸¹

The investigators at the participating hospitals were required to perform outcome and process surveillance by completing forms, which were then sent for their monthly analysis to the INICC office in Buenos Aires.⁸¹

Outcome Surveillance

The INICC Surveillance Program is focused on the methods and definitions for DAI developed by the U.S. Centers for Disease Control and Prevention (CDC) for the National Nosocomial Infection Surveillance System (NNIS)/ National Health Safety Network (NHSN) program.^{82,83} However, the INICC methods have taken into consideration the different socioeconomic status and specific limitations of limited-resource countries, and were adapted for their application in this setting.⁸¹ Outcome surveillance includes rates CLAB per 1000 device-days; microorganism profile, bacterial resistance, length of stay, and mortality in their ICUs.

Process surveillance

Preventive strategies in INICC member hospitals are based on simple, inexpensive, evidence-based measures, which include outcome surveillance, process surveillance, education and performance feedback of outcome surveillance and process surveillance.⁸¹

Process surveillance is designed to monitor compliance with easily measurable, key infection control measures. It includes the surveillance of compliance rates for hand hygiene practices and some specific infection control measures for the prevention of CLAB.^{60,62,63,76}

Hand-hygiene (HH) compliance by healthcare workers (HCWs) is determined by measuring the frequency of HH performances when clearly

indicated, and such practices are monitored by the hospital's ICP during randomly selected 1-hour observation periods, 3 times a week. Although HCWs know that HH practices are regularly monitored, they are not actually aware of the precise moment in which observations are taking place.⁸¹

ICPs were trained to detect HH compliance and record HH opportunities and compliance through direct observation. The INICC direct observation comprises the "Five Moments for Hand Hygiene," as recommended by the World Health Organization (WHO). The "Five Moments" were designed on the basis of the evidence concerning DAI prevention and control, and include the monitoring of the following moments: (1) before patient contact, (2) before an aseptic task, (3) after body fluid exposure risk, (4) after patient contact, and (5) after contact with patient surroundings.⁸⁴

Training and Validation

Investigators are self-trained by means of a manual and training tool that describe how to perform surveillance and complete surveillance forms. Investigators have continuous e-mail and telephone access to a support team at the INICC Central Office in Buenos Aires, Argentina, which is in charge of responding to all queries within 24 hours. The INICC Chairman further reviews all queries and responses.

Surveillance forms for individual patients allow internal and external validation, because they include every clinical and microbiological criterion for each type of DAI, such as temperature, blood pressure, use of invasive devices, cultures taken, culture results, antibiotic use. Surveillance also includes a form where positive cultures are registered and matched with patients' forms.

On a monthly basis, participating hospitals submit the completed surveillance forms to the INICC

Central Office, where the validity of each case was checked and the recorded signs and symptoms of infection and the results of laboratory studies, radiographic studies, and cultures were scrutinized to assure that the NNIS System criteria for device-associated infection were fulfilled.

The ICT member who reviewed the forms completed at the participating AICU was able to verify that criteria for infection had been met accurately in each case. Additionally, the original patient data forms were further validated at the INICC Central Office, before data on the reported infection were entered into the INICC's database. To that end, queries were submitted from INICC office in Buenos Aires to the ICT teams at each hospital, challenging those cases with suspected CLAB, and data were uploaded after receiving the reply from hospital teams. Finally, the INICC team performed consistency analyses of database, such as age, gender, dates, among other data, and reviews of medical records that compared data registered in forms and data in medical records.

Performance Feedback

The concept of using performance feedback of outcome surveillance and process surveillance as a valuable control measure in limited-resource hospitals was based on its effectiveness as proved in previous INICC studies.^{60,62,63,76,80,85}

The INICC Central Office team prepared and sent monthly chart reports to each participating hospital that detailed their rates of CLAB, microbiology profile, and rates of adherence to hand hygiene, among other infection related data. The participating ICU staff received feedback on their performance at monthly meetings, by means of the review of said charts, which were posted in a prominent location in the ICU.

Bundle Background

Within the INICC program, the infection prevention bundle was based on the guidelines published by the Society for Health Care Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA) in 2008,⁶⁷ the Center for Diseases Control and Prevention (CDC) in 2011,⁸⁶ and the Joint Commission for Health Care Accreditation (JCAHO) in 2012.⁸⁷ All them describe evidence-based interventions and recommendations for CLAB prevention in the ICU. Within the international context, outcome and process surveillance, integrated in an intervention bundle with performance feedback of infection control practices, has been shown to successfully reduce and control DAIs in different studies conducted in INICC member hospitals.^{60,62,63,80,85,88-91}

This bundle provides feasible and cost-effective infection control measures applicable internationally.

The INICC bundle consist on the following interventions:

1. Educate healthcare personnel regarding indications for intravascular catheter use, proper procedures for insertion and maintenance, and appropriate infection control measures to prevent intravascular catheter-related infections.^{65,92-97} Designate only trained personnel that has demonstrated competency for insertion and maintenance of central intravascular catheters.
2. Periodically assess knowledge of and adherence to guidelines among personnel involved in the insertion and care of intravascular catheters.
3. Performance of active surveillance for CLAB.⁹⁸
4. Use of an all-inclusive catheter cart or kit.⁹⁹
5. Use of a catheter checklist to ensure adherence to infection prevention practices at the time of CVC insertion.⁹⁹
6. Use a subclavian site, rather than a jugular or a femoral site, in adult patients to minimize infection risk for notunneled CVC placement.¹⁰⁰⁻¹⁰³ Weigh the risks and benefits of placing a central venous device at a recommended site to reduce infectious complications against the risk for mechanical complications (e.g., pneumothorax, subclavian artery puncture, subclavian veinlaceration, subclavian vein stenosis, hemothorax, thrombosis, air embolism, and catheter misplacement). Avoid using the femoral vein for central venous access in adult patients.
7. Use a CVC with minimum number of ports or lumens essential for patient care.¹⁰⁴⁻¹⁰⁶
8. When possible use ultrasound to guide the placement of central venous catheters to reduce cannulation attempts and mechanical complications. Ultrasound guidance should only performed by professionally trained staff
9. Perform hand hygiene, either by washing hands with soap and water or with alcohol – based hand rubs (ABHR). Hand hygiene should be performed before palpating catheter insertion sites as well as before and after inserting, replacing, accessing, repairing, or dressing an intravascular catheter.⁷³ Palpation of the insertion site should not be performed after the application of antiseptic, unless aseptic technique is maintained.^{61,107-109}
10. Maintain aseptic technique for the insertion and care of intravascular catheters.¹¹⁰⁻¹¹² When aseptic technique cannot be instituted (i.e. catheters inserted during a medical emergency), replace the catheter as soon as possible, i.e, within 48 hours
11. Use maximal sterile barrier precautions, including the use of a cap, mask, sterile gown, sterile gloves, and a sterile full body drape, for the insertion of CVCs, PICCs, or guidewire exchange.¹¹²⁻¹¹⁴
12. Prepare skin by applying alcohol-based disinfectant containing $\geq 0.5\%$ chlorhexidine before central venous catheter insertion and dressing changes.¹¹⁵⁻¹²⁰ Antiseptics should be allowed to dry prior to placing the catheter.
13. Use either sterile gauze or sterile, transparent, semipermeable dressing to cover catheter site.¹²¹⁻¹²⁶ Change dressing when it is dampened, loosened, or visibly soiled.^{121,122} Change transparent dressing used on short-term CVC at least every 7 days, except in pediatric patients for which the risk for dislodging catheter may outweigh the benefit of dressing change.¹²⁴ Change gauze dressing used on short-term CVC sites every 2 days. Visual check insertion sites during dressing change, if patient's condition permits. If patients have tenderness at the insertion site, fever without obvious source, and/or other clinical symptoms suggesting a local infection or bloodstream infection, the dressing should be removed to allow thorough examination of the site.
14. Do not routinely replace CVCs, PICCs, hemodialysis catheters, or pulmonary artery catheters to prevent catheter related infections.^{127,128}
15. Do not submerge catheter or catheter site in water
16. Disinfection of line hubs, needleless connectors, and infection ports before accessing the CL.^{129,130}
17. In patients not receiving blood, blood products or fat emulsions, replace administration sets that are continuously used, including secondary sets and add-on devices, no more frequently than at 96-hour intervals, but at least every 7 days.¹³¹⁻¹³⁵ Replace tubing used to administer blood, blood products, or fat emulsions (those combined with amino acids and glucose in a 3-in-1 admixture or infused separately) within 24 hours of initiating the infusion.¹³⁶⁻¹³⁹ Replace tubing used to administer propofol infusions every 6 or 12 hours, when the vial is changed, per the manufacturer's recommendation.¹⁴⁰
18. Employ hospital-specific or collaborative-based performance improvement initiatives in which multifaceted strategies are 'Bundled' together to improve compliance with evidence-based recommended practices.^{57,63,141}

19. Daily assessment the necessity of catheter, and promptly remove unnecessary catheters.¹⁴²⁻¹⁴⁴ Removal of nonessential catheters.^{145,146}
20. Performance of direct observation of hand hygiene compliance; placement and condition of sterile gauze or sterile polyurethane dressing on the insertion site;^{15,68} recording of the date of catheter insertion and last administration set change;^{15,67} gauze dressing replacement every 48 hours and replacement of transparent semi-permeable membrane dressings, at least, every 7 days, with the recording of the date and time of the dressing replacement; using structured observation tools at regularly scheduled intervals.^{15,147}
21. Do not administer systemic antimicrobial prophylaxis routinely before insertion or during use of an intravascular catheter to prevent catheter colonization or CLABSI.
22. Do not use topical antibiotic ointment or creams on insertion sites, except for dialysis catheters, because of their potential to promote fungal infections and antimicrobial resistance

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