
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. From the available literature, it is highly visible that the adverse consequences of HAI in the developing world—that is, attributable mortality, prolonged length of stay, extra hospital costs, and increased bacterial resistance—are more far-reaching in terms of severity than in the developed world. The prevalence of HAI internationally was found to at least double the rates published by the European Centre for Disease Prevention and Control, and triple those found in the USA.

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; 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).

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 DAIs in critically ill patients was found to be from two- to 19-fold higher than those reported from developed countries.

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.

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%. 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%.

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.

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%.

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%.

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.\textsuperscript{41}

**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.\textsuperscript{44-47} 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.\textsuperscript{46,48-51} 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.\textsuperscript{52,53} 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 \[p=0.86\]).\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{46}

**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.\textsuperscript{54} Surveillance data are essential to have an accurate knowledge of the burden of HAI and focus efforts on the areas that need more attention.\textsuperscript{8,74} 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.\textsuperscript{29,40,41,56,58,64}

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.\textsuperscript{45,70}

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..
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 CLAB control practices. After intervention, the CLAB rate 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). 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.

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-HAI 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 DA-AIs, 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. 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).

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.

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. 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. 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. 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. 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. 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.

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 if 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. 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, the Center for Diseases Control and Prevention (CDC) in 2011, and the Joint Commission for Health Care Accreditation (JCAHO) in 2012. 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. This bundle provides feasible and cost-effective infection control measures applicable internationally.

The INICC bundle consist on the following interventions:

Educate:
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. 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.

Outcome Surveillance:
3. Performance of active surveillance for CLAB.

Hand Hygiene and Aseptic Technique:
4. 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. Palpation of the insertion site should not be performed after the application of antiseptic, unless aseptic technique is maintained.
5. Maintain aseptic technique for the insertion and care of intravascular catheters. 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.
6. 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.
7. Prepare skin by applying alcohol-based disinfectant containing ≥ 0.5% chlorhexidine before central venous catheter insertion and dressing changes. Antiseptics should be allowed to dry prior to placing the catheter.

Specific Interventions:
8. Use of an all-inclusive catheter cart or kit.
9. Use of a catheter checklist to ensure adherence to infection prevention practices at the time of CVC insertion.
10. Use a subclavian site, rather than a jugular or a femoral site, in adult patients to minimize infection risk for notunneled CVC placement. 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 vein laceration, subclavian vein stenosis, hemotherax, thrombosis, air embolism, and catheter misplacement). Avoid using the femoral vein for central venous access in adult patients.
11. Use a CVC with minimum number of ports or lumens essential for patient care.
12. 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.
13. Use either sterile gauze or sterile, transparent, semipermeable dressing to cover catheter site. Change dressing when it is damped, loosened, or visibly soiled. 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. 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.
15. Do not submerge catheter or catheter site in water.
16. Three Ways Stopcocks should be avoided, as they represent a potential portal of entry for microorganisms into vascular access catheters and IV fluids. Closed catheter access systems are associated with fewer infections than open systems and should be used preferentially. When needleless systems are used, a split septum may be preferred over mechanical...
valves due to increased risk of infection with the mechanical valves.128-131

17. With multi-dose vials, 10 steps required to aseptically flush CVC vs. 4 steps with a **single use prefilled flushing device**. Flushing is an important element of intermittent I.V. therapy. Flushing with preservative-free 0.9 % sodium chloride (USP) or other flush solutions shall be performed before and after the administration of incompatible medications and solutions. Strongly encourages use of **single use prefilled flushing device**. Single-use IV flush vials reduce the risk of CLAB. 86

18. **Disinfection** of line hubs, needleless connectors, and infection ports before accessing the CL.132,133

19. 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.134-136 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.137,138 Replace tubing used to administer propofol infusions every 6 or 12 hours, when the vial is changed, per the manufacturer’s recommendation.143

20. Employ hospital-specific or collaborative-based performance improvement initiatives in which multifaceted strategies are **‘Bundled’** together to improve compliance with evidence-based recommended practices.96,62,144

21. Daily assessment the necessity of catheter, and promptly remove unnecessary catheters. **Removal of nonessential catheters.**145-147

**Performance Feedback:**

22. Performance of **direct observation** of hand hygiene compliance; placement and condition of sterile gauze or sterile polyurethane dressing on the insertion site;42,67 recording of the date of catheter insertion and last administration set change;42,66 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.42,130

**Avoid the following:**

23. Do not administer **systemic antimicrobial prophylaxis** routinely before insertion or during use of an intravascular catheter to prevent catheter colonization or CLABSI.

24. 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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