

**Preventing CLABSIs: Experimental Interventions and Opportunities for Diagnostic and Antimicrobial Stewardship in Solid Organ Transplant Patients**

by

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# **Preventing CLABSI: Experimental Interventions and Opportunities for Diagnostic and Antimicrobial Stewardship in Solid Organ Transplant Patients**

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## **Abstract**

Central line-associated bloodstream infections (CLABSI) are one of the deadliest healthcare-associated infections (HAIs) and are associated with mortality and longer hospital stays. One population that is at a higher risk of having a CLABSI is patients who have recently received solid organ transplants, due to their frequent hospital stays and immunocompromised status. Current best practices to avoid CLABSI are sterile insertion techniques of central venous catheters, proper line maintenance and daily checks for central line necessity. However, for the most vulnerable patients, further measurements may need to be taken. This literature review examined four experimental interventions—compliance audits, antimicrobial coated/impregnated catheters, antimicrobial dressings and patches at line entry site, and CHG bathing—for ease of use, cost, ease of implementation, and overall CLABSI reduction. CHG bathing and CHG dressings were found to be the most effective in reducing CLABSI rates and were cost effective, but compliance audits may be the most crucial in facilities with uncontrolled CLABSI, since adherence to best practice guides is necessary. Antimicrobial and diagnostic stewardship was also examined, as both practices play a critical role in reducing CLABSI rates, especially in solid organ transplant patients. Smart culturing to eliminate positives in the absence of true bloodstream infection, as well as prescribing antibiotics only when infectious signs and symptoms are present can all help decrease the risk of CLABSI and overuse of antibiotics, which can be detrimental for immunosuppressed patients. Infection prevention in healthcare settings is very significant to public

health, since reducing infections will not only decrease morbidity and mortality among patients but also reduce financial strain on healthcare systems. Implementing the right interventions, along with diagnostic and antimicrobial stewardship, can help reduce the rate of CLABSIs in healthcare settings and can keep patients safe.

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## **Preface**

I would like to first and foremost thank my Essay Advisor, Dr. Graham Snyder, for agreeing to help me formulate an in-depth literature review and guiding me on the research opportunities in the field of clinical infection prevention. Without his continuous support and content expertise, this literature review would not have been possible.

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## **1.0 Part One: Central Line Associated Bloodstream Infections (CLABSI) and Epidemiology**

According to the Centers for Disease Control and Prevention (CDC), there were 21,399 central line-associated bloodstream infections (CLABSI) in 2020.<sup>1</sup> The National Healthcare Safety Network (NHSN) defines a CLABSI as a laboratory-confirmed bloodstream infection in a patient where the central line was in place for >48 hours from the date of blood culture collection. Central venous catheters (CVCs) are inserted into major veins in order to administer drugs, draw blood, and give fluids in large amounts over a period of time. These central lines are necessary for some critically ill patients for monitoring and treatment, but they also pose a high risk for infection given the direct access to the patient's bloodstream.

CLABSI are associated with increased mortality and longer hospital stays, as well as higher costs for the healthcare system.<sup>2-5</sup> CLABSI are one of the most deadly healthcare-associated infections (HAIs), with a mortality rate between 12-25%.<sup>6</sup> Even after adjusting for severity of illness, CLABSI is associated with a doubling of the risk of mortality<sup>3</sup> and increased hospital stay of 24 days.<sup>5</sup> A single CLABSI event can cost approximately \$48,000, a significant burden for the healthcare system.<sup>7</sup>

Certain populations are at higher risk of developing a CLABSI from a central line given certain patient, provider, and device characteristics.<sup>8</sup> Patients who are immune-compromised, have chronic illness, are malnourished, have severe skin burns, or have been in the hospital for a long stay prior to insertion are at higher risk for developing infection. Emergency line insertion, frequent manipulation of the line, and lack of daily line care are also risk factors in developing CLABSI. Certain device characteristics, such as the anatomical placement and number of lumens,

can also place a patient at higher risk for developing CLABSI.<sup>9</sup> Proper insertion and maintenance, as well as minimizing use, are critical in preventing a CLABSI.<sup>8,10</sup>

### **1.1 Current Recommendations for Reducing CLABSI**

The CDC released a checklist in 2014 with prevention guidelines for both the insertion and maintenance of central lines.<sup>14</sup> The first set of recommendations focus on sterile procedures during insertion and maintenance of central lines. One of the most important recommendations, not only for the insertion and care of central lines but for all healthcare, is proper hand hygiene practice. This includes washing hands with soap and water or using an alcohol-based hand rub before donning gloves and after leaving a patient room. The World Health Organization (WHO) “5 Moments for Hand Hygiene” campaign details the importance of hand hygiene in patient safety.<sup>15</sup> Secondly, adherence to aseptic technique, as well as using maximal sterile barrier precautions during insertion and maintenance, is also recommended to reduce environmental contaminants. Thirdly, a disinfecting wash must be used prior to line insertion and maintenance to reduce the burden of skin commensals.

Placement of the central line can also impact the probability of a CLABSI. Placement of a CVC in the femoral vein in adults is not preferred due to its close proximity to the inguinal fold and its probability of staying moist, as well as its tendency to make patient ambulation difficult.<sup>16</sup> Subclavian catheterization is associated with the lowest risk for infection, followed by femoral and jugular catheterization.<sup>17</sup> Once inserted, a sterile transparent, semipermeable dressing should be placed over top of the insertion site to keep it clean and dry. Gauze dressings should be avoided and if necessary, changed every two days and transparent, semipermeable dressings are preferred

and should be changed every seven days. The site should only be accessed using sterile technique and dressing should be immediately changed if soiled, wet, or the dressing integrity is compromised.<sup>14</sup>

Lastly, all central lines should be monitored daily for necessity and checked for approved indications for removal of the CVC.<sup>14,18</sup> These approved indications are end of drug treatment, no central venous pressure measurement, infection, persistent occlusion, and damaged device. All central lines should be removed when there is no longer an indication for a CVC. If complications such as thrombosis, occlusion, or phlebitis occur, is necessary.<sup>18</sup>

Within the University of Pittsburgh Medical System (UPMC), a CLABSI best strategy guide is available through the employee portal.<sup>19</sup> Within this guide are standard practices for insertion and maintenance of CVCs at all UPMC facilities. This guide also includes checklists for competencies for central line maintenance, dressing changes, and various blood culture collection methods. Links for education modules are also included. The best strategies included in this guide are all recommended practices listed within the CDC checklist, as well as further measures such root cause analysis for identified CLABSI cases and the use of maintenance kits. Maintenance kits created for nurses and practitioners have step-by-step instructions and all of the materials needed to successfully change a central line dressing, including maximal sterile barrier materials and chlorhexidine gluconate (CHG) impregnated sponges. The use of maintenance kits ensures that all items needed are already organized and packaged together to reduce breaks in the sterile field to retrieve forgotten items during manual picking. These kits have proven to increase adherence to best practices during dressing maintenance and changes.<sup>20</sup>

## **1.2 Central Lines in Solid Organ Transplant (SOT) Patients**

Central lines are commonly found in patients who are receiving or have recently received a solid organ transplant (SOT). CVCs are used to help deliver medications to the SOT patient over an extended period of time, however, they can have additional uses for certain types of transplants, such as aiding in dialysis and measuring central venous pressure in kidney transplant recipients.<sup>21,22</sup> This makes medication administration, blood transfusions, and blood draws easier while undergoing and recovering from this major surgery. While central lines can be necessary to treat SOT patients, CLABSI are one of the primary infections seen in immunosuppressed patients, due to contamination of the CVC with normal skin flora<sup>23</sup> as well as increased frequency of healthcare and antimicrobial exposure. SOT recipients are given immunosuppressive drugs to reduce the chance of transplant rejection, making them more susceptible to infection, including those due to endogenous flora.<sup>24,25</sup>

Bloodstream infections still remain a notable life-threatening complication in SOT recipients.<sup>26</sup> Mortality rates from bloodstream infections vary based on type of transplant but range from as low as 3% in kidney transplant recipients to as high as 52% in liver transplant recipients.<sup>24</sup> Precautions such as housing SOT patients in positive-pressure rooms and starting them prophylactically on antimicrobials can reduce overall risk of infection following the transplant, but further measures may be needed in order to specifically reduce CLABSI in this high-risk population. The interventions outlined by the CDC focus on preventing site infections and on continued education for patients and providers and should be effective even for immunosuppressed patients with long-term catheterization, however, there are also experimental interventions that could be helpful in reducing CLABSI in high-risk groups if they cannot be controlled through these basic measures.<sup>23</sup>

## 2.0 In-Depth Review of Potential Interventions

To further reduce CLABSI incidence, many studies have investigated interventions that could be utilized in settings where the previously described interventions have not been successful in controlling CLABSIs. Using the special approaches mentioned in the 2014 update of the CDC CLABSI guidelines,<sup>14</sup> A literature search was conducted on PubMed for novel interventions to reduce CLABSI. Key words and phrases used were “CLABSI intervention,” “CHG bathing,” “antimicrobial catheters,” “performance feedback,” “antimicrobial patches,” “CLABSI reduction,” and “novel intervention for CLABSI.” Twelve articles were chosen to illustrate current findings (**Table 1**). The four most prevalent techniques—compliance audits, antimicrobial coated/impregnated catheters, antimicrobial dressings and patches, and CHG bathing— are outlined below.

**Table 1. Potential Interventions to Reduce CLABSI Incidence**

Intervention	Reference	Design	Setting	CLABSI Reduction?
Compliance audits/performance feedback	Cherifi, et al., 2013 <sup>27</sup>	Multicenter quasi-experiment	Five adult ICUs in two Belgian tertiary care hospitals	Yes
	Wall, et al., 2005 <sup>28</sup>	Program implementation/quality improvement	MICU at UW Medical Center	Yes

	Balla, et al., 2018 <sup>29</sup>	Program implementation/quality improvement	Tertiary-care NICU in India	Yes
Intervention	Reference	Design	Setting	CLABSI Reduction?
Antimicrobial coated/impregnated catheters	Yousif, et al., 2016 <sup>30</sup>	Randomized control trial (RCT)	Infusion therapy unit at The University of Texas MD Anderson Cancer Center	Yes
	Storey, et al., 2016 <sup>31</sup>	RCT	cardiovascular thoracic, MICU, and oncology units at a large, 800-bed tertiary community hospital	No
	Kramer, et al., 2017 <sup>32</sup>	Meta-analysis	N/A	Yes
Antimicrobial dressings and patches at line entry site	Karlnoski, et al., 2019 <sup>33</sup>	Retrospective cohort study	Seven different ICUs at Tampa General Hospital	Yes
	Webster, et al., 2017 <sup>34</sup>	RCT	929-bed tertiary-care hospital	No
	Righetti, et al., 2016 <sup>35</sup>	Prospective randomized crossover study	Hemodialysis unit at Uboldo Hospital in Italy	Yes
CHG Bathing	Frost, et al., 2016 <sup>36</sup>	Meta-analysis	N/A	Yes

	Dixon, et al., 2010 <sup>37</sup>	Observational cohort study	Surgical ICU at a level 1 trauma center	Yes
	Shah, et al., 2016 <sup>38</sup>	Meta-analysis	N/A	Yes

## 2.1 Compliance Audits and Performance Feedback

Despite detailed intervention bundles being put in place, hospitals can still struggle to keep CLABSI rates low.<sup>28</sup> Continued maintenance and adherence to all aspects of central line insertion and maintenance bundles can sometimes be difficult to maintain. Tracking only CLABSI rates can make it difficult to pinpoint the root causes of these infections, since there are so many possible steps that infection may be introduced. Implementing continuous quality improvement through the auditing of central lines and performance feedback could be one strategy to implement in systems where maintenance of these intervention bundles is an issue. These measures could include observations of line insertion, checklists for insertion and maintenance, and continued feedback on individual performance.

A quality improvement study conducted in an adult medical intensive care unit (MICU) found a reduction in incidence rate from 7.0 to 3.8 per 1,000 catheter days by creating checklists that had to be scanned into the computer for review.<sup>28</sup> This checklist included hand hygiene, trainee supervision, maximal sterile barriers, CHG skin prep, and conditions of CVC (emergent versus elective). There was also audit feedback for the healthcare workers after review of the checklists. This reduction in CLABSIs was sustained two years after the study ended.<sup>28</sup>

A similar study from Belgium used an observation method to determine if all bundle interventions were being performed during CVC maintenance.<sup>27</sup> This multicenter quasi-experimental model used three phases: a baseline assessment, introduction of education and supervision during maintenance and the removal of procedure supervision. This study found that the incidence rate from phase I to phase II decreased from 4.00 to 1.81 per 1,000 catheter days but increased from phase II to phase III from 1.81 to 2.73 per 1,000 catheter days. This indicates that monthly meetings have some impact on CLABSI reduction but is overall more effective when combined with procedure supervision.<sup>27</sup> These methods of supervision and periodic feedback have proven to be effective, even in settings with high CLABSI incidence. A study implementing a quality improvement initiative in a tertiary-care neonatal intensive care unit (NICU) in India found an incidence rate reduction from 31.7 to 3.5 per 1,000 catheter days when implementing strict hand hygiene completion times, use of checklists, and performance feedback.<sup>29</sup>

The biggest limitation to using continuous quality improvement measures is need for the continued upkeep.<sup>28</sup> Two of these studies measured post-implementation adherence to protocol<sup>27,28</sup> and both found that while still better than the baseline, providers had begun to slip from their performance during the intervention period. Creating an interdisciplinary team of physicians, nurses, and infection preventionists to continue to support this intervention would be needed.<sup>28</sup> However, given the current staffing shortages,<sup>39</sup> this may not be feasible. Another limitation noted in the Balla, et al. study was the inability to link CLABSI reduction to one specific intervention.<sup>29</sup> This specific study design included improved hand hygiene protocol along with the implementation of a quality improvement team, making it harder to pinpoint the most effective intervention in reducing CLABSI rates at this hospital.



Cost was not mentioned in any of these studies, but the cost to adequately staff a team to oversee this effort could be great. Cost analysis to determine additional staffing compared to a facility's CLABSI reduction would have to be calculated on a case-by-case basis.

## **2.2 Antimicrobial-coated/Impregnated Catheters**

Antimicrobial-coated/impregnated catheters have been commercially available as an intervention for CLABSI, however, efficacy studies have had varied results.<sup>32</sup> Since first becoming available, many different variations of antimicrobial catheters have been created and tested. Catheters can be coated or impregnated with various antimicrobial agents, such as therapeutic drugs with systemic use (minocycline, rifampin), topical asepsis agents (chlorhexidine), antimicrobial metals (silver), or a combination of these.<sup>40</sup>

A month-long, controlled clinical trial in an infusion therapy unit at the University of Texas MD Anderson Cancer Center showing an incidence rate of 1.7 per 1,000 catheter days in the non-CHG impregnated catheters as compared to 0 per 1,000 catheter days in the CHG-impregnated catheters group.<sup>30</sup> However, other studies did not find a significant difference between CHG and non-CHG-impregnated catheters, with a 18-month-long study in three high-risk units within an 800-bed tertiary-community hospital published in 2016 finding no significant difference between CLABSIs in CHG and non-CHG catheters.<sup>31</sup> A meta-analysis comparing eight studies with three different antimicrobial coatings—CHG, rifampin, and minocycline—found an overall reduction in CLABSIs in the coated catheters (2.40 per 1,000 catheter days) when compared to the uncoated catheters (1.23 per 1,000 catheter days). Additionally, this analysis found an 80% reduction in

CLABSIs in high-risk patients (burn patients, critically ill patients, and patients with cancer) when using coated catheters.<sup>32</sup>

While some of these studies found increased protection against CLABSIs, two of the studies also found that CHG-impregnated catheters were harder to insert and led to adverse events. In the Yousif, et al. study, the failure to thread rates were 11% and 2% in CHG and non-CHG coated catheters, respectively.<sup>30</sup> The Storey, et al. study found a similar result with 96% of the post-insertion bleeding requiring a thrombogenic dressing belonging to the CHG-coated catheter group.<sup>31</sup> Replacing current catheters with antimicrobial-coated catheters could be harder to implement than simply switching the product due to this increased failure to thread rate.

With antimicrobial-coated catheters costing approximately \$20 more each, this could be a cost-effective approach if there was clear evidence of reduction in CLABSI incidence. A cardiac intensive care unit in a children's hospital in Argentina found that using impregnated catheters in their population did not decrease the risk of CLABSI, making this intervention more expensive than uncoated catheters.<sup>41</sup> Without concrete evidence of CLABSI reduction, cost savings is difficult to determine.

### **2.3 Antimicrobial Dressings and Patches at Catheter Entry Site**

Similar to antimicrobial-coated catheters, antimicrobial dressings and patches placed at the entry site of the catheter have also been studied for potential CLABSI reduction. Since many CLABSIs occur due to exposure at the entry site of the central line<sup>35</sup> and can be caused by normal skin flora,<sup>23</sup> using an antimicrobial patch at the entry site may reduce possibility of infection.

Sponges can be impregnated with topical asepsis agents and antimicrobial metals and placed over the catheter entry site to reduce bacterial and fungal growth for at least seven days.<sup>34</sup>

Chlorhexidine gluconate (CHG) dressings have been tested and shown to be effective, with a randomized control trial spanning two six-month periods in hemodialysis patients in Italy citing a difference in incidence to be 1.21 and 0.28 per 1,000 catheter days in standard polyurethane dressing and CHG dressings, respectively.

Another randomized control trial at a 929-bed tertiary care hospital in Australia compared a less costly broad-spectrum antimicrobial, polyhexamethylene biguanide (PHMB), with CHG discs over five months and found no significant difference between the two treatments, indicating that PHMB could still be an effective treatment in preventing CLABSI while also providing some cost savings.<sup>34</sup>

A 2019 study from the University of South Florida's academic tertiary care hospital had a novel use of silver dioxide dressings, commonly used for surgical site wounds, as a central line insertion site dressing.<sup>33</sup> After a 12 month study period, there was a significant difference in incidence rate of CLABSI between the CHG impregnated sponge and silver dioxide dressings, 2.38 and 1.28 per 1,000 catheter days in CHG impregnated sponges and silver dioxide dressing, respectively.

The Righetti, et al. study found a significant cost savings of \$269,000 annually.<sup>35</sup> PHMB, while no significant difference was found between this treatment and the CHG discs, PHMB discs are cheaper and were proven to be just as effective, making it another cost savings option.<sup>34</sup> There was also a cost savings with silver dioxide dressings, estimated between \$4,000 and \$36,000 per 1,000 catheter days. Since there is little evidence of bacterial resistance to silver dioxide, this could be particularly useful for high-risk populations.<sup>33</sup>

## 2.4 CHG Bathing

CHG bathing is an intervention used at UPMC as part of the CLABSI best strategy guide, but there has been some varied evidence on its efficacy in preventing CLABSI.<sup>42,43</sup> Initial studies using 2% CHG-impregnated cloths show significant reduction in incidence ratio from 12.07 to 3.17 per 1,000 catheter days.<sup>37</sup> More recent meta-analyses further support this finding. One analysis looking at seventeen clinical trials found a 56% reduction in CLABSIs across the initial findings.<sup>36</sup> Another study analyzing results from four trials found the relative risk of 0.46 with a 95% confidence interval (0.34-0.63), supporting the reduction of CLABSIs with the use of 2% CHG-impregnated cloths.

The Shah, et al. study looked further into the costs associated with the addition of CHG bathing using impregnated cloths and found that the overall cost of a CHG-impregnated cloth was \$4.10 more than a nonmedicated cloth but was still ten times less expensive than a single CLABSI.<sup>38</sup> Looking strictly at cost savings from using CHG to reduce CLABSI, CAUTI, and *C. diff.*, there was an annual savings of more than \$815,000 from 20 averted infections across two studies.<sup>44</sup>

While seemingly an easy intervention to implement, there are significant challenges to successfully adding CHG bathing to a facility's standard of care.<sup>45</sup> One of the biggest challenges to daily CHG implementation is pushback from nurses and administrators.<sup>46</sup> Demonstrating the impact daily CHG bathing can have on bloodstream infection reduction is necessary. Standardizing CHG bathing procedure is also needed to implement this intervention.<sup>45,47</sup> There is also significant clinician concern towards

patients' skin sensitivities and their discomfort as CHG can be sticky until it has dried.<sup>46</sup> All of these challenges can make CHG bathing a complex behavioral intervention to implement.

**Table 2. Summary of Potential Interventions**

Intervention	Ease of Use	Cost	Ease of Implementation
Compliance audits/performance feedback	+	\$\$	+++
Antimicrobial coated/impregnated catheters	++	\$\$	++
Antimicrobial dressings and patches at line entry site	+++	\$	+++
CHG Bathing	+++	\$	++

To display ease of use and ease of implementation, a range from + to +++ is used, with + representing a more difficult intervention and +++ representing an easier intervention. Cost is represented with \$, with more costly interventions being represented with more \$.

## **2.5 Interventions Recommendations**

Since there are many different root causes that can be attributed to a CLABSI, the best approach to prevention is a bundle of interventions rather than one single intervention.<sup>48</sup> A combination of these experimental interventions, along with the current CDC recommendations, could be helpful in preventing CLABSI in high-risk populations. The four interventions were

compared for ease of use, cost, and ease of implementation (**Table 2**). Antimicrobial-coated lines do not currently show enough efficacy to justify implementation. However, CHG bathing, CHG dressings, and compliance audits have shown to be effective in reducing CLABSI incidence and cost effective overall. Silver dioxide dressings show promise, but with only one study trialing these patched with patients, further studies are currently needed. As always, adherence to best strategy guides is of utmost importance in preventing infection. Research studies provide insight as to how these interventions work in a controlled environment, but maintenance and adherence to these techniques remains critical in infection prevention.

### 3.0 Considerations of SOT and Immunosuppression

One special consideration that must be taken for immunosuppressed SOT patients is increased central line audits to check for necessity of central lines in these patients. Checking line necessity is included in the CDC checklist for all patients with CVCs, but this becomes especially important for patients with compromised immune systems who are likely to have a long-term CVC.<sup>24</sup> Balancing the ease of treatment and monitoring with the increased risk for infection can be difficult. More data is needed in this field to further understand how to maximize care and minimize infection risk in patients with long-term central venous catheterization.

Despite the plethora of basic and experimental interventions, there are still barriers to getting to zero. In order to further reduce CLABSI, integrated stewardship must be at the forefront. Along with the interventions for prevention of CLABSI discussed, antimicrobial and diagnostic stewardship are also necessary to reducing HAIs.<sup>49</sup> Even in immunocompromised patients, such as SOT recipients, antimicrobial usage should be restricted to only what is necessary to prevent the formation of multidrug resistant organisms (MDROs). Diagnostic stewardship in the form of smart blood culturing and peripheral blood draws can also decrease potential risk of CLABSI, as well as help to minimize the number of misidentified CLABSIs using the NHSN definition, as overcaptured CLABSI events under the current NHSN definition can lead to inappropriate antibiotic use.<sup>50</sup>

### 3.1 Antimicrobial Stewardship in SOT Patients

Antimicrobial resistant bacteria have become a major healthcare challenge, causing higher morbidity and mortality in infected patients, as well as higher healthcare costs associated with these longer stays. Antibiotic resistance mechanisms are naturally occurring in bacteria, but overuse and misuse of antibiotics in both humans and animals has accelerated this issue.<sup>51</sup> To prevent the over-prescription of antibiotics, antimicrobial stewardship programs have been formed. These programs aim to reduce the misuse of antibiotics through hospital leadership commitment, pharmacy expertise, tracking, and education.<sup>52</sup> In SOT patients, antimicrobial stewardship programs face unique challenges, most notably the elevated risk of infectious complications associated with immunosuppression, multidrug-resistant organisms due to prolonged exposure to prophylactic antibiotics, and donor-derived infections.<sup>53</sup>

Antibiotic-resistant bacteria can be the causative agent in CLABSIs. A retrospective study comparing three years of NHSN data on antibiotic resistance in CLABSI pathogens in oncology units versus the non-oncology adult populations in the same hospitals found that rates of CLABSI from fluoroquinolone-resistant *E. coli* and vancomycin-resistant *E. faecium* were 15% higher in the oncology unit when compared to non-oncology locations.<sup>54</sup> This could be due to the prophylactic use of antibiotics like fluoroquinolones in immunosuppressed patients, such as oncology and SOT patients.<sup>54</sup> One strategy that may be useful in reducing drug-resistant bacterial infections in immunosuppressed patients is through the consult of an infectious disease specialist to ensure the prophylactic regimen is stewardship-concordant. The consultation could decrease the current issues with antimicrobial stewardship in SOT patients, such as lack of de-escalation, antimicrobial spectrum being too broad, and duration being too long.<sup>53</sup>



### 3.2 Diagnostic Stewardship for Blood Culturing

Diagnostic stewardship is another important consideration in order to reduce the incidence of reportable CLABSI cases in SOT patients. Physicians significantly overestimate the likelihood of BSI in their patients, leading to excess blood culturing in patients.<sup>55</sup> However, there is a fine line between using blood culturing as a useful diagnostic tool and the overuse of blood culturing. Many issues can arise from too many blood cultures being collected, most notably potential exposure to infection from accessing the central line too often and the incorrect classification of other bloodstream infections as CLABSIs due to the NHSN definition.<sup>56</sup>

Optimization of blood culturing can reduce contamination of common skin commensals and avoid false-positive cultures.<sup>57</sup> False-positive blood cultures resulting from contamination or from a colonization found from surveillance blood culturing on a patient without symptoms of infection can be costly for the hospital and detrimental to the patient. False positive blood cultures that meet the criteria for a CLABSI still must be reported to the NHSN, resulting in a financial penalty, as well as covering the costs of the patient's extended hospital stay for treatment. The increased length of stay, along with the extra charges for pharmaceuticals to treat each patient, could result in over \$1,000,000 in extra funds annually for a 400 bed hospital.<sup>58</sup> There is also a significant clinical burden on patients with false-positive blood cultures. Along with an increased hospital stay, inappropriate exposure to antibiotics can lead to further complications including allergic reaction, development of antimicrobial-resistant bacterial strains, and increased risk of developing *C. diff* infection.<sup>57</sup> In order to reduce false-positives, peripheral blood draws can reduce detection of common commensals from the central line.<sup>59</sup> Potential changes in to the NHSN definition of a CLABSI to distinguish between true CLABSI and contaminated cultures may also help in reducing false-positive CLABSI cases.

The NHSN definition of CLABSI is designed for surveillance purposes and is not meant for clinical evaluation or patient care.<sup>59</sup> While NHSN definitions have always included some “background data noise” from being too broad and not encompassing all aspects of CLABSI within their criteria, with current, highly effective insertion and maintenance bundles reducing CLABSIs down to small numbers, there is a high likelihood that no system will ever reach zero.<sup>60</sup> Continued reporting of CLABSIs decreases hospital funding, damages provider morale, and hurts the reputation of the institution.<sup>60</sup> CLABSI reporting has become a bucket to include other BSIs from a secondary source in patients that have a central line. This could include infections from other inserted devices, surgeries, skin contaminants, or abdominal translocations that do not have adequate proof that this is the source are then classified as a CLABSI due to the lack of documentation proving it otherwise.<sup>60</sup> Current NHSN definitions lack specificity for complex patient populations and need revision.<sup>61</sup> Some suggest a revision to the definition to include “indeterminate source” as an option for a bloodstream infection could reduce the misclassification of some bloodstream infections as CLABSIs and thus reduce some of this current burden.<sup>60</sup>

#### **4.0 Public Health Significance and Conclusions**

Infection prevention in healthcare settings as a whole is deeply rooted in public health, since reducing infections will not only decrease morbidity and mortality among patients but also reduce financial strain on healthcare systems. As many as 28,000 patients die from CLABSI annually in the United States.<sup>62</sup> With public health infrastructure focusing on improving population health, prevention, and health promotion,<sup>63</sup> it is important that within the hospital, HAIs are reduced through interventions and considerations for all populations.

CLABSIs are one of the four most common HAIs and can result in severe disease and death. The current prevention measures outlined by the CDC are comprehensive, but additional measures may be needed in particular high-risk groups or in settings where these approved interventions cannot control CLABSIs. CHG bathing and CHG dressings have shown to be the most effective in reducing CLABSI incidence and are cost effective. However, implementing compliance audits and performance feedback could be the most crucial in facilities with uncontrolled CLABSIs, since adherence to insertion and maintenance bundles is necessary.

To get CLABSI rates to zero, especially in SOT patients, antimicrobial and diagnostic stewardship must be implemented. Reducing the number of false positive BSIs through smart blood culturing will save on cost and reduce on unnecessary antibiotic treatments, which can be detrimental for immunosuppressed patients. The biggest limitation to this review is the lack of data surrounding the epidemiology and prevention of CLABSIs in SOT patients. Future efforts focusing on checking for central line necessity in this population could help to find a balance between optimizing care and minimizing infection risk.

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