# Risk Factors for Central Venous Line Associated Bloodstream Infection in Pediatric Patients 0-18 Years of Age: A Cohort Study

by

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## DEDICATION

I dedicate this thesis to my mom and dad, Chris and Claude. They have supported me through this and every other endeavor I have taken on. Without their words of advice and encouragement, you would not be reading this. For that, and everything else, I am grateful.

To my brother, Alex, thank you for the humour to distract me when I needed it, and of course, the tech support. To Brandon, thank you for your support, your advice, and your convincing words when this seemed impossible. To the rest of my family and friends, I also extend my appreciation and gratitude.

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## ABSTRACT

This cohort study examined Central Venous Line (CVL) use and risk of Central Line Associated Bloodstream Infection (CLABSI) in patients 0 to 18 years of age at a pediatric tertiary care referral center serving 2.3 million people in Halifax, NS. [1] Data was collected between 1995 and 2013 and held in two prospectively maintained databases used for routine hospital surveillance and quality assurance practices. There were 666 CLABSI cases in 9,067 CVLs. The CLABSI rate per 1,000 line-days decreased over time with a large decrease in 2012. This may be due to infection control interventions, including a centre-wide hand hygiene campaign. Risk factors identified in this study are: Care group (an approximation of underlying illness), the use of double lumen CVLs, subclavian CVL insertion, and the use of dressings with gauze, absorbent pads, or pressure cuffs. The use of Port-A-Cath CVLs was the only protective factor identified in this study.

## LIST OF ABBREVIATIONS USED

| | |
|---|---|
| CDC | Centers for Disease Control and Prevention |
| CIHI | Canadian Institute of Health Information |
| CLABSI | Central Line Associated Blood Stream Infection |
| CLUR | Central Line Utilization Ratio |
| CNISP | Canadian Nosocomial Infection Surveillance Program |
| CONS | Coagulase Negative Staphylococcus |
| CVAD | Central Venous Access Database |
| CVL | Central Venous Line |
| HAID | Hospital Acquired Infection Database |
| ICU | Intensive Care Unit |
| IPCS | Infection Prevention and Control Service |
| IT Services | Information Technology Services |
| IWK | Izaak Walton Killam Health Centre |
| MSBP | Maximal Sterile Barrier Precautions |
| NHSN | National Healthcare Safety Network |
| NICU | Neonatal Intensive Care Unit |
| PICC | Peripherally Inserted Central Catheter |
| PICU | Pediatric Intensive Care Unit |
| TCPS | The Tri-Council Policy Statement |

## GLOSSARY

**Blockage:** Defined in this study as: difficulty or inability to flush or withdraw from the CVL, having a clot in the CVL, or otherwise having between one lumen and the entire CVL partially or completely blocked.

**Care group:** An approximation for underlying illness based on the hospital care unit most frequently accessed by participants.

**Central line:** See central venous line.

**Central venous access device:** See central venous line.

**Central venous line (CVL):** An intravenous device which allows medications and fluids to be administered directly to the main blood vessels of the body.

**Disconnect:** Any part of the line of the CVL becoming separated from the hub or external endpoint.

**External endpoint:** The external portion of the CVL that commonly lies outside the body but can lie just beneath the skin and must be accessed with a needle, as is the case with Port-A-Caths.

**Fracture:** The CVL being broken at some point between the exit site and the internal tip.

**In situ:** Positioned beneath the skin or otherwise within body tissues.

**Infiltration**: The internal tip of the CVL being outside the blood vessel.

**Internal endpoint:** The internal tip of the CVL that lies inside a main blood vessel.

**Leakage:** The CVL leaking fluids interstitially or at the exit site.

**Mechanical complication:** Any physical problem with a CVL that interferes with the device's functionality. See blockage, disconnect, fracture, infiltration, leakage, and migration.

**Migration:** The internal tip of the CVL becoming misplaced.

**Totally implantable CVL:** A CVL which must be accessed by needle through a hub which lays just beneath the skin.

**Tunnelled CVL:** A CVL intended for long-term use which lays flat beneath the skin for some length before entering the insertion vein.

**Nontunnelled CVL:** A CVL intended for short-term use which has a direct route between the insertion vein and the external environment.

**Peripherally Inserted Central Catheter:** A CVL intended for long-term use which is inserted in the extremities and threaded through peripheral blood vessels to reach main blood vessels.

**Port-A-Cath:** A brand name commonly used interchangeably with totally implantable CVLs. See totally implantable CVLs.

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# CHAPTER 1: INTRODUCTION

## 1.1. CENTRAL VENOUS LINES

Central Venous Lines (CVLs) are an essential part of care for many hospital patients. CVLs allow health care professionals to inject fluids directly into main blood vessels. This allows nutrition, medications, or chemotherapies to enter the blood stream quickly and at high volumes.[2] Traditional peripheral intravascular devices, which inject materials into the extremities, are not able to deliver fluids in this manner because peripheral blood vessels are too small to accept large volumes over a short period of time.[2] Additionally, CVLs may remain in situ long-term, which avoids excessive skin punctures for patients requiring frequent injections. CVLs are used with patients of all ages. CVL use in children is common for both inpatients and outpatients with illnesses such as cancer, gastrointestinal disorders, or cystic fibrosis.[2]

## 1.2. CENTRAL LINE ASSOCIATED BLOOD STREAM INFECTION

CVLs provide access for microbes to enter the intravascular space. Because of this, it is common for microbes to colonize CVLs while they are in situ. This colonization can be benign or it may result in infections of the device tunnel, exit site, or, most seriously, in an infection of the blood called a Central Line Associated Blood Stream Infection (CLABSI). In severe CLABSI cases, organisms in the blood may travel to, and establish themselves in, other parts of the body.[3] CLABSI complicates patient care, increases cost of treatment and length of hospital stay, often requires the placement of a new CVL and thus another surgery, and has a mortality rate of up to 25%.[4, 5]

The definition of CLABSI as stated by the Centers for Disease Control and Prevention (CDC) has become standard in North America and is used by the Canadian Nosocomial Infection Surveillance Program (CNISP). [4, 6] Based on this definition, patients are considered to have CLABSI if they have a blood culture positive for a known pathogen where another site could not be the source of infection, or if they have two blood cultures positive for microbes that are not known to be pathogens and one of the following symptoms are present: fever (>38°C), chills, hypotension, or appearance of infection at the insertion site. In patients under one year of age, these symptoms may include fever, hypothermia, apnea, or bradycardia. [6] These symptoms must be present in addition to positive blood cultures to avoid a false positive diagnosis due to transient bacteremia or contamination of the blood sample.

## 1.3. GAPS IN THE LITERATURE

The body of CLABSI research that focuses on pediatric populations is smaller than work with adult populations and studies are not as often replicated to confirm results. Furthermore, there is very little research on CLABSI in Canadian populations. The literature search yielded only four studies examining CLABSI risk in Canadian children. [7-10] These studies mainly focused on populations from Ontario and Quebec, with only one study including data from a pediatric subpopulation (infants < 32 weeks gestation) from the Maritime provinces. [8]

Most studies on CLABSI are based on US populations and thus within the US healthcare system. Investigating CLABSI in a Canadian pediatric population would provide more insight into CVL care and CLABSI within the context of Canadian health

care delivery. This enables the comparison of CVL use in Canadian versus other healthcare systems.

## CHAPTER 2: STUDY OBJECTIVES

The overall objective of this study is to improve the care of children who require Central Venous Lines (CVLs) This can be separated into two specific objectives:

1. To describe the incidence of Central Line Associated Bloodstream Infection (CLABSI) in patients ages 0-18 years who had CVLs placed at the Izaak Walton Killam Health Centre (IWK).
2. To determine risk factors and protective factors for CLABSI in patients ages 0-18 years.

# CHAPTER 3: LITERATURE REVIEW

A literature search was conducted for reviews and primary studies examining Central Line Associated Bloodstream Infection (CLABSI) in pediatric populations. The aim of this search was to identify potential risk factors for CLABSI in children (ages 0 - 18) and to evaluate the evidence of the effects these risk factors have on CLABSI risk. These variables could then be sought for inclusion in this study, if available.

## 3.1. SEARCH STRATEGY

A literature search was conducted within the MEDLINE PubMed database (*National Center for Biotechnology Information*, U.S. National Library of Medicine; Bethesda, Maryland). The PubMed search strategy can be found in Appendix A. To capture as many potentially relevant studies as possible, no restrictions on study design were included in this search strategy. Literature was also identified outside of the PubMed search. Relevant studies cited in articles retrieved from the PubMed search were incorporated into the literature review. Additionally, contact with experts in the field yielded several relevant studies to be included. Finally, national reports from the Centers for Disease Control (CDC), National Health and Safety Network (NHSN), and Canadian Nosocomial Infection Surveillance Program (CNISP) were found through Google searches. A flowchart of the literature search results can be found in Appendix B.

## 3.2. LITERATURE IDENTIFIED

The PubMed literature search yielded 444 studies. The titles of these were reviewed and 110 studies were identified as potentially relevant. Of these, 16 reviews were

identified and examined, with consideration given to study design, population of interest, and potential sources of bias. Five reviews were found to be suitable based on population age (0-18 years inclusive) and outcome of interest (CLABSI). Only one of these, published in 2005 by De Jonge et al, was a systematic review. The findings of the systematic review formed a preliminary outline of CLABSI risk factors to consider in primary studies. The other narrative reviews served as background information on CLABSI pathophysiology and prevention.

Using the risk factors mentioned in the De Jonge review, the abstracts of the 94 remaining studies were compiled into one electronic file and subjected to a keyword search for specific risk factors, as outlined in the De Jonge review. Abstracts containing keywords specific to desired risk factors were subject to full article review. For example, to compare evidence of the effect ICU exposure has on CLABSI risk, the abstracts of the 94 potentially relevant studies were searched electronically using applicable key-words, such as “intensive care” and “ICU”. The full article for any study considering ICU exposure’s effect on CLABSI was then reviewed. Study designs, populations of interest, and potential sources of bias were noted and results regarding ICU exposure as a risk factor for CLABSI were compared. Similar searches were conducted for all other risk factors outlined in the De Jonge review. Ultimately, 61 studies were identified in this manner and included in the literature review.

Additionally, 24 reports and studies found outside of the PubMed search. These were identified in citations from articles the retrieved from PubMed, through expert recommendation, and by Google search. Any report or study deemed relevant and useful was included in the literature review.

3.3. INCIDENCE OF CLABSI

CLABSI surveillance has become essential to quality assurance in health care. The reporting of CLABSI rates is now standardized in accordance with the National Healthcare Safety Network (NHSN), a surveillance program coordinated by the Centers for Disease Control and Prevention (CDC). This ensures consistency in denominators when reporting CLABSI rates, making the comparisons between reports simple. A summary of CLABSI rates in various prospective cohort studies that define CLABSI by NHSN standards can be found in Table 1.

**Table 1.** Summary of crude CLABSI rates from prospective cohort studies using pediatric populations

| Authors | Title | Year Published | Crude CLABSI Rate |
|---|---|---|---|
| Mahieu et al. [11] | Risk factors for central vascular catheter-associated bloodstream infections among patients in a neonatal intensive care unit | 2001 | 4.4/1000 Line-Days |
| Chien et al.[8] | Variations in central venous catheter-related infection risks among Canadian neonatal intensive care units | 2002 | 7.2 – 12.1/1000 Line-Days |
| Couto et al.[12] | Risk Factors for Nosocomial Infection in a Neonatal Intensive Care Unit | 2006 | 9.8% of participants |
| Pinon et al.[13] | A prospective 7-year survey on central venous catheter-related complications at a single pediatric hospital | 2009 | 0.46/1000 Line-Days |
| Abou Elella et al. [14] | Impact of Bloodstream Infection on the Outcome of Children Undergoing Cardiac Surgery | 2010 | 25.8/1000 Line-Days |
| Niedner et al.[15] | Epidemiology of Central Line–Associated Bloodstream Infections in the Pediatric Intensive Care Unit | 2011 | 3.1/1000 Line-Days |

| | | | |
|---|---|---|---|
| Zingg et al.[16] | Individualized Catheter Surveillance among Neonates: A Prospective, 8-Year, Single-Center Experience | 2011 | 8.0/1000 Line-Days |
| Touré et al.[17] | Totally implantable central venous access port infections in patients with digestive cancer: Incidence and risk factors | 2012 | 0.76/1000 Line-Days |
| Dudeck et al.[18] | National Healthcare Safety Network (NHSN) report, data summary for 2012, Device-associated module | 2013 | 1.4/1000 Line-Days (Pediatric Medical/Surgical Units) |

-CLABSI = Central line associated bloodstream infection

This table lists CLABSI rates in populations with varying heterogeneity. The variation in CLABSI rates listed may be partially explained by the variation in population characteristics or subgroups included in each study. It is important to note that CLABSI rates may vary greatly among subgroups of the same population. For example, a 2010 NHSN report stated that CLABSI rates for pediatric inpatient wards for medical/surgical, orthopedic, and rehabilitation patients had mean CLABSI rates of 1.5, 1.6, and 2.8 per 1000 line-days, respectively.[19] The variation in these CLABSI rates is likely related to the variation in patients' characteristics, or risk factors for CLABSI, among the inpatient wards mentioned.

### 3.4. RISK FACTORS AND PROTECTIVE FACTORS

CLABSI cases in children may be prevented by understanding risk factors and protective factors for CLABSI in pediatric patients. This may occur by avoiding modifiable risk factors, taking extra preventative measures for patients with non-modifiable risk factors, or promoting protective factors. A summary of risk factors and protective factors for CLABSI proposed in the literature can be found in Table 2.

**Table 2.** Summary of literature suggested risk factors and protective factors for CLABSI in pediatric populations

| Predictor | Increases or Decreases Risk of CLABSI? | Modifiable? |
|---|---|---|
| CVL types | Variable | No |
| Underlying Illness/ Immunocompromise | Increase | No |
| Age | Increase | No |
| Insertion Complications | Increase | Yes |
| Duration in Situ | Increase | Yes |
| Dressing Type | Increase | Yes |
| Clots and Blockages | Increase | Yes |
| Mechanical Complications | Increase | Yes |
| Parenteral Nutrition | Increase | Yes |
| Location of Insertion | Increase | Yes |
| Time Spent in the ICU | Increase | Yes |
| Antibiotics | Decrease | Yes |
| Barrier Precautions/Insertion Timing | Decrease | Yes |

-CLABSI = Central line associated bloodstream infection
-ICU = Intensive Care Unit

### *3.4.1. Non-modifiable Risk Factors*

#### 3.4.1.1. Types of CVLs

There are several types of CVLs used in clinical practice. The underlying disease to be treated and the urgency with which the CVL must be inserted influence which type of CVL will be used. Every type of CVL carries risks of infection, but some have greater risks than others. The main types of CVLs are tunnelled, nontunnelled, peripherally inserted, and totally implantable. Diagrams of each type of CVL can be found in Appendix C and their descriptions are to follow.[20]

Each CVL type consists of a tube with one end in a main blood vessel and the other end outside the body. The former is the "internal endpoint" where fluids and medications are released into the blood stream. The "external endpoint" is the site of injection of said materials, which is accessible to caregivers. The main differences

among CVL types are the distances between the internal and external endpoints and the structure of the external endpoint.

Tunnelled CVLs are placed near the blood vessel into which they will be inserted, but the line lies flat just below the skin for a distance before curving inward to enter the blood vessel. This tunneling provides a longer route for microbes to travel from the external endpoint to the internal endpoint, and so is thought to decrease the likelihood of clinical illness. Previous literature has found these CVLs to be less prone to infection than nontunnelled CVLs and can remain in situ for long periods of time.[2, 21, 22]

To the contrary, nontunnelled CVLs have the shortest and most direct route between the internal and external endpoints. The line leads directly into the blood vessel without being tunnelled. This makes them simple to insert, but also simple for microbes to migrate through. These CVLs are often used in emergency situations outside the operating room and are meant to be temporary until a more secure longer term CVL can be inserted.[21] This type of CVL has the highest rate of infection compared to other CVL types.[21]

Peripherally Inserted Central Catheter (PICCs), however, can be over 20 centimeters long and have external endpoints in the arms, legs, or head.[21] These CVLs are inserted by threading the line through peripheral blood vessels to reach main blood vessels. The extra distance between the external and internal endpoints hinders microbial migration, thereby discouraging CLABSI and making the CVL appropriate for long term use.[2, 21]

Lastly, totally implantable CVLs are tunnelled beneath the skin like tunnelled CVL, but do not have truly external endpoints. The Port-A-Cath chamber lies just beneath the skin and is accessed by a needle that must puncture the skin in order to reach

the CVL.[21] These CVLs require very little maintenance. The most likely way through which they may become infected are through poor aseptic technique when materials are injected or through colonization of the CVL upon insertion. These CVLs are very rarely infected and can remain in situ for years.[21]

3.4.1.2. Underlying Illness & Immunocompromise

CVLs are used to treat patients with many different conditions, some of which are associated with immunocompromise. Prospective studies have supported immunocompromise as an independent risk factor for CLABSI.[13, 23] However, many studies investigating risk factors for CLABSI in children limit their study sample to children with certain underlying illnesses or immunocompromise without a comparison group of children with other illnesses or who are not immunocompromised.[13, 23, 24] This leaves room for investigation of the effect of underlying illnesses and immunocompromise has on the risk of CLABSI with appropriate comparison groups.

3.4.1.3. Age

The literature also suggests that the younger a patient is, the more susceptible they are to CLABSI.[25-28] This also applies to prematurity in neonates, with a prospective study indicating that neonates weighing less than 750 grams at birth have an increased risk of CLABSI compared to heavier, more mature, neonates.[16] However, a more recent retrospective study by Yumani et al. (2013) suggested the increase in CLABSI risk associated with prematurity and low birth weight may be explained by prolonged hospital stay.[29]

The systematic review by De Jonge et al found older children have similar risks for CLABSI as adults, while younger children may be at increased risk.[17] This review cites

several studies, both prospective and retrospective, concluding that CLABSI risk decreases as patient age increases, with a plateau sometime during late childhood or adolescence where risk levels match those of young adults. [30-34] This finding was challenged by a prospective cohort study that found no association between age and risk of CLABSI. [35] The age threshold of vulnerability is difficult to pinpoint, though one study suggested children younger than four years of age are especially vulnerable. [36] However, this study was a retrospective case review so its findings should be further validated with a prospective study. [36]

There is a lack of recent studies on age and CLABSI risk (all but one of the studies cited above were all performed before 2000). In the past decade, standard practices in neonatal, cancer, and intensive care have also improved. These improvements may have altered the survival and/or infection rates for young patients, which could affect the role age has in CLABSI risk – as is suggested by Yumani et al. [29]

### *3.4.2. Modifiable Risk Factors*

#### 3.4.2.1. Insertion Complications

Ideally, all CVLs would be successfully placed during the first attempt at insertion. However, this is often not feasible and consequently several attempts at placement are required before the CVL is properly inserted. This provides multiple opportunities for skin flora to enter the internal tissues of the body, after which they may colonize the CVL and potentially cause CLABSI. This phenomenon has been examined and increased complexity and/or difficulty of CVL insertion has been linked to increased risk of CLABSI in pediatric patients in both prospective and retrospective cohort studies. [37-39]

3.4.2.2. Duration in Situ

CVLs may be more likely to develop CLABSI over time because of the extended opportunity for microbes to establish themselves on the device and cause infection. Duration in situ has been identified as a risk factor for CLABSI consistently in literature from North America, South America, Europe, and Asia since 2000. [14, 16, 40-43] The only challenge to this trend comes from a study by Downes et al[44], which reported no statistically significant association between duration in situ and development of CLABSI. However, this study found a statistically non-significant trend toward a critical period between 30 and 90 days in situ, where CLABSI was most likely to occur.

A chart review of children (mean age of 22 months) by Mohammed et al[42], and a retrospective cohort study of neonates by Sengupta et al[40], found this critical time to be after approximately one month in situ, similar to Downes et al. On the other hand, Neidner et al[15] conducted a prospective cohort study that found this critical period to be after seven days in situ. A recent retrospective study on PICCs in neonates also found a critical period for CLABSI risk of two weeks post insertion. [45]

3.4.2.3. Dressing Type

The external endpoint of a CVL is usually covered in a bandage or dressing. The type of dressing and the frequency with which it is changed may affect the risk of developing CLABSI. The De Jonge systematic review and a prospective multicentre study suggested that an air- and water-tight dressing, such as a transparent tape-like dressing, may reduce CLABSI risk because it prevents microbes from establishing themselves on the external portion of the CVL. [26, 46] However, these same studies, along with a prospective study and a meta-analysis, made the argument that the lack of air and

water exchange may compromise the integrity of the skin under said dressing, thus promoting infection. Therefore, a gauze-like dressing which allows gas and moisture exchange may be more protective against infection compared to transparent dressings. [26, 37, 46, 47] These findings were refuted, however, by a randomized clinical trial comparing transparent and gauze-like dressings showed little difference between the risk of CLABSI associated with each dressing. [48]

3.4.2.4. Mechanical Complications

CVLs may break, leak, shift in position, or malfunction in another mechanical way. When this occurs, colonized microbes may break free and enter the bloodstream, which can lead to CLABSI. [49] When CVLs are mechanically compromised, they may need to be repositioned, repaired, or replaced. These processes often require additional skin punctures, which presents the opportunity for microbes to establish themselves inside the body and cause CLABSI. This has been observed by Langley et al. in an early analysis of this data from 1994-2000, who reported statistically significant associations between CVL fracture, migration, or leakage and later CLABSI. [49] These findings are supported by other studies having found an association between mechanical complications and CLABSI.[50]

Difficulty administering fluids, withdrawing blood, or flushing the CVL may indicate a blockage in the CVL. One way these blockages may occur is by blood clots. When a CVL is inserted, the body responds by coating the CVL in proteins and coagulant factors, forming a fibrin sheath. [22] This provides a good medium upon which microbes may grow and form a biofilm, thereby increasing the risk of CLABSI. [22, 49, 51] Occasionally, the fibrin sheath may extend inside the lumen of the CVL essentially

forming a blood clot that blocks the CVL. [22] CVLs may also become blocked by an accumulation of crystallized medication, upon which a fibrin sheath may form. This may provide an additional medium for a biofilm, promoting further microbial growth. This has been supported by literature suggesting blood clots and blockages in CVLs increase CLABSI risk.[52]

CVL blockages may also be an indication that CLABSI is present. The excessive microbial growth and immune response to this growth may form a clot and/or blockage in the CVL. [22] Thus, blockages appear to be both a cause and consequence of CLABSI. This likely increases the association between blockages and CLABSI, but also poses a challenge in determining causation.

To prevent biofilm formation and blood clots, anticoagulants may be used. This has been found to reduce the risk of CLABSI. [53] However, some studies examining the effect of anticoagulants on the CLABSI risk have found little or no reduction in CLABSI risk with anticoagulant use. [21]

3.4.2.5. Parenteral Nutrition

Parenteral nutrition, or administering intravenous nutrition, is a necessary part of care for some patients. This may include total parenteral nutrition (TPN), where an array of non-fat nutrients is administered. If the patient requires fats to be administered intravenously, lipid therapy is used alone or along with TPN. The role of TPN as a risk factor for CLABSI has been repeatedly confirmed by prospective, retrospective, and case-control studies. [11, 43, 54, 55] The mechanism by which intravenous nutrition may increase the risk of CLABSI are increased microbial sustainability in the blood due to

lipid contamination, fluctuations in blood sugar, and compromised gut mucosa (through which microbes can enter the blood) due to a lack of enteral nutrition. [43, 54]

3.4.2.6. Location of Insertion

Several cross-sectional studies on pediatric CLABSI have found that CVL placement in the torso or upper extremities has a lower risk of CLABSI than femoral placement. [15, 55-57] This may be explained by the greater presence of microbes in the femoral area due to its proximity to the groin. However, other cross sectional and retrospective studies have found that femoral site insertions actually led to fewer CLABSI cases. [56, 58] One of these studies was set in a Neonatal Intensive Care Unit (NICU) and suggested that the femoral site led to fewer CLABSI cases because neonates are more often handled around the chest and neck, potentially disturbing CVLs placed in the upper body. [58] This raises the question of whether older patients, whose walking may disturb a femoral site CVL, would show different findings.

3.4.2.7. Time spent in the ICU

Time spent in the intensive care unit (ICU) has also been associated with an increased risk of CLABSI through case control and cohort studies. [5, 43, 54, 55, 59] However, it is difficult to conclude that presence in the ICU is an independent risk factor for CLABSI because patients in the ICU are already at an increased risk due to the severity of their underlying conditions and the frequency with which their CVLs are accessed. [43] For example, having been cared for in an ICU prior to CVL insertion has been linked to an increase in risk of CLABSI, suggesting ICU time is correlated with other factors affecting CLABSI risk. [55] Furthermore, many studies on CLABSIs were restricted to ICU patients, thereby eliminating the possibility to compare ICU and non-ICU patients.

[14, 54, 55, 59, 60] This leaves room for research into the role of ICU care on CLABSI risk, with comparisons between ICU and non-ICU patients.

### *3.4.3. Protective Factors for CLABSI*

#### 3.4.3.1. Antibiotics

Administration of antibiotics has been shown through prospective and cross-sectional studies to reduce risk of CLABSI in patients requiring CVLS as the presence of antibiotics prevents microbial growth and could plausibly inhibit the development of CLABSI. [21, 22, 55, 61] This may include the use of antibiotic impregnated CVLs, perioperative administration of antibiotics, or the administration of antibiotics for any purpose. Using preventative antibiotics as standard procedure may seem an obvious remedy for CLABSI, but the potential for antibiotic resistant microbes highlights the importance of identifying and controlling CLABSI risk factors instead of relying solely on antibiotics for CLABSI prevention.

#### 3.4.3.2. Barriers and Insertion Area

Ensuring an aseptic environment during CVL placement is perhaps the most effective way to avoid future CLABSI. This can be done through the use of Maximum Sterile Barrier Precautions (MSBP). [21, 26, 62, 63] MSBP were shown to be an effective method of CLABSI avoidance by Raad et al in 1994 through a randomized trial. [64] In the years following, other randomized trials showed similar results. [64-68] Ideally, all CVLs would be inserted using MSBP. However, in an emergency situation, CVLs are inserted outside the operating room in the emergency room, ICU, or care unit, where MSBP are not possible. Pediatric patients who had their CVLs inserted with without MSBP have

been found to be at an increased risk for CLABSI compared to patients who had their CVLs inserted under MSBP. [21, 26, 62, 63]

## 3.5. IMPLICATIONS OF LITERATURE SEARCH FOR THIS STUDY

Inconsistency in the literature surrounding some of the suspected risk factors for CLABSI and paucity of studies in pediatric populations indicates the need for further research in this area. Most risk factors mentioned in the previous sections contain some uncertainty or opportunity for further research. Where possible, these risk factors should also be examined further to establish or confirm best practice for CVL care and CLABSI prevention.

# CHAPTER 4: METHODS

## 4.1. STUDY DESIGN

A cohort of children ages 0-18 years who were treated at the Izaak Walton Killam Health Centre (IWK) between 1995 and 2013 was constructed and followed from Central Venous Lines (CVLs) insertion to removal. The outcome of interest was Central Line Associated Bloodstream Infection (CLABSI); exposures were known or suspected risk factors for CLABSI.

### *4.1.1. Rationale for Study Design*

Randomization was not feasible for this study due to the desire to examine several risk factors at once and the resources required to conduct a randomized controlled trial. Additionally, the seriousness of the outcome of interest (CLABSI) and the established clinical practice for avoiding and treating said outcome made randomization difficult to justify in an ethical sense. In order to conduct a randomized trial, the exposure must have clinical equipoise, meaning it is unclear whether it will affect the outcome of interest or cause harm. For example, the literature search yielded five randomized clinical trials examining the effect of Maximal Standard Barrier Precautions (MSBP) on CLABSI risk, which was a relationship not yet established. [64-68] Each of these studies found MSBP to be protective against CLABSI, making randomization of MSBP in subsequent studies unethical. This concept applied to several risk factors in this study.

Another way CLABSI has been examined is through case-control study designs. [41, 44, 54, 69-73] Case-control studies are limited, however, by the difficulties inherent to their

designs. First, as is often the case with retrospective designs, many of these studies used hospital records, which can vary greatly in their completeness and consistency of reporting.[44, 70, 71, 73] Second, incidence rates associated with specific exposures cannot be determined because the study design prevents the establishment of appropriate denominators.

Cohort studies are the most common study design used to examine CLABSI in pediatric populations.[9, 11-17, 33, 39, 59, 62, 74-79] The literature search yielded eight prospective cohort studies examining CLABSI in children. The CLABSI rates reported in these studies are listed in Table 1 of section 3.3. Cohort study designs suggest causation more reliably than case-control studies because exposure status may be assessed before the outcome occurs, thus establishing temporality. Although cohort studies cannot offer the same control over participant homogeneity as randomized clinical trials, they offer an internally valid way to examine harmful exposures that would be unethical to study through a randomized clinical trial. Thus, cohort study design is the most suitable choice for a study of CLABSI risk factors.

However, retrospectively collected data, which has been used in many cohort studies examining pediatric CLABSI, often has shortcomings with regard to data quality. Sources of retrospective data, such as chart review, participant interviews, or administrative databases maintained for another purpose, are often subject to missing values or inconsistent detail. Because of this, prospectively maintained data collected with the intent to be used in research, such as the data used in this study, is favorable for a cohort study examining CLABSI.

## 4.2. DATA SOURCES

This study uses data from the IWK Central Venous Access Database (CVAD) linked with the IWK Hospital Acquired Infection Database (HAID). The CVAD holds a record of every CVL inserted at the IWK since 1994. It was designed to collect exposure data for several elements associated with CVLs, such as age of patient, environment of CVL insertion, underlying illnesses, etc. prior to the outcomes of CVL complication or removal of the CVL without complication. The data was and continues to be collected prospectively during the course of patient care.

Targeted hospital acquired infections, including CLABSI, are identified by trained Infection Prevention and Control Service (IPCS) nurses in an ongoing surveillance program. All hospital acquired infections since 2006 are recorded in the HAID. This database includes information on admission dates, underlying illness, reason for admission to the IWK, unit of admission, infection date, infecting pathogen, etc. This data has been and continues to be collected prospectively through routine hospital surveillance.

## 4.3. LINKAGE

The HAID and CVAD were linked to create a cohort of children who had CVLs inserted at the IWK. The HAID contained information on CLABSI cases from 2006 onward. CLABSI rates prior to 2006 were determined from information in the CVAD.

The HAID and the CVAD were linked first through a deterministic linkage and then a probabilistic linkage. The deterministic linkage was performed using a combination of the K Number (identification number used at the IWK) and date of CVL insertion. Due to missing data or data entry errors, the match was less than 100%, so

probabilistic linkage based on name and date of birth was performed. After the linkage was performed, all identifiers were removed.

## 4.4. ETHICAL CONSIDERATIONS

The Tri-Council Policy Statement (TCPS) on Ethical Conduct for Research Involving Humans outlines guidelines for research involving secondary datasets. [80] These guidelines raise several ethical issues that are applicable to this study. These issues and strategies to resolve them in accordance with TCPS requirements are outlined in this section.

The databases used in this study were created by the IPCS for patient care and quality assurance. The IPCS has ongoing access to these databases. The supervisor for this study, Dr. Joanne Langley, is part of the IPCS. She, too, has regular access to the full databases.

This study held minimal potential risk to participants as there was no intervention or change to patient care. All data were collected as part of routine patient care and infection surveillance. Because of the minimal risk to participants and the sample size being too large to practically obtain consent, it was justifiable that this study be conducted without acquiring consent from individual participants.

The main ethical consideration for this study was the potential loss of privacy if re-identification of participants occurred. Measures were taken to maintain data security. Access to the dataset was only available through password-protected IWK computers. Cells with five or fewer participants and data that allow back-calculation to individual values (such as date of birth calculated from age in days at insertion and date of CVL insertion) were suppressed in all outputs produced from the dataset.

Date of CVL insertion was suppressed in the dataset, but month and year of CVL insertion were included. To approximate patient age without re-identifying participants, each insertion was assumed to occur on the 15th day of the listed month of insertion. From that point on, the number of line-days was added to the patient's age at insertion to create an approximate age variable. The same technique was used to approximate an ongoing date variable. These variables allowed the examination of outcomes by patient age rather than age at CVL insertion, and seasonality of CLABSI rates – both of which were vital to this study.

This dataset will be stored for five years after study publication. After that time, the data will be stored according to IWK Research Ethics Board guidelines. The IWK Research Ethics Board gave approval of this project on October 22, 2013 (approval number: 1014859).

## 4.5. INCLUSION AND EXCLUSION CRITERIA

Patients were eligible if they had their CVLs inserted between 1995 and 2013 at the IWK while they were between ages 0-18 years. Patients were followed beyond this age restriction until CVL removal if they reached their 18th birthday with their CVL in situ. Patients who had their CVLs inserted at another facility were excluded as there was no information on CVL insertion for these patients. Patients who were discharged with their CVLs in situ but still receiving care from the IWK through day clinics were included in the sample. Patients who transitioned their care to adult facilities while their CVLs were in situ were considered lost to follow up and their data were censored in the analyses.

## 4.6. POWER CALCULATION

There are 9,067 CVLs from 5,648 patients in the dataset. However, the univariate and multivariate analyses were conducted using only the first CVL in each patient. This limited the sample to 5,648 patients with 5,648 CVLs. A matrix was created to show power levels to detect differences in CLABSI rate with varying proportions of participants exposed to a theoretical risk factor with the assumption that the CLABSI rate in the unexposed group is 10%. This matrix was based on a sample size of 5,648 CVLs and can be found in Table 3. A difference in CLABSI rate of 10% or more between exposed and unexposed groups is considered clinically significant in many studies.[59, 74, 81] This matrix shows that greater than 90% power could be achieved for all differences in CLABSI rate equal to or greater than 5%, meaning that this study had ample power to detect clinically relevant differences.

**Table 3.** Matrix of power calculations over varying CLABSI rates and risk factor exposure levels

| | Proportion of Sample Exposed | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| CLABSI Rate in those Exposed | 10% | 20% | 30% | 40% | 50% | 60% | 70% | 80% | 90% |
| 5% | 0.99 | >0.99 | >0.99 | >0.99 | >0.99 | >0.99 | >0.99 | >0.99 | 0.99 |
| 6% | 0.89 | 0.99 | >0.99 | >0.99 | >0.99 | >0.99 | >0.99 | 0.99 | 0.91 |
| 7% | 0.61 | 0.88 | 0.95 | 0.97 | 0.98 | 0.97 | 0.96 | 0.90 | 0.69 |
| 8% | 0.29 | 0.51 | 0.64 | 0.71 | 0.73 | 0.72 | 0.66 | 0.56 | 0.36 |
| 9% | 0.09 | 0.15 | 0.19 | 0.22 | 0.23 | 0.23 | 0.21 | 0.17 | 0.11 |
| 10% | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 11% | 0.11 | 0.16 | 0.19 | 0.21 | 0.22 | 0.21 | 0.18 | 0.14 | 0.09 |
| 12% | 0.30 | 0.48 | 0.59 | 0.64 | 0.65 | 0.63 | 0.57 | 0.44 | 0.25 |
| 13% | 0.57 | 0.80 | 0.89 | 0.93 | 0.94 | 0.93 | 0.89 | 0.78 | 0.50 |
| 14% | 0.79 | 0.96 | 0.99 | 0.99 | 0.99 | 0.99 | 0.99 | 0.95 | 0.75 |
| 15% | 0.92 | 0.99 | >0.99 | >0.99 | >0.99 | >0.99 | >0.99 | 0.99 | 0.91 |

**Note:** Calculations are based on a sample size of 5,648 and an assumption that 10% of the unexposed group develops CLABSI.
-CLABSI = Central line associated bloodstream infection

## 4.7. STATISTICAL ANALYSES

### *4.7.1. Software*

All analyses, including the construction of the power matrix seen in Table 3, were conducted using Stata/SE 13 (Stata Corp., College Station, TX, US) on computers at the IWK.

### *4.7.2. Unit of Analysis*

If a patient had multiple CVLs, either consecutively or concurrently, those CVLs could not be considered independent. The descriptive analyses included all CVLs regardless of multiple CVLs per patient in order to provide the clearest picture of CVL use and CLABSI at the IWK. Here, using patients as the unit of analysis would have neglected all but the first CVL. Therefore, CVLs were used as the units of analysis in the descriptive analyses. To incorporate multiple CVLs per patient into the univariate and regression analyses used in this study, each CVL would have been considered separately, regardless of how many CVLs each patient had. This would have violated the lack of independence between multiple CVLs per patient and resulted in an under estimation of standard error and subsequent erroneous findings. Due to these complications with dependence, only the first CVL per patient was used in the univariate and regression analyses. Because the number of patients equaled the number of CVLs in the univariate and regression analyses, patients were used as the units of analysis for these analyses.

### *4.7.3. Data Management*

Each participant had observations for each day they had their CVL in situ for a total of 896,402 observations. Many variables were constant over all line-days for one participant (e.g. type of line). However, many variables changed for each patient based

on daily observations (e.g. presence of fever), which had to be manipulated prior to analyses. Additionally, several variables had categories with small groups, which needed to be aggregated to obtain stable estimates in the analysis. The following sections outline the data management used to remedy these issues.

#### 4.7.3.1. Missing Data

If a patient was discharged with their CVL in situ, they did not have data for the days they spent out of hospital. These patients were assumed to have had no new CVL complications during their time out of hospital unless otherwise documented and were followed until CVL removal. If data were missing due to transfer to another facility, patients were considered lost to follow up and censored in the analyses.

A similar strategy was used for the dressing type variable. Dressing type was only recorded on the day it was changed, leading to empty values for the remaining days it was in place. To remedy this, the last known dressing type replaced empty values. However, this strategy was not appropriate for Port-A-Caths as they often do not require dressings. To remedy this variability, patients with Port-A-Caths were placed in a separate dressing type category.

Information on antibiotic use was available only on the date of insertion. Only information on antibiotic use immediately before and after the CVL insertion was available. Unfortunately, there was no way to track antibiotic use over time after CVL insertion.

Unrecorded observations were approached differently depending on the covariate. For dichotomous yes/no variables, missing values were assumed to be “no.” This was reflected in all analyses. For variables with multiple categories with fewer than

5% of observations missing, hot deck imputation was used, whereby a missing value was imputed from a randomly selected record from the same insertion year. If a variable category had more than 5% of observations missing, these missing variables were separated into a category titled "unknown."

#### 4.7.3.2. Referent Categories

Referent categories were consistent for all univariate and regression analyses. Dichotomous yes/no variables used the "no" category as referent. For chronological variables, such as date of insertion and age at CVL insertion, the last category in chronological order was used as the referent category for all univariate and regression analyses. The most frequent category of non-chronological variables was used as the referent category.

#### 4.7.3.3. Small Groups

Many variables contained categories with very few participants. These are outlined in Table 4. This was a problem because such small categories often prevented regression models from converging. The strategy for handling small groups was slightly different depending on the type of category.

Variables with multiple categories often had an "other" category, which was recorded purposefully and did not reflect missing values. If a variable had an "other" category containing fewer than 5% of observations, this category was lumped with the most frequently observed non-"other" category that was not the referent category. Otherwise, "other" categories were left as stand-alone categories.

Remaining categories containing fewer than 5% of variable observations were not altered if they represented a clinically significant group dissimilar to other categories

within the same variable. If there was no clinically important reason to keep the small group separate, it was combined with the largest non-"other" category that was not the referent category.

#### 4.7.3.4. Time Lag to CLABSI

In order to capture associations between risk factors and CLABSI, and assuming the date the risk factor occurred preceeded the outcome by more than one day, a time lag to CLABSI was established for certain variables, where appropriate. This was done for variables that may theoretically exert their effect on CLABSI risk for a period of time after their occurrence. For example, assuming mechanical complications increase the risk of CLABSI, a CLABSI associated with a mechanical complication is not likely to manifest on the same day as the mechanical complication. Rather, there is likely period of time after the mechanical complication when a CLABSI associated with said complication could appear. Based on expert opinion (IPCS), the lag period to CLABSI was established as one month after applicable complications. Therefore, if a mechanical complication occurred in a CVL, the complication was considered to occur for the following 30 days, during which time the development of CLABSI could be partially attributed to the complication. These variables were used in the univariate and multivariate analyses.

#### 4.7.3.5. Handling of Risk Factor Variables

Data on specific underlying diagnosis was not recorded in the database. Since patients are cared for in subspecialty settings, the subspeciality care area assignment in which the child spent most of their line-days was used as an approximation of underlying condition (e.g. cancer, chronic renal failure, intensive care)

A CVL blockage was defined as having difficulty or being unable to flush or withdraw from the CVL, having between one lumen and the entire CVL blocked, or having a clot in the CVL. There was no distinction made between partial and complete blockages. Infiltration describes the internal tip of the CVL being outside the blood vessel into the surrounding tissues and is an indication for line removal. Similarly, migration describes the internal tip of the CVL being misplaced. In these cases, tip placement may be readjusted without CVL removal. Disconnect describes any part of the line of the CVL becoming separated from the hub or external endpoint. This problem may be solved without CVL removal. Leakage and fracture describe the CVL being broken or unable to deliver fluids to the appropriate tip location without leaking. Due to small cell counts all mechanical complications variables were combined except blockage, which remained separate from other mechanical complications.

Table 4 shows a summary of the data management used to prepare for the univariate and regression analyses. The frequencies displayed in this table represent counts of CVLs once the dataset was limited to first CVL per patient. It is important to note that the frequencies seen for "Blockage Within 30 Days" and "Mechanical Complication" variables represent line-days, not CVLs. These events could occur multiple times in one CVL and were listed as occurring every day during the 30 day time lag, as described in section 4.7.3.4, making it complex to identify a simple yes/no for these complications within each CVL. Thus, the total line-days each of these variables were listed as "yes" or "no" were reported instead of CVL-specific frequencies.

**Table 4.** Summary of variable manipulation and data management for regression analyses

| Variable | | CVLs [n (%)] | Action Taken |
|---|---|---|---|
| *Age* | | | |
| | Neonate (0-28 Days) | 2471 (43.8) | --- |
| | Infant (28 Days – 1 Year) | 831 (14.7) | --- |
| | Toddler (1-4 Years) | 704 (12.5) | --- |
| | School Age (5-9 Years) | 574 (10.2) | --- |
| | Teen (10-16 Years) | 1004 (17.8) | --- |
| | 17 Years & Older | 64 (1.1) | Referent |
| *Year of CVL Insertion* | | | |
| | 1995 | 286 (5.1) | --- |
| | 1996 | 251 (4.4) | --- |
| | 1997 | 245 (4.3) | --- |
| | 1998 | 262 (4.6) | --- |
| | 1999 | 234 (4.1) | --- |
| | 2000 | 252 (4.5) | --- |
| | 2001 | 278 (4.9) | --- |
| | 2002 | 226 (4.0) | --- |
| | 2003 | 264 (4.7) | --- |
| | 2004 | 311 (5.5) | --- |
| | 2005 | 300 (5.3) | --- |
| | 2006 | 311 (5.5) | --- |
| | 2007 | 368 (6.5) | --- |
| | 2008 | 325 (5.8) | --- |
| | 2009 | 366 (6.5) | --- |
| | 2010 | 359 (6.4) | --- |
| | 2011 | 350 (6.2) | --- |
| | 2012 | 366 (6.5) | --- |
| | 2013*** | 294 (5.2) | Referent |
| *Care Group* | | | |
| | Oncology/Hematology | 106 (1.9) | --- |
| | Nephrology | 815 (14.4) | --- |
| | Surgery(General/Specialty) | 720 (12.8) | --- |
| | General Pediatrics | 570 (10.1) | --- |
| | PICU | 1221 (21.6) | --- |
| | NICU | 2171 (38.4) | Referent |
| | Other | 15 (0.3) | Combined with PICU |
| | Missing | 30 (0.5) | Imputed |

| | | | |
|---|---|---|---|
| *Insertion Reason* | | | |
| | Oncology | 672 (11.9) | --- |
| | Difficult Peripheral | 587 (10.4) | --- |
| | Short Term ICU/OR Monitoring | 546 (9.7) | --- |
| | Intensive Care | 547 (9.7) | --- |
| | Malabsorption | 90 (1.6) | --- |
| | Prolonged Access | 2362 (41.8) | Referent |
| | Renal Failure | 43 (0.8) | --- |
| | Missing | 801 (14.2) | Categorized as “unknown” |
| *Insertion Timing* | | | |
| | Elective | 3464 (61.3) | Referent |
| | Urgent | 615 (10.9) | --- |
| | Emergency | 256 (4.5) | --- |
| | Missing | 801 (14.2) | Categorized as “unknown” |
| *CVL Type* | | | |
| | PICC | 3028 (53.6) | Referent |
| | Short-Term Nontunnelled | 1687 (29.9) | --- |
| | Long-Term Tunnelled | 146 (2.6) | --- |
| | Port-A-Cath | 723 (12.8) | --- |
| | Other | 64 (1.1) | Combined with short-term nontunnelled |
| *Concurrent CVL* | | | |
| | No | 5351 (94.7) | Referent |
| | Yes | 297 (5.3) | --- |
| *Lumen Count* | | | |
| | Single | 3661 (64.8) | Referent |
| | Double | 1820 (32.2) | --- |
| | Triple | 167 (3.0) | --- |
| *Insertion Side* | | | |
| | Right | 2365 (41.9) | Referent |
| | Left | 1900 (33.6) | --- |
| | Missing | 1383 (24.5) | Categorized as “Unknown” |
| *Insertion Area* | | | |
| | OR | 2322 (41.1) | Referent |
| | ER | 7 (0.1) | --- |
| | ICU | 509 (9.0) | --- |
| | NICU | 1936 (34.3) | --- |
| | Unit | 678 (12.0) | --- |
| | Other | 125 (2.2) | Combined with NICU |
| | Missing | 71 (1.3) | Categorized as “Unknown” |

| | | | |
|---|---|---|---|
| *Antibiotics Pre-Insertion* | | | |
| | No | 3125 (55.3) | Referent |
| | Yes | 2523 (44.7) | --- |
| *Antibiotics Post-Insertion* | | | |
| | No | 5582 (98.8) | Referent |
| | Yes | 66 (1.2) | --- |
| *Dressing Type* | | | |
| | Clear Transparent | 3521 (62.3) | Referent |
| | Clear Transparent with Absorbent Pad | 1302 (23.0) | --- |
| | Gauze | 8 (0.1) | Combined with Clear Transparent with Absorbent Pad |
| | Pressure | < 5 | Combined with Clear Transparent with Absorbent Pad |
| | Semi-Clear Woven | 96 (1.7) | --- |
| | Port-A-Cath | 723 (12.8) | --- |
| | Other | < 5 | Combined with Clear Transparent with Absorbent Pad |
| *Insertion Vein* | | | |
| | Jugular | 1386 (24.5) | Referent |
| | Arm | 1383 (24.5) | --- |
| | Head (Cephalic) | 817 (14.5) | --- |
| | Leg | 1253 (22.2) | --- |
| | Subclavian | 775 (13.7) | --- |
| | Other | 7 (0.1) | Combines with Arm |
| | Missing | 27 (0.5) | Imputed |
| *Tip Location* | | | |
| | SVC/RA | 2831 (50.1) | Referent |
| | Subclavian/Bracheocephalic | 777 (13.8) | --- |
| | Inferior Vena Cava | 617 (10.9) | --- |
| | Not Specified/Unknown | 1036 (18.3) | Combined with Missing |
| | Missing | 388 (6.9) | Categorized as “Unknown” |

| | | | |
|---|---|---|---|
| *Blockage in Past 30 Days*<br>*Frequencies reported are line-days | | | |
| | No | 503293 (90.6) | Referent |
| | Yes | 51980 (9.4) | --- |
| *Mechanical Complication in Past 30 Days*<br>*(Includes disconnect, fracture, leakage, and/or migration)*<br>*Frequencies reported are line-days | | | |
| | No | 549309 (90.6) | Referent |
| | Yes | 5964 (1.1) | --- |

-PICU = Pediatric intensive care unit
-NICU = Neonatal intensive care unit
-Imputed = Combined with other categories within the same variable at weighted random
-ICU = Intensive care unit
-OR = Operating room
-PICC = Peripherally inserted central catheter
-ER = Emergency room
-SVC = Superior vena cava
-RA = Right atrium

### *4.7.4. Descriptive Statistics*

Summary statistics on sociodemographics and clinical characteristics for all children with one or more CVLs were described in this section. For continuous variables, means with 95% confidence intervals were calculated. For categorical variables, frequencies were displayed as counts and percent represented [n (%)].

The proportion of IWK inpatients with CVLs each year was determined by calculating the Central line utilization ratio (CLUR). The formula for this measure is [n(central line days)/t(patient days)]. [82] Hospital-wide patient-day data were not available before 2006. Therefore, CLUR values could only be calculated for 2006 onward. It has been suggested that a low CLUR can be used as an indication of efficient CVL use and reduced CLABSI risk. [82] A facility's CLUR may also be an indication of CVL use policies and patient characteristics over time.

CLABSI rates and their 95% confidence intervals were calculated per 1000 line-days for the whole sample, by year, and by the covariates listed in Appendices D and E.

In addition to tabulating descriptive data, CVL use and CLABSI rates over time were summarized in graphs to display any changes in incidence of either of these over time. Tables and figures summarizing CLABSI rates were replicated using only the first CVL per patient and can be found in Appendix F.

### *4.7.5. Univariate Analysis*

#### 4.7.5.1. Logrank Tests

Logrank tests were performed on all covariates to compare expected and observed CLABSI incidences for each covariate. These findings were further investigated in the regression analyses.

#### 4.7.5.2. Kaplan Meier Curves

Several Kaplan Meier curves measuring time to CLABSI were generated. An unstratified curve was generated to describe time to CLABSI over the first year after CVL insertion for the entire sample. The shape of the unstratified Kaplan Meier curve was used to estimate the appropriate length of follow up for subsequent curves. Stratified curves were generated to describe time to CLABSI for different age groups, insertion year groups, care groups, and CVL types. In addition to describing CLABSI over time in situ, these curves were used to determine whether risk of CLABSI was constant or variable over time.

### *4.7.6. Regression Analyses*

Clinically, reason for insertion is highly affected by underlying condition, which was represented as care group for this study. The variables for insertion reason and care group would have contributed similar information to the multivariate analyses. Insertion

reason was included in the univariate regression analysis, but care group was chosen over insertion reason for the multivariate regression analysis.

#### 4.7.6.1. Justification for Cox Proportional Hazard Model

The binary outcome of this study (CLABSI vs. no CLABSI) suggested the use of either Cox Proportional Hazards or other types of survival analysis, logistic regression, or Poisson regression. Previous studies similar to this one have used these types of analyses. [11, 17, 59, 74] Further considerations in the choice of analysis included the unequal length of the observation period/time at risk and covariates that may change over time (e.g. presence of blockage).

Poisson and logistic regressions were not suitable as they assume equal time to follow up for all participants. CLABSI can occur days or years after CVL insertion, so defining a set follow up period for all participants was not suitable. Furthermore, methods to alter these models to adjust for varying time to follow up were cumbersome among simpler options.

Survival analyses are ideal for non-recurrent events such as death or immunity-inducing disease. Although CLABSI can occur twice in one person or CVL, this study only considered the first instance of CLABSI in each CVL as an outcome for the univariate and regression analyses. Thus, a multivariate survival analysis was deemed appropriate. The Cox Proportional Hazard was chosen for its simplicity to incorporate multiple covariates and its ability to adjust for time-varying covariates.

#### 4.7.6.2. Univariate Cox Proportional Hazards models

Hazard ratios with 95% confidence intervals for CLABSI were calculated for each covariate using Cox Proportional Hazards models. This allowed the individual

association between each variable category and CLABSI to be examined. Continuous variables, such as age at insertion, were divided into categories for the regression analyses.

#### 4.7.6.3. Multivariate Cox Proportional Hazards model

All covariates were entered into a Cox Proportional Hazards Model, regardless of significance levels in the univariate analysis. All analyses were controlled for year of insertion as this variable was included throughout the modeling procedure and remained in the final model. A backward elimination method was used to develop the final model. Variables not statistically significantly associated with CLABSI were removed from the model. If the removal of a covariate altered the coefficient of another covariate by 15% or greater, the removed covariate was placed back into the model and considered a confounder. If a variable was removed and not considered a confounder, a log-likelihood test was run between the new and previous models. If the log-likelihood test yielded a p-value > 0.05, the variable in question was permanently removed from the model. The final model contains only confounders, statistically significant covariates, and the year of insertion variable. Variables with statistically significant associations with CLABSI were considered risk factors or protective factors, depending on the direction of the association.

# CHAPTER 5:RESULTS

## 5.1. OBJECTIVE 1: TO DESCRIBE THE INCIDENCE OF CLABSI IN IWK INPATIENTS AGES 0-18 YEARS.

### *5.1.1. Sample Characteristics*

There were 5,648 patients with 9,067 Central Venous Lines (CVLs) in the sample, meaning that many patients had more than one CVL inserted during the study period. Figure 1 shows the age distribution of CVL recipients, both for the entire sample and limited to first CVL per patient. The figure shows the distribution of age at insertion is right skewed. Most CVLs were used in infants and neonates. The age distribution did not change substantially when the sample was limited to first time CVL users.

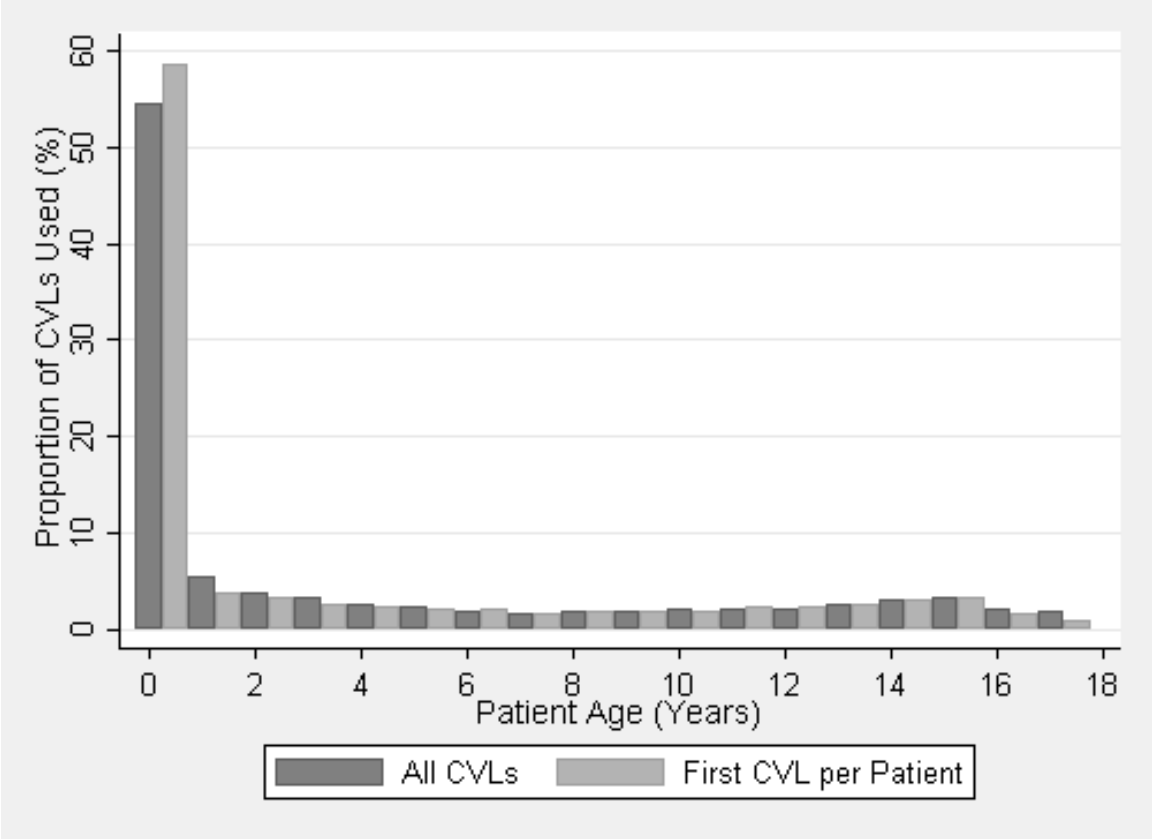


**Figure 1.** Distribution of patient age at CVL insertion for all CVLs and first CVL per patient
**Note:** n = 9,067 for all CVLs; n = 5,648 for first CVL per patient
-CVL = Central Venous Line

Because the majority of CVL users were under two years of age, a second graph of the age distribution of CVL users was created for patients 24 months and younger. This graph can be found in Figure 2 and shows that most CVL users under two years of age are newborns. Additionally, this graph shows no major differences between all CVLs and first CVL per patient.

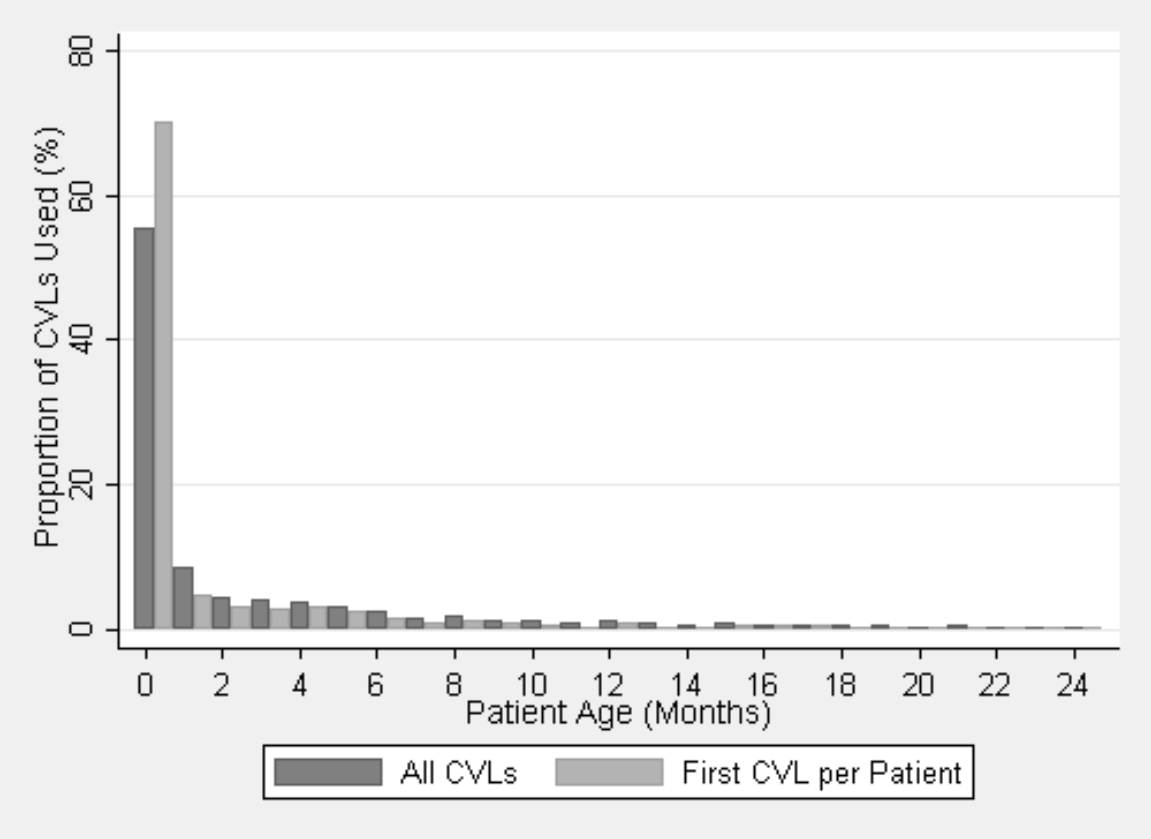


**Figure 2.** Distribution of patient age at CVL insertion for patient 24 months or younger for all CVLs and first CVL per patient
**Note:** n = 9,067 for all CVLs; n = 5,648 for first CVL per patient
-CVL = Central Venous Line

The distribution of patients in each care group can be found in Table 5. The frequencies found in this table are specific to patients, regardless of how many CVLs each patient had. The majority of patients requiring CVLs were cared for in the Neonatal Intensive Care Unit (NICU), followed by the Pediatric Intensive Care Unit (PICU).

**Table 5.** List of care groups with patient frequencies

| Care Group | Patient Count [n (%)] |
|---|---|
| Nephrology | 106 (1.9) |
| Oncology/Hematology | 815 (14.5) |
| Surgery(General/Specialty) | 720 (12.8) |
| General Pediatrics | 570 (10.1) |
| PICU | 1221 (21.6) |
| NICU | 2171 (38.4) |
| Other | 15 (0.3) |
| Missing | 30 (0.5) |
| Total | 5648 (100.0) |

-PICU = Pediatric intensive care unit
-NICU = Neonatal intensive care unit

### *5.1.2. CVL Characteristics*

A total of 9,067 CVLs were used in 5,648 patients over 171,877 in-hospital line-days and 896,402 total line-days in this population. There were five types of CVLs used: Port-A-Caths (totally implanted CVLs), Peripherally Inserted Central Catheters (PICCs), long-term tunnelled CVLs, short-term nontunnelled CVLs, and CVLs of miscellaneous structure. The frequencies each CVL type used in the dataset are summarized in Table 6. This table includes all CVLs, so patients with more than one CVL are represented more than once. PICCs are the most frequently used CVL structure, followed by short-term nontunnelled CVLs.

**Table 6.** List of CVL types with usage frequencies

| CVL type | CVLs [n (%)] |
|---|---|
| Short-Term Nontunnelled | 2943 (32.5) |
| Long-Term Tunnelled | 433 (4.8) |
| Other | 178 (1.96) |
| PICC | 4375 (48.2) |
| Port-A-Cath | 1138 (12.6) |
| **Total** | 9067 (100.0) |

-CVL = Central venous line
-PICC = Peripherally inserted central catheter

A large proportion of patients had more than one CVL, either consecutively or concurrently. A summary of the number of CVLs each patient required can be found in Table 7. At least half the participants had two or more CVLs. Most patients with multiple CVLs had each one at a time, with fewer patients having multiple concurrent CVLs.

**Table 7.** Number of CVLs in patients

| **Descriptor** | | **CVLs per Patient** |
|---|---|---|
| Mean | | 2.55 |
| Median | | 2 |
| Range | | 1-23 |
| Concurrent CVLs per Patient | | |
| | *One at a time* | 5355 |
| | *Two at a time* | 289 |
| | *Three at a time* | 5 |
| | *Four at a time* | 2 |

**Note:** n = 9,067 CVLs
-CVL = Central venous line

The central line utilization ratio (CLUR) from 2006 to 2013 is displayed in Figure 3. The CLUR is nearly constant over time. However, there was a drop in the CLUR during 2013.

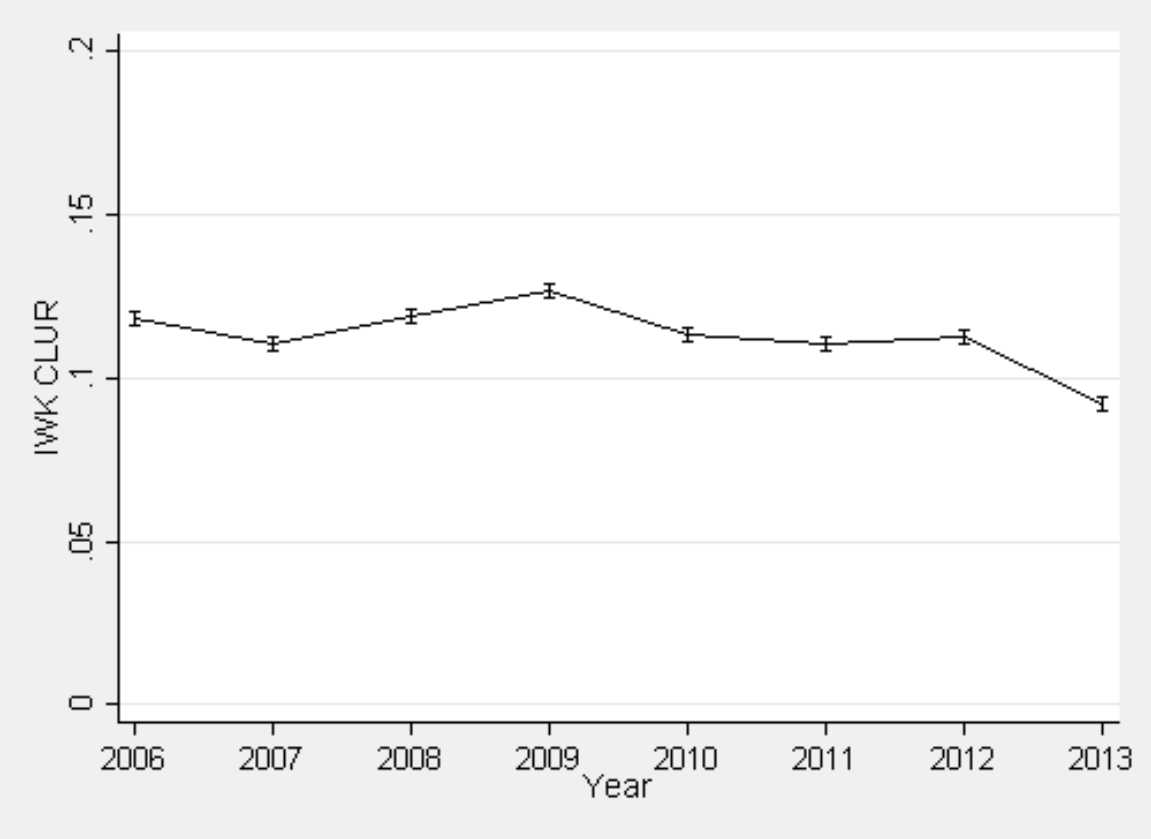


**Figure 3.** IWK CLUR between 2006 and 2013
**Note:** Central line utilization ratio (CLUR) is calculated for each calendar year using the following formula: [n(central line days)/t(patient days)]; Vertical lines indicate 95% confidence intervals around CLUR point estimates.
-IWK = Izaak Walton Killam Health Centre
-CLUR = Central line utilization ratio
-Central line = Central Venous Line (CVL)

*5.1.3. Mechanical Complications*

Table 8 summarizes the number of CVLs ever having mechanical complications at the IWK during this study period. This table represents the proportion of the total CVLs in this sample, regardless of whether patients required more than one CVL. Nearly one quarter of CVLs at the IWK became blocked, either completely or partially, at some point while in situ.

**Table 8.** Summary of mechanical complications in CVLs

| Mechanical Complication | Frequency [n (%)] |
|---|---|
| Blockage | 2140 (23.6) |
| Fracture | 117 (1.3) |
| Leakage | 540 (6.0) |
| Infiltration | 375 (4.1) |
| Disconnect | 253 (2.8) |
| Migration | 185 (2.0) |

**Note:** Denominators equal total CVLs in the sample (9,067).
-CVL = Central venous line
-Infiltration = Internal CVL tip lies outside the blood vessel, allowing fluids to spill into surrounding tissues

### *5.1.4. CLABSI*

Of the 9,067 CVLs used, 666 developed CLABSI at some point during the study period. A series of graphs and tables describing CLABSI rates over time are found in this section. The denominator for all CLABSI rates is in-hospital line-days. Tables and figures describing CLABSI rates were replicated using only the first CVL per patient and can be found in Appendix F.

Figure 4 shows the hospital-wide CLABSI rates over time. Overall, CLABSI rates have been decreasing from 1995 to 2013. Most notably, there was a substantial drop in CLABSI incidence between 2010 and 2012, which was sustained into 2013.

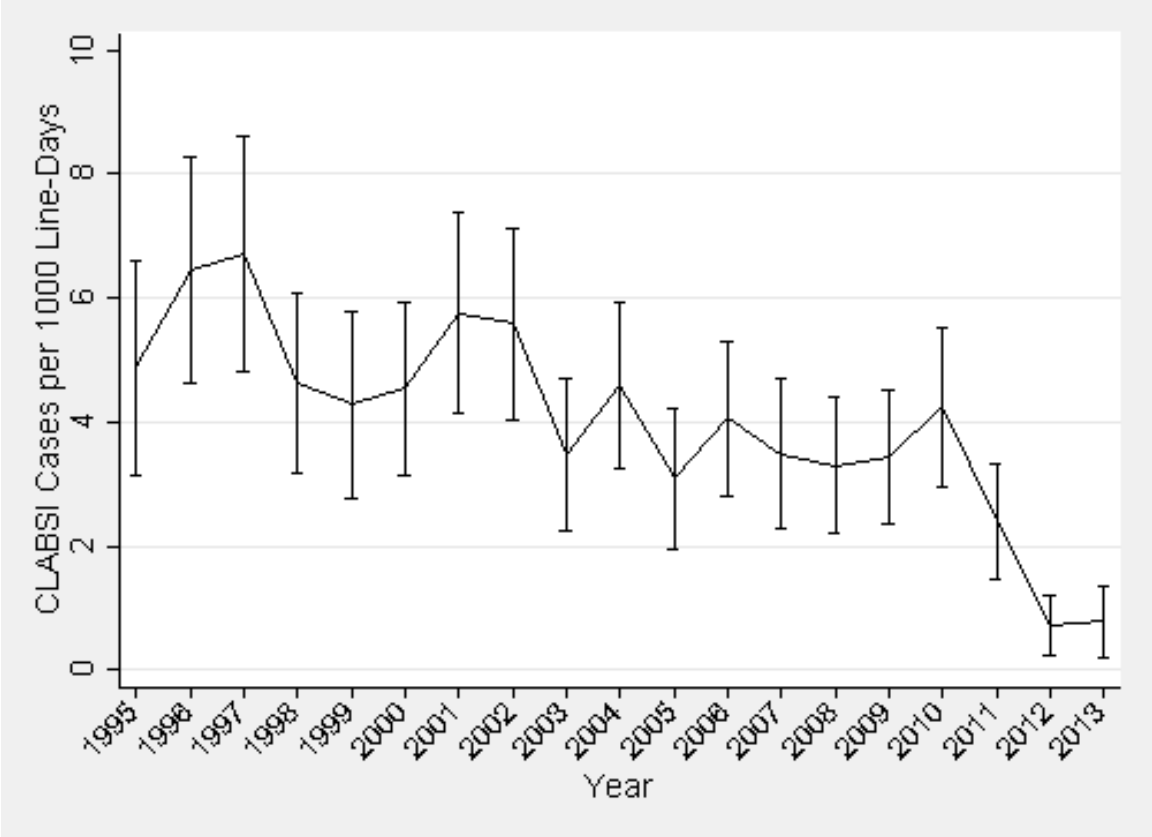


**Figure 4.** Hospital-wide CLABSI rate over time as cases per 1000 in-hospital line-days; vertical lines indicate 95% confidence intervals
**Note:** n = 9,067 CVLs
-CLABSI = Central line associated bloodstream infection

Table 9 shows the hospital-wide CLABSI rates by seasonal quarter over the entire study period. There appears to be no trend in CLABSI rates as seasons change.

**Table 9.** Hospital-wide CLABSI rates by season as cases per 1000 in-hospital line-days

| Quarter | CLABSI Cases per 1000 Line-Days | 95% Confidence Interval |
|---|---|---|
| 1 (January – March) | 3.9 | 3.4-4.5 |
| 2 (April – June) | 3.6 | 3.1-4.2 |
| 3 (July – September) | 4.2 | 3.6-4.8 |
| 4 (October – December) | 3.7 | 3.1-4.2 |

**Note:** n = 9,067 CVLs
-CLABSI = Central line associated bloodstream infection

CLABSI rates across age groups at time of insertion are displayed in Figure 5. Neonates appear to have the highest risk of CLABSI with CLABSI rates decreasing with age.

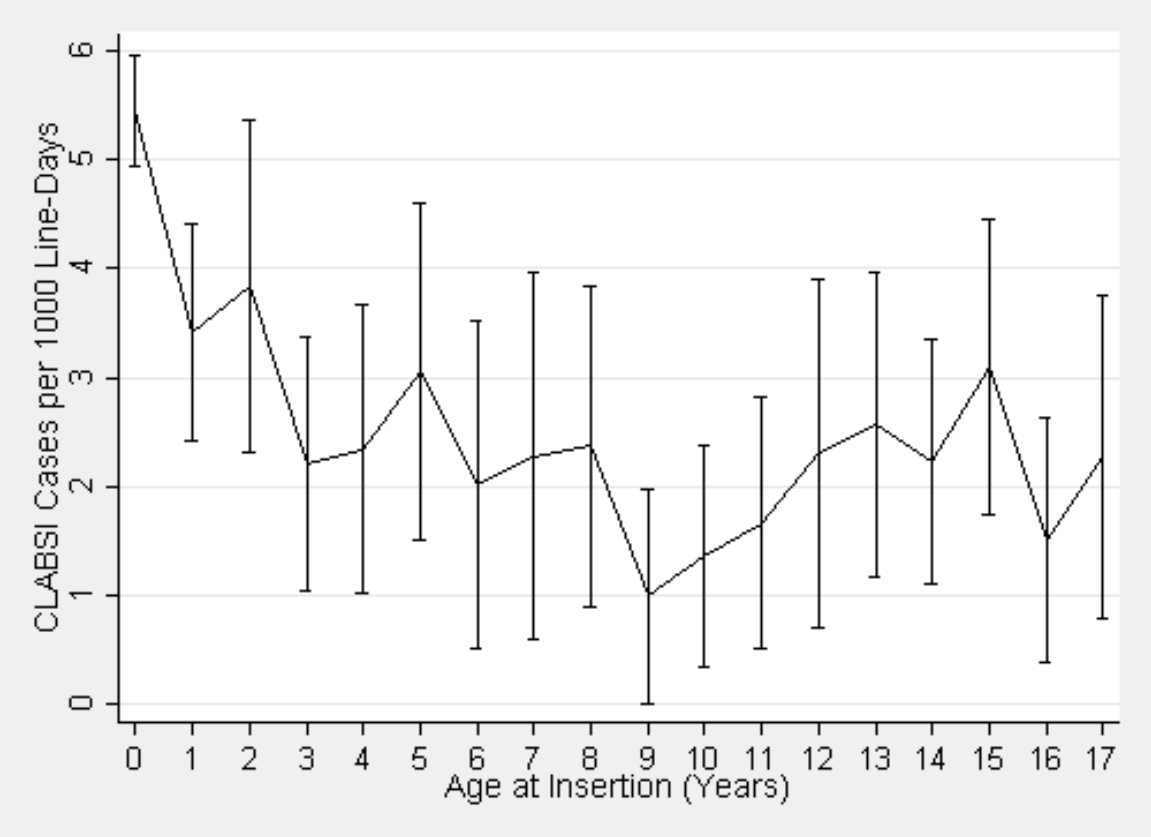


**Figure 5.** Hospital-wide CLABSI rate over age at CVL insertion as cases per 1000 in-hospital line-days; vertical lines indicate 95% confidence intervals
**Note:** n = 9,067 CVLs
-CLABSI = Central line associated bloodstream infection

Table 10 lists care group specific CLABSI rates over the study period. Patients with missing care group data ("unknown" category) showed the highest average CLABSI rate. Of the patients with known care groups, NICU patients had the highest CLABSI rates, followed by PICU patients. The corresponding table in patients with their first CVL can be found in Appendix F.

**Table 10.** Hospital-wide CLABSI rates stratified by care group as cases per 1000 in-hospital line-days; 95% confidence intervals also shown

| Care Group | CLABSI Cases per 1000 Line-Days | 95% Confidence Interval | CVL Count |
|---|---|---|---|
| Nephrology | 3.5 | 2.4-4.6 | 274 |
| Oncology/Hematology | 2.6 | 2.1-3.0 | 1301 |
| Surgery (General/Specialty) | 1.4 | 0.9-2.0 | 1232 |
| General Pediatrics | 2.3 | 1.7-2.8 | 1078 |
| PICU | 4.7 | 3.6-5.7 | 2212 |
| NICU | 6.3 | 5.7-7.0 | 2900 |
| Other | 4.6 | 0.0-11.0 | 23 |
| Unknown | 6.6 | 0.2-13.0 | 47 |
| Total | --- | --- | 9067 |

**Note:** n = 9,067 CVLs
-CLABSI = Central line associated bloodstream infection
-PICU = Pediatric intensive care unit
-NICU = Neonatal intensive care unit

Table 11 shows the relative frequencies of organisms that were isolated in the blood culture of patients with CLABSI. Gram positive bacteria, namely Coagulase Negative Staphylococcus (CONS), were implicated in the majority of CLABSI cases.

**Table 11.** Summary of infecting organisms

| Pathogen Type | Pathogen | Cases [n (%)] |
|---|---|---|
| **Gram Positive** | **---** | **479 (71.9)** |
| | CONS | 361 (54.2) |
| | *Staphylococcus aureus* | 60 (9.0) |
| | *Non-Hemolytic Streptococcus sp.* | 44 (6.6) |
| | *Bacillus sp.* | 8 (1.2) |
| | *Staphylococcus aureus* (Methicillin resistant) | ≤ 5 |
| | *Streptococcus pneumoniae* | ≤ 5 |
| | *Enterococcus sp.* | ≤ 5 |
| | *Rhodococcus* | ≤ 5 |
| **Gram Negative** | **---** | **134 (20.1)** |
| | *Enterobacter sp.* | 48 (7.2) |
| | *Escherichia coli sp.* | 26 (3.9) |
| | *Klebsiella sp.* | 26 (3.9) |
| | *Pseudomonas aeruginosa* | 21 (3.2) |
| | *Acinetobacter* | ≤ 5 |
| | *Stenotrophomonas maltophilia* | ≤ 5 |
| | *Serratia marcesans* | ≤ 5 |
| | *Morganella morganii* | ≤ 5 |
| **Fungus** | **---** | **20 (3.0)** |
| | *Candida Sp.* | 20 (3.0) |
| **Other** | **---** | **20 (3.0)** |
| **Unknown** | **---** | **13 (2.0)** |
| **Total** | | **666 (100.0)** |

-CONS = Coagulase Negative Staphylococcus

## 5.2. OBJECTIVE 2: TO DETERMINE RISK FACTORS AND PROTECTIVE FACTORS FOR CLABSI IN CHILDREN WITH CVLS.

All analyses serving Objective 2 were conducted using only the first CVL for each patient and patients were considered the units of analysis. Since season of insertion showed no association with CLABSI (see Table 8), month of insertion was not included in the univariate and regression analyses.

### *5.2.1. Univariate Analyses*

#### 5.2.1.1. Logrank Tests

Logrank tests were performed on each variable to detect any statistically significant differences between expected and observed events. The results of these tests are summarized in Table 12. There were statistically significant differences in CLABSI risk between the categories of the following variables: age, year of CVL insertion, care group, insertion reason, CVL type, insertion side, insertion area, antibiotics pre-insertion, antibiotics post-insertion, dressing type, insertion vein, and tip location. This means the occurrence of CLABSI over the categories in these variables was more or less common than expected based on the number of patients in each category.

**Table 12.** Summary of logrank tests exploring CLABSI risk across variables

| Variable | | CLABSI Cases Observed | CLABSI Cases Expected | P-Value |
|---|---|---|---|---|
| *Age* | | | | |
| | Neonate (0-28 Days) | 266 | 127 | <0.001* |
| | Infant (28 Days – 1 Year) | 24 | 32 | |
| | Toddler (1-4 Years) | 37 | 72 | |
| | School Age (5-9 Years) | 17 | 59 | |
| | Teen (10-16 Years) | 35 | 88 | |
| | Young Adult (17 Years & Older) | 5 | 7 | |

| | | | | |
|---|---|---|---|---|
| *Year of CVL Insertion* | | | | |
| | 1995 | 19 | 19 | <0.001* |
| | 1996 | 24 | 18 | |
| | 1997 | 25 | 18 | |
| | 1998 | 24 | 22 | |
| | 1999 | 26 | 21 | |
| | 2000 | 20 | 19 | |
| | 2001 | 27 | 21 | |
| | 2002 | 29 | 29 | |
| | 2003 | 17 | 22 | |
| | 2004 | 24 | 25 | |
| | 2005 | 16 | 21 | |
| | 2006 | 19 | 18 | |
| | 2007 | 22 | 24 | |
| | 2008 | 22 | 22 | |
| | 2009 | 22 | 21 | |
| | 2010 | 29 | 20 | |
| | 2011 | 12 | 18 | |
| | 2012 | 5 | 22 | |
| | 2013 | 2 | 15 | |
| *Care Group* | | | | |
| | Oncology/Hematology | 73 | 154 | <0.001* |
| | Nephrology | 8 | 10 | |
| | Surgery(General/Specialty) | 6 | 37 | |
| | General Pediatrics | 10 | 43 | |
| | PICU (includes “other”) | 27 | 20 | |
| | NICU | 260 | 119 | |
| *Insertion Reason* | | | | |
| | Oncology | 60 | 129 | <0.001* |
| | Difficult Peripheral | 39 | 34 | |
| | Short Term ICU/OR Monitoring | 10 | 8 | |
| | Intensive Care | 21 | 12 | |
| | Malabsorption | 5 | 6 | |
| | Prolonged Access | 176 | 139 | |
| | Renal Failure | 7 | 4 | |
| | Unknown | 66 | 52 | |
| *Insertion Timing* | | | | |
| | Elective | 249 | 244 | 0.36 |
| | Urgent | 35 | 45 | |
| | Emergency | 12 | 14 | |
| | Unknown | 88 | 81 | |

| | | | | |
|---|---|---|---|---|
| *CVL Type* | | | | |
| | PICC | 259 | 163 | <0.001* |
| | Short-Term Nontunnelled (includes "other") | 41 | 39 | |
| | Long-Term Tunnelled | 25 | 22 | |
| | Port-A-Cath | 54 | 155 | |
| *Concurrent CVL* | | | | |
| | No | 374 | 375 | 0.75 |
| | Yes | 10 | 9 | |
| *Lumen Count* | | | | |
| | Single | 295 | 297 | 0.82 |
| | Double | 83 | 82 | |
| | Triple | 6 | 5 | |
| *Insertion Side* | | | | |
| | Right | 130 | 127 | 0.03* |
| | Left | 127 | 149 | |
| | Unknown | 127 | 107 | |
| *Insertion Area* | | | | |
| | OR | 131 | 218 | <0.001* |
| | ER/ICU | 15 | 13 | |
| | NICU (includes "other") | 232 | 118 | |
| | Unit | 6 | 35 | |
| *Antibiotics Pre-Insertion* | | | | |
| | No | 223 | 186 | <0.001* |
| | Yes | 161 | 198 | |
| *Antibiotics Post-Insertion* | | | | |
| | No | 374 | 380 | <0.001* |
| | Yes | 10 | 4 | |
| *Dressing Type* | | | | |
| | Clear Transparent/Pressure (includes "other") | 105 | 93 | <0.001* |
| | Clear Transparent Absorbent Pad/ Pressure/Gauze (includes "other") | 109 | 34 | |
| | Semi-Clear Woven | 1 | 2 | |
| | Port-A-Cath | 169 | 255 | |
| *Insertion Vein* | | | | |
| | Jugular | 68 | 122 | <0.001* |
| | Arm (includes "other") | 131 | 79 | |
| | Head (Cephalic) | 40 | 40 | |
| | Leg | 89 | 46 | |
| | Subclavian | 56 | 97 | |

| | | | | |
|---|---|---|---|---|
| *Tip Location* | | | | |
| | SVC/RA | 215 | 265 | <0.001* |
| | Subclavian/Bracheocephalic | 41 | 41 | |
| | Inferior Vena Cava | 68 | 33 | |
| | Unknown | 60 | 45 | |
| *Blockage in Past 30 Days* | | | | |
| | No | 373 | 372 | 0.79 |
| | Yes | 11 | 12 | |
| *Mechanical Complication in Past 30 Days (Includes disconnect, fracture, leakage, and/or migration)* | | | | |
| | No | 381 | 382 | 0.67 |
| | Yes | 3 | 2 | |

-PICU = Pediatric intensive care unit
-NICU = Neonatal intensive care unit
-ICU = Intensive care unit
-OR = Operating room
-PICC = Peripherally inserted central catheter
-ER = Emergency room
-SVC = Superior vena cava
-RA = Right atrium

5.2.1.2. Kaplan Meier Curves of Time to CLABSI

Figure 6 shows a Kaplan-Meier curve for all pediatric patients with their first CVL. The risk of CLABSI changes over time in situ. The risk of CLABSI is highest in the first 60 days after CVL insertion and then gradually decreases. After day 180 CLABSI risk was very small and therefore, all further Kaplan-Meier curves were truncated at day 180.

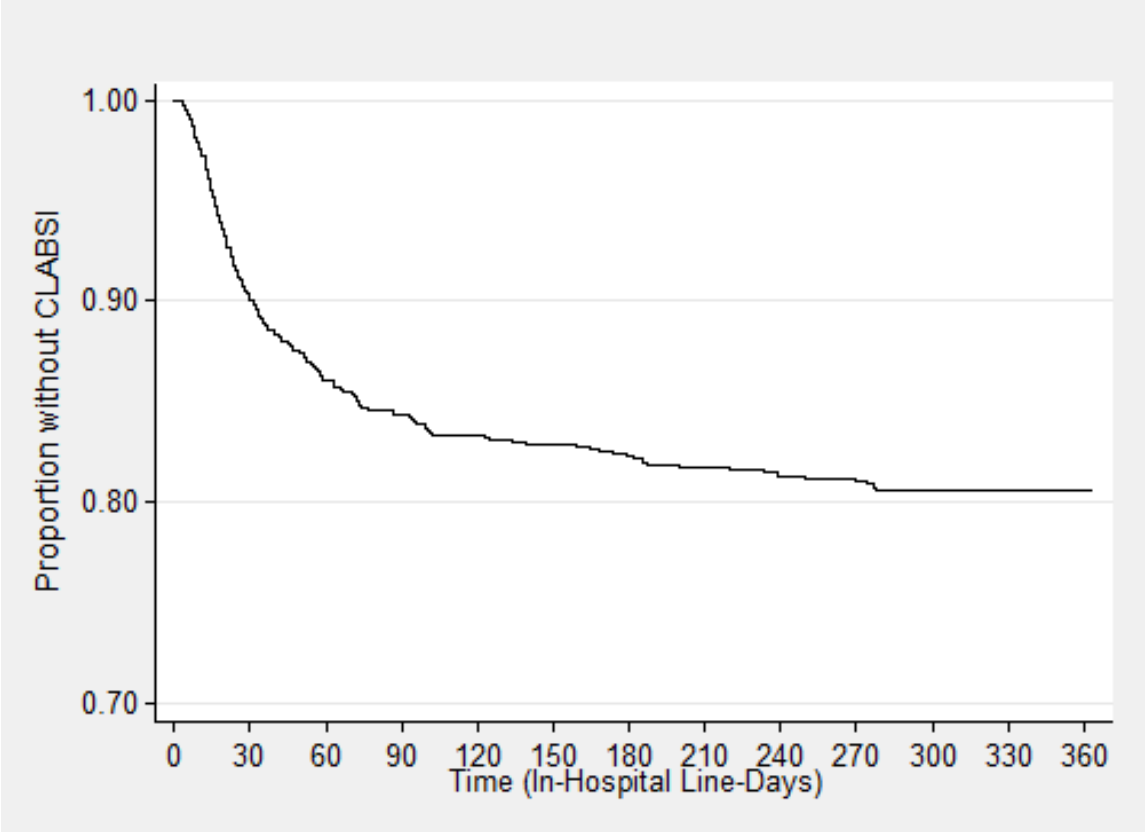


**Figure 6.** Kaplan Meier curve of time to CLABSI over one year after CVL insertion
**Note:** n = 5,648 CVLs
-CLABSI = Central line associated bloodstream infection
-CVL = Central venous line

A Kaplan-Meier curve of time to CLABSI by age group is shown in Figure 7. There is a large difference between neonates and other age groups in CLABSI cases over time. Like the unstratified curve in Figure 6, many neonatal CLABSI cases occurred within the first 60 days. This continued until approximately 90 days, when the curve flattens. The risk of CLABSI remains relatively constant over time for the other age categories.

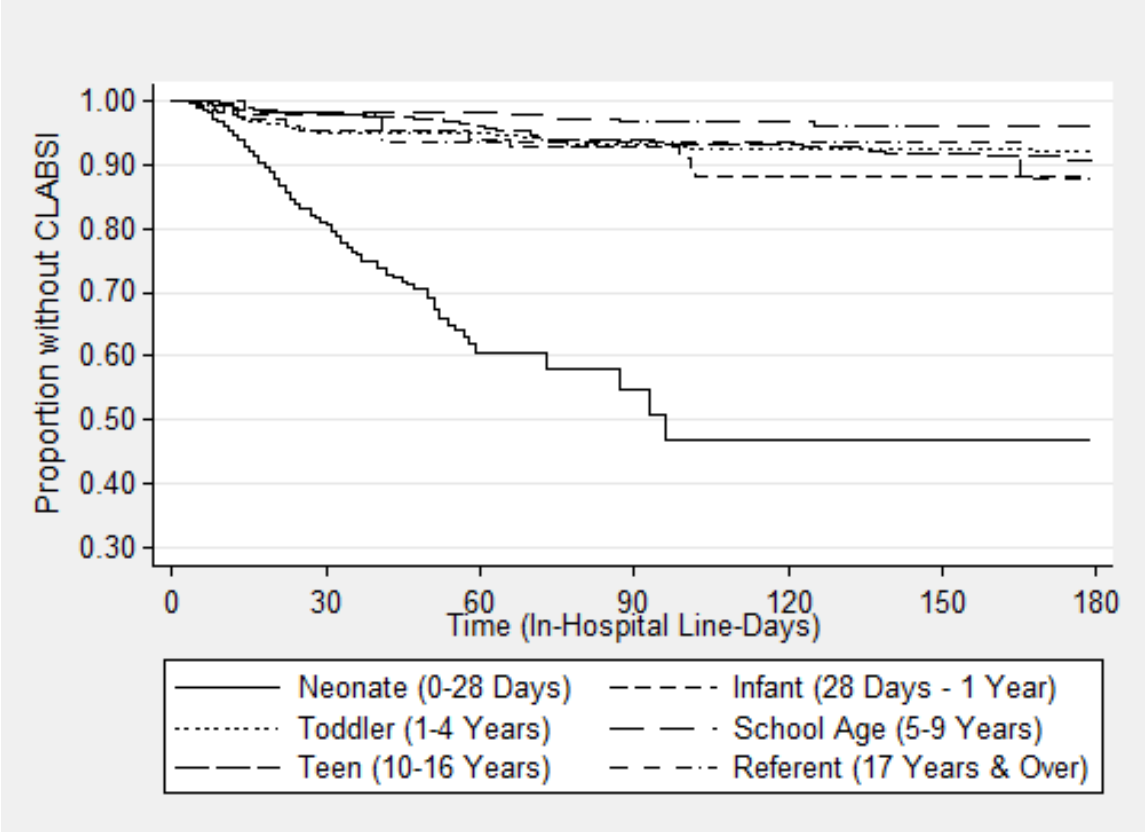


**Figure 7.** Kaplan Meier curve of time to CLABSI over 180 days after CVL insertion by age group
**Note:** n = 5,648 CVLs
-CLABSI = Central line associated bloodstream infection
-CVL = Central venous line

Figure 8 shows a Kaplan-Meier curve of CLABSI stratified by date of CVL insertion. CLABSI risk was highest in the first 60 days, The 2010-2013 group had a lower overall risk of CLABSI compared to the other time periods with approximately 88% of participants remaining CLABSI free after 60 days.

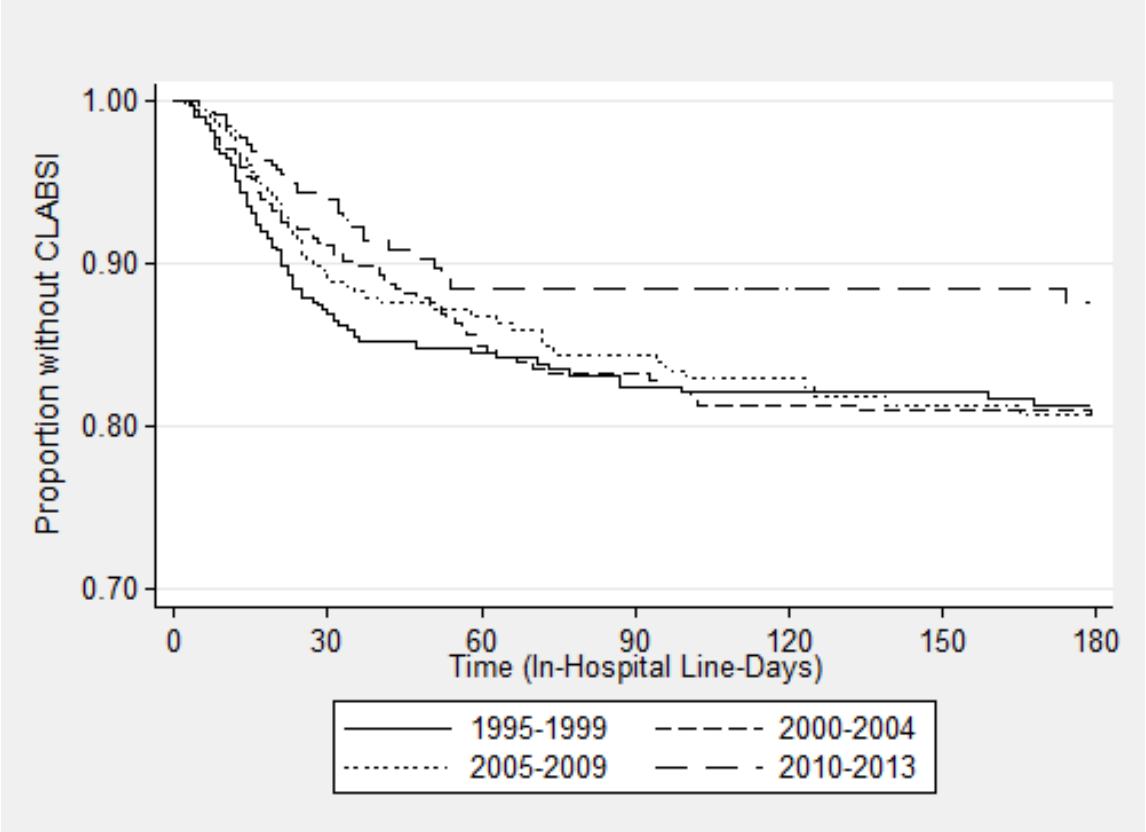


**Figure 8.** Kaplan Meier curve of time to CLABSI over 180 days after CVL insertion by year of insertion
**Note:** n = 5,648 CVLs
-CLABSI = Central line associated bloodstream infection
-CVL = Central venous line

A Kaplan-Meier curve of CLABSI risk by care group can be found in Figure 9. NICU and PICU patients had the highest incidence of CLABSI compared to the other care groups.

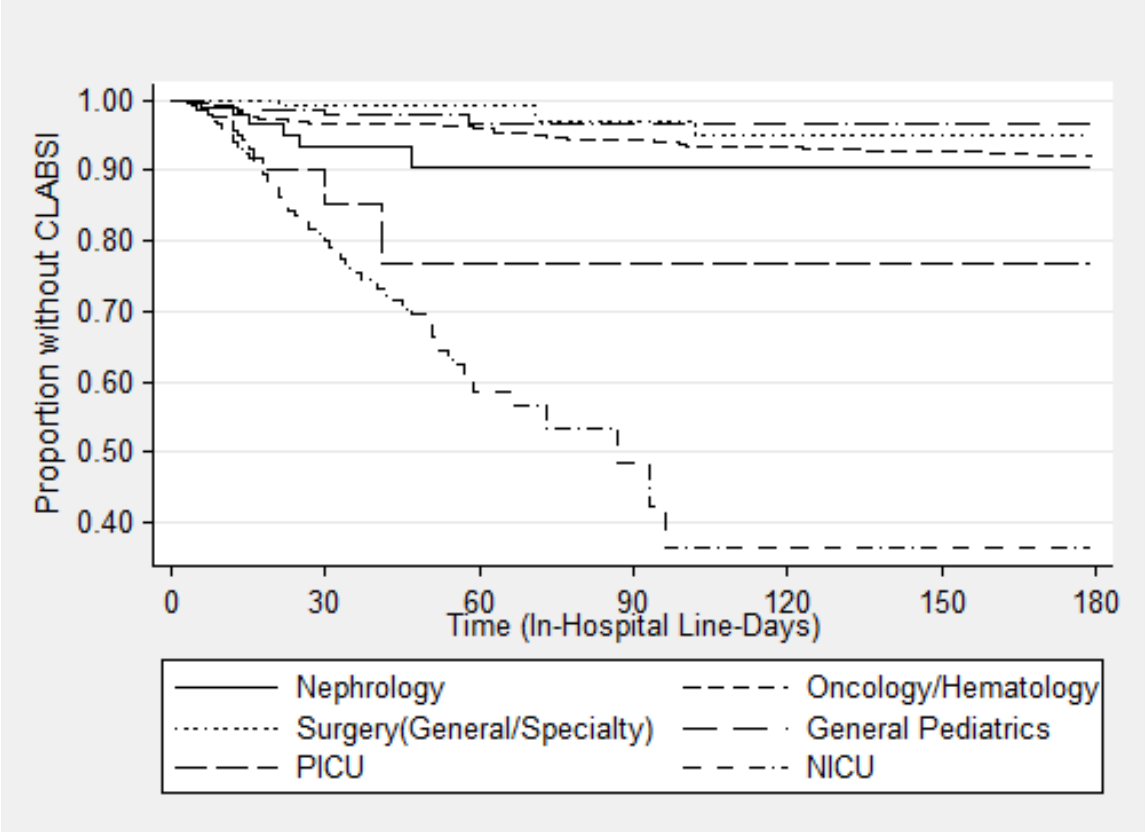


**Figure 9.** Kaplan Meier curve of time to CLABSI over 180 days after CVL insertion by care group
**Note:** n = 5,648 CVLs
-CLABSI = Central line associated bloodstream infection
-CVL = Central venous line
-NICU = Neonatal Intensive Care Unit
-PICU = Pediatric Intensive Care Unit

Figure 10 shows a Kaplan-Meier curve stratified by CVL type. PICCs appear to have the highest risk of CLABSI compared to other catheter types.

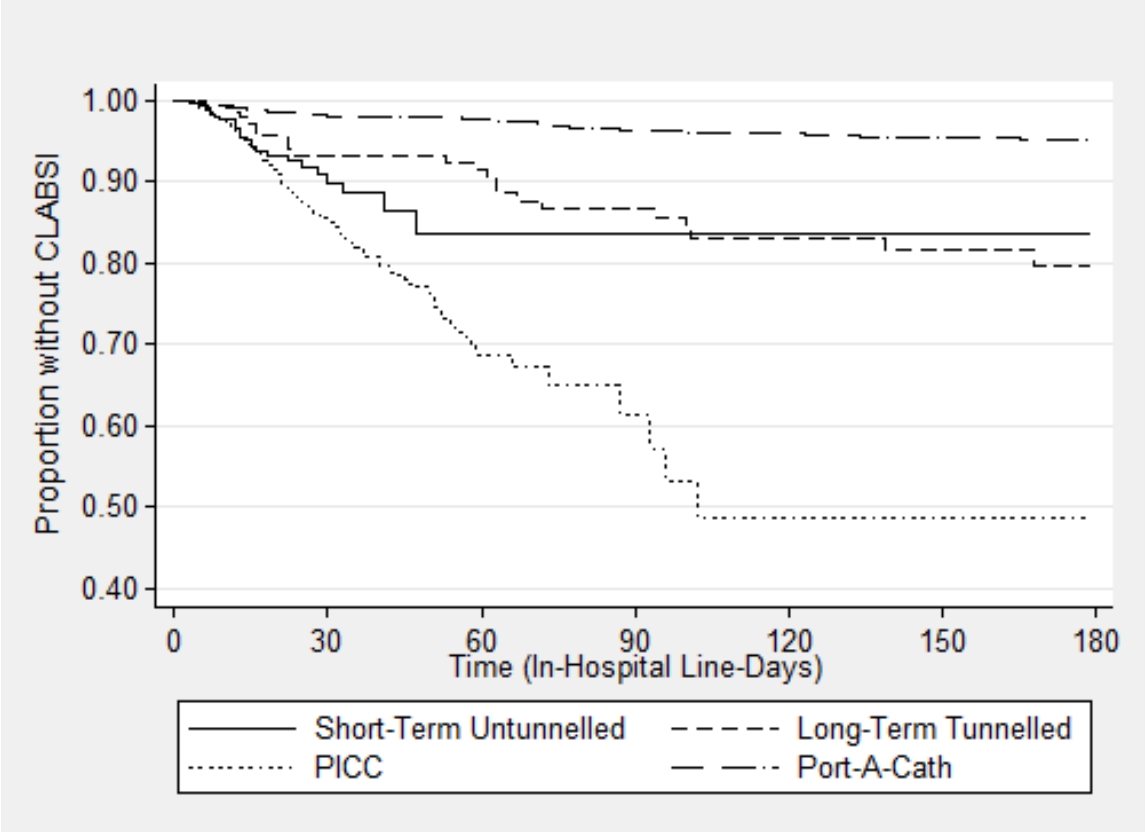


**Figure 10.** Kaplan Meier curve of time to CLABSI over 180 days after CVL insertion by CVL type
**Note:** n = 5,648 CVLs
-CLABSI = Central line associated bloodstream infection
-CVL = Central venous line
-PICC = Peripherally inserted central catheter

*5.2.2. Regression Analyses*

Hazard ratios for CLABSI and their 95% confidence intervals for each of the variables studied were obtained from univariate and multivariate Cox Proportional Hazards models. A summary of the unadjusted and adjusted model results can be found in Table 13.

Nephrology, oncology/hematology, surgery, and general pediatrics care groups showed a statistically significant reduction in CLABSI risk compared to the referent NICU care group. PICU patients showed no statistically significant difference from NICU patients in terms of CLABSI risk.

CLABSI risk in patients with Port-A-Caths was statistically significantly lower than patients with PICC CVLs. No other statistically significant associations were found between CVL types.

CVLs with two lumens showed a statistically significantly higher risk of CLABSI than single lumen CVLs. Triple lumen CVLs showed no statistically significant difference in CLABSI risk compared to single lumen lines.

CVL dressings with gauze, absorbent pads, or pressure cuffs showed a statistically significant increase in CLABSI risk compared to clear transparent dressings. No other associations were found for dressing types.

CVLs inserted into the subclavian vein showed a statistically significant increase in CLABSI risk compared to the referent jugular vein. No other insertion veins showed significant associations with CLABSI risk.

**Table 13.** Summary of regression analyses

| | | Univariate | | Full Model | |
|---|---|---|---|---|---|
| **Variable** | | **HR** | **95% CI** | **HR** | **95% CI** |
| *Age* | | | | | |
| | Neonate (0-28 Days) | 4.26 | 1.73-10.46* | 0.78 | 0.27-2.21 |
| | Infant (28 Days – 1 Year) | 1.17 | 0.44-3.06 | 0.63 | 0.23-1.75 |
| | Toddler (1-4 Years) | 0.58 | 0.23-1.49 | 0.76 | 0.29-1.99 |
| | School Age (5-9 Years) | 0.34 | 0.13-0.93* | 0.38 | 0.14-1.04 |
| | Teen (10-16 Years) | 0.53 | 0.21-1.35 | 0.47 | 0.18-1.23 |
| | Young Adult (17 Years & Older) | 1 | - | 1 | - |
| *Care Group* | | | | | |
| | NICU | 1 | - | 1 | - |
| | Nephrology | 0.25 | 0.12-0.51* | 0.34 | 0.12-0.95* |
| | Oncology/Hematology | 0.10 | 0.07-0.14* | 0.36 | 0.15-0.84* |
| | Surgery(General/Specialty) | 0.05 | 0.02-0.12* | 0.12 | 0.04-0.35* |
| | General Pediatrics | 0.07 | 0.04-0.14* | 0.20 | 0.08-0.51* |
| | PICU (includes “other”) | 0.62 | 0.42-0.94* | 0.60 | 0.29-1.24 |

| | | | | | |
|---|---|---|---|---|---|
| *Insertion Reason* | | | | | |
| | Prolonged Access | 1 | - | --- | --- |
| | Difficult Peripheral | 0.90 | 0.64-1.28 | --- | --- |
| | Short Term ICU/OR Monitoring | 1.18 | 0.62-2.25 | --- | --- |
| | Intensive Care | 1.49 | 0.94-2.35 | --- | --- |
| | Malabsorption | 0.66 | 0.27-1.60 | --- | --- |
| | Oncology | 0.30 | 0.22-0.41* | --- | --- |
| | Renal Failure | 1.22 | 0.57-2.60 | --- | --- |
| | Unknown | 0.93 | 0.70-1.24 | --- | --- |
| *Insertion Timing* | | | | | |
| | Elective | 1 | - | 1 | - |
| | Urgent | 0.76 | 0.53-1.08 | --- | --- |
| | Emergency | 0.86 | 0.48-1.53 | --- | --- |
| | Unknown | 1.07 | 0.84-1.36 | --- | --- |
| *CVL Type* | | | | | |
| | PICC | 1 | - | 1 | - |
| | Short-Term Nontunnelled (includes “other”) | 0.69 | 0.50-0.95* | 0.75 | 0.36-1.57 |
| | Long-Term Tunnelled | 0.36 | 0.23-0.58* | 0.58 | 0.25-1.32 |
| | Port-A-Cath | 0.08 | 0.05-0.12* | 0.13 | 0.05-0.34* |
| *Lumen Count* | | | | | |
| | Single | 1 | - | 1 | - |
| | Double | 1.02 | 0.78-1.30 | 1.80 | 1.19-2.72* |
| | Triple | 1.29 | 0.57-2.91 | 2.31 | 0.86-6.16 |
| *Insertion Side* | | | | | |
| | Right | 1 | - | --- | --- |
| | Left | 0.83 | 0.65-1.06 | --- | --- |
| | Unknown | 1.16 | 0.90-1.48 | --- | --- |
| *Insertion Area* | | | | | |
| | OR | 1 | - | 1 | - |
| | ER/ICU | 2.53 | 1.45-4.41* | 1.09 | 0.58-2.05 |
| | SCN (includes “other”) | 4.13 | 3.23-5.27* | 1.18 | 0.81-1.73 |
| | Unit | 0.37 | 0.16-0.84* | 0.55 | 0.22-1.40 |
| *Antibiotics Pre-Insertion* | | | | | |
| | No | 1 | - | --- | --- |
| | Yes | 0.67 | 0.55-0.82* | --- | --- |
| *Antibiotic Post-Insertion* | | | | | |
| | No | 1 | - | --- | --- |
| | Yes | 2.42 | 1.29-4.54* | --- | --- |

| | | | | | |
|---|---|---|---|---|---|
| *Dressing Type* | | | | | |
| | Clear Transparent | 1 | - | 1 | - |
| | Clear Transparent Absorbent Pad/Gauze /Pressure (includes "other") | 3.01 | 2.30-3.95* | 2.01 | 1.39-2.91* |
| | Semi-Clear Woven | 0.35 | 0.05-2.52 | 0.31 | 0.04-2.25 |
| | Port-A-Cath | 0.52 | 0.40-0.68* | 1.56 | 0.88-2.79 |
| *Insertion Vein* | | | | | |
| | Jugular | 1 | - | 1 | - |
| | Arm (includes "other") | 4.23 | 3.04-5.89* | 0.87 | 0.55-1.36 |
| | Head (Cephalic) | 2.55 | 1.68-3.89* | 0.66 | 0.40-1.11 |
| | Leg | 4.95 | 3.48-7.03* | 0.84 | 0.55-1.30 |
| | Subclavian | 1.05 | 0.73-1.49 | 1.56 | 1.02-2.39* |
| *Tip Location* | | | | | |
| | SVC/RA | 1 | - | --- | --- |
| | Subclavian/Bracheocephalic | 1.32 | 0.94-1.86 | --- | --- |
| | Inferior Vena Cava | 2.66 | 2.00-3.52* | --- | --- |
| | Unknown | 1.75 | 1.30-2.35* | --- | --- |
| *Blockage in Past 30 Days* | | | | | |
| | No | 1 | - | --- | --- |
| | Yes | 0.92 | 0.50-1.68 | --- | --- |
| *Mechanical Complication in Past 30 Days (Includes disconnect, fracture, leakage, and/or migration)* | | | | | |
| | No | 1 | - | --- | --- |
| | Yes | 1.28 | 0.41-4.00 | --- | --- |

**Note:** All hazard ratios in the full model are controlled for year of insertion as this variable was included in the model but not subject to the backward elimination procedure.

-PICU = Pediatric intensive care unit
-NICU = Neonatal intensive care unit
-ICU = Intensive care unit
-OR = Operating room
-PICC = Peripherally inserted central catheter
-ER = Emergency room
-SCN = Special care nursery
-SVC = Superior vena cava
-RA = Right atrium

# CHAPTER 6:DISCUSSION

## 6.1. MAJOR FINDINGS

### *6.1.1. Objective 1: To describe the incidence of CLABSI in patients ages 0-18 years who had CVLs placed at the IWK*

#### 6.1.1.1. CVL Usage Trends

The Central Line Utilization Ratio (CLUR) remained nearly constant from 2006 to 2012, suggesting the clinical practice related to the decision to insert Central Venous Lines (CVLs) and/or the patient population did not vary greatly over time. There was a drop in the CLUR in 2013. This coincided with a drop in the hospital-wide Central Line Associated Bloodstream Infection (CLABSI) rate.

Most patients in this study required more than one CVL, either consecutively or concurrently. This information is useful for monitoring CVL usage at the Izaak Walton Killam Health Centre (IWK). However, the effects multiple CVLs may have on CLABSI risk were not examined in this study.

Children two years of age or younger were the most frequent users of CVLs. Inherent to age, this group likely has higher risk of infection (including CLABSI) than older groups. Thus, the group requiring CVLs most frequently may also be the most vulnerable to CLABSI.

#### 6.1.1.2. CLABSI

Of the 9,067 CVLs included in this study, 666 developed CLABSI. Gram positive bacteria, mostly Coagulase Negative Staphylococcus (CONS), were the most common infecting organisms. This is consistent with previous literature listing CONS and other

gram positive skin commensals as the most frequent causative agents of CLABSI. [6, 21, 22] This suggests the majority of CLABSI causing bacteria enter through the skin.

There were no seasonal differences in CLABSI rates. However, there was a clear and consistent trend toward hospital-wide CLABSI rate reduction over time. Such a trend was also seen through National Health and Safety Network (NHSN) reports. The 2006 NHSN summary of device associated infections listed the pediatric medical/surgical CLABSI rate as 5.3 cases per 1,000 line-days. [83] This rate later dropped with the 2012 version of this summary reporting 1.4 CLABSI cases per 1,000 line-days for pediatric medical/surgical units. [18] This study found CLABSI rates of approximately 4 cases per 1,000 line-days and 1 case per 1,000 line-days in 2006 and 2012, respectively. These rates are below the corresponding NHSN reported rates, but reflect hospital-wide CLABSI cases as opposed to medical/surgical units only. Nonetheless, the trends in CLABSI rates in this population appear to correspond with trends seen elsewhere.

Drops in CLABSI rate may be indicative of effective infection control interventions. In discussion with the IWK Infection Prevention and Control Service (IPCS), a number of interventions that may have affected CLABSI rates were identified. In 2010, a hand hygiene campaign began in the IWK Neonatal Intensive Care Unit (NICU). In 2011, this campaign was expanded to the rest of the hospital. It is possible these campaigns contributed to the drop in CLABSI rates seen between 2010 and 2012. More recently, 2012 saw the introduction of chlorohexidine, a topical antiseptic, to the NICU. Chlorohexidine use with CVLs was later introduced to the rest of the hospital. This may have affected the 2013 CLABSI rate, but more follow up data is needed.

Neonates and infants had the highest CLABSI rates of any age group. CLABSI rates reduced with age for the first three years of life, then remained roughly constant. This finding is consistent with previous literature indicating high CLABSI rates in very young patients.[25-28] Likely related to average patient age in this care group, the NICU held the most patients and had the highest CLABSI rate.

Additionally, the risk of CLABSI appears to change with time since insertion: The majority of CLABSI cases occurred within approximately 60 days of CVL insertion. This pattern was apparent over the whole sample and after stratification by age, date of CVL insertion, care group, and CVL type. Several studies have identified periods of increased CLABSI risk ranging from seven days to over 30 days after CVL insertion.[15, 16, 40, 42, 45, 74] Although there is always a risk of CLABSI while a CVL is in place, patients' risk of CLABSI may diminish with time.

### *6.1.2. Objective 2: To determine risk factors and protective factors for CLABSI in patients ages 0-18 years*

Patients in the nephrology, oncology/hematology, surgery, and general pediatrics care groups had a significantly lower CLABSI risk compared to NICU patients. CLABSI risk in the PICU care group did not statistically differ from NICU patients. These findings lend some support the association between time spent in intensive care environments and CLABSI, which has been established in previous studies.[5, 54, 55, 59, 74] It should be noted, however, that the high risk of CLABSI seen in NICU patients was likely confounded by the young age of these patients. Neonates are inherently more susceptible to infection than children of other ages.

Port-A-Caths were associated with a statistically significant reduced risk of CLABSI than PICCs. This is consistent with previous literature, as totally implantable

CVLs have been repeatedly linked to low CLABSI rates. [21, 22] Double lumen CVLs showed a statistically significant increase in CLABSI risk compared to single lumen CVLs. Triple lumen CVLs were associated with an increase in CLABSI risk but the association was not statistically significant, possibly due to the relatively low number of children in this group (167, or 3.0% of the sample).

A statistically significant association between CLABSI and dressing type was established. CVLs with clear transparent dressings with absorbent pads, gauze, or pressure cuffs showed an increased hazard of CLABSI compared to CVLs with clear transparent dressings alone. This may suggest these types of dressings provide a medium for bacterial growth leading to CLABSI. However, several studies have suggested gauze-like dressings are protective against CLABSI. [26, 37, 46, 47]

There was a slight but statistically significant increase in CLABSI risk for CVLs inserted in the subclavian vein compared to CVLs inserted in the jugular vein. This increase in risk is small enough that it may not be clinically significant. However, it may be explained by the fact that CVLs are not commonly inserted in the jugular vein and so may be more likely to be inserted under Maximal Sterile Barrier Precautions (MSBP).

The use of Port-A-Caths over other CVL types was the only protective factor against CLABSI identified in this study. This finding was expected given the structure of the device (external endpoint lies beneath the skin) and its inherent requirement for surgical insertion. Additionally, previous literature has supported a protective association between Port-A-Caths and CLABSI.[21]

Turning to notable yet non-significant findings, age was not found to be a significant predictor of CLABSI in the multivariate analysis, which contradicts literature supporting age as a predictor for CLABSI. [25-28] This may be explained by confounding

with the care group variable. Risk of CLABSI in NICU patients was significantly higher than patients in other care groups. These significant associations in each variable were likely related, as NICU patients would represent neonates and infants, who had the highest rate of CLABSI in the descriptive analyses. The confounding between these two variables may explain the lack of significance for patient age within the model.

Blockages and other mechanical complications showed no statistically significant association with CLABSI. It is possible that the chosen time window of 30 days between blockages or other mechanical complications and CLABSI (see Methods, section 4.7.3.4) may have been too long or too short. One notable finding with mechanical complications is that nearly one quarter of CVLs became blocked at some point, either partially or completely. This is notable regardless of an association with CLABSI as blockages can complicate care.

There was no significant association between antibiotic use prior to CVL insertion and CLABSI, but antibiotic use post CVL insertion was associated with a statistically significant increase in CLABSI risk. This is unexpected given the established relationship between antibiotics and infection prevention.[21, 22, 55, 61] However, it is not common practice to give prophylactic antibiotics for CVL insertions at the IWK. Antibiotic use in this setting was for another suspected or established bacterial infection, which could increase the risk of CLABSI. [22, 81]

This study found no significant associations between the site in the hospital where the CVL was inserted and risk of CLABSI. This contradicts previous literature, as the environment in which CVLs are inserted has been linked to CLABSI risk, with operating room (OR) insertion having the lowest risk. [21, 26, 62, 63] One potential reason for this contradiction with the literature is that patients with inherently high risk of CLABSI may

have been more likely to have their CVLs inserted in the OR in an attempt to avoid infection. The higher likelihood of MSBP in the OR may have lowered these patients' risk of CLABSI to resemble that of inherently lower risk patients who had their CVLs inserted outside the OR. This difference in risks combined with the differences in aseptic technique used in these environments could have caused the apparently equivalent risk of CLABSI between these groups.

## 6.2. IMPLICATIONS FOR HEALTHCARE

Gram positive skin commensals were the causative agents of the majority of CLABSI cases, which suggests hand hygiene and skin preparation at CVL insertion play a large role in CLABSI risk. The drop in CLABSI rates following a hand hygiene campaign suggests such an intervention may be an effective means of future CLABSI prevention.

Infants and ICU patients held the highest risk of CLABSI. These findings were likely correlated, as NICU patients are both infants and under intensive care. However, both infants and ICU patients may benefit from extra infection prevention precautions when inserting and handling their CVLs.

CVL dressings with absorbent pads, gauze, and/or pressure cuffs are associated with an increased risk of CLABSI. Avoiding these dressings when possible may prevent future CLABSI.

Finally, interventions to prevent CVL blockages may be useful to patient care, as nearly one quarter of CVLs inserted at the IWK during the study period became blocked. Prophylactic anticoagulants, such as low dose heparin, have been explored for this

purpose. Two Cochrane reviews suggest this practice does not effectively prevent CVL blockages. However, both reviews acknowledge the need for further investigation.[84, 85]

## 6.3. STRENGTHS

One of the strengths of this study is the quality of the data and the broad scope of information collected. The Central Venous Access Database (CVAD) was constructed with this study in mind and has been maintained prospectively with the detail ideal for a cohort study. The Hospital Acquired Infection Database (HAID) is also maintained prospectively and in great detail as it is required for infection accountability. The size of the database is also a major strength as it adds statistical power. Studies like this one commonly have sample sizes of less than 2,000 patients.[11, 17, 59, 74] This study, on the other hand has a sample size of over 5,600 patients.

Another strength of this study was that it spanned 18 years of patient care. During the study period aseptic techniques and CVL insertion procedures changed as new therapies became available. This provided an opportunity to evaluate the effectiveness of these changes in preventing infection.

Another strength of this study is the variety of groups represented in the sample. Most CLABSI research focuses on a very specific group of patients in terms of illness, age, care setting, or a combination of these. This study captured all ages, illnesses, and care settings of the pediatric inpatients at a tertiary care center serving three provinces. This resulted in a very comprehensive account of CVL use and CLABSI risk across a diverse population. This suggests the results to this study are generalizable to other populations, namely those with similar strategies of health care delivery.

Finally, this study established baseline CLABSI rates and characteristics in a Canadian Maritime Pediatric population. It is unlikely that there are biological differences in CLABSI between this population and the more commonly studied US population. However, the differences in the administration and delivery of healthcare between the US and Canada could play a role in infection. This study enables comparison of CLABSI between different healthcare systems.

## 6.4. LIMITATIONS

One notable limitation to this study is inherent to cohort study designs: Causation must be inferred from observed events – which is less robust than if exposures were randomized. Little could be done to remedy this as randomization was not suitable for this study.

Many variables or variable categories had to be merged with others due to small size or missing values. These included all non-blockage mechanical complication variables and categories of the care group, CVL type, insertion area, dressing type, insertion vein, and tip location variables. This may have diluted significant associations, resulting in Type II error. Additionally, only the first CVL per patient was considered for the univariate and regression analyses. This eliminated the ability to consider having multiple CVLs as a risk factor.

Finally, the dataset did not capture underlying illnesses or medications used in patient care other than antibiotics at the time of insertion. There was no suitable approximation for medications, but care group information was used to approximate principal underlying illnesses. Problems with this include the potential for misclassification of illnesses and the fact that other diagnoses could not be

approximated. Ideally, datasets used in future studies should capture medication administration, underlying illness, and comorbidities or be linked to another database containing this information, such as those from the Canadian Institute of Health Information (CIHI).

## 6.5. FUTURE RESEARCH

There were several findings in this study that require further exploration. The hand hygiene campaign preceding the 2010-2012 drop in CLABSI rates is suggestive of a causal relationship. Such a relationship could not be established in this study, but future studies should seek to confirm whether hand hygiene campaigns are an effective means of CLABSI prevention.

In 2012, chlorohexidine (a topical antiseptic) was introduced to standard practice at the IWK for CVL care in the NICU, and later to the rest of the hospital. The effects of this intervention could not be fully investigated in this study as there was insufficient follow up time since the intervention. However, future studies should examine the effects of this intervention.

The data used in this study did not capture underlying illness or comorbidities. An approximation was made for underlying illness, but future studies should include more robust measures of underlying illness and comorbidity. This may be done by incorporating CIHI data to the dataset used here.

Data on antibiotic use in this study was limited to observations on the day of CVL insertion. There was no information on other medications administered. Future studies could benefit from daily records of medication administration, especially antibiotics.

The relationship between dressing type and CLABSI found in this study warrants future research. Further studies should aim to confirm and elaborate on this relationship. For example, an increased risk of CLABSI associated with gauze dressings may be altered by changing these dressings more or less often.

Finally, mechanical complications should be prevented and their relationship with CLABSI should be explored. This study found nearly one quarter of CVLs became either partially or completely blocked. Efforts to prevent these complications should be evaluated in future studies, with specific attention to the evaluation of anticoagulant therapy. [84, 85] This study found no association between mechanical complications and CLABSI within 30 days of said complications. Future studies could explore the effects widening or narrowing this period has on the association between these complications and CLABSI risk.

# CHAPTER 7:CONCLUSIONS

Central Line Associated Bloodstream Infection (CLABSI) is a clinically significant morbidity in the Canadian Maritime Pediatric population. CLABSI rates have decreased over time. The majority of CLABSI cases in this population were caused by gram positive skin commensals. Risk factors identified in this study are: Care group (an approximation of underlying illness), the use of double lumen Central Venous Lines (CVLs,) subclavian CVL insertion, and the use of dressings with gauze, absorbent pads, or pressure cuffs. The protective factor identified in this study is: The use of Port-A-Cath CVLs. This information can be used to guide CVL insertion and care practices and to evaluate new and existing CLABSI prevention strategies.

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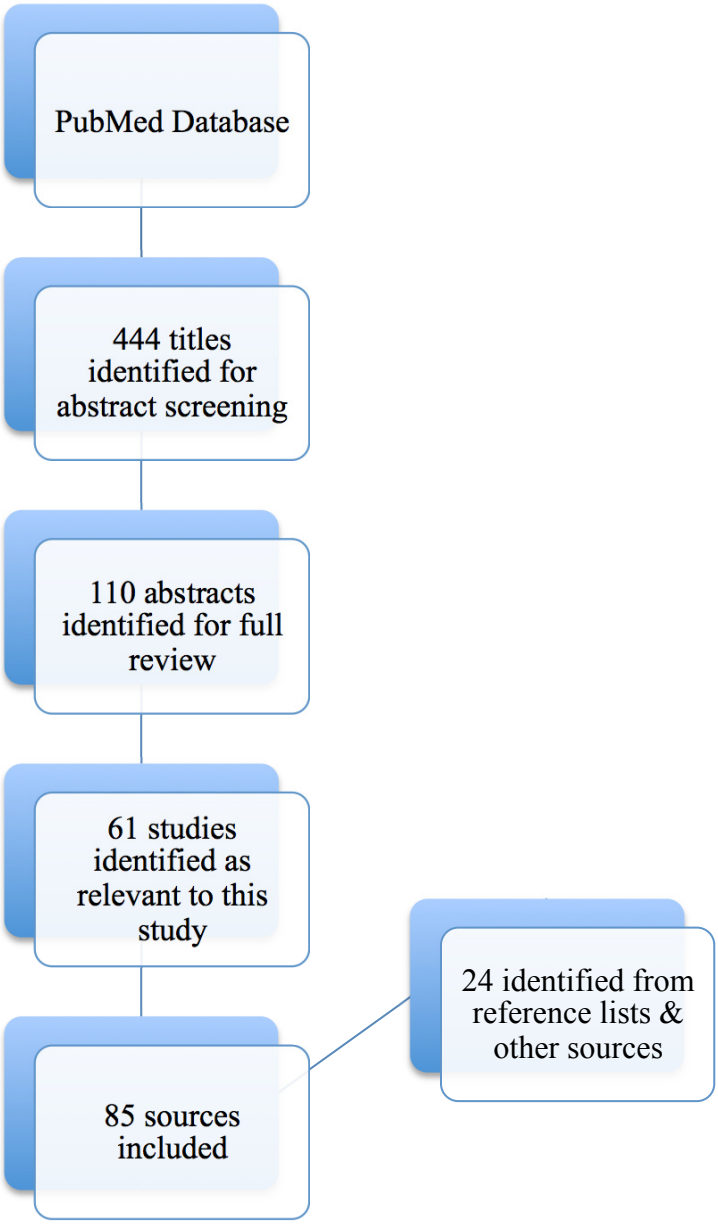
## APPENDIX A: PUBMED LITERATURE SEARCH STRATEGY

| | AND | AND | AND | AND | AND |
|---|---|---|---|---|---|
| OR | "vascular access devices"[MeSH Terms] | "outcome and process assessment (health care)"[MeSH Terms] | "epidemiologic factors"[MeSH Terms] | "infant, newborn"[MeSH Terms] | "2000/01/01"[PDAT] : "3000/12/31"[PDAT] |
| OR | "central venous catheters"[MeSH Terms] | infection[Text Word] | "causality"[MeSH Terms] | "infant"[MeSH Terms] | |
| OR | "catheterization, central venous"[MeSH Terms] | "catheter-related infections"[MeSH Terms] | "risk factors"[MeSH Terms] | child"[MeSH Terms] | |
| OR | "catheters, indwelling"[MeSH Terms] | "catheter related infections/blood"[MeSH Terms] | "precipitating factors"[MeSH Terms] | "adolescent"[MeSH Terms] | |
| OR | | "catheter related infections/epidemiology"[MeSH Terms] | | | |
| OR | | "catheter related infections/etiology"[MeSH Terms] | | | |
| OR | | "sepsis"[MeSH Terms] | | | |
| OR | | "sepsis/blood"[MeSH Terms] | | | |
| OR | | "sepsis/epidemiology"[MeSH Terms] | | | |
| OR | | "sepsis/etiology"[MeSH Terms] | | | |

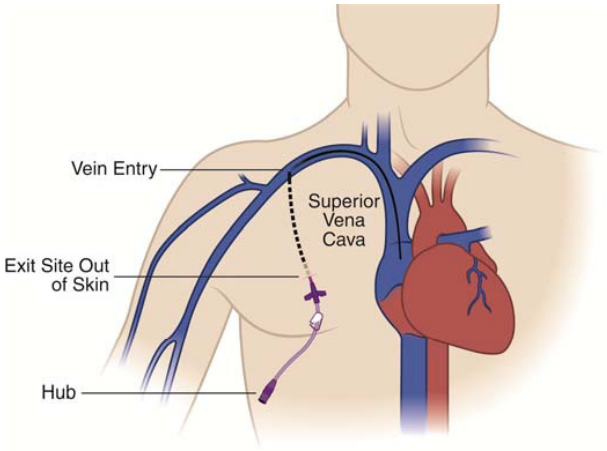
| | | | | | |
|---|---|---|---|---|---|
| OR | | "equipment failure"[MeSH Terms] | | | |
| OR | | "equipment failure/adverse effects"[MeSH Terms] | | | |
| OR | | "equipment failure/etiology"[MeSH Terms] | | | |
| OR | | "equipment failure analysis"[MeSH Terms] | | | |
| OR | | "thrombosis"[MeSH Terms]) | | | |
| OR | | "thrombosis/epidemiology"[MeSH Terms] | | | |
| OR | | "thrombosis/etiology"[MeSH Terms] | | | |

## APPENDIX B: LITERATURE SEARCH RESULTS



## APPENDIX C: DIAGRAMS OF CVL TYPES

1. TUNNELLED CVL




Power Hickman® Tunneled Central Venous Catheter

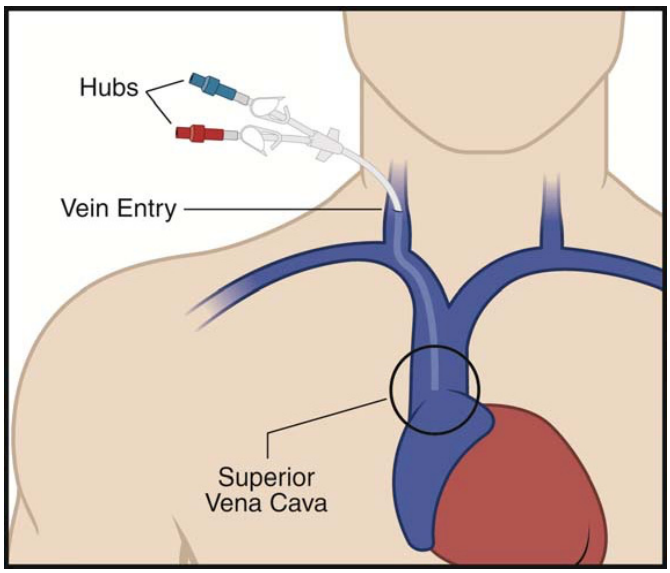
Multi-lumen Hickman® or Broviac® Long-Term Dialysis Catheters

Groshong® Tunneled Central Venous Catheter



Picture taken from The Joint Commission CLABSI Toolkit (2013).[20]

2. NONTUNNELLED CVL

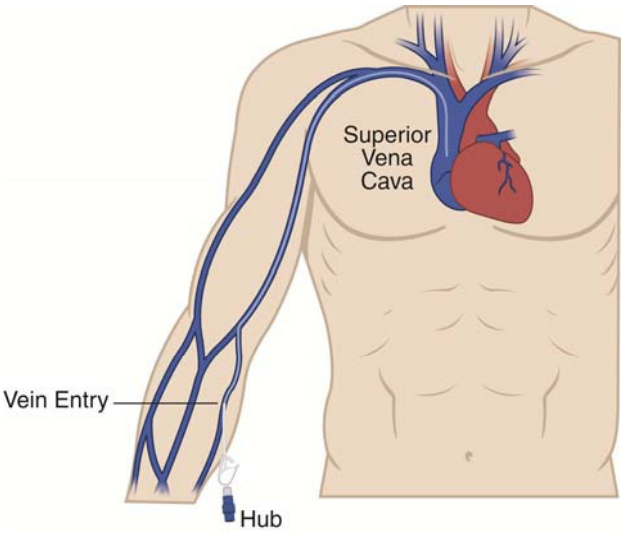



MAHURKAR™ Elite Dialysis Catheter

Image provided courtesy of Covidien. MAHURKAR is a trademark of Sakharam D. Mahurkar, MD.

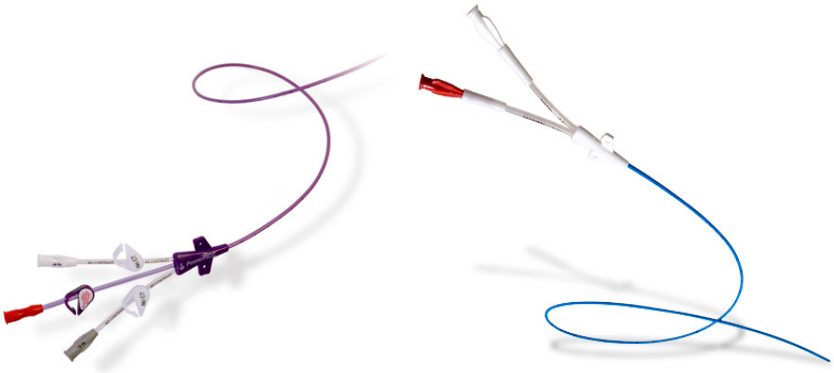

Picture taken from The Joint Commission CLABSI Toolkit (2013).[20]

3. PICC




**Multi-lumen Peripherally Inserted Catheters**

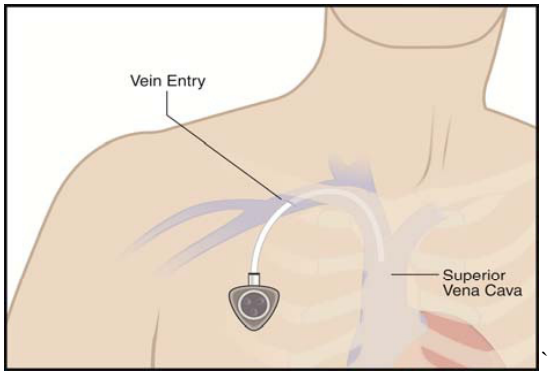
PowerPICC® Catheter Groshong® Catheter

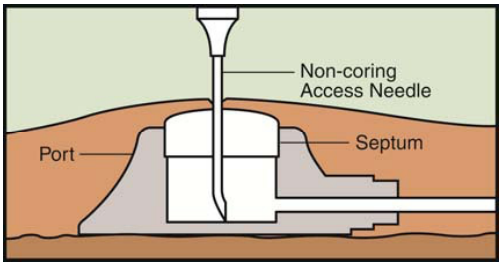




Picture taken from The Joint Commission CLABSI Toolkit (2013).[20]

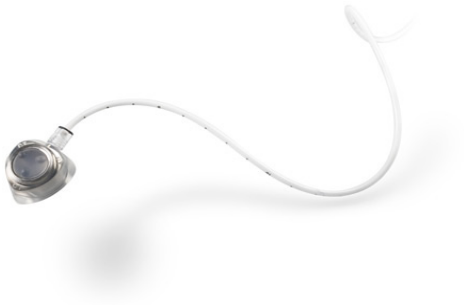
4. TOTALLY IMPLANTABLE CVL




**Single lumen**

PowerPort® Vue Implantable Port



Titanium Dome Port

**Dual lumen**

SlimPort® Dual-lumen Rosenblatt™ Implantable Port



Picture taken from The Joint Commission CLABSI Toolkit (2013).[20]

## APPENDIX D: POTENTIAL CLABSI RISK FACTORS (FROM CVAD)

| Variable | Description | Type of Data | Categories |
|---|---|---|---|
| Date of insertion | Month and year of CVAD insertion | Numerical | Date in month and year |
| Age | Age at the time of CVAD insertion | Continuous | Age in days |
| Location of insertion | The care environment in which the CVAD was placed | Categorical | OR, NICU, PICU, care area |
| Vein used | Which blood vessel the CVAD accessed | Categorical | Jugular, femoral, other |
| Tip location | Where in the body the tip of the CVAD was placed | Categorical | Neck, chest, leg |
| Type of line | The CVAD structure of the line in question | Categorical | Port-A-Cath, Broviac, Hickman, Dialysis (cuffed), Dialysis (non-cuffed), PICC, Arrow/Cook, Other |
| Number of Lumens | The number of lumens present in the CVAD in question | Categorical | Single, double, or triple lumen CVADs |
| Antibiotics | Whether antibiotics were given before insertion, after insertion, or not at all. | Categorical | Yes (before insertion), yes (after insertion), no |
| Chlorohexidine used | Whether chlorohexidine solution was used on the CVAD at insertion | Categorical | Yes/No |
| Alcohol Used | Whether alcohol was used on the CVAD at insertion | Categorical | Yes/No |
| Barrier precautions | During the CVAD insertion, what aseptic barrier precautions were taken? Include masks, gloves, etc. | Categorical | Maximal, moderate, minimal |
| Underlying illness | Illness of the child requiring the CVAD | Categorical | chronic, injury, immunosuppressing |
| Insertion timing | How planned or rushed the CVAD insertion was | Categorical | elective, urgent, and emergency |

| | | | |
|---|---|---|---|
| Insertion complications | Number of skin punctures necessary during CVAD insertion. | Numerical | # punctures |
| Dressing type | What type of dressing was placed over the CVAD insertion site | Categorical | semi-permanent transparent, gauze transparent, gauze-like, and tape over gauze/other. |
| Complications | Whether there were mechanical complications or blockages while the CVAD was in use. | Dichotomous | Yes/No |

## APPENDIX E: OUTCOME VARIABLES (FROM HAID)

| Variable | Description | Type of Data | Categories |
|---|---|---|---|
| Time to first CLABSI symptoms | How many days the line was in place before CLABSI symptoms appeared | Numerical | # days in situ |
| Time to first CLABSI diagnosis | How many days the line was in place before CLABSI was diagnosed | Numerical | # days in situ |
| Unit where symptoms were first identified | Where was the patient when they became symptomatic of CLABSI? | Categorical | OR, NICU, PICU, care area |
| Polymicrobial infection? | How many microbes were identified by the blood culture? | Numerical | # microbial species identified |
| Causative organism | What microbe(s) was/were identified in with blood culture? | Categorical | Species name of organism(s) |
| Previous mechanical complication | Did the patient have a mechanical complication associated with the CVAD prior to the onset of CLABSI? | Dichotomous | Yes/No |
| Previous blockage | Did the patient have a blockage associated with the CVAD prior to the onset of CLABSI? | Dichotomous | Yes/No |
| Time between complication and CLABSI symptoms | If a mechanical complication or blockage occurred prior to the onset of CLABSI, how many days before the onset of CLABSI symptoms did this complication occur? | Numerical | # days between onset of complication and CLABSI symptoms |
| Time between complication and CLABSI diagnosis | If a mechanical complication or blockage occurred prior to the onset of CLABSI, how many days before the onset of CLABSI diagnosis did this complication occur? | Numerical | # days between onset of complication and CLABSI diagnosis |

## CHAPTER 8: APPENDIX F: CLABSI RATES FOR FIRST CVL PER PATIENT

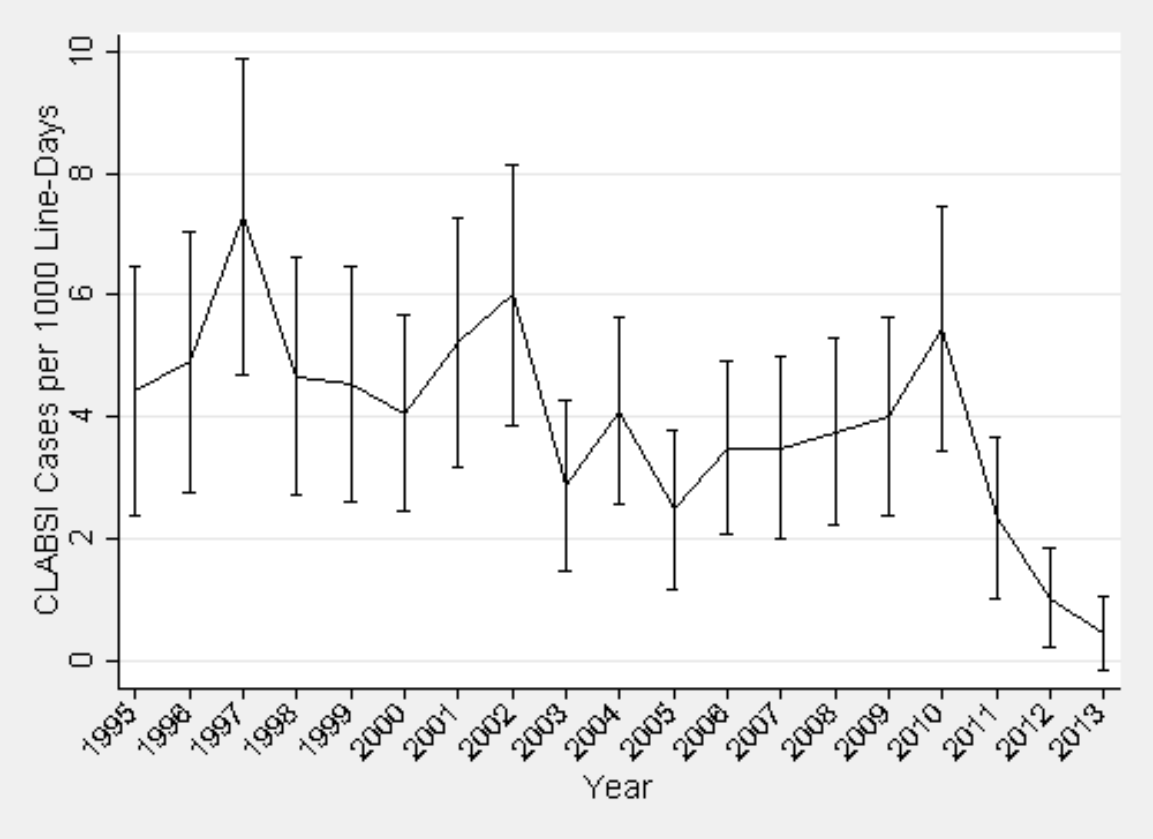



**Figure 11.** Hospital-wide CLABSI rate over time as cases per 1000 in-hospital line-days for first CVL per patient; vertical lines indicate 95% confidence intervals
**Note:** n = 5,648 CVLs
-CLABSI = Central line associated bloodstream infection

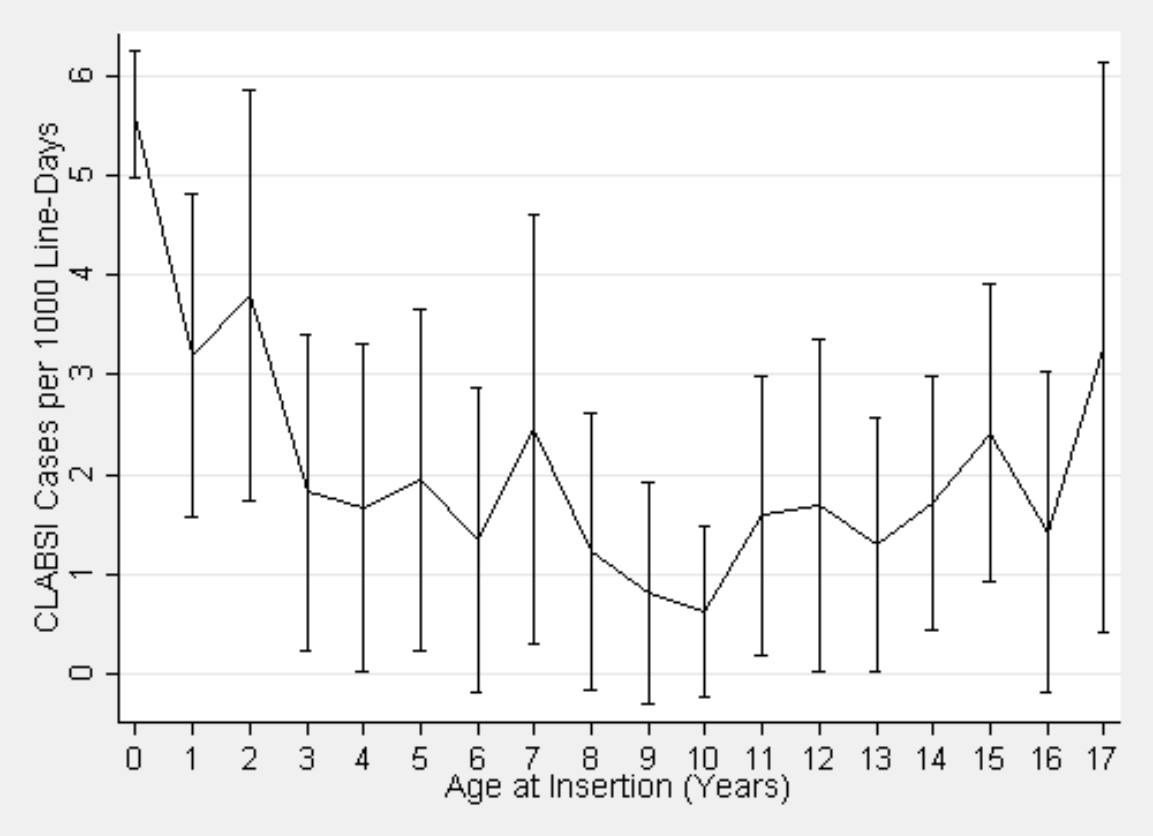



**Figure 12.** Hospital-wide CLABSI rate over age at CVL insertion as cases per 1000 in-hospital line-days for first CVL per patient; vertical lines indicate 95% confidence intervals

**Note:** n = 5,648 CVLs

-CLABSI = Central line associated bloodstream infection

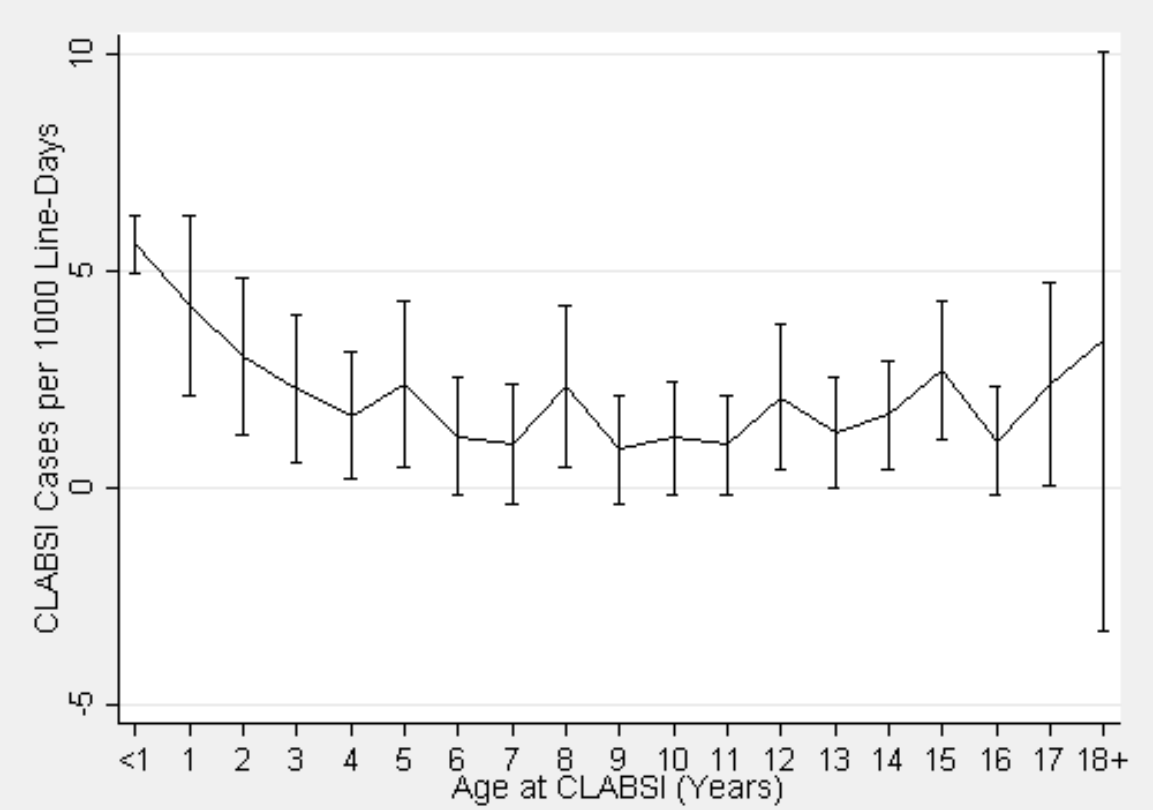



**Figure 13.** Hospital-wide CLABSI rate over age at CLABSI occurrence as cases per 1000 in-hospital line-days for first CVL per patient; vertical lines indicate 95% confidence intervals

**Note:** n = 5,648 CVLs

-CLABSI = Central line associated bloodstream infection

**Table 14.** Hospital-wide CLABSI rates by season as cases per 1000 in-hospital line-days for first CVL per patient

| Quarter | CLABSI Cases per 1000 Line-Days | 95% Confidence Interval |
|---|---|---|
| 1 (January – March) | 3.5 | 3.1-4.7 |
| 2 (April – June) | 3.6 | 2.7-4.2 |
| 3 (July – September) | 3.9 | 3.6-5.2 |
| 4 (October – December) | 4.4 | 2.8-4.3 |

**Note:** Numerators are season specific CLABSI cases; denominators are season specific in-hospital line-days. The crude rate is multiplied by 1,000 to find the CLABSI rate per 1,000 line-days. n = 5,648 CVLs.
-CLABSI = Central line associated bloodstream infection

**Table 15.** Hospital-wide CLABSI rates stratified by care group as cases per 1000 in-hospital line-days for first CVL per patient; 95% confidence intervals also shown

| Care Group | CLABSI Cases per 1000 Line-Days | 95% Confidence Interval |
|---|---|---|
| Nephrology | 2.1 | 0.6-3.5 |
| Oncology/Hematology | 2.6 | 2.0-3.2 |
| Surgery (General/Specialty) | 0.7 | 0.1-1.2 |
| General Pediatrics | 0.8 | 0.3-1.4 |
| PICU | 3.3 | 2.0-4.5 |
| NICU | 6.7 | 5.8-7.5 |
| Other | --- | --- |
| Unknown | --- | --- |

**Note:** Numerators are care group specific CLABSI cases; denominators are care group specific in-hospital line-days. The crude rate is multiplied by 1,000 to find the CLABSI rate per 1,000 line-days. n = 5,648 CVLs.
-CLABSI = Central line associated bloodstream infection
-PICU = Pediatric intensive care unit
-NICU = Neonatal intensive care unit