Surveillance of Central Line-Associated Bloodstream Infections in Quebec Intensive Care Units

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November 2011

A thesis submitted to McGill University in partial fulfilment of the requirements of the degree of Doctor in Philosophy (Ph.D.)

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ABSTRACT

Central line-associated bloodstream infections (CLABSI) figure as one of the most important healthcare-associated infections (HAI), particularly in intensive care units (ICU). Despite their clinical and public health importance, little is known about CLABSI in Canadian ICUs. Thus, the first objective of this thesis was to describe the epidemiology of CLABSI in Quebec ICUs, using data from the *Surveillance Provinciale des Infections Nosocomiales – Bactériémies Associées aux Cathéters Centraux* (SPIN-BACC) program. We showed that CLABSIs are an important problem in Quebec ICUs, but CLABSI incidence rates have decreased since 2007. Moreover, the proportion of methicillin-resistant *Staphylococcus aureus* has declined to <40% since 2006 (chapter 6).

Surveillance programs are essential to establish benchmarks. In the last years, several regional and national CLABSI surveillance programs have decided to eliminate continuous participation requirements from hospitals. This might have jeopardized the validity of these programs' results because the minimal number of months hospitals should participate in such programs to generate valid annual benchmarks for CLABSI incidence rates have yet to be determined. Our second objective was to determine, through simulation, the impact of different participation requirements on the ability of national and provincial/regional surveillance programs to yield valid estimates of the true annual ICU CLABSI pooled incidence rates. We demonstrated that shortening participation requirements might be suitable for national ICU CLABSI surveillance programs

if data are randomly collected. Nevertheless, regional/provincial programs should opt for continuous participation to avoid biased benchmarks (chapter 7).

Furthermore, surveillance programs can also be used as a tool to reduce CLABSI incidence rates in ICUs. However, the magnitude of this effect has not been definitely determined as earlier studies presented a wide range of effect estimates. We hypothesized that the effect of surveillance on CLABSI rates differs depending on the characteristics of participating ICUs. Our third objective was to determine the effect of SPIN-BACC on the CLABSI incidence rates in Quebec ICUs, and identify ICU-level variables associated with higher CLABSI incidence rates. There were important reductions in the CLABSI incidence rates of "surveillance-naïve" (31%) and of non-university affiliated ICUs (27%) that participated in SPIN-BACC for 3 years. However, due to our small sample size, these results were not statistically significant. Neonatal and "surveillance-naïve" units were associated with higher CLABSI incidence rates (chapter 8).

In conclusion, our first study described the CLABSI burden on ICU patients in Quebec. Our simulation study suggested that small and medium sizes surveillance programs should perform continuous surveillance to avoid biased benchmarks. Finally, we suggested that reductions in ICU CLABSI incidence rates associated with targeted surveillance may be more pronounced among "surveillance-naïve" and non-university affiliated ICUs. All the different applications of CLABSI surveillance data demonstrated in this thesis have the ultimate goal of improving patient care and safety.

ABRÉGÉ

Parmi les infections associées aux soins de santé, les bactériémies associées aux cathéters centraux occupent une place prédominante, particulièrement dans les unités de soins intensifs. Malgré leur importance aux niveaux de la clinique et de la santé publique, l'épidémiologie des bactériémies associées aux cathéters centraux au niveau canadien est peu connue. Dès lors, le premier objectif de cette thèse était de décrire l'épidémiologie des bactériémies associées aux cathéters centraux dans les unités de soins intensifs du Québec en utilisant les données du programme de Surveillance Provinciale des Infections Nosocomiales – Bactériémies Associées aux Cathéters Centraux (SPIN-BACC). Nous démontrons que les bactériémies associées aux cathéters centraux sont un problème majeur dans les unités de soins intensifs du Québec. Toutefois, les taux d'incidence de bactériémies associées aux cathéters centraux ont progressivement baissé depuis 2007 et la proportion de *Staphylococcus aureus* résistants à la méthicilline se maintient à moins de 40% depuis 2006, ce qui est considérablement inférieure aux données américaines de surveillance (chapitre 6).

Les programmes de surveillance sont essentiels pour générer des étalons externes. Toutefois, au cours des dernières années, plusieurs programmes régionaux et nationaux ont aboli la participation continue comme préalable. Cette décision pourrait avoir compromis la validité de leurs résultats car le nombre minimal de mois lesquels les établissements doivent soumettre des données à ces programmes afin d'obtenir des taux d'incidence régionaux/provinciaux ou

nationaux valides est inconnu. Notre deuxième objectif était de déterminer, à l'aide de simulations, l'impact de différents seuils minimum de participation sur la capacité des programmes de surveillance régionaux/provinciaux et nationaux à fournir des estimations valides du vrai taux d'incidence des bactériémies associées aux cathéters centraux dans les unités de soins intensifs. Nous démontrons que la réduction des seuils de participation peut être appropriée pour les programmes nationaux si les données sont soumises de façon aléatoire. Toutefois, les programmes régionaux/provinciaux, ainsi que les petits sous-ensembles des unités de soins intensifs, devraient opter pour une participation continue afin d'éviter le risque de générer des étalons externes biaisés (chapitre 7).

Par ailleurs, les programmes de surveillance peuvent aussi être utilisés comme outils pour réduire le taux d'incidence des bactériémies associées aux cathéters centraux dans les unités de soins intensifs. Toutefois, l'importance de cet effet n'a pas encore été déterminée de façon définitive, car les études antérieures ont presenté une vaste gamme d'effets de tailles différentes. Il est possible que l'impact de la surveillance sur les taux d'incidence de bactériémies associées aux cathéters centraux soit différent selon les caractéristiques des unités de soins intensifs participantes aux programmes de surveillance. Dès lors, notre troisième objectif était de déterminer l'effet de SPIN-BACC sur les bactériémies associées aux cathéters centraux dans les unités de soins intensifs du Québec et d'identifier les variables, au niveau des unités de soins intensifs, associées à un taux d'incidence des bactériémies associées aux cathéters centraux plus élevé. Nous

observons des réductions importantes des taux d'incidence des bactériémies associées aux cathéters centraux parmi les unités de soins intensifs qui n'avaient jamais été exposées à la surveillance (31%), ainsi que parmi les unités de soins intensifs non-universitaires (27%) qui ont participé à SPIN-BACC pendant 3 années. Toutefois, ces résultats n'étaient pas statistiquement significatifs à cause de notre petite taille d'échantillon. Les unités de soins intensifs néonatales et les unités qui n'avaient jamais été exposées à la surveillance étaient associées à un taux d'incidence des bactériémies associées aux cathéters centraux plus élevé (chapitre 8).

En bref, notre première étude a démontré que les bactériémies associées aux cathéters centraux constituent un lourd fardeau au sein de la population de patients admis aux unités de soins intensifs dans la province de Québec. Notre étude de simulation a suggéré que les programmes de surveillance de petite et moyenne tailles devraient effectuer leur surveillance de façon continue afin de réduire le risque de présenter des étalons externes biasés. Enfin, l'effet d'un programme de surveillance ciblé sur les taux d'incidence des bactériémies associées aux cathéters centraux semble être plus prononcé au sein des unités de soins intensifs n'ayant jamais exposées à la surveillance et les unités de soins intensifs qui ne sont pas affiliées à des universités. L'utilisation et la compréhension des données de surveillance, tel que démontré dans cette thèse, ont l'objectif final de améliorer la qualité de soins et la sécurité des patients.

ACKNOWLEDGEMENTS

I dedicate this thesis to my husband Dr. Jesse Papenburg and my parents, Rui Fontela and Nelsi Scolari Fontela. Their unconditional support, love and faith kept me going, and made my life much more colourful and beautiful. I will never be able to thank them enough for that. I will never be able to love them enough for that.

I would like to thank my supervisors Dr. Caroline Quach and Dr. Robert Platt for their mentorship, guidance and pleasant mood. I would also like to express my gratitude to them for providing me with an extraordinary work environment, where ideas could be shared, questions could be asked and answers could be found together. In addition, I thank Dr. Barry Pless, my former supervisor, who helped me enter the PhD program and trained me to "see the big picture".

I also thank Dr. David Buckeridge and Dr. Madhukar Pai for their guidance and availability, as well as their interest in my research project. Finally, I would like to thank all the manuscripts' co-authors, for providing invaluable input, and Mr. Luc Villandré, Dr. Dana Teltsch and Dr. Annie Hoen for their kindness and availability to answer my (numerous) questions regarding the statistical methods used in this thesis.

I am very grateful to the *Institut National de Santé Publique du Québec* and the *Surveillance Provinciale des Infections Nosocomiales* (SPIN) group for granting us permission to use the SPIN-BACC database for this thesis. I would like to thank Ms. Isabelle Rocher, from the SPIN-BACC group, for her precious help and kindness, Dr. Charles Frenette, who was kind enough to tell me the SPIN history, as well as all the SPIN-BACC participating hospitals and their infection control teams.

I thank Mrs. Suzanne Larivière, Mrs. Katherine Hayden and Mr. André-Yves Gagnon, from the Department of Epidemiology, Biostatistics and Occupational Health, and Ms. Sofia Bamboulas, from the Montreal Children's Hospital, for their great administrative support throughout my doctoral studies. I also thank them for not only being extremely competent professionals, but also for being generous people who go beyond their duties to help students.

I would like to thank the Division of Pediatric Critical Care at the Montreal Children's Hospital for encouraging my doctoral studies. In particular, I would like to thank Dr. Ronald Gottesman for his guidance, mentorship, generosity and unrestricted support, which have been really important to me and which I will never forget.

I thank my colleagues and dear friends Dr. Robin Taylor and Dr. Arnaud Chiolero for filling my days at Purvis Hall with joy. I am very grateful for the moments, discussions and laughs that we shared, as well as our lunches at Jo's. I

also want to thank my dear friend Dr. Evelyn Constantin for her support and friendship.

Finally, I would like to thank the *Fonds de la Recherche en Santé Québec* (FRSQ), the Montreal Children's Hospital Research Institute, the McGill University Health Center Research Institute, the Department of Pediatrics of the Montreal Children's Hospital, McGill University, Dr. Davinia Withington, and Dr. Madhukar Pai for providing the financial support that enabled me to pursue my doctoral studies.

CONTRIBUTION OF AUTHORS

I developed the original research questions for this thesis in collaboration with my thesis supervisors, Dr. Caroline Quach and Dr. Robert Platt. I was responsible for the definition of the thesis objectives, which were approved by my thesis committee. With the guidance of my thesis supervisors, I selected or developed the design, the methods and the statistical analysis used in each study.

Dr. Quach obtained the SPIN-BACC data used in this thesis. I processed all data and built specific databases for each of the studies. Consequently, I carried out all statistical analyses and was responsible for the first result interpretation. After discussing the results with my thesis supervisors and thesis committee members, I was in charge of drafting the manuscripts, which were revised and edited by Dr. Caroline Quach and Dr. Robert Platt, as well as other co-authors. Finally, I wrote all chapters of this PhD thesis.

The contributions of co-authors to the manuscripts included in this thesis are described in detail below:

1. Patricia S. Fontela, Robert W. Platt, Isabelle Rocher, Charles Frenette, Dorothy Moore, Élise Fortin, David Buckeridge, Madukhar Pai, Caroline Quach. ***Surveillance Provinciale des Infections Nosocomiales*** **(SPIN) Program: implementation of a mandatory surveillance program for central line-associated bloodstream infections.** Am J Infect Control 2011;39(4):329-35.

Conception: PS Fontela, C Quach, R Platt; Design: PS Fontela, C Quach, R Platt, D Buckeridge, M Pai; *Data acquisition:* I Rocher, C Frenette, D Moore, E Fortin, C Quach; *Analysis:* PS Fontela, C Quach, R Platt; *Data interpretation:* PS Fontela, C Quach, R Platt, D Buckeridge, M Pai, I Rocher, C Frenette, D Moore, E Fortin; *Writing:* PS Fontela, C Quach, R Platt, I Rocher, C Frenette, D Moore, E Fortin; *Critical revision:* C Quach, R Platt, D Buckeridge, M Pai, I Rocher, C Frenette, D Moore, E Fortin. *Supervision:* C Quach

2. Patricia S. Fontela, Robert W. Platt, Isabelle Rocher, Charles Frenette, Dorothy Moore, Élise Fortin, David L. Buckeridge, Madukhar Pai, Caroline Quach. **Epidemiology of central line-associated bloodstream infections in Quebec intensive care units: a 6-year review.** Am J Infect Control. 2011 Aug 6. [Epub ahead of print]

Conception: PS Fontela, C Quach, R Platt; *Design:* PS Fontela, C Quach, R Platt, D Buckeridge, M Pai; *Data acquisition:* I Rocher, C Frenette, D Moore, E Fortin, C Quach; *Analysis:* PS Fontela, C Quach, R Platt; *Data interpretation:* PS Fontela, C Quach, R Platt, D Buckeridge, M Pai, I Rocher, C Frenette, D Moore, E Fortin; *Writing:* PS Fontela, C Quach, R Platt, I Rocher, C Frenette, D Moore, E Fortin; *Critical revision:* C Quach, R Platt, D Buckeridge, M Pai, I Rocher, C Frenette, D Moore, E Fortin. *Supervision:* C Quach

3. Patricia S. Fontela, Caroline Quach, David L. Buckeridge, Madhukar Pai, Robert W. Platt. **Effect of surveillance program participation**

requirements on the validity of benchmarks for central line-associated bloodstream infection incidence rates in intensive care units

Conception: PS Fontela, C Quach, R Platt; *Design:* PS Fontela, R Platt; *Data analysis:* PS Fontela, R Platt; *Data interpretation:* PS Fontela, C Quach, R Platt; *Writing:* PS Fontela, C Quach, R Platt, DL Buckeridge, M Pai; *Critical revision:* C Quach, R Platt, D Buckeridge, M Pai; *Supervision:* RW Platt.

4. Patricia S. Fontela, Caroline Quach, David L. Buckeridge, Madukhar Pai, Robert W. Platt. **Effect of targeted surveillance on central line-associated bloodstream infection incidence rates in intensive care units**

Conception: PS Fontela, C Quach, R Platt; *Design:* PS Fontela, R Platt, C Quach, DL Buckeridge; *Data analysis:* PS Fontela, R Platt, DL Buckeridge; *Data interpretation:* PS Fontela, C Quach, R Platt, DL Buckeridge; *Writing:* PS Fontela, C Quach, R Platt, DL Buckeridge, M Pai; *Critical revision:* C Quach, R Platt, D Buckeridge, M Pai; *Supervision:* RW Platt, C Quach.

STATEMENT OF ORIGINALITY

The work presented in this thesis represents an original contribution to the domain of infectious disease epidemiology. Specifically, it contributes to the areas of surveillance of healthcare-associated infections (HAI) and infection control.

Central line-associated bloodstream infections (CLABSI) represent an important toll on patients admitted to intensive care units (ICUs). Many countries have implemented national surveillance systems to gather data about the epidemiology of CLABSI and other HAI. In Canada, the only source of data available is the Canadian Nosocomial Infection Surveillance Program, which collects data from 49 sentinel hospitals, mostly university-affiliated centres, from across the country. In Quebec, a provincial surveillance program for CLABSI in ICUs (SPIN-BACC) was launched in 2003 and currently includes 62 of the province's ICUs. The description of CLABSI epidemiology in Quebec ICUs contributed to a better comprehension of the ICU CLABSI problem in the country, as it also provides data from community-based hospitals. Our study showed that CLABSI is still a prominent problem in Quebec ICUs, but rates have declined in recent years.

In the last decades, many countrywide and regional HAI surveillance networks have allowed hospitals to shorten their annual participation in programs. However, the effect of non-continuous participation requirements on benchmarks validity generated by these programs had yet to be studied. Our study showed that

non-continuous participation might be feasible for nationwide CLABSI surveillance programs, if data are collected randomly. However, regional/provincial programs should rely on continuous participation to avoid increasing the risk of biased benchmarks.

Finally, in the last decades, surveillance programs have been used as an intervention to decrease HAI rates. Nevertheless, the magnitude of its effect on ICU CLABSI incidence rates has yet to be determined, as earlier studies were unable to adjust for potential confounders, providing only crude estimates of the effect. Our study showed that the effect of surveillance on ICU CLABSI incidence rate is not uniform and is probably larger in ICUs that had not been previously exposed to surveillance before and in non-university affiliated units. Furthermore, we showed that neonatal units and ICUs never previously exposed to surveillance are associated with higher CLABSI rates

While I received essential guidance from my supervisors and committee members, and input from the co-authors on clinical, methodological and statistical aspects of this thesis, the studies presented in the forthcoming chapters represent my original work.

STATEMENT OF SUPPORT

This thesis was supported by various sources of funding. I am very grateful for having received a Doctoral Training Award from the *Fonds de la Recherche en Santé Québec* (FRSQ), a Foundation of Stars/Montreal Children's Hospital Research Fellowship from the Montreal Children's Hospital Research Institute, a McGill University Health Center Research Institute Studentship Award, as well as the Allan Ross Fellowship from the Department of Pediatrics of the Montreal Children's Hospital. Furthermore, I also received a Principal's Graduate Fellowship and a Graduate Studies Fellowship, both from McGill University, for which I am also thankful. Finally, I am very grateful to Dr. Davinia Withington and Dr. Madhukar Pai, who provided complimentary funding in the form of a research assistantship during the first year of my doctoral studies.

Our project was supported by the *Institut National de Santé Publique du Québec* and the *Surveillance Provinciale des Infections Nosocomiales* (SPIN) group, which gave us permission to use data from the SPIN-BACC program. The views presented in this thesis are those of the authors, and do not necessarily reflect those of the *Institut National de Santé Publique du Québec* or the SPIN group.

LIST OF ABBREVIATIONS

CI: Confidence interval

CLABSI: Central line-associated bloodstream infection

CVC: Central venous catheter

CVCUR: Central venous catheter utilization ratio

HAI: Healthcare-associated infections

ICU: Intensive care unit

IQR: Interquartile range

KISS: *Krankenhaus Infektions Surveillance System*

NICU: Neonatal intensive care units

NHSN: National Healthcare Safety Network

NNIS: National Nosocomial Infections Surveillance System

OR: Odds ratio

PICU: Pediatric intensive care unit

REACAT: *Surveillance Nationale des Infections Nosocomiales liées aux Cathéters Veineux Centraux en Réanimation Adulte*

RR: Rate ratio

SD: Standard deviation

SENIC: Study on the Efficacy of Nosocomial Infection Control

SIR: Standardized incidence ratio

SPIN-BACC: *Surveillance Provinciale des Infections Nosocomiales - Bactériémies associées aux cathéters centraux*

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CHAPTER 1 - INTRODUCTION

Surveillance is a critical activity in public health.[1] This continuous and dynamic process involves the collection, analysis, interpretation and dissemination of health data with the final objective of using the obtained results for prevention and control.[2, 3] To be successful in this purpose, surveillance systems depend on attributes such as high sensitivity to identify cases, simplicity, timeliness and flexibility.[2]

In the hospital setting, surveillance is used to gather information on patient safety. This includes the monitoring of healthcare-associated infections (HAI), which are associated with high morbidity and mortality worldwide. According to the World Health Organization, HAI are estimated to affect more than 1.4 million patients worldwide at any given time.[4] Of all HAI, central line-associated bloodstream infections (CLABSIs) are considered one of the most important due to their severe impact on mortality, morbidity, and hospitalization costs, especially in intensive care unit (ICU) patients.

Despite the clinical and public health implications of CLABSI in ICUs, little has been published about its epidemiology in Canada. Currently, the Canadian Nosocomial Infection Surveillance Program, a network consisting of 49 self-selected sentinel hospitals in 9 different provinces, is the only available source of data.[5] A comprehensive analysis of the CLABSI situation in Quebec ICUs would contribute to a better understanding of the CLABSI problem not only

in Quebec but also in the rest of Canada. Therefore, the first objective of this thesis was to describe the epidemiology of CLABSI in Quebec ICUs from October 2003 to March 2009. To do so, we used data from the *Surveillance Provinciale des Infections Nosocomiales - Bactériémies Associées aux Cathéters Centraux* (SPIN-BACC) program, launched in 2003 by the Quebec Ministry of Health (*Ministère de la santé et des services sociaux*) and the *Institut National de Santé Publique du Québec*.[6-9]

Different strategies can be employed to perform CLABSI surveillance. Independently of the chosen strategy, surveillance should be performed as an ongoing process, as continuity enables the recognition of changes in trends and detection of outbreaks. However, running a continuous surveillance program is labour intensive and costly, and many hospitals do not have the resources to comply with this requirement. Many national and regional/provincial CLABSI surveillance programs acknowledged this reality and consequently eliminated the requirement for continuous participation from their protocols, as a way of increasing the number of participating hospitals.[10-13]

Shortening the surveillance period performed per year raises concerns about the validity of the obtained results by these programs. Thus far, no study has determined the minimal number of months hospitals must participate in a surveillance program to yield a valid benchmark for the annual pooled incidence rate of CLABSI. Thus, the second objective of this thesis is to determine, through simulation, the impact of different participation requirements on the ability of

national and provincial/regional surveillance programs to yield valid estimates of the true annual ICU CLABSI incidence rate.

Finally, it is hypothesized that HAI surveillance can also be used as a tool to reduce CLABSI incidence rates. Two mechanisms through which surveillance would achieve this objective were proposed by the Study on the Efficacy of Nosocomial Infection Control (SENIC).[14] Initially, surveillance might influence healthcare practice through a Hawthorne effect, meaning that feeling watched, healthcare professionals tend to provide better care to patients when the surveillance team is physically present.[15] However, this effect is expected to be transitory, as it is not feasible to perform HAI surveillance on hospital wards 24 hours per day, 7 days per week. The second and most powerful mechanism through which surveillance may lead to a decrease in CLABSI incidence rates is the dissemination of its results. The reporting of provincial/national surveillance results to infection control teams, as well as administrative and hospital staff may trigger changes, i.e., improvements in infection control practices, which in turn may reduce the risk of infection.[16]

In the last decades, the use of targeted surveillance, which focuses on a specific HAI and/or group of patients, has become very popular worldwide, due to its lower cost and the fact that it generates risk-adjusted results. So far, the effect of targeted surveillance on ICU CLABSI rates was assessed by a few before-after studies, which reported decreases in CLABSI rates ranging from 13.1% to 77.2% after 2 and 5 years of surveillance, respectively.[17-22] We hypothesized that the

wide range of observed effects is due to the fact that the targeted surveillance effect is modified by certain characteristics of participating ICU. Knowing the magnitude of this effect would allow the setting of realistic objectives when implementing CLABSI surveillance programs in ICUs. Therefore, the third objective of this thesis is to determine the effect of a targeted surveillance program (SPIN-BACC) on the CLABSI incidence rate in Quebec ICUs and identify ICU-level characteristics associated with higher CLABSI incidence rates.

CHAPTER 2 - LITERATURE REVIEW

2.1. Central line-associated bloodstream infections

HAIs are defined by the World Health Organization as "an infection occurring in a patient during the process of care in a hospital or other healthcare facility which was not present or incubating at the time of admission".[4] Infections acquired in hospital with signs and symptoms starting after discharge are also considered HAIs, as long as they meet time windows specified in standard definitions.

HAIs cause a substantial burden of illness worldwide.[23] It is currently impossible to obtain an accurate global estimate due to the limited availability of reliable data and different surveillance methods and definitions used in different countries.[4, 24] Despite this, the World Health Organization estimates that, at any time, more than 1.4 million patients are affected by HAI worldwide.[24] In the U.S. alone, the Centers for Disease Control and Prevention estimated that 1.7 million HAIs occurred in 2002, associated with approximately 99,000 deaths and with an economic impact of $ 4.5 billion.[25] In Europe, the European Centre for Disease Prevention and Control calculates that the yearly burden of HAI includes 4.5 million infections, 111,000 deaths, 16 million extra days of hospitalization and a total cost of € 7 billion.[26] The situation is even worse in developing countries, where HAI prevalence is estimated to be 15.5 per 100 hospitalized patients.[27]

In Canada, HAI prevalence in adult and pediatric hospitals is estimated to be 11.6 cases per 100 patients and 8 cases per 100 patients, respectively.[28, 29] The Canadian Nosocomial Infection Surveillance Program estimates that CLABSI prevalence is 1.2 cases per 100 adults patients, but 2.5 cases per 100 pediatric patients.[28, 29] Among Canadian ICU patients, the median excess length of hospital stay attributable to CLABSI is 13.5 days, while the average attributable cost per case survivor is CAN$ 35,000.[30]

CLABSIs are generally considered the most severe HAI because of their high mortality, morbidity and important economic burden. For surveillance purposes, the Centers for Disease Control and Prevention define CLABSI as a bloodstream infection in a patient with a central venous catheter (CVC) at the time of diagnosis or within the 48 hours prior.[31, 32] In addition, the bloodstream infection cannot be related to any other infectious process the patient might have and must not have been present or incubating at the moment of hospital (or ICU) admission.[33]

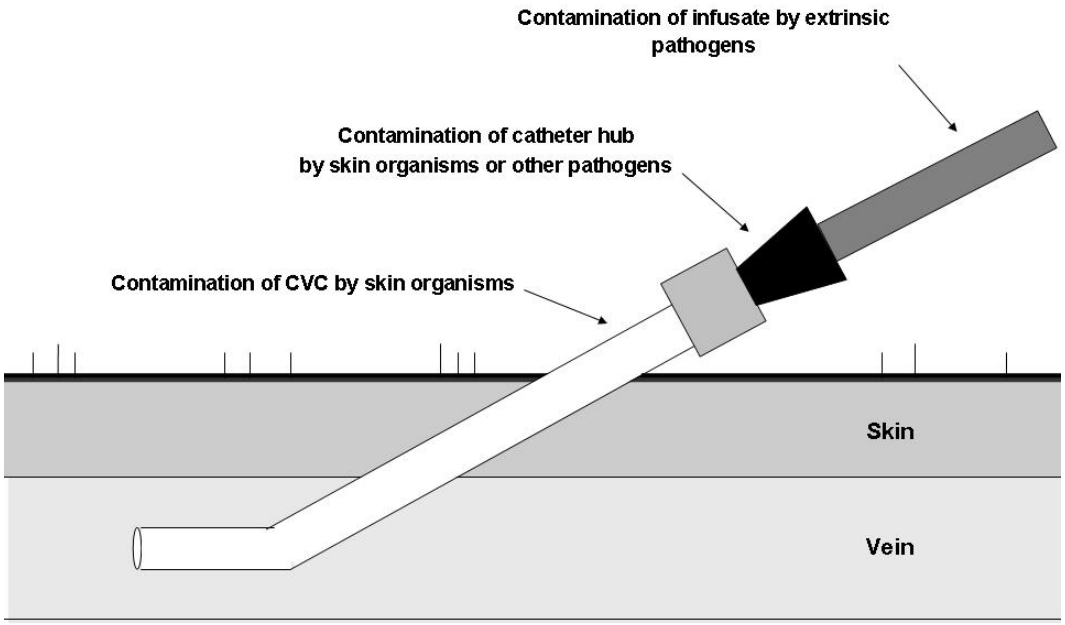
The current definition of bloodstream infection used by the National Healthcare Safety Network (NHSN), which is the national surveillance program in the U.S., is based on the presence of positive blood cultures.[34] It includes at least one of the following criteria:

1. Patient has a recognized pathogen cultured from at least 1 blood culture, AND organism cultured from blood is not related to an infection at another site, OR
2. Patient has at least 1 of the following signs or symptoms: fever (>38°C), chills, or hypotension, AND signs and symptoms and positive laboratory results are not related to an infection at another site, AND common skin commensals (i.e., diphtheroids - *Corynebacterium* spp -, *Bacillus* - not *B. anthracis* - spp, *Propionibacterium* spp, coagulase-negative staphylococci - including *S epidermidis* -, viridans group streptococci, *Aerococcus* spp, *Micrococcus* spp) is cultured from at least 2 blood cultures drawn on separate occasions, OR
3. Patient <1 year of age has at least 1 of the following signs or symptoms: fever (>38°C, rectal), hypothermia (<37°C, rectal), apnea, or bradycardia, AND signs and symptoms and positive laboratory results are not related to an infection at another site, AND common skin commensals (i.e., diphtheroids - *Corynebacterium* spp -, *Bacillus* spp - not *B. anthracis* -, *Propionibacterium* spp, coagulase-negative *Staphylococci* - including *S epidermidis* -, viridans group *Streptococci*, *Aerococcus* spp, *Micrococcus* spp) is cultured from at least 2 blood cultures drawn on separate occasions.

CLABSIs occur most commonly after contamination of a CVC by bacteria present on the skin (Figure 2.1).[35] After penetrating through the CVC cutaneous insertion site, microbes follow the external catheter tract and colonize its tip,

which leads to infection of the bloodstream.[36] The CVC contamination may happen at the time of insertion, or later, during its manipulation. In addition, CLABSIs may develop after the contamination of the catheter hub or the use of contaminated intravenous fluids.[36, 37]

Figure 2.1 – Mechanisms of central venous catheter contamination (Adapted from Maki DG. Infections caused by intravascular devices used for infusion therapy: pathogenesis, prevention, and management. In: Bisno AL, Waldvogel FA, editors. Infections associated with indwelling medical devices. 2nd ed. Washington, DC: American Society for Microbiology Press, 1994:155-212)



CVC colonization and development of CLABSIs are a consequence of the interaction of pathogens, CVC characteristics, as well as extrinsic and host factors. In terms of pathogens, data from the NHSN (U.S.), for the period between 2006-2007, and EDCD, for the year of 2008, show that Gram-positive cocci cause between 50 and 60% of CLABSI cases (Table 2.1).[38, 39] Within the Gram-positive cocci group, coagulase-negative *Staphylococci* are the most frequent pathogens associated with CLABSIs (around 30%). Gram-negative bacteria are present in 17% of CLABSI cases in the U.S., but are considerably more frequent in Europe (35%).[38, 39] While *Klebsiella* spp and *Enterobacter* spp are the most common CLABSI-associated Gram-negative pathogens in the U.S., most of the Gram-negative CLABSI in Europe are due to *Pseudomonas aeruginosa* (8%). Finally, *Candida* spp (a yeast) accounts for 6 to 12% of cases and is associated with the highest attributable mortality rates (9%).[38-40] No specific data exist regarding pathogens associated with CLABSI in Canadian ICUs.

Some pathogens, e.g., coagulase-negative *Staphylococci*, *S. aureus* and certain *Candida* spp, have increased adherence capacities due to their ability to produce extracellular polysaccharides, known as "slime", which envelope their external surfaces. Extracellular polysaccharides allow bacteria to adhere to the CVC surface while acting as a barrier against leukocytes and antimicrobials.[41, 42] The adhesion of the first bacteria to the intravenous catheter facilitates the settlement of other pathogens, which will proliferate and form multilayered bacterial colonies enclosed in a matrix of extracellular polymeric substances known as "biofilm".[43, 44]

Table 2.1 – Main pathogens associated with central line-associated bloodstream infections

Pathogens	**CDC (2006-2007)**	**ECDC (2008)**
Bacteria		
Gram-positive cocci	60%	53.4%
- Coagulase- negative *staphylococci*	34.1%	28%
- *Enterococcus* spp	16%	12.5%
- *Staphylococcus aureus*	9.9%	11.4%
Gram-negative bacilli	17.6%	35.2%
- *Klebsiella* spp	4.9%	6.5%
- *Enterobacter* spp	3.9%	5.5%
- *Pseudomonas aeruginosa*	3.1%	7.9%
- *Escherichia coli*	2.7%	7.5%
Yeast		
Candida spp	11.8%	6.3%

CDC = Centers for Disease Control and Prevention, ECDC = European Centre for Disease Prevention and Control

The material with which the catheter is made may also increase the risk of colonization. Silicone catheters are more prone to bacterial adherence than polyurethane or Teflon catheters, probably due to the direct toxic effect of silicone on neutrophils.[45] In addition, certain materials predispose to the formation of thrombi, which later serve as a nidus for microbial colonization.[35] Finally, irregularities present on the catheter surface also enhance bacterial adhesion.[35]

Extrinsic factors associated with medical interventions entail a higher risk of catheter colonization. The administration of parenteral nutrition fluids through the CVC, which are rich in glucose and lipids, is associated with microbial growth, especially *Candida* spp.[46] Most importantly, the non-observation of infection control practices by healthcare workers is thought to be the major contributor to nosocomial transmission of microorganisms and CVC contamination. Infection control measures supported by well-designed studies include the use of sterile gloves and maximal sterile barrier precautions at the moment of CVC insertion, as well as the use of >0.5% chlorhexidine gluconate preparations with 70% alcohol for skin antisepsis.[31] Among other evidence-based recommendations for CVC maintenance, the most important are prompt removal of CVCs that are no longer needed, and use of >0.5% chlorhexidine gluconate preparations with 70% alcohol for dressing changes and to scrub access ports.[31]

Finally, hosts with a compromised immune system are at high risk for developing CLABSI from both pathogenic and commensal microorganisms. Patients in the extremes of age, i.e., infants and elders, are more susceptible not only to CLABSI, but to all types of HAIs.[47-49] This may be due to the presence of an immature immune system, in the case of newborns and infants, or chronic diseases in older patients, such as diabetes, that impair the normal patient's immune response, as well as immunosenescence.[50-52] Furthermore, the disease process that led to hospitalization can also play a role in decreasing the host immune status. For example, severe burns cause important losses of skin, a physical barrier against infections, increasing the risk of CVC contamination.[53]

Finally, many therapeutic strategies currently used also compromise host defenses, e.g., immunosuppressive and immunomodulatory drugs.

2.1.1. Central line-associated bloodstream infections in intensive care units

ICU patients are particularly at risk for the development of CLABSIs.[48] The use of a CVC is an essential part of the standard care provided to this patient population. As CVCs are frequently the only route to administer intravenous drugs and nutrition to ICU patients, sometimes for long periods of time, they tend to be manipulated multiple times per day, increasing the risk of contamination.[54] In addition, ICU patients are severely debilitated, many of them presenting decreased immune defenses due to concurrent disease processes such as neutropenia, human immunodeficiency virus infection, cancer, poor nutritional status, and extremes of age.[53, 55] Importantly, ICU endemic nosocomial microorganisms are more resistant to antimicrobials than those found in other hospital areas, due to the selection of multidrug resistant strains caused by the extensive use of antimicrobials in these units.[39, 56] Consequently, ICU nosocomial infections tend to be more aggressive and difficult to treat.[53]

The public health implications of CLABSIs in ICU patients are quite evident. From the 250,000 estimated CLABSI cases that occur annually in the U.S., approximately 80,000 (32%) occur in ICUs despite the fact that ICUs represent only 5 to 10% of all hospital beds.[25, 55] A systematic review including data from 4

European countries (United Kingdom, France, Germany and Italy) estimated that around 40,000 CLABSI episodes are diagnosed annually in ICUs, generating between 264,000 and 369,000 additional hospital days and extra costs ranging from € 270 to 344 million per year.[57]

2.1.2. Central line-associated bloodstream infections in Canadian intensive care units

Despite its clinical and public health importance, little has been published about the CLABSI epidemiology in ICUs in Canada. Currently, the only source of data is the Canadian Nosocomial Infection Surveillance Program, which was established in 1994 and uses data from 49 self-selected sentinel hospitals, mostly university-affiliated centres, in 9 Canadian provinces to provide HAI rates and trends and develop national guidelines.[5, 58] According to the Canadian Nosocomial Infection Surveillance Program, the pooled annual CLABSI incidence rates for adult, pediatric and neonatal ICUs in 2006 were 2.3, 2.6 and 5.7 CLABSI/1,000 CVC-days, respectively.[58]

In 2003, the *Ministère de la santé et des services sociaux* and the *Institut National de Santé Publique du Québec* launched the SPIN-BACC program, with the objectives of gathering data on the epidemiology of CLABSI in the Province of Quebec and to promote HAI surveillance.[6] SPIN-BACC requires all participating hospitals to perform active and prospective CLABSI surveillance in ICUs throughout the year in a standardized way. SPIN-BACC data were used to

create a provincial database about CLABSI incidence and mortality rates and have been used as provincial benchmarks since 2005.[7-9] Once participation became mandatory for all Quebec ICUs with 10 beds or more in 2007, SPIN-BACC was implemented in 62 of the province's ICUs (100% of eligible units).

Given the paucity of data about the CLABSI epidemiology in Canadian ICUs, carrying out a comprehensive analysis of the CLABSI situation in Quebec ICUs would contribute to a better understanding of the CLABSI problem in Canada, as SPIN-BACC also provides data for community-based hospitals. Furthermore, this would allow Canadian ICUs to benchmark their infection rates using Canadian data.

Therefore, the first objective of this thesis was to describe the epidemiology of CLABSI in Quebec ICUs from October 2003 to March 2009.

2.2. Surveillance of healthcare-associated infections

Hospital surveillance programs are essential to provide information on the HAI burden, through the quantification of the baseline rates for different infections, the monitoring of trends, and the detection of outbreaks. However, purposes of HAI surveillance go beyond this, as its results can also be used for the planning or evaluation of infection control measures, comparison of infection rates between hospitals and hypothesis testing.[59] In addition, it is believed that surveillance may be a tool to reduce HAI rates.[60]

HAI surveillance encompasses programs that are single hospital-based but also programs that are international, multicenter, electronic systems that receive data from hospitals from different countries. Independently of the program's size, surveillance is an ongoing process that requires the long-term collaboration of many different individuals. Thus, to improve acceptability and collaboration, a surveillance system must have a simple structure and be easily operated.[59] Moreover, it should be flexible to accommodate other information needs, changes in case definitions, and integration with other systems.

Other desired attributes of a surveillance system include representativeness, timeliness, stability, sensitivity, positive predictive value and data quality.[59, 61] Representativeness is crucial for the accurate description of HAI rates over time and their distribution in different patient populations. Its absence results in the impossibility of generalizing surveillance results to the population as a whole, which may affect planning of infection control interventions. One problem encountered by multicenter surveillance programs that rely on voluntary participation is the self-selection of participants. In this particular case, representativeness might be impaired because participating hospitals may differ from non-participants in important aspects, including case-mix, quality of their infection control programs and HAI rates.[62, 63]

Timeliness and stability are attributes directly associated with the performance and usefulness of a surveillance system, which are determinants of its viability.[64] In the case of HAI, timeliness alludes to the time required to

recognize and control an outbreak, or to identify a change in trends, while stability is defined as the level of reliability of a surveillance system.[59] The timeliness of a surveillance system can be significantly impaired by a lack of stability, as this will lead to a delay in problems recognition.

Sensitivity and positive predictive value provide different viewpoints about the efficiency of a surveillance system. Sensitivity is the extent to which cases are detected in the target population, and must be tailored according to the surveillance objectives. The monitoring of HAI trends can be performed by surveillance systems that do not have high sensitivity, if this latter is kept constant over time.[59] However, if outbreak investigations are predicted to happen, a highly sensitive case definition should be used to ensure identification of cases and to monitor change in rates over time.[61] In such instances, a high positive predictive value is also required, because high rates of false positives could mislead the detection of an outbreak.[65]

Nevertheless, the prevalence of HAI may be significantly different depending on HAI type and geographical region. For example, the prevalence of CLABSI in Canada (2007) and Europe (2009) was estimated to be 1.2 and 1.9 cases per 100 adult ICU patients, while the prevalence of ventilator-associated pneumonia in Europe (2009) was 6.5 cases per 100 ICU patients.[29, 66] Whereas sensitivity and specificity are conditioned on the "true" numbers of cases and non-cases, positive and negative predictive values are measures that are proportionally dependent on the prevalence of condition.[66] Therefore, due to the

variability in the prevalence of different HAI, it may not always be possible to have surveillance programs with high positive predictive values, independent of the quality of the methods employed.

The quality of collected data refers to data validity and completeness and has a direct influence on the surveillance results. The assessment of the quality of surveillance programs' data is essential to ensure their scientific credibility, as well as to identify methodological problems. As explained above, HAI surveillance systems must ideally present high sensitivity and high positive predictive values. However, cut-offs for both measures that could be used to classify the quality of data reporting have yet to be determined.[67] In 1998, the quality of reporting of the American National Nosocomial Infection Surveillance (NNIS) system was assessed by a pilot study that included 9 participating hospitals and had as gold standard the result of a chart review performed by previously trained data collectors.[68] Regarding the reporting of CLABSI, the sensitivity, specificity and positive predictive value were 85%, 98.3% and 87%, respectively (95% confidence intervals - CI - not provided).

The quality of data reporting of two other national surveillance systems has also been similarly evaluated. In 2007, Zuschneid et al showed that the sensitivity and specificity of CLABSI reporting to the national German surveillance program were 66% and 99.4% (95% CI not provided), respectively.[69] Finally, Versporten et al assessed the validity of the reporting of CLABSI data to the National Surveillance of Infections in Hospitals program in Belgium between

1997 and 2001.[70] Their sensitivity was 59.3% (95%CI 39.0-76.9), specificity was 99.1% (95%CI 98.2-99.6), and the positive predictive value was 65.3% (95%CI 43.6-82.4).

The use of case definitions intends to establish uniform criteria for HAI reporting, while balancing the needs of sensitivity, specificity and feasibility.[71] In the last decade, surveillance systems have moved towards increasing specificity of CLABSI definitions (and also other HAIs). While still using a combination of clinical findings and laboratory results for its determination, the current NHSN CLABSI definition and other surveillance networks only include cases that have been confirmed by positive blood cultures, i.e., laboratory-confirmed CLABSI.[34, 72] To improve feasibility and simplicity, case definitions used for surveillance purposes tend to be more restrictive than clinical diagnoses made by physicians, as these latter also use their disease knowledge and their own understanding of the patient's clinical course.[71] Consequently, it is not recommended to use surveillance definitions for clinical diagnosis and/or therapeutic decisions.[13, 73]

2.2.1. Surveillance methods

The methods used for data collection are another essential element of surveillance systems. Nowadays, several different HAI surveillance strategies are available. The NHSN, whose methods are considered by many to be the current gold standard, requires all participating hospitals to perform active, patient-based, prospective surveillance.[12, 74] Active surveillance is the process of proactively

seeking HAI incident cases using trained personnel.[13, 75] For this purpose, information gathered from various data sources is used to determine the occurrence of a HAI. Alternatively, passive surveillance relies on people other than the infection control practitioners to report the cases. Nevertheless, their lack of training in surveillance may lead to misclassification, underreporting and absence of data timeliness.

Patient-based surveillance is characterized by the identification of HAI cases through patient monitoring, using all data sources available.[74] It requires considerable resources, as infection control practitioners must visit patient care areas, review medical charts and laboratory results, and have discussions with caregivers. In contrast, laboratory-based surveillance relies on reports of positive laboratory results for cases detection. Despite being faster and comparatively inexpensive, it has the disadvantages of increasing the risks of misclassification – classifying as an infection what was really a colonization -, as well as a lack of information regarding patients' characteristics.[71]

Prospective surveillance requires patients to be followed while hospitalized. Ideally, the post-discharge period should be included to capture HAIs with clinical findings that only become evident after hospital discharge. As a major advantage, prospective surveillance enables the identification of clusters of infection and outbreaks in a timely fashion.[13] In addition, data collected tend to have better quality compared to data obtained from chart reviews but is expensive and labour intensive.

One very popular alternative to prospective surveillance of incident cases is the use of prevalence surveillance. Prevalence surveillance monitors all active HAI cases at a given point in time for a given location. It can be performed in a single day (point prevalence) or over a period of time (period prevalence). Despite being a rapid and low-cost strategy, it is associated with both over- and underestimation of patients' risk of infection due to, respectively, length-biased sampling and insufficient sample size in small hospitals.[13, 76] Moreover, it does not allow for outbreak detection.

Finally, HAI data can be collected using hospital-wide or targeted strategies. Hospital-wide surveillance is a comprehensive method where all types of HAIs on all wards are monitored, providing a broad view of what happens in the hospital.[12] It involves the use of active, prospective, and patient-based surveillance methods. The major disadvantage is that this strategy is time and resource consuming.

In 1986, the Centers for Disease Control and Prevention's predecessor to NHSN, the NNIS program, introduced 3 standardized protocols, called "surveillance components", targeting different patient groups: adult and pediatric ICUs, high-risk nurseries and surgical patients.[77] While the surgical patients component focused exclusively on surgical site infections, both the ICU and the high-risk nurseries components aimed to collect data on all HAIs. The main advantages of these targeted surveillance programs include their lower cost and

the generation of data for a group of patients that were all exposed to a similar risk of acquiring these infections, i.e., risk-adjusted results.[13, 78]

The use of targeted surveillance, associated with standardization of case definition and surveillance methods, helps to improve the comparability of interhospital rates, which is one of the fundamental purposes of HAI surveillance.[78] However, stratification by ICU type only solves part of the problem, as case-mix between same-type ICUs may vary considerably. Consequently, the non-adjustment for case-mix may lead to biased comparisons, as some ICUs will certainly present high HAI rates because of patient populations with high intrinsic risk for HAI or undergoing specific therapies/procedures placing them at higher risk, rather than higher rates because of the quality of the infection control program and patient care.[79, 80]

Some attempts have been made to build case-mix adjustment models using both patient- and hospital-level factors, but the definitive set of variables have yet to be defined. At the hospital-level, surveillance results are usually stratified by academic profile (university affiliation) and size. Nonetheless, Tong et al observed that some hospital services were associated with high rates of healthcare-associated bloodstream infections, such as oncology (rate ratio - RR - 1.60; 95%CI 1.29-1.98), infectious diseases (RR 2.72; 95%CI 1.97-3.96), bone marrow transplant (RR 1.52; 95%CI 1.14-2.03) and acquired immune deficiency syndrome wards (RR 2.14; 95%CI 1.20-3.82).[81] At the patient-level, Kritsotakis et al proposed the following variables to adjust for case-mix differences:

neutropenia (odds ratio - OR - 3.9; 95%CI 1.5-9.9), emergency admission (OR 2.2; 95%CI 1.3-3.7), infection as primary diagnosis (OR 4.1; 95%CI 1.7-10.1), "ultimately fatal disease" (OR 2.1; 95%CI 1.3-3.5) or "rapidly fatal disease" (OR 6.3; 95%CI 3.2-12.6), impaired functional status (OR 1.7; 95%CI 1.1-2.6), length of stay <15 days at risk for infection (OR 2.0; 95%CI 1.3-3.1), mechanical ventilation (OR 3.5; 95%CI 1.6-7.5), and surgical procedure within 30 days of the onset of infection (OR 2.4; 95%CI 1.5-3.8).[80]

Initially, CLABSI data were collected as part of a HAI hospital-wide surveillance program. The higher frequency of CLABSI in ICUs compared to other hospital wards as well as their high case-fatality proportion in this particular patient population led to the development of a CLABSI surveillance strategy that specifically targets ICU patients.[12, 13, 77]

Like the hospital-wide strategy, ICU targeted CLABSI surveillance was designed to be a continuous, active and prospective process. Continuity enables the recognition of changes in trends and detection of outbreaks. However, running a continuous surveillance program is labour intensive and costly, and many hospitals do not have the resources to comply with it. Moreover, in the specific case of ICU targeted CLABSI surveillance, resources are concentrated in only one area and on one HAI, which leaves the infection control team unaware of problems arising in other hospital wards or relating to other types of HAI.

2.2.2. Targeted surveillance programs and hospital participation requirements

As a way to better use available resources and to reduce the risk of missing clusters of infection on the remaining wards, many hospitals have decided to shorten the duration of the ICU targeted CLABSI surveillance performed throughout the year. As a result, more time is available for HAI surveillance in the rest of the hospital and for other important infection control activities. However, this strategy probably has a negative impact on the validity of the local CLABSI incidence rates. When calculating the annual rates for a single ICU, the total number of CLABSI cases and CVC-days that occur in a one-year period is low. Thus, CLABSI rates produced will be statistically very unstable, as removing one-month of data could substantially change the annual CLABSI incidence rate.

Nevertheless, many national and regional/provincial CLABSI surveillance programs acknowledged this new reality and consequently eliminated continuous participation requirements from their protocols in order to increase the number of participating hospitals. For example, NHSN requires a minimum participation of 1 month per year from hospitals, while in England the cut-off is 3 months.[11, 82] In the Netherlands, hospitals participate at their own discretion in the national surveillance program.[10, 83]

Similarly to what happens to single ICUs, the elimination of continuous participation requirements may also negatively impact results of multicenter surveillance programs. The gaps in the data collected by different ICUs raise concerns about the validity of the obtained benchmarks. As described above, the cut-offs for the minimal hospital participation in multicenter CLABSI surveillance programs has been set arbitrarily and are variable. No one has yet determined the minimum number of months hospitals must participate in a national or regional/provincial surveillance program to yield a valid estimate of the annual CLABSI pooled incidence rate.

Thus, the second objective of this thesis was to determine, through simulation, the impact of different participation requirements on the ability of national and regional/provincial surveillance programs to yield valid estimates of the true annual ICU pooled CLABSI incidence rates.

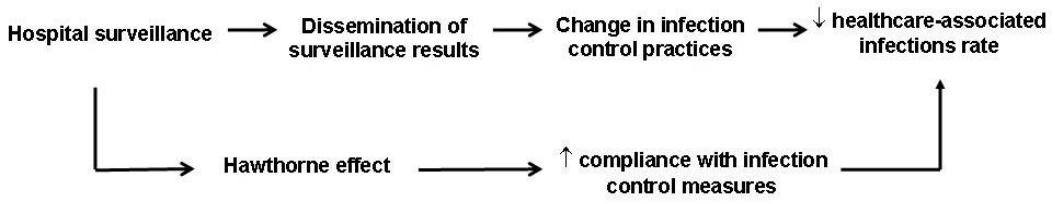
2.3. Surveillance as an infection control tool

The final objective of surveillance is to use of its results for prevention and control. It is believed that surveillance leads to the decrease of HAI rates through 2 different mechanisms (Figure 2.2). Initially, surveillance might influence healthcare practice through a Hawthorne effect. As demonstrated by Kohli et al, compliance of healthcare professionals with infection control measures tends to be transitorily better when the surveillance team is physically present on units.[84] The researchers observed that compliance with hand hygiene

on 3 different inpatient care units decreased from 65% to 58% ($p = 0.1$) when the known observer was not present, a result that was clinically significant due to the consequent increase in the CLABSI risk among these patients. The effect was even more pronounced on a highly compliant unit, where adherence to hand hygiene procedures dropped from 98% to 79% ($p = 0.03$).

Dissemination of surveillance results is the second mechanism through which surveillance could lower HAI incidence rates. Differently from the Hawthorne effect, its impact on HAI rates is expected to be sustained.[14, 60] The use of benchmarks and the reporting of provincial/national surveillance results to the infection control team, as well as to medical and administration staff of hospitals that present higher HAI rates compared to benchmarks should trigger changes in infection control programs, which in turn should lead to improvement in patient-care practices that could be linked to a higher risk of infections.[14, 60]

Figure 2.2 – Conceptual model regarding the effect of surveillance on healthcare-associated infection incidence rates (Adapted from Haley RW et al. Study on the efficacy of nosocomial infection control (SENIC project): summary of study design. Am J Epidemiol 1980;111:472-85)



The efficacy of hospital-wide surveillance programs was evaluated by the nationwide observational Study on the Efficacy of Nosocomial Infection Control (SENIC), launched by the Centers for Disease Control and Prevention in 1980.[14, 60] SENIC used a controlled before-after design and included only hospitals that were "surveillance-naive" during the before period, i.e., hospitals that had never done surveillance before. SENIC showed that hospitals that had implemented a high quality infection control program experienced a 15% decrease (95%CI 3.7-25.1) in their bloodstream infection incidence rates between 1970 and 1975-1976. High-quality infection control programs implied that programs made use of the current scientific literature, had written policies and promoted teaching activities to healthcare providers. Nevertheless, the presence of a high quality infection control program and a high or mid-high quality surveillance program (active, patient-based program that analyzed and disseminated their results), including at

least 1 infection control nurse per 250 hospital beds and 1 hospital epidemiologist, led to a 35% decrease (95%CI 19.7-47.6) in the bloodstream infection incidence rates during the same 5-year period.

No specific information about ICUs and CLABSIs was provided by the SENIC study. The results for this patient population and HAI type are diluted in the pooled results of hospital-wide surveillance. Moreover, SENIC does not indicate the number of participating hospitals with ICUs. Therefore, based on the SENIC study alone, we do not precisely know the extent to which surveillance affects CLABSI incidence rates in ICUs.

Due to time and economical constraints, and the increasing need for data in HAI high-risk patient populations, the use of hospital-wide surveillance has been progressively abandoned in favour of targeted surveillance. However, the magnitude of a targeted surveillance program's effect on CLABSI rates has yet to be defined. It is conceivable that the implementation of a national/regional targeted surveillance would be more effective for CLABSI prevention than a hospital-wide surveillance program, as all infection control efforts would be focused on one specific area.

After the publication of the SENIC study, many hospitals implemented infection control programs and performed surveillance on a regular basis for many years, using benchmark data from established programs such as NHSN. As a result, in contrast to hospitals that participated in the SENIC study, most of

hospitals/ICUs that now join national/regional surveillance programs should not be "surveillance-naive". This implies that they should have already been exposed to the effect of "results dissemination", and may have acted on identified problems. Consequently, this could dilute the observed effect of national/regional targeted surveillance programs on ICU CLABSI incidence rates.

A systematic search of the literature identified 7 before-after studies that have tried to estimate the effect of ICU-targeted surveillance on CLABSI rates. In 3 of these studies, "surveillance-naive" ICUs were evaluated, and no adjustment for confounding was performed.[19-21] Orsi et al showed that the crude CLABSI incidence rate in a single adult ICU decreased by 13.1% (from 19.1 to 16.6 CLABSI/1000 CVC-days; $p = 0.54$) after results from the first year of surveillance were disseminated and infection control measures were enforced during the second year of the program.[19] Nonetheless, it is possible that the observed result was partially due to a decrease in the use of CVC during the before and after periods (83% vs. 71%; $p < 0.05$). Yoo et al described a 69% reduction in CLABSI incidence rates over 3.5 months (from 4.2 to 1.3 CLABSI/1000 CVC-days; $p = 0.14$) in a single mixed (adult and pediatric) ICU.[21] However, this study had only 6 CLABSI cases during the entire surveillance period and unblinded chart review was used to determine CLABSI rates in the pre-intervention period. Despite having showed clinically significant reductions in CLABSI incidence rates, the results of Orsi's and Yoo's studies did not reach statistical significance. The only statistically significant results reported thus far are those of Venberghe et al who observed a 40% reduction in the crude CLABSI

incidence rate in a single mixed ICU during a 5-year period (from 7.2 to 4.3 CLABSI/1000 CVC-days; p = 0.0045).[20]

Regarding the effect of multicenter surveillance programs, the Centers for Disease Control and Prevention described the evolution of CLABSI incidence rates in different ICUs for the period between 1990 and 1999.[85] A decrease in CLABSI rates was observed in medical (44%), coronary (43%), pediatric (32%) and surgical ICUs (31%). As discussed by the authors, the reported findings were subject to some confounding, such as the effect of other national infection control strategies (e.g., prevention guidelines) and a shift from hospital- to nonhospital-based delivery of services in the healthcare system.

Three multicenter before-after studies evaluated the impact of targeted surveillance on CLABSI rates in adult ICUs.[17, 18, 22] L'Heriteau et al published the results of the first 5 years of the *Surveillance Nationale des Infections Nosocomiales liées aux Cathéters Veineux Centraux en Réanimation Adulte* (REACAT) network in France.[18] The REACAT case definition for catheter-related infections included both CLABSIs and localized infections at the catheter insertion site – without bloodstream infection. L'Heriteau described a 58.6% reduction in the crude catheter-related infections incidence rate in 35 adult ICUs that continuously participated in the program over a 3-year period (from 5.99 to 2.48 CLABSI/1000 CVC-days; p value and 95%CI not reported). When analyzing data from 10 ICUs that continuously participated for 5 years, the drop in the

incidence rate was 77.2% (from 7.63 to 1.74 CLABSI/1000 CVC-days; p value and 95%CI not reported).

In the L'Heriteau study, analysis was not performed using CLABSI incidence rates as the outcome. However, data published in the REACAT annual reports for the first 3 years of surveillance showed that CLABSI rates dropped by 32% (from 1.5 to 1.0 cases/1,000 CVC-days; p-value and 95%CI not provided).[86] Furthermore, the CLABSI case definition initially used by REACAT was changed for a stricter one in the third year of the surveillance program.[87, 88] As a result, fewer patients met the criteria for catheter-related infections during the last 2 years of surveillance, leading to an overestimation of the decrease in rate observed between the first and fifth year. Finally, the duration of the surveillance period was variable (4 months in the first 3 years and 6 months in the last 2 years), and so was the time of year when surveillance was performed, which may have impaired the comparability of CLABSI rates presented.

In Germany, the *Krankenhaus Infektions Surveillance System* (KISS) was introduced in 1997. KISS is an ICU targeted surveillance program that recommends continuous surveillance for all participating hospitals. However, the team responsible for KISS acknowledges that a proportion of hospitals chose to shorten the duration of participation per year in the ICU CLABSI targeted surveillance to allow for monitoring of HAI rates on other wards.[89] Zuschneid at al reported a 28.6% decrease in the pooled CLABSI incidence rate in participating ICUs in the KISS program for at least 2 years from 1997 to 2001 (from 2.1 to 1.5

CLABSI/1000 CVC-days; p = 0.04).[22] Also using the KISS database, Gastemeier et al showed a 19% reduction in the pooled CLABSI incidence rate in ICUs that continuously participated for 3 years during the period between 1997 and 2003 (from 2.1 to 1.7 CLABSI/1000 CVC-days; p value and 95%CI not reported).[17] It is possible that some of the effect observed in these 2 papers was due to confounding. In 2001, a law for protection of patients against HAI was introduced in Germany, which led to the implementation of new infection control programs in many hospitals across the country.[62] Consequently, it was impossible to tease out the extent to which the law and KISS contributed to the observed decrease in the CLABSI incidence rate.

All the multicenter studies described above used a before-after design without adjustment for potential confounders and interaction factors, such as ICU type, publication of CLABSI prevention guidelines, or previous exposure to surveillance. In addition, REACAT and KISS methods present important problems, such as short and unequal annual surveillance duration and missing data.

Unlike REACAT and KISS, the Quebec provincial surveillance program (SPIN-BACC) requires all participating hospitals to perform prospective ICU targeted surveillance for CLABSI in a continuous fashion. As a unique feature, participation in the SPIN-BACC program became mandatory for all Quebec ICUs with 10 beds or more in 2007. Moreover, the SPIN group trains all hospital-based infection control practitioners to perform active surveillance in a standard way

and a quality assurance system exists to reduce the risk of measurement error. Finally, SPIN-BACC results are disseminated through an annual report to all participating hospitals. For these reasons, the quality of data collected by the SPIN program may be considered better in comparison to REACAT and KISS.

The aforementioned studies tried to determine the effect of ICU targeted surveillance on CLABSI incidence rates. However, because of the methodological problems mentioned above, the magnitude of this effect has not been definitely estimated. In addition, it is possible that the variability in the studies' results is due to the heterogeneity of the effect of targeted surveillance among ICUs. We hypothesize that the reduction in CLABSI incidence rate associated with surveillance would be more pronounced among "surveillance-naïve" ICUs, i.e., ICUs where surveillance had not been performed before participation in regional/national surveillance program, and among non-university affiliated units.

Personnel at "surveillance-naïve" units are not aware of the presence and magnitude of their CLABSI problem. Furthermore, they are not capable of evaluating the effectiveness of their infection control programs. Zoutman et al showed that non-university affiliated ICUs tend to have less structured surveillance and infection control programs compared to teaching ICUs.[90] In joining a national/regional surveillance program, both "surveillance-naïve" and non-university affiliated units would have the opportunity to not only measure their own CLABSI rates, but also compare them to benchmarks. Consequently,

improvements in infection control practices could be prompted by the recognition of high rates, and also by the participation in infection control activities sponsored by many national/regional surveillance programs.

A study using data from a high quality surveillance program such as SPIN-BACC along with statistical methods that adjust for potential confounders and address possible interactions could help determine the extent to which ICU targeted-surveillance reduces CLABSI incidence rates. This knowledge would allow infection control programs and public health officers to make realistic projections about the expected results of this type of surveillance.

Therefore, as the third objective of this thesis, we determined the effect of a targeted surveillance program (SPIN-BACC) on the CLABSI incidence rate in Quebec ICUs. Furthermore, we identified ICU-level variables associated with higher CLABSI incidence rates.

CHAPTER 3 - THESIS OBJECTIVES

The objectives of this thesis are:

1. To describe the epidemiology of CLABSIs in Quebec ICUs from October 2003 to March 2009;

2. To determine, through simulation, the impact of different participation requirements on the ability of national and provincial/regional surveillance programs to yield valid estimates of the true annual ICU pooled CLABSI incidence rates;

3. To determine the effect of a targeted surveillance program (SPIN-BACC) on the CLABSI incidence rate in Quebec ICUs and to identify ICU-level variables associated with higher CLABSI incidence rates.

CHAPTER 4 - STUDY SETTING

For this thesis, we used data from the SPIN-BACC program, implemented in the province of Quebec, which is situated in the central region of Canada. Quebec is the country's largest province, and the second most populated. In 2010, its population was 7,907,400 inhabitants.[91]

In 1996, the *Association des Médecins Microbiologistes et Infectiologues du Québec* created the *Surveillance Provinciale des Infections Nosocomiales* (SPIN) group. In collaboration with the *Association des Infirmières en Prévention des Infections* and the *Ordre des Infirmières et Infirmiers du Québec*, the SPIN group performed a first study (SPIN-1) on the epidemiology of CLABSI in Quebec hospitals, which demonstrated that CLABSI incidence rates in ICUs were 400% higher compared to other wards.[92] In 2000-2001, the second phase of this study (SPIN-2) was carried out, this time focusing exclusively on CLABSI incidence rates in ICUs.[93]

In 1999, the *Association des Médecins Microbiologistes et Infectiologues du Québec* and the *Institut National de Santé Publique du Québec* joined forces to create the *Comité sur les Infections Nosocomiales du Québec* to provide scientific expertise in the domain of HAI prevention and control.[6] Its mandate includes the development of recommendations with respect to surveillance and prevention of HAI, as well as the development of infection control directives for Quebec hospitals.

. The SPIN program was transferred to the *Comité sur les Infections Nosocomiales du Québec* in 2002, becoming responsible for HAI surveillance in Quebec hospitals.[94] The main objectives of the SPIN program are to monitor HAI incidence rates in order to establish priorities for provincial infection control programs, and to evaluate the results of implemented measures. In addition, SPIN aims to allow rates comparison among Quebec hospitals by use of standardized surveillance methods.

Based on the current scientific literature, SPIN developed surveillance programs for 4 different HAI known for their association with high morbidity and/or mortality for specific patient populations: 1) *Clostridium difficile*-associated diarrhea, 2) Methicillin-resistant *Staphylococcus aureus* bloodstream infections, 3) Vancomycin-resistant *enterococci* infections, and 4) Healthcare-associated bloodstream infections. The latter is subdivided into 3 programs: 1) Global surveillance of healthcare-associated bloodstream infection (SPIN-BACTOT), 2) Surveillance of healthcare-associated bloodstream infection in hemodialysed patients (SPIN-HD), and 3) Surveillance of central line-associated bloodstream infections in ICU patients (SPIN-BACC).

The SPIN-BACC program has continuously collected data on CLABSIs in Quebec ICUs since its inception in October 2003. The surveillance methods used by the SPIN-BACC program are described in detail in Chapter 5. For the first objective of this thesis, we used data from the SPIN-BACC database for the period between October 2003 and April 2009 (Chapter 6). For the second

objective of this thesis, we used data from ICUs that continuously submitted data to the program during 1 year from April 2007 to March 2009 (Chapter 7). For the third and last objective, we used data from ICUs that continuously participated in SPIN-BACC for 3 years from April 2004 to March 2011 (Chapter 8).

We have obtained permission from the *Institut National de Santé Publique du Québec* to use SPIN-BACC data for this thesis. In addition, this project was approved by the Institutional Review Board at McGill University.

CHAPTER 5 - SPIN-BACC PROGRAM

5.1. Preamble

Due to the frequent use of CVC in ICUs, CLABSI is one of the most common HAI in this patient population. This, as well as its high morbidity and mortality, and potential preventability, led to the choice of CLABSI as one of the priorities of the SPIN program and the launching of the SPIN-BACC program in Quebec ICUs with 6 beds or more in October 2003. Initially, participation in the SPIN program was voluntary, but it became mandatory for ICUs with 10 beds or more in January 2007.

In 2009, a survey organized by the SPIN-BACC group showed that there were 121 ICUs in Quebec, 44 of which had 10 beds or more.[95] Currently, all eligible ICUs (100%) continuously submit data to the program. In addition, around 30% of the ICUs with less than 10 beds (20 units) voluntarily participate in SPIN-BACC.

The surveillance methods used by SPIN-BACC as well as its implementation process were described in a manuscript entitled "*Surveillance Provinciale des Infections Nosocomiale*s (SPIN) Program: implementation of a mandatory surveillance program for central line-associated bloodstream infections". Overall CLABSI incidence rates for the period between 2003 and 2009 for adult ICUs (including pooled data for surgical, cardiac, medical,

combined - medical and surgical or cardiac-, and burn units), PICUs and NICUs were presented. This manuscript was published in the American Journal of Infection Control (Am J Infect Control 2011;39(4):329-35).

5.2. *Surveillance Provinciale des Infections Nosocomiales* (SPIN) Program: implementation of a mandatory surveillance program for central line-associated bloodstream infections (Am J Infect Control 2011;39(4):329-35)

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Keywords:

Cross-infection; intensive care unit; central catheterization; epidemiology.

Conflicts of interest:

None to report

ABSTRACT

Background: In 2003, the *Surveillance Provinciale des Infections Nosocomiales* (SPIN) program was launched to gather data about central line-associated bloodstream infections (CLABSI) incidence rates in intensive care units (ICUs) located in the Province of Quebec. To improve the generalizability of SPIN benchmarks, participation in SPIN became mandatory for ICUs with ≥ 10 beds in 2007.

Objective: To describe the implementation process, surveillance methods and overall results of the SPIN program between 2003 and 2009.

Methods: SPIN surveillance methods are based on the National Healthcare Safety Network. Participation is open to all Quebec ICUs, but mandatory for units with ≥10 beds as of January 2007. Results include CLABSI incidence rates for 2003-2009 and the epidemiology of CLABSI cases.

Results: Mandatory participation increased the number of ICUs by 100% (from 30 to 60 units). Between 2003 and 2009, the overall CLABSI incidence rates for adult, pediatric, and neonatal ICUs were 1.67, 2.24 and 4.40 CLABSI/1,000 catheter-days, respectively. CLABSI cases were predominately female (60%), with a mean age of 44 years (SD 32 years). The use of regular central lines was present in 64% of CLABSI.

Conclusions: The implementation of mandatory participation was essential to increase the generalizability of SPIN CLABSI rates, which also improved their quality as the provincial benchmarks.

INTRODUCTION

Central line-associated bloodstream infections (CLABSI) are a major problem in intensive care units (ICUs), as they result in a considerable burden of illness.[1] Moreover, it is estimated that CLABSIs prolong the length of hospital stay by 1 to 4 weeks, with an increased hospitalization cost of up to CAN$ 35,000 per patient.[2]

Due to the clinical and public health importance of CLABSI, the *Institut National de Santé Publique du Québec*, Canada, launched the *Surveillance Provinciale des Infections Nosocomiales* (SPIN) program in 2003, which aims to gather data about the epidemiology and incidence of CLABSI in ICUs located in the Province of Quebec.

The objectives of the SPIN program are: [3-5]

1. To estimate the incidence and mortality rates of CLABSI in Quebec ICUs;
2. To describe the underlying conditions associated with CLABSI;
3. To identify the pathogens associated with this type of healthcare-associated infection (HAI);
4. To create a database that allows for benchmarking of CLABSI incidence rates observed in hospitals across the Province of Quebec and to follow these rates over time;
5. To provide data that can be used for interfacility comparisons;

6. To reduce the CLABSI incidence rate in Quebec ICUs to a minimum;
7. To encourage all Quebec ICUs with ≥6 beds to participate in SPIN.

Since 2005, annually published SPIN results have been used as the provincial ICU benchmarks. From the inception of the program in October 2003, until December 2006, participation in SPIN was voluntary. This changed in January 2007, when the Quebec Ministry of Health made this participation mandatory for all Quebec ICUs with ≥10 beds. This article describes the implementation process and the current surveillance methods used by the SPIN program, as well as the overall results for the period between 2003 and 2009.

METHODS

Location

The province of Quebec, situated in the central region of Canada, is the country's largest province, and the second most populated. In 2009, its population was 7,828,900 inhabitants.[6]

Characteristics of participating hospitals

All adult, pediatric, and neonatal ICUs in the Province of Quebec are eligible to participate in the SPIN program. Thirty ICUs (26 adult, 2 pediatric and 2 neonatal units) reported data to SPIN during its first surveillance period, which started in October 2003 and lasted 6 months. Until January 2007, participation in

SPIN was voluntary, and increased participation was sought by educational activities, publicity and active recruitment.

As of January 2007, all eligible ICUs (with ≥10 beds) are required to continuously participate in SPIN throughout the year. Cardiac ICUs were encouraged to participate but were not part of the mandatory surveillance, as their CLABSI rates were close to zero during the first year of the program.

Definitions

Definitions used by SPIN are in accordance with the Nosocomial Infection Surveillance (NNIS)/National Healthcare Safety Network (NHSN) criteria.[7-9] Central venous catheters (CVC) are defined as intravenous catheters that end at or near the heart, or in a great vessel close to the heart, such as the subclavian, internal jugular, or femoral veins. Peripherally inserted CVC (e.g., catheters inserted into the basilic, cephalic, or brachial veins that enter the superior vena cava), tunneled CVC, totally implanted catheters and umbilical vessel catheters (inserted into the umbilical artery or vein) are also considered CVCs.

Bloodstream infections are defined as:

1. Patient has a recognized pathogen cultured from ≥1 blood culture AND organism cultured is not related to an infection at another site, OR
2. Patient has at least 1 of the following signs or symptoms: fever (>38°C), chills, hypotension (or hypothermia - <37°C -, apnea, or

bradycardia if patient <1 year of age) AND a common skin contaminant (e.g. diphtheroids, *Bacillus* spp, *Propionibacterium* spp, coagulase-negative *Staphylococci*, viridans group *Streptococci* or *Micrococci*) is cultured from ≥2 blood cultures, or from ≥1 blood culture if appropriate antimicrobial therapy initiated by the treating physician AND signs and symptoms and positive laboratory results are not related to an infection at another site.

The definition of CLABSI in SPIN requires the presence of a CVC upon bloodstream infection diagnosis or in the previous 48 hours.[8] To be eligible for inclusion in the SPIN database, the onset of a CLABSI must occur while the patient was admitted to an ICU or within 48 hours following ICU discharge. The CLABSI must not be present or incubating upon the patient's admission to the ICU. The onset of a CLABSI is defined as the time when the first positive blood culture was obtained, or at the time of first clinical sign if that was earlier. Finally, ICUs are classified according to their academic profile.[3-5, 10] An ICU is classified as a "teaching unit" if the majority of the clinical services of the hospital to which it belongs are part of a teaching and research program of a medical school at the undergraduate and post-graduate levels.

Data collection

SPIN requires all participating hospitals to perform active prospective surveillance of CLABSI in ICUs throughout the year. This means that all CLABSI cases must be proactively sought while patients are still in the ICU or

within 48 hours after their discharge from ICU.[3-5, 11] Annual data collection starts on April 1st and is divided into 13 four-week surveillance sub-periods per year.

Data are collected for 7 types of ICU: adult (surgical, cardiac, medical, combined - medical and surgical or cardiac - and burn); and pediatric (PICU) and neonatal (NICU). In each of the ICUs, at least 1 hospital-based infection control practitioner, in collaboration with the hospital epidemiologist, is responsible for recording and uploading data regarding CLABSI cases and denominators.

The strategy used to identify CLABSI cases includes a daily search for new positive blood culture results in ICU patients. The infection control practitioner then goes to the ICU to verify if patients with positive blood cultures currently have CVCs, or had CVCs in the previous 48 hours. If the presence of a CVC is confirmed, the medical and nursing charts are reviewed to determine if the case fulfils the criteria for CLABSI diagnosis. All CLABSI with an onset of symptoms before the patient's admission to the ICU are excluded. All patients with ≥1 CVC are followed until 48 hours after CVC removal or discharge from ICU, whichever comes first.

When a CLABSI diagnosis is confirmed, the following patient data are collected: date of birth, gender, birth weight (for NICU patients only), hospital and ICU admission date, date of CLABSI onset, number of positive blood culture sets, type of catheter, presence of infection at catheter site, and death within 30 days and its association with the CLABSI episode (directly associated, indirectly

associated or unrelated). The presence of risk factors for CLABSI is also recorded: renal failure requiring dialysis or hemofiltration, use of total parenteral nutrition, neutropenia, leukemia, neoplasia, diabetes mellitus, and bone marrow or solid organ transplantion in the last 3 months. Finally, data collectors also record the microorganisms isolated from blood cultures and antimicrobial resistance patterns.

The denominator data collected for each of the surveillance sub-periods include CVC-days and patient-days. Both denominators are defined according to the NNIS/NHSN criteria.[9, 12] The number of CVC-days is defined as the total number of days of exposure to CVCs by all patients in a selected ICU for each 28-day period. For its calculation, the number of patients with ≥1 CVC is collected daily, and summed at the end of the 28-day period. The use of multiple CVCs in 1 patient is counted as 1 CVC-day. [9, 10] The number of patient-days is defined as the total number of days that patients are in the ICU during the 28-day period.

Data uploading

According to the SPIN protocol, non-nominative data must be uploaded within the month following the end of each surveillance sub-period on the SPIN web portal located on the *Laboratoire de Santé Publique du Québec* website.

Quality assurance

A manual of operation containing a detailed description of how the data collection must be carried out was sent to all SPIN participants before they started

the surveillance program. The manual included definitions for CLABSI cases and denominators, as well as information about how and when to upload collected data on the SPIN web portal.

Quality assurance is also ensured by built-in input fields' masks and by automatic validation of fields and denominators entered. As background data on denominators (patient-days and CVC-days) were available in the SPIN database, validation rules were implemented to ensure that denominators entered were within 2 standard deviations of the background data for each given participating unit. Moreover, patients' age must be in concordance with the type of ICU (e.g., patients aged ≥18 years cannot be reported as NICU patients) and the ICU admission date had to be after or the same as the hospital admission date. The program also ensured that mandatory fields are not left empty by precluding submission of the CLABSI to SPIN.

In addition, all hospital-based infection control practitioners involved in the data collection were required to participate in a one-day web-training session chaired by the SPIN CLABSI coordination team at the moment their hospital enrolled in the program. The objective of this activity was to make local staff thoroughly familiar with the SPIN methods. During this session, they were trained on the elements of a surveillance system: case definition, data collection strategy and instruments, and on how to upload data to the SPIN web portal. This ensured that data were collected in a standardized way across ICUs and that the case definitions were appropriately understood.

Quality control

A hospital-based infection control practitioner, supported by a medical microbiologist or infectious disease specialist/hospital epidemiologist, adjudicates all CLABSI cases diagnosed in their hospital's ICU(s) to minimize outcome misclassification. Furthermore, all data uploaded to the SPIN web portal are monthly perused by a trained member of the SPIN coordination team, and an email is sent directly to the site when data seem out of the ordinary. Data are also monitored and adjudicated a second time, on a quarterly basis, at the *Institut National de Santé Publique du Québec*. Data generating concerns about possible misclassification or incorrect values are sent back to the respective hospitals for review.

At the end of the surveillance year, the SPIN data are adjudicated one last time by an infection control physician with training in Epidemiology before being analyzed. Criteria for CLABSI diagnosis, such as interval between ICU admission and development of infection and pathogen identified, are reviewed. A search for discrepant values is performed, and all data suspected of having been erroneously entered are sent back to the respective hospital for revision.

Finally, the SPIN CLABSI coordination team organizes meetings every second year with the objective of exchanging experience between participating hospitals. During these meetings, the group discusses problems encountered by infection control practitioners when collecting or uploading data. Furthermore,

workshops on case scenarios, calculation of rates, dissemination of data, and development of infection control programs are offered.

SPIN data analysis

SPIN uses descriptive statistics, including mean (standard deviation - SD) and median (interquartile range – IQR), to summarize the characteristics of the CLABSI cases and the associated underlying conditions. Annual ICU CLABSI pooled incidence mean rates (per 1,000 CVC-days) and CVC utilization ratios (CVCUR) are calculated according to the NNIS/NHSN specifications and stratified by ICU type (adult, pediatric and neonatal) and academic profile ("teaching" and "non-teaching" units):[10, 12]

$$\text{ICU CLABSI pooled incidence mean rate} = \frac{\sum \text{annual ICU CLABSI cases}}{\sum \text{annual ICU CVC-days}} * 1{,}000$$

$$\text{ICU CVCUR} = \frac{\text{Sum of annual ICU CVC-days}}{\text{Sum of annual ICU patient-days}}$$

Pooled annual CLABSI incidence rates and CVCUR stratified by ICU type are compared to the SPIN rates from previous years, as well as with data published by NHSN (data not presented). Furthermore, annual ICU CLABSI incidence rates and CVCUR are also calculated for each individual center and used to produce medians and percentiles (10^{th}, 25^{th}, 75^{th} and 90^{th} percentiles), which are also stratified by ICU type and academic profile. For categorical data,

similar comparisons are performed, and chi-square or Fisher exact test are used to test for statistical significance.

Data dissemination

The SPIN CLABSI coordination team produces an annual report describing the status of CLABSI incidence rates in participating Quebec ICUs for the current year. A comparison between the current CLABSI incidence rates, CVCURs, and frequency distribution of pathogens and antimicrobial resistance patterns, with data from previous surveillance years, as well as data from the NHSN program, is provided. The report is distributed to all SPIN participating ICUs yearly. Each participating ICU receives a code that allows them to confidentially compare their rates to those of other similar ICUs in the province, and to their own previous results.

Statistical analysis

For this study, we calculated the pooled CLABSI incidence mean rate for the period between 2003 and 2009, as well as its 10^{th}, 50^{th} and 90^{th} percentiles. Results were stratified according to ICU type (adult, pediatric and neonatal) and academic profile ("teaching" and "non-teaching" units). Descriptive statistics, including mean (SD) and median (IQR), and frequency distribution were used to describe the characteristics of the CLABSI cases.

RESULTS

At the inception of the SPIN program in October 2003, 30 ICUs (26 adult, 2 pediatric and 2 neonatal units) contributed data to the SPIN database. The implementation of mandatory participation in January 2007 led to a substantial increase in the number of participating ICUs, bringing the total number of units from 30 to 60 currently participating (48 adult, 5 pediatric and 7 neonatal units).

Between October 2003 and March 2009, a total of 891 CLABSI were identified for 446,137 CVC-days monitored. Table 5.2.1 presents the overall CLABSI incidence rates for 2003-2009, as well as the 10^{th} and 90^{th} percentiles, which are used by SPIN as the cut-offs for low and high outliers, respectively.

CLABSI cases occurred predominately in females (60%), with a mean age of 44 years (SD 32 years) and median of 56 years (IQR 4 months – 71 years). When analyzing the age distribution among CLABSI cases, we observed 2 peaks: neonates and elderly patients. Short-term CVCs were the most frequent type of catheter associated with bloodstream infections (64%). Previously reported CLABSI risk factors were identified in a majority of cases: 13% had renal failure requiring dialysis or hemofiltration, 43% were on total parenteral nutrition, and 3% had a bone marrow or solid organ transplantation in the last 3 months. In addition, 6%, 4%, 5% and 21% of CLABSI patients had neutropenia, leukemia, neoplasia, and diabetes mellitus, respectively.

During 2003-2009, coagulase-negative *Staphylococci* was the most frequently pathogen associated to CLABSI (53%), followed by *Staphylococcus aureus* (15%) and *Candida* spp (13%). Of all *S. aureus*, the proportion of methicillin-resistant *S. aureus* declined from 70% to less than 40% after the 2006-2007 period.

DISCUSSION

Surveillance is essential to provide information on the epidemiology of HAI, which are associated with high mortality and morbidity worldwide.[13] When monitoring CLABSI, ICU patients are a priority, as this group has disproportionately more CLABSI compared to other patient populations. From the 250,000 estimated CLABSI cases that occur annually in the U.S. approximately 80,000 (32%) occur in ICUs, despite the fact that these patients only comprise 5 to 10% of all hospital beds.[14]

The clinical and public health importance of CLABSI in ICU patients led the *Institut National de Santé Publique du Québec* to create the SPIN program in 2003. SPIN results presented for the period between 2003 and 2009 show that CLABSI is an important problem for Quebec ICUs, with summary pooled CLABSI incidence rates for 2003-2009 for adult, pediatric and neonatal ICUs of 1.67, 2.24 and 4.40 CLABSI/1,000 CVC-days, respectively.

The surveillance methods used in SPIN were based on the NNIS/NHSN system and the comparison of the methodological aspects of SPIN and NHSN is presented in Table 5.2.2. Both SPIN and NNIS/NHSN require ICUs to perform active prospective surveillance while patients are still in the ICU and also for the 48 hours following their discharge. This allows for the detection of the estimated 10% of CLABSI cases that would be missed if surveillance after ICU discharge was not performed.[15]

In contrast with NNIS/NHSN, which included clinical sepsis as one of the CLABSI criteria in all ICUs up until 2006 and for patients ≤1 year until 2010, SPIN only includes laboratory-confirmed bloodstream infections in order to increase the validity of CLABSI report.[7, 9, 12] In addition, SPIN has not yet changed its CLABSI definition, which is still based on the NNIS program, since the program inception in 2003. This measure allows SPIN to maintain comparability of CLABSI rates over time. As of April 2010, the new NHSN definition is now in use but comparability is maintained because incidence rates using both definitions have been calculated since January 2007.

Furthermore, the SPIN program collects data about characteristics of the CLABSI cases. In doing so, we aim to have a better understanding of the patient population who develops CLABSI. This knowledge has helped us to make decisions about which targeted-prevention programs should be implemented at the hospital and provincial levels. Given the high proportion of methicillin-resistant *Staphylococcus aureus* causing CLABSI in Quebec ICUs, surveillance results

have been used to prioritize methicillin-resistant *Staphylococcus aureus* infection control guidelines and promote their importance. Moreover, with the objective of decreasing CLABSI rates to a minimum, process surveillance for catheter insertion and maintenance has also been prioritized. Hospitals with high CVCUR have audited their CVC use and some have managed to decrease their duration of catheterization. The high incidence rates in NICUs have also served to set priorities in action plans and quality improvement.

Mandatory participation in SPIN, however, is the major difference with NHSN. While NHSN allows ICUs to report a minimum of 1 surveillance period per year, SPIN requires participating units to continuously report data throughout the year. The SPIN CLABSI coordination team considered that the introduction of mandatory participation was necessary to increase the participation of Quebec ICUs in the program with the objectives of better estimating the magnitude of the CLABSI problem in the province. This measure increased not only the generalizability of SPIN results, but also their quality when they are used as the provincial benchmark.

The establishment of mandatory participation in SPIN was clearly successful as the number of participants increased from 30 to 60 ICUs after 2007. Currently, 93% of all Quebec eligible ICUs report data to SPIN. Non-participating ICUs cite a lack of adequate resources as the reason for not having joined SPIN yet. Therefore, the number of ICUs is expected to increase further in the following

years, as non-participating ICUs acquire the necessary infrastructure and human resources to join the program.

The use of sound surveillance methods, which ensure the high quality of the data collected, was also essential to achieve the objective of estimating the magnitude of the CLABSI problem in Quebec ICUs and to use SPIN results as the provincial benchmarks. The SPIN CLABSI coordinating team trained all hospital-based infection control practitioners to perform active surveillance in a standardized way, is available to discuss more complex cases as needed, and a quality assurance system was developed to reduce the risk of misclassification of CLABSI cases and risk factors. Despite the measures already undertaken, the accuracy of the collected data remains a priority. Consequently, a study to evaluate the reporting validity of CLABSI data to the SPIN program is being performed in 2010.

The importance of the SPIN program has grown since its inception. Since its first report in 2005, annual results have been used as Quebec benchmark rates. In addition, hospital-based and provincial infection control committees have used SPIN results to plan CLABSI prevention and control strategies. Finally, the Quebec Ministry of Health is now using SPIN data as performance indicators in infection prevention and control for hospitals across the province. Aware of the importance of the contribution of SPIN to public health in Quebec, the coordination team continues to work towards the development of strategies that could lead to more effective surveillance, such as the linkage between the

provincial surveillance system and hospital databases to avoid duplicate data entry, as well as the development of a program to monitor the process of healthcare practices.

CONCLUSION

CLABSI result in a substantial burden of illness in hospitalized patients. The SPIN program launched in 2003 by the *Institut National de Santé Publique du Québec* has contributed to define the importance of this problem in Quebec ICUs. The implementation of mandatory participation was essential to increase the generalizability of the results, as well as the quality of SPIN rates as the provincial benchmarks. In order to continue to provide high-quality data, the SPIN research team has worked on the improvement of the current surveillance methods and the expansion of the program.

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Table 5.2.1 – Summary of pooled central line-associated bloodstream infection incidence mean rates for the period between 2003 and 2009 inclusively

ICU type	Number of ICUs	CLABSI cases	CVC-days	Pooled CLABSI incidence rate*	Percentiles[δ]		
					10th	50th	90th
Adult ICUs	49	618	369,209	1.67	1.40	1.61	1.83
Teaching	26	493	278,806	1.77	1.07	1.74	2.03
Non teaching	23	125	90,403	1.38	1.03	1.33	2.45
PICUs	5	68	30,317	2.24	1.42	2.20	2.82
NICUs	7	205	46,611	4.40	3.23	4.06	5.17

ICU = intensive care unit, CLABSI = central line-associated bloodstream infection, CVC = central venous catheter, PICU = pediatric intensive care unit, NICU = neonatal intensive care unit

* per 1,000 CVC-days

[δ] Percentiles derived from the annual pooled CLABSI mean incidence rates for 2003 to 2009

Table 5.2.2 - Comparison of methodological features of SPIN and NHSN (device-associated module) systems

Feature	SPIN	NHSN
Surveillance type	targeted, active and prospective	targeted, active and prospective
Post-ICU discharge surveillance	yes	yes
Participation	mandatory	voluntary
Minimal participation	continuous throughout the year	minimum of 1 calendar month
Definitions	CDC	CDC
	only includes LCBSI	included BSIs defined by clinical sepsis criteria for neonates and infants ≤1 year until December 2009
	LCBSI is diagnosed by: · ≥1 positive blood culture for a recognized pathogen not related to an infection at another site OR · ≥1 sign of sepsis AND ≥2 positive blood cultures for usual skin contaminants AND signs / symptoms and (+) laboratory result are not related to an infection at another site OR · ≥1 sign of sepsis AND ≥1 positive blood culture for usual skin contaminants AND institution of appropriate antimicrobial therapy AND signs / symptoms and (+) laboratory result are not related to an infection at another site	LCBSI is diagnosed by: · ≥1 positive blood culture for a recognized pathogen not related to an infection at another site OR · ≥1 sign of sepsis AND ≥2 positive blood cultures for usual skin contaminants AND signs / symptoms and (+) laboratory result are not related to an infection at another site
Data collection about CLABSI risk factors	yes	no
NICU component	results are not stratified by birth weight	results are stratified by birth weight
Data report	results are not stratified by CVC type internet-based data interface upload within 30 days of the end of each surveillance sub-period	results are stratified by CVC type internet-based data interface upload within 30 days of the end of the month
Training of data collectors	yes	yes

ICU = intensive care unit, SPIN = *Surveillance Provinciale des Infections Nosocomiales*, NHSN = National Healthcare Safety Network, CDC = Centers for Disease Control and Prevention, LCBSI = laboratory-confirmed bloodstream infection, NICU = neonatal intensive care units, CLABSI = central line-associated bloodstream infection, CVC = central venous catheter

CHAPTER 6 - EPIDEMIOLOGY OF CENTRAL LINE-ASSOCIATED BLOODSTREAM INFECTIONS IN QUEBEC INTENSIVE CARE UNITS

6.1. Preamble

In Canada, the only source of data about CLABSI epidemiology in ICUs is the Canadian Nosocomial Infection Surveillance Program, which uses data from 49 self-selected sentinel hospitals across the country.[5, 58] Unfortunately, the majority of the Canadian Nosocomial Infection Surveillance Program participating hospitals are university-affiliated, which impairs the generalizability of its results to community-based hospitals.[58]

To contribute to the understanding of the CLABSI problem in Canada and provide benchmark data for community-based hospitals, this thesis had as its first objective to describe the epidemiology of CLABSI in Quebec ICUs. To do so, we used the SPIN-BACC database and designed a retrospective dynamic cohort study, which included ICUs that joined SPIN-BACC at different points in time. Sixty-two of the Quebec ICUs participate in this provincial surveillance program, including 23 non-university affiliated units. As an important feature, participation in SPIN-BACC became mandatory to all ICUs with 10 beds or more as of 2007, which improved the generalizability of its results.

In this manuscript, which was published in the American Journal of Infection Control (Am J Infect Control 2011 Aug 6 [Epub ahead of print]), we provided a comprehensive analysis of the CLABSI incidence rates in Quebec ICUs and we discussed the impact of mandatory participation on rates. Furthermore, we reported the main pathogens associated with CLABSI and their antimicrobial resistance patterns. Finally, we compared our results to those of both the Canadian Nosocomial Infection Surveillance Program and the NHSN in the U.S., and discussed the difference in surveillance methods used by this latter and SPIN-BACC.

6.2. Epidemiology of central line-associated bloodstream infections in Quebec intensive care units: a 6-year review (Am J Infect Control 2011 Aug 6 [Epub ahead of print])

Authors

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Keywords:

Healthcare-associated infections; bloodstream infections; central lines; central-line associated bloodstream infections (CLABSI); intensive care units; surveillance

Conflicts of interest:

None to report.

ABSTRACT

Background: The burden of central line-associated bloodstream infections (CLABSI) in Canadian intensive care units (ICUs) is not well established. Our study aims to describe CLABSI epidemiology in Quebec ICUs during 2003-2009.

Methods: Retrospective dynamic cohort of 58 ICUs that participated in the *Surveillance Provinciale des Infections Nosocomiales* (SPIN) during 2003-2009. We calculated annual CLABSI incidence rates, central venous catheter utilization ratios (CVCUR) and case-fatality proportions, and described the pathogens involved. Data were analyzed using descriptive statistics and standardized incidence ratios.

Results: 891 CLABSI were identified during 446,137 CVC-days. During 2003-2009, the CLABSI incidence rates of adult, pediatric, and neonatal ICUs were 1.67, 2.20 and 4.40 CLABSI/1000 CVC-days, respectively. Since 2007, CLABSI incidence rates in adult, pediatric, and neonatal ICUs have decreased by 11, 50 and 18%, respectively. Pediatric ICUs had the highest CVCUR (median 0.61, interquartile range 0.57-0.66). Coagulase-negative staphylococci caused 53% of the CLABSI. The proportion of *S. aureus* resistant to methicillin declined from 70% to <40% after 2006.

Conclusion: CLABSI result in a considerable burden of illness in Quebec ICUs. However, CLABSI incidence rates have decreased since 2007 and the methicillin-resistant *Staphylococcus aureus* proportion has remained <40% since 2006. Continuous surveillance is essential to determine if these changes are sustainable.

INTRODUCTION

Healthcare-associated infections (HAI) are estimated to affect more than 1.4 million patients worldwide at any time.[1] Among all HAI, central line-associated bloodstream infections (CLABSI) have a particularly severe impact on morbidity, mortality and hospitalization costs. From the 250,000 estimated CLABSI cases that occur annually in the U.S., approximately 80,000 (32%) take place in intensive care units (ICUs).[2] The severe debilitation of ICU patients, many of them presenting decreased immune defenses due to concurrent disease processes, along with their need of central venous catheters (CVCs) for treatment purposes and/or hemodynamic monitoring, partly explain the high incidence of CLABSI in this setting.[3-5]

Despite the clinical and public health importance of CLABSI, little has been published about its epidemiology in Canadian ICUs. A prospective cohort study carried out in 2006 described CLABSI incidence rates after 1 year of surveillance in 63 university-affiliated ICUs that participated in the Canadian Nosocomial Infection Surveillance Program.[6, 7] The pooled CLABSI incidence rates for adult, pediatric (PICU), and neonatal (NICU) ICUs were 2.3, 2.6, and 5.7 cases/1000 CVC-days, respectively. In 2003, the *Institut National de Santé Publique du Québec* launched the *Surveillance Provinciale des Infections Nosocomiales* (SPIN) program, which aimed to promote HAI surveillance and understand the epidemiology of CLABSI in ICUs in the Province of Quebec.[8-10] SPIN CLABSI incidence rates have been used as provincial benchmarks since

2005. Given the paucity of data regarding CLABSI epidemiology in a Canadian setting and to allow Canadian ICUs to benchmark their infection rates using Canadian data, we conducted a retrospective dynamic cohort study to describe the epidemiology of CLABSI in Quebec ICUs from October 2003 to March 2009.

METHODS

SPIN program

A detailed description of the SPIN surveillance definitions and methods has been previously published.[11]

Surveillance methods

SPIN requires all participating hospitals to perform active and prospective CLABSI surveillance in ICUs throughout the year.[8, 12-14] At the time of its inception in 2003, 28 ICUs voluntarily submitted data to the program. In January 2007, the Quebec Ministry of Health determined that participation in SPIN was mandatory for all Quebec ICUs with ≥10 beds. There are currently 62 ICUs registered in the program: 50 adult, 5 pediatric and 7 neonatal units. Despite their participation not being mandatory, 20 (32%) out of the 62 Quebec ICUs with <10 beds send data to SPIN.

Definitions

Reported CLABSI must have been acquired while patients were admitted to or within 48 hours of their discharge from an ICU. Patients must also have a CVC

at the time of or within the 48 hours preceding the onset of a bloodstream infection.[3] CVCs are defined as intravenous catheters that end at or near the heart, or in a great vessel close to the heart (e.g., subclavian, internal jugular, or femoral veins). Peripherally inserted catheters that enter the superior vena cava, tunneled catheters, totally implanted catheters, and umbilical vessel catheters are also considered CVCs.

The bloodstream infection definition used in SPIN was that of the National Nosocomial Infections Surveillance (NNIS) program published in 1988.[14, 15] Briefly, patients must 1) have a recognized pathogen cultured from ≥1 blood culture AND the organism cultured is not related to an infection at another site, OR 2) have ≥1 of the following signs or symptoms: fever (>38°C), chills, hypotension (or hypothermia - <37°C -, apnea, or bradycardia if patient <1 year of age) AND a common skin contaminant (e.g., diphtheroids, *Bacillus* spp, *Propionibacterium* spp, coagulase-negative *Staphylococci*, viridans group *Streptococci* or *Micrococci*) cultured from ≥2 blood cultures, or from ≥1 blood culture if appropriate antimicrobial therapy initiated by the treating physician AND signs, symptoms and positive laboratory results are not related to an infection at another site.

Data collection and patient eligibility

All patients who had a CVC while in the ICU were followed for up to 48 hours after CVC removal or ICU discharge, whichever came first. CLABSI cases were identified by infection control practitioners, who performed a daily search

for new positive blood culture results in ICU patients. Consequently, infection control practitioners went to the ICU to verify if patients with positive blood cultures currently had CVCs, or had one in the previous 48 hours. If the presence of a CVC was confirmed, the medical and nursing charts were reviewed to determine if the case fulfilled the criteria for CLABSI diagnosis. All CLABSI with an onset of symptoms before the patient's admission to the ICU were excluded. If a CLABSI case was confirmed, data about patient demographics, death at 30 days and its association or not with CLABSI (according to the evaluation of the hospital epidemiologist), and data on pathogens and antimicrobial resistance patterns were collected. Data on denominators (CVC-days and patient-days) were collected daily by hospital-based infection control practitioners.

All infection control practitioners involved in the surveillance process and clinical verification of the collected data were trained by the SPIN group. Rates are available on a monthly basis on the *Institut National de Santé Publique du Québec* website and reports are produced annually to allow for benchmarking against comparable institutions.

Study population and outcomes

We analyzed the annual pooled CLABSI incidence mean rates, CVC utilization ratios (CVCUR) and CLABSI case-fatality proportions for ICUs that participated in SPIN for ≥6 months in a year between 2003 and 2009. We also compared our results to those reported by the National Healthcare Safety

Network (NHSN) and the Canadian Nosocomial Infection Surveillance Program, and described the distribution of CLABSI pathogens and their patterns of antimicrobial resistance. The McGill University Institutional Review Board approved this study and waived the need of informed consent.

Statistical analysis

Continuous outcomes were presented using medians, percentiles and interquartile range (IQR), while discrete variables were presented with their frequency distribution. The ICU pooled CLABSI incidence mean rates (per 1000 CVC-days), CVCUR, CLABSI case-fatality and antimicrobial resistance proportions were calculated according to the NHSN specifications using R 2.8.1.[8, 16] Results were stratified by surveillance year, ICU type (adult, pediatric, or neonatal) and academic profile ("teaching units", if the hospital is part of a teaching and research program of a medical school, or "non-teaching units"). To compare CLABSI rates, we used t-test or standardized incidence ratio (SIR) and its 95% confidence interval (CI).

SIR is a summary measure that uses an indirect standardization method to compare rates by dividing the number of observed CLABSI by the number of expected CLABSI.[17, 18] The number of expected CLABSI is calculated by multiplying the CVC-days for different SPIN ICU types for a determined period of time by a reference population rate, e.g., NHSN or Canadian Nosocomial Infection Surveillance Program CLABSI rates, for the same ICU type and period. A SIR equal to 1 means that there is no difference between the observed and the

expected number of CLABSI, while SIRs <1 or >1 mean that the (SPIN) CLABSI rate is lower or higher than the rates found in the reference population, respectively.

To calculate the SIR of SPIN over NHSN, we had to estimate the NHSN CLABSI incidence rate for adult, pediatric and neonatal ICUs. For the calculation of NHSN adult and pediatric ICU CLABSI rates, we combined data from all ICUs classified as adult and pediatric, respectively. When calculating the NICU rate, we combined NHSN data from level III and II/III NICUs, and included CVC and umbilical catheter-associated infections.

RESULTS

Between October 2003 and March 2009, 58 ICUs participated in the surveillance program. Overall, 891 CLABSI were detected for 446,137 CVC-days. Adult ICUs contributed to the highest proportion of CLABSI cases (69%), CVC-days (83%), patient-days (73%) and all-cause mortality (80%). Table 6.2.1 presents the characteristics of participating ICUs. As the first period of SPIN surveillance lasted 6 months (October 2003-March 2004), the absolute numbers of CLABSI cases, CVC-days and all-cause mortality are lower.

CLABSI incidence rates

Figure 6.2.1 shows the annual pooled CLABSI incidence rates for 2003-2009 stratified by ICU type, academic profile, and surveillance year. The

summary pooled CLABSI annual incidence rate was the highest in NICUs and lowest in adult ICUs, 4.40 and 1.67 CLABSI/1000 CVC-days, respectively. Starting at the 2005-2006 period, adult teaching ICUs showed CLABSI incidence rates 28 to 88% higher than non-teaching units (p 0.004). An increase in the CLABSI incidence rates for all ICU types, ranging from 30 to 57%, was observed during the 2006-2007 period, coinciding with a substantial number of new ICUs joining the SPIN program (Figure 6.2.1). Overall, the new participating units had CLABSI incidence rates that were 68% higher on average than those with previous participation in SPIN (SIR 1.68, 95%CI 1.30-2.12). In the subsequent years, adult and pediatric ICUs showed an 11% (SIR 0.89, 95%CI 0.75-1.04) and 50% (SIR 0.51, 95%CI 0.22-1.01) decline in their rates, respectively. For NICUs, an 18% decrease of the CLABSI incidence rate (SIR 0.82, 95%CI 0.61-1.07) only occurred during the 2008-2009 period.

When compared to the 2006 Canadian Nosocomial Infection Surveillance Program results, the SPIN CLABSI rate for NICUs for the same period (April 2006-March 2007) was considerably lower (4.25 vs. 5.70 CLABSI/1,000 CVC-days – SIR 0.66; 95%CI 0.30-1.76). The rates for adult teaching (2.15 vs. 2.30 CLABSI/1,000 CVC-days – SIR 0.93; 95%CI 0.77-1.12) and pediatric ICUs (1.38 vs. 2.60 CLABSI/1,000 CVC-days – SIR 0.53; 95%CI 0.11-1.53) were similar.[6]

However, when comparing the pooled CLABSI incidence rates of Quebec ICUs for April 2006 to March 2009 to the rates calculated using published NHSN data for January 2006 to December 2008, the SPIN rates were lower for adult

ICUs (1.77 vs. 1.99 CLABSI/1,000 CVC-days – SIR 0.89; 95%CI 0.81-0.98), similar for PICUs (2.38 vs. 2.94 CLABSI/1,000 CVC-days – SIR 0.81; 95%CI 0.58-1.11), and higher for NICUs (4.87 vs. 2.59 CLABSI/1,000 CVC-days – SIR 1.88; 95%CI 1.60-2.20).[19] When using the new NHSN CLABSI definition published in 2008, thus removing CLABSI caused by usual skin contaminants where only 1 blood culture is positive, SPIN rates for adult ICUs (1.31 CLABSI/1000 CVC-days) and PICUs (2.03 CLABSI/1000 CVC-days) decreased further as expected, with new SIRs of 0.66 (95%CI 0.59-0.73) and 0.69 (95%CI 0.48-0.96), respectively. The rate for NICUs was also reduced (3.19 CLABSI/1000 CVC-days), but remained significantly higher than the NHSN rate (SIR 1.23; 95%CI 1.01-1.49).[20]

CVCUR

Figure 6.2.2 provides data on CVCUR for 2003-2009. PICUs presented the highest CVCURs (median 0.61, IQR 0.57-0.66), while NICUs had the lowest ratios (median 0.22, IQR 0.21-0.34). Among adult ICUs, the CVCUR in teaching ICUs (median 0.61, IQR 0.59-0.64) was between 1.7 and 2.0 times that of non-teaching units (median 0.34, IQR 0.33-0.35). Both PICUs and NICUs showed a decline in their CVCURs over time, while in adult ICUs the CVCUR remained stable during the study period.

Case-fatality proportions

Regarding case-fatality proportions, no trend involving all-cause mortality was identified from 2003 to 2009. Adult ICUs presented the highest case-fatality

proportions (median 34%, IQR 32-37%), while NICUs had the lowest (median 14%, IQR 9-16%). Excepting the 2003-2004 period, the case-fatality proportion in non-teaching adult ICUs was consistently higher (between 15 to 57%) compared to adult teaching units. When using only CLABSI related deaths for its calculation, we observed, in adult ICUs, a decrease from 20 to 4% in the case-fatality proportion from 2003 to 2009. For NICUs and PICUs, no temporal trends were observed.

Microbiology and antimicrobial resistance

Coagulase-negative *Staphylococcus* was the most frequently identified organism (53%), followed by *Staphylococcus aureus* (15%) and *Candida* spp (13%). Other pathogens, such as *Enterococcus* spp (8%), *Klebsiella* spp (4%), *Enterobacter* spp (3%), *Pseudomonas aeruginosa* (2%), and *Escherichia coli* (2 %), were responsible for <20% of the CLABSI. No trend regarding the distribution of the pathogens was identified.

The proportion of *Staphylococcus aureus* resistant to methicillin declined from 70% to less than 40% after the 2006-2007 period. Resistance to fluconazole in Candida spp has remained stable around 10% since 2006-2007. Finally, no *Enterococcus* spp resistant to vancomycin were detected until 2008-2009, when resistance was observed in 6% of *Enterococcus faecalis* and *Enterococcus faecium* causing CLABSI.

DISCUSSION

CLABSI is an important problem for Quebec ICUs. Summary pooled CLABSI incidence rates for 2003-2009 for adult, pediatric, and neonatal ICUs were 1.67, 2.24, and 4.40 CLABSI/1000 CVC-days, respectively. However, a decrease in the CLABSI incidence rates has been noticed since 2007.

The comparison between SPIN and the Canadian Nosocomial Infection Surveillance Program CLABSI incidence rates for university-affiliated ICUs showed that they were not significantly different. The same could not be said after we compared SPIN and NHSN results, the latter also a program that includes non-teaching ICUs. SPIN rates for adult ICUs were considerably lower, while our NICU rates were higher.[19] Despite similar surveillance methods and definitions, SPIN and NHSN have important differences that should be accounted for when comparing their results. NHSN reports include ICUs that contributed data to the program for ≥1 month/year, whereas we included data from ICUs that participated in SPIN for ≥6 months/year. In doing so, we believe that our results become more stable and better reflect the CLABSI rates of participating ICUs. This is especially true after the 2006-2007 period as, from this point on, >95% of ICUs continuously sent data to SPIN.

Also, while SPIN still includes CLABSI diagnosed by 1 positive blood culture with potential skin contaminants in the presence of clinical signs of sepsis with the initiation of appropriate antimicrobial therapy (NNIS criterion 2b for

bloodstream infection diagnosis), NHSN, since 2008, requires 2 positive blood cultures procured at different times or sites in the same setting.[15, 20] As demonstrated in the NHSN 2006-2007 report, the proportion of CLABSI cases that fits NNIS criterion 2b was 35% in NICUs, 30% in PICUs and 15% in adult ICUs.[21] To enable the comparison between SPIN and NHSN data, we applied the new NHSN definition, adopted by SPIN as of April 2010, to our rates for 2006-2008.[20] Consequently, our CLABSI rates for adult, pediatric, and neonatal units decreased by 26, 15, and 35%, respectively, thus improving our performance compared to NHSN.

The lower CLABSI rates presented by SPIN in comparison to NHSN may be due to different factors. First, a considerable proportion of the adult and pediatric ICUs that volunteered to participate in SPIN before the program became mandatory belonged to hospitals with long-standing established infection control programs. Despite the absence of Canadian benchmarks, these units were using NNIS/NHSN data for comparison and acting upon the observed results. Thus, it is possible that many units had already lowered their rates over time, reaching a plateau mostly driven by their case-mix. This may not be true for NICUs, as only 1 out of the 6 units that participated during 2006-2008 had an already established surveillance program. Second, we cannot rule out a difference between the case-mix of patients of ICUs participating in SPIN and NHSN, as well as differences in infection control practices. To address the latter, a survey about infection control practices is being prepared and will be sent to SPIN participating hospitals.

We showed that CLABSI incidence rates in Quebec ICUs significantly increased during the 2006-2007 period. This may be explained by the large number of units without prior surveillance programs that joined SPIN during that year. A decline in the ICU CLABSI rates has been observed since. It would be precipitous to interpret this observation as a trend, especially in light of the change in the composition of the group of participating ICUs that took place in 2006-2007. To detect a secular trend, we must follow this now stable group of ICUs prospectively.

The distribution of CLABSI pathogens in Quebec ICUs parallels the results obtained by the NHSN (2006-2007) and the Hospitals in Europe Link for Infection Control through Surveillance (HELICS) network (2000-2004), where coagulase-negative *Staphylococci* is the most frequently isolated microorganism (34.1 and 24.7%, respectively).[22, 23] However, our proportions of methicillin-resistant *Staphylococcus aureus* (below 40% since 2006) and vancomycin-resistant *Enterococci* (6%) are considerably lower than in the NHSN program (56.8 and 36.4%, respectively). The mandatory participation of SPIN hospitals in a concurrent provincial methicillin-resistant *Staphylococcus aureus* bacteremia surveillance program since 2007, as well as the publication of revised provincial methicillin-resistant *Staphylococcus aureus* prevention guidelines in 2006 may partly explain this result.[24, 25]

One of the study's limitations is the paucity of data on ICUs with <10 beds, whose participation in SPIN remains voluntary. As the case-mix of patients in

these ICUs may be different from those participating in SPIN, we do not recommend the generalization of our results to this group. Furthermore, because of the small number of some ICU sub-categories, e.g., adult burn, we decided to divide ICUs into 3 broad groups: adult, pediatric, and neonatal. We acknowledge that this classification is not ideal, as it may not reflect the case-mix and thus describe the CLABSI rates and trends of certain more specific ICU types.

However, this study presents important public health implications. Because participation is mandatory, the number of SPIN participating ICUs is high, as is the diversity of the healthcare facilities involved. We believe that the use of mandatory participation is the best option, especially for regional surveillance programs, as it improves the representativeness and the generalizability of the results. Thus, our results add to the current state of knowledge about the CLABSI problem in Canadian ICUs and allows for benchmarking data in the Canadian healthcare system. Moreover, they have helped in the development of provincial infection control strategies for CLABSI prevention, as well as in monitoring their effects. We are currently in the process of implementing quality improvement interventions, such as bundles for central line insertion and maintenance, and workshops about evidence-based infection control measures for CLABSI, whose results we expect to report in a near future.

CONCLUSION

CLABSI is a significant problem in Quebec ICUs. After reaching a peak in 2006-2007, CLABSI incidence rates have decreased. In the 2008-2009 period, the CLABSI incidence rates in adult, pediatric and neonatal ICUs were 1.69, 1.45, and 4.64 CLABSI/1000 CVC-days. Moreover, the methicillin-resistant *Staphylococcus aureus* proportion has remained below 40% since 2006, which is considerably lower than American data (NHSN) for the same period. To determine if these changes in the CLABSI rates and resistance patterns will be maintained, it is essential to pursue surveillance in a continuous fashion.

ACKNOWLEDGEMENTS

The authors would like to thank Dr. Jesse Papenburg for his critical review of this manuscript.

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This article was published in the American Journal of Infection Control, 2011 Aug 6 [Epub ahead of print], Fontela PS, Platt RW, Rocher I, Frenette C, Moore D, Fortin E, Buckeridge D, Pai M, Quach C., **Epidemiology of central line-associated bloodstream infections in Quebec intensive care units: a 6-year review**, Copyright Elsevier (2011).

Table 6.2.1 – Characteristics of SPIN participating intensive care units during 2003-2009

ICU type	Surveillance year						Total
	2003-2004	2004-2005	2005-2006	2006-2007	2007-2008	2008-2009	
Adult ICUs							
Number of units	24	30	23	41	47	46	-
Adult non-teaching							
Number of units	14	18	13	20	24	24	-
CLABSI cases	15	23	9	24	32	22	125
CVC-days	5,087	11,765	9,898	19,824	22,086	21,743	90,403
All-causes deaths	4	10	4	11	14	5	48
Adult teaching							
Number of units	10	12	10	21	23	22	-
CLABSI cases	15	53	58	113	126	128	493
CVC-days	17,480	37,992	35,896	52,499	67,643	67,296	278,806
All-causes deaths	8	15	21	37	35	25	141
Pediatric ICUs							
Number of units	2	2	2	4	4	5	-
CLABSI cases	3	13	11	18	15	8	68
CVC-days	2,174	5,716	5,199	6,350	5,375	5,503	30,317
All-causes deaths	-	6	4	4	5	3	22
Neonatal ICUs							
Number of units	2	2	3	6	6	7	-
CLABSI cases	9	19	18	44	63	52	205
CVC-days	2,403	4,921	6,640	10,357	11,076	11,214	46,611
All-causes deaths	1	3	1	7	10	4	26

ICU = intensive care unit, CLABSI = central line-associated bloodstream infection, CVC = central venous catheter All pediatric and neonatal ICUs are teaching units
Participation in SPIN became mandatory for ICUs ≥ 10 beds during the 2006-2007 period

Figure 6.2.1 - Central line-associated bloodstream infection incidence rates stratified by surveillance year, intensive care unit type and academic profile

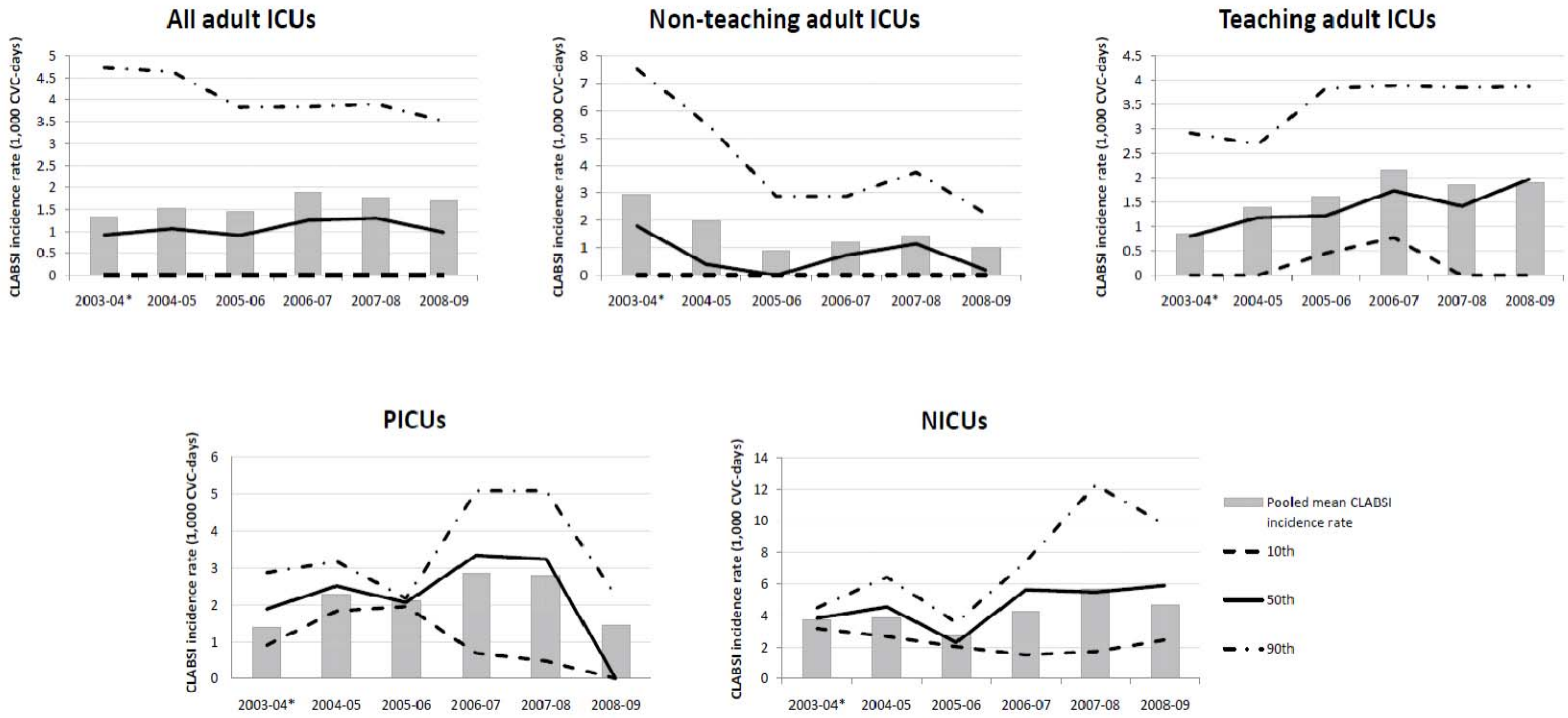
* The 2003-2004 period lasted only 6 months (from October 1st 2003 to March 31st 2004)

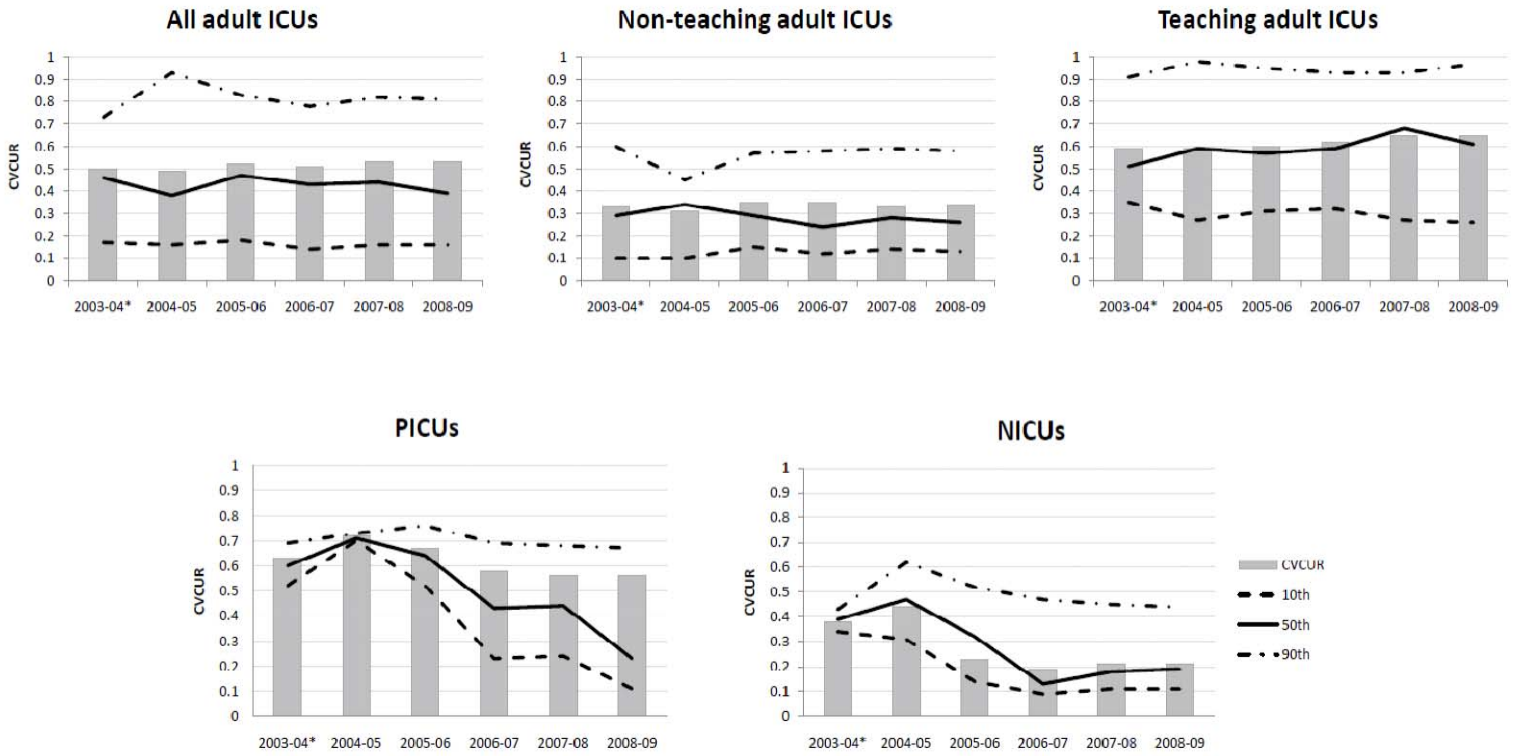
ICU = intensive care unit, PICU = pediatric intensive care units, NICU = neonatal intensive care unit, CLABSI = central line-associated bloodstream infection

Figure 6.2.2 - Central venous catheter utilization ratios stratified by surveillance year, intensive care unit type and academic profile

* The 2003-2004 period lasted only 6 months (from October 1st 2003 to March 31st 2004)

ICU = intensive care unit, PICU = pediatric intensive care units, NICU = neonatal intensive care unit, CVCUR = central venous catheter utilization ratio


All adult ICUs
Non-teaching adult ICUs
Teaching adult ICUs
PICUs
NICUs
CLABSI incidence rate (1,000 CVC-days)
2003-04*
2004-05
2005-06
2006-07
2007-08
2008-09
Pooled mean CLABSI incidence rate
10th
50th
90th


All adult ICUs
Non-teaching adult ICUs
Teaching adult ICUs
PICUs
NICUs
CVCUR
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
2003-04*
2004-05
2005-06
2006-07
2007-08
2008-09
CVCUR
10th
50th
90th

APPENDIX A

Table 6.2.2 – Pooled central line-associated bloodstream infection incidence rates stratified by surveillance year, intensive care unit type and academic profile

Variables	2003-04	2004-05	2005-06	2006-07	2007-08	2008-09
Adult ICUs (n)	24	30	23	41	47	46
Pooled CLABSI IR	1.33	1.53	1.46	1.89	1.76	1.69
- 10th percentile	0	0	0	0	0	0
- 25th percentile	0	0	0.18	0	0	0
- 50th percentile	0.92	1.06	0.91	1.25	1.30	0.98
- 75th percentile	2.86	2.34	2.18	2.17	2.42	2.26
- 90th percentile	4.73	4.64	3.83	3.84	3.90	3.52
Adult teaching ICUs (n)	14	18	13	20	24	24
Pooled CLABSI IR	0.86	1.40	1.62	2.15	1.86	1.90
- 10th percentile	0	0	0.45	0.77	0	0
- 25th percentile	0.09	0.09	0.89	1.18	0.71	0.69
- 50th percentile	0.80	1.18	1.22	1.73	1.42	1.97
- 75th percentile	1.89	2.31	2.18	2.43	3.25	2.79
- 90th percentile	2.92	2.69	3.83	3.89	3.85	3.87
Adult non-teaching ICUs (n)	10	12	10	21	23	22
Pooled CLABSI IR	2.95	1.96	0.91	1.21	1.45	1.01
- 10th percentile	0	0	0	0	0	0
- 25th percentile	0	0	0	0	0	0
- 50th percentile	1.80	0.40	0	0.73	1.14	0.19
- 75th percentile	4.78	3.30	1.21	1.92	2.18	1.08
- 90th percentile	7.52	5.54	2.88	2.88	3.75	2.25
PICUs* (n)	2	2	2	4	4	5
Pooled CLABSI IR	1.38	2.27	2.12	2.84	2.79	1.45
- 10th percentile	-	-	-	0.69	0.47	0
- 25th percentile	-	-	-	1.72	1.18	0
- 50th percentile	-	-	-	3.34	3.23	0
- 75th percentile	-	-	-	4.63	4.96	0.87
- 90th percentile	-	-	-	5.08	5.08	2.24
NICUs* (n)	2	2	3	6	6	7
Pooled CLABSI IR	3.75	3.86	2.71	4.25	5.69	4.64
- 10th percentile	-	-	-	1.50	1.72	2.45
- 25th percentile	-	-	-	2.73	2.93	3.70
- 50th percentile	-	-	-	5.62	5.48	5.90
- 75th percentile	-	-	-	6.12	7.91	7.80
- 90th percentile	-	-	-	7.42	12.26	9.78

ICU = intensive care unit, CLABSI = central line-associated bloodstream infection, IR = incidence rate, PICUs = pediatric intensive care units, NICUs = neonatal intensive care units
*All PICUs and NICUs are teaching units

Table 6.2.3 – Pooled central venous catheter utilization ratios stratified by surveillance year, intensive care unit type and academic profile

Variables	2003-04	2004-05	2005-06	2006-07	2007-08	2008-09
Adult ICUs (n)	24	30	23	41	47	46
CVCUR	0.50	0.49	0.52	0.51	0.53	0.53
- 10th percentile	0.17	0.16	0.18	0.14	0.16	0.16
- 25th percentile	0.31	0.32	0.29	0.24	0.24	0.24
- 50th percentile	0.46	0.38	0.47	0.43	0.44	0.39
- 75th percentile	0.61	0.66	0.67	0.62	0.68	0.69
- 90th percentile	0.73	0.93	0.83	0.78	0.82	0.81
Adult teaching ICUs (n)	14	18	13	20	24	24
CVCUR	0.59	0.59	0.60	0.62	0.65	0.65
- 10th percentile	0.35	0.27	0.31	0.32	0.27	0.26
- 25th percentile	0.39	0.37	0.47	0.39	0.45	0.37
- 50th percentile	0.51	0.59	0.57	0.59	0.68	0.61
- 75th percentile	0.72	0.75	0.75	0.76	0.80	0.79
- 90th percentile	0.91	0.98	0.95	0.93	0.93	0.97
Adult non-teaching ICUs (n)	10	12	10	21	23	22
CVCUR	0.33	0.31	0.35	0.35	0.33	0.34
- 10th percentile	0.10	0.10	0.15	0.12	0.14	0.13
- 25th percentile	0.18	0.22	0.18	0.20	0.19	0.17
- 50th percentile	0.29	0.34	0.29	0.24	0.28	0.26
- 75th percentile	0.44	0.40	0.39	0.50	0.40	0.38
- 90th percentile	0.60	0.45	0.57	0.58	0.59	0.58
PICUs (n)	2	2	2	4	4	5
CVCUR	0.63	0.72	0.67	0.58	0.56	0.56
• 10th percentile	-	-	-	0.23	0.24	0.11
• 25th percentile	-	-	-	0.26	0.33	0.21
• 50th percentile	-	-	-	0.43	0.44	0.23
• 75th percentile	-	-	-	0.62	0.56	0.58
• 90th percentile	-	-	-	0.69	0.68	0.67
NICUs (n)	2	2	3	6	6	7
CVCUR	0.38	0.44	0.23	0.19	0.21	0.21
- 10th percentile	-	-	-	0.09	0.11	0.11
- 25th percentile	-	-	-	0.12	0.16	0.15
- 50th percentile	-	-	-	0.13	0.18	0.19
- 75th percentile	-	-	-	0.32	0.33	0.31
- 90th percentile	-	-	-	0.47	0.45	0.44

ICU = intensive care unit, CLABSI = central-line-associated bloodstream infection, CVCUR = central venous catheter utilization ratio, PICUs = pediatric intensive care units, NICUs = neonatal intensive care units

*All PICUs and NICUs are teaching unit

CHAPTER 7 – SURVEILLANCE PARTICIPATION AND VALIDITY OF BENCHMARKS FOR CENTRAL LINE-ASSOCIATED BLOODSTREAM INFECTION INCIDENCE RATES IN INTENSIVE CARE UNITS

7.1. Preamble

Surveillance was developed to be a continuous activity. However, in the last years, many national/regional CLABSI surveillance programs have eliminated continuous participation requirements from their protocols.[10] New participation cut-offs proposed were set in an arbitrarily manner and may have endangered the validity of the CLABSI incidence rate benchmarks generated by these programs, as no study has determined the minimal annual duration of hospital participation that yields valid annual pooled CLABSI incidence rates at a regional and national level.

Thus, the second objective of this thesis was to determine the impact of different participation requirements on annual ICU CLABSI incidence rate benchmarks produced by national and provincial/regional surveillance programs. To do so, we used simulation techniques and different scenarios in which the surveillance participation had been randomly and non-randomly shortened. For scenarios involving provincial/regional surveillance programs, we used the SPIN-BACC database from April 2007 to March 2009. For scenarios involving

countrywide benchmarks, we simulated a database for a national surveillance program including 600 ICUs.

Our results showed that shortening participation requirements may be suitable for surveillance programs with a large number of participants, i.e., national programs, if data are collected in a random way. However, regional/provincial programs should rely on continuous participation to decrease the risk of biased benchmarks.

This manuscript was prepared for submission.

7.2. Effect of surveillance program participation requirements on the validity of benchmarks for central line-associated bloodstream infections incidence rates in intensive care units

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Keywords:

Healthcare-associated infections; bloodstream infections; central-line associated bloodstream infections (CLABSI); intensive care units; surveillance; benchmarks.

Conflicts of interest:

None to report

ABSTRACT

Introduction: Several central line-associated bloodstream infections (CLABSI) surveillance programs allow shortened hospital participation. We evaluated the effect of different participation cut-offs on the validity of annual CLABSI incidence rate benchmarks for intensive care units (ICUs).

Methods: We estimated the true annual pooled CLABSI incidence rate for both a real provincial (Quebec, <100 ICUs) and a simulated national (600 ICUs) surveillance program. We simulated scenarios where the annual surveillance participation was randomly or non-randomly shortened. Each scenario's annual pooled CLABSI incidence rate was estimated and compared to the true rates in terms of validity, bias, and proportion of simulation iterations that presented valid estimates (ideal if ≥90%).

Results: All random scenarios generated valid CLABSI incidence rates estimates (bias -0.37 to 0.07 CLABSI/1000 CVC-days), while non-random scenarios presented 0 to 100% valid iterations and higher bias (-2.18 to 1.27 CLABSI/1000 CVC-days). For random scenarios, the higher the number of ICUs in the surveillance program, the lower the participation cut-off to generate ≥90% valid iterations. The cut-offs for a countrywide program were 3, 13, and 13 months, when ICUs participated equally, and 3, 12, and 8 months, when participation was unequal, for adult, pediatric and neonatal units, respectively. At a provincial level, the cut-offs were 9, 12, and 10 months (equal participation), and 9, 13, and 12 months (unequal participation), for adult, pediatric, and neonatal units, respectively.

Conclusions: The shortening of participation requirements may be suitable for national ICU CLABSI surveillance programs if participation months are randomly chosen. Regional/provincial programs should opt for continuous participation to avoid biased benchmarks.

INTRODUCTION

Surveillance is essential to provide information on the epidemiology of central line-associated bloodstream infections (CLABSI). However, national and provincial/regional surveillance programs face significant challenges when recruiting participating hospitals. Most hospitals cite limited resources for infection control as the reason for not participating.

To increase the number of participating hospitals, many multicenter CLABSI surveillance programs have eliminated the continuous participation requirement from their protocols. For example, the National Healthcare Safety Network (NHSN) in the U.S. requires hospitals to participate a minimum of 1 month/year in the CLABSI surveillance program, while in England the cut-off is 3 months.[1, 2] In the Netherlands, hospitals participate at their own discretion in the national surveillance program.[3, 4]

Nevertheless, limiting the amount of surveillance data submitted per year raises concerns about the validity of the obtained benchmarks, as the aforementioned cut-offs are arbitrary and variable. Furthermore, no study has yet determined the minimum number of months hospitals must participate in a surveillance program to generate valid benchmarks for annual pooled CLABSI incidence rates.

The purpose of this study was thus to determine, through simulation, the impact of different participation requirements on the ability of countrywide and provincial/regional surveillance programs to yield valid estimates of the true annual Intensive Care Units (ICU) pooled CLABSI incidence rates.

METHODS

This study was approved by the McGill University Institutional Review Board and had the need of informed consent waived.

Simulation involving a national (large) CLABSI surveillance program

We simulated data collected by a countrywide ICU CLABSI surveillance program containing 600 ICUs (480 adult, 48 pediatric ICU - PICU -, and 72 neonatal ICU - NICU -; 60% teaching units) during a one-year period. To do so, we used published data from NHSN and the *Surveillance Provinciale des Infections Nosocomiales* (SPIN) database, an ICU CLABSI surveillance program in the province of Quebec, Canada, to model the ICU population structure and annual CLABSI incidence rate, respectively.[5-10] A detailed explanation of the simulation model can be found in Appendix A.

Calculation of the reference (true) annual pooled CLABSI incidence rates

The simulation model containing the population characteristics and the equations to model ICU number of beds, CLABSI, and central venous catheters-

days (CVC-days) for each of the 13 4-week surveillance periods/year was run 1000 times. This generated 1000 independent complete, i.e., no missing data, databases. We took a random subset of 100 simulated databases and calculated their individual adult, pediatric, and neonatal ICU annual pooled CLABSI incidence rates:

$$\text{CLABSI incidence rate} = (\sum \text{CLABSI cases} / \sum \text{CVC-days}) * 1000$$

These rates were considered the "true rates" for each simulated database, as they were calculated using 100% of the data. Furthermore, we calculated intervals which limits were values 10% above and below the annual true rates.

Simulation involving the provincial (small) CLABSI surveillance program (SPIN)

Data source

Using the original SPIN database for 2007-2009 as the data source, we built a new dataset with no missing values including 44 ICUs (34 adult ICUs, 4 PICUs, and 6 NICUs) that continuously participated in SPIN during 2007-2008 (complete dataset I).[6] The variables contained in this dataset were: number of CLABSI cases and CVC-days per surveillance period for each ICU (13 blocks/year), academic profile, and ICU type.

Calculation of the reference (true) annual pooled CLABSI incidence rate

We used the complete dataset I to calculate the "true" annual adult, pediatric, and neonatal ICU CLABSI incidence rates for the 2007-2008 period, as well as intervals whose limits were values 10% above and below the annual rates. To check the reliability of the results obtained for the complete dataset I, we repeated the steps above using the complete dataset II, which included 53 ICUs (43 adult ICUs, 4 PICUs, and 6 NICUs) that continuously sent data to SPIN during 2008-2009.

Simulation procedures to compare the different proposed scenarios

Generation of scenarios

The complete national and provincial datasets were used as references for the creation of scenarios where the duration of the ICU surveillance participation was progressively shortened. To do so, data were removed in 2 ways:

1. Random removal of surveillance blocks:

    1.1. Equal participation scenarios:

In these scenarios, the surveillance program determines the number of surveillance blocks that ICUs should commit to per year, making all ICUs participate for the same number of blocks, but allowing ICUs to choose, in advance, when the data will be collected. We assumed that the ICUs' choice of surveillance blocks is made in an independent and random way.

We started by generating a scenario where each ICU had not sent data (i.e., number of CLABSI and CVC-days) for 1 of the 13 surveillance periods/year. We progressively removed 1 additional period per ICU, until we reached 12 periods of missing completely at random data.

1.2. Unequal participation scenarios:

In these scenarios, the surveillance program determined that the minimal required ICU participation was 1 block/year. ICUs were free to decide in advance if they wanted to send data for 1 or more blocks, and for which periods the data were collected. Again, we assumed that ICUs had chosen the surveillance blocks in an independent and random way.

Initially, we created a scenario where the total ICU population had an average participation of 12 surveillance blocks/year. We progressively decreased the average participation 1 block at a time, until we reached an average participation of 1 block. Blocks were randomly removed.

The generation of each of the 12 equal/unequal participation scenarios was repeated 1000 times. The adult, pediatric and neonatal ICU annual CLABSI incidence rates were calculated for each iteration. We built a distribution of the 1000 estimates of the different CLABSI incidence rates and calculated their expected means, which were compared to the “true rates”.

2. Non- random removal of surveillance periods:

These scenarios examine a situation where the surveillance program determines the number of surveillance blocks that ICUs must participate per year and when the data will be collected. The options in which surveillance lasts 9, 6, and 3 blocks/year were evaluated. We investigated 4 different alternatives for when the data were required to be collected: 1) continuous data collection for the first 9, 6, or 3 blocks, 2) the last 9, 6, or 3 blocks, 3) the 9, 6, or 3 middle blocks, and 4) alternated data collection for a total 9, 6, or 3 blocks. The adult, pediatric and neonatal ICU annual CLABSI incidence rates were estimated for all 12 scenarios and compared to the "true rates".

Simulation outcomes

The primary outcome was defined as the validity of the estimate of the adult, pediatric, and neonatal annual ICU CLABSI incidence rates for a provincial and a national surveillance program (see "Statistical comparisons"). An estimate was considered valid if it was within 10% of the "true rate". As secondary outcomes, we evaluated the estimate average bias and the proportion of valid simulated iterations.

Statistical comparison

All simulations were performed using R 2.11.0. The performance of our model for the national surveillance program was evaluated through the assessment of bias and root mean square error.[11, 12] To do so, we compared the mean

simulated adult, pediatric and neonatal ICU CLABSI incidence rates to the SPIN adult, pediatric and neonatal ICU CLABSI incidence rates for 2007-2009.

The comparison between the estimates of the annual CLABSI incidence rates and the "true rates" was performed in 3 ways:[13]

1. Validity: an estimate, including the expected mean calculated for the random data removal scenarios, was considered to be valid if it was within 10% of the "true rate". The 10% range was determined based on the judgment of infection control experts.
2. Average bias: calculated by subtracting the mean estimate from the "true rate".
3. Proportion of iterations whose CLABSI incidence rate estimates were valid: exclusive to the random data removal scenarios. A scenario was considered acceptable if the estimated rate was valid, i.e., was within 10% of the true rate, in at least 90% of the iterations.

The means of the distribution of 1000 CLABSI incidence rate estimates calculated for the random scenarios and the CLABSI incidence rate estimates generated for the non-random scenarios involving the provincial surveillance program were directly compared to the "true rates". For the random scenarios involving the national surveillance program, we calculated the mean of the distribution of 1000 CLABSI incidence rate estimates per scenario for each of 100 databases, as well as the CLABSI incidence rate estimates generated for the non-

random scenarios. Consequently, we calculated the mean of the 100 estimates and calculated the average bias, validity and proportion of valid iterations.

RESULTS

Performance of the national surveillance program simulation model

Estimation of the adult, pediatric, and neonatal ICU pooled CLABSI incidence rates presented bias of -0.23, -0.05, and -0.33 CLABSI/1000 CVC-days, respectively. The maximum amount of bias (NICU) represented a decrease of 6.6% of the true CLABSI IR and was considered acceptable. Adult, pediatric, and neonatal ICU CLABSI incidence rates presented random mean square errors of 0.053, 0.119, and 0.240, respectively.

National (large) surveillance program

Estimated "true" rates for adult, pediatric, and neonatal ICUs were 1.52, 2.13, and 4.67 CLABSI/1000 CVC-days, respectively.

Random scenarios with equal ICU participation

All scenarios presented valid estimates for all ICU CLABSI incidence rates (bias -0.0091 to 0.0119 CLABSI/1000 CVC-days – Figure 7.2.1). The minimum participation required for adult ICUs to yield 90% of valid iterations was 3 surveillance blocks, while PICUs and NICUs required participation during the entire surveillance year.

Random scenarios with unequal ICU participation

Valid estimates of all ICU CLABSI incidence rates were obtained in all scenarios (bias -0.017 to 0.0054 CLABSI/1000 CVC-days – Figure 7.2.2). The cut-offs of average participation for having 90% of valid iterations were 3, 12, and 8 surveillance blocks for adult, pediatric, and neonatal ICUs, respectively.

Non-random scenarios

The scenarios that evaluated a total surveillance duration of 9 blocks per year generated estimates for adult ICU CLABSI incidence rate that were valid for 100% of the sample of 100 simulated databases, while the proportion of valid NICU and PICU estimates ranged between 96 to 98%, and 68 to 78%, respectively. Overall, bias ranged from -0.0301 to 0.0337 CLABSI/1000 CVC-days (Figure 7.2.3).

Regarding the scenarios in which surveillance lasted 6 blocks, 100% of estimates were valid for adult ICU CLABSI incidence rate, while NICUs presented proportions that varied from 84 to 92% (overall bias -0.035 to 0.015 CLABSI/1000 CVC-days). Less than 53% of PICUs estimates were valid, with a much higher bias (-1.583 to 0.070 CLABSI/1000 CVC-days – Figure 7.2.3).

Finally, the scenarios evaluating a 3-block surveillance duration had the worst overall performance. While the estimates for adult ICU CLABSI incidence rate produced validity proportions ≥96% and minimal bias (-0.0080 to 0.0068 CLABSI/1000 CVC-days), the estimates for NICU and PICU were ≤70% and

≤37% valid, respectively, with bias between -0.0958 and 0.1118 CLABSI/1000 CVC-days (Figure 7.2.3).

Provincial (small) simulation program

True rates for adult, pediatric, and neonatal ICUs for 2007-2008 were 1.83, 2.79, and 5.69 CLABSI/1000 CVC-days, respectively. For the 2008-2009 periods, true rates were 1.68 CLABSI/1000 CVC-days (adult ICUs), 1.52 CLABSI/1000 CVC-days (PICUs), and 4.18 CLABSI/1000 CVC-days (NICUs).

Random scenarios - equal participation

All scenarios presented valid estimates for all ICU CLABSI incidence rates (bias -0.1782 to 0.0352 CLABSI/1000 CVC-days – Figure 7.2.1). To yield 90% of valid iterations, the minimum participation required for adult and neonatal ICUs was the same for the 2007-2008 and 2008-2009 surveillance years: 9 blocks and 10 blocks, respectively. For PICUs, while the minimal participation required in 2007-2008 was 12 blocks, the 90% validity proportion could not be achieved in any scenario in 2008-2009.

Random scenarios - unequal participation

Valid estimates for all ICU CLABSI incidence rates were obtained in all scenarios (bias -0.3745 to 0.0743 CLABSI/1000 CVC-days – Figure 7.2.2). The average participation requirements for achieving 90% of valid iterations were 10 (2007-2008) and 9 (2008-2009) blocks for adult units, and 12 blocks for NICUs.

The 90% validity proportion could not be achieved for PICUs in either of the surveillance years.

Non-random scenarios

The scenarios in which surveillance lasted 9 blocks generated estimates of adult and neonatal ICU CLABSI incidence rates that were valid ≥80% of the time during the 2007-2009 period. PICUs presented the worst results, with only 40% (2007-2008) and 20% (2008-2009) of valid estimates. Overall bias ranged between -1.2291 and 0.6381 CLABSI/1000 CVC-days (Figure 7.2.3).

For the scenarios evaluating a 6-block surveillance duration (bias -1.9026 to 1.2666 CLABSI/1000 CVC-days – Figure 7.2.3), between 71% (2007-2008) and 86% (2008-2009) of estimates were valid for adult ICU CLABSI incidence rates, while NICUs and PICUs presented validity proportions that were 57% and <43%, respectively, for the same period.

Again, the scenarios that studied a surveillance duration of 3 blocks had the worst overall performance. While the validity proportion for NICU CLABSI incidence rate estimates were 40% (2007-2008) and 60% (2008-2009), respectively, PICUs could not achieve valid estimates (0%) in both years and adult ICUs presented 40% of valid estimates during 2008-2009 and 0% during 2007-2008. Overall bias ranged between -2.1752 and 3.4614 CLABSI/1000 CVC-days (Figure 7.2.3).

DISCUSSION

Our study simulated the effect of different participation cut-offs on the validity of national and provincial/regional benchmarks for CLABSI incidence rates and demonstrated that surveillance programs should base their minimum participation requirements on the number of participating ICUs. If data are collected for random intervals during the year, it is possible to generate valid estimates of the true CLABSI incidence rates using less data. Nevertheless, this outcome will only be achieved if a surveillance program has a high number of participating ICUs, as is the case for countrywide surveillance programs.

In our random scenarios, our approach was to use all available data for the calculation of the annual CLABSI incidence rates. Furthermore, we assumed that the periods when data were collected were randomly chosen, something that may be achieved by asking ICUs to select *a priori* when data will be collected; e.g., before each surveillance period. In using this strategy, missing completely at random data were produced by design, which allowed the calculation of unbiased estimates of the annual CLABSI incidence rates.[12, 14, 15] However, as the estimates were calculated based on a lower number of observations, there was loss of precision, which could be partially compensated for by either a longer participation or a higher number of participants.

Based on our results, we do not recommend the elimination of a continuous participation requirement for small (<100 ICUs) CLABSI surveillance

programs, i.e., regional/provincial, due to the limited number of participating ICUs. This strategy seems suitable only for national surveillance programs, which have enough participating units to compensate for the reduction in surveillance time. However, even national programs should be careful when doing so, as further stratification of CLABSI rates according to ICU types (e.g., adult cardiac or adult burn units), would cause a substantial decrease in sample size for incidence rate calculation, thereby threatening benchmark validity. This problem was exemplified by the lower precision and validity of the PICU and NICU estimates compared to adult ICUs', which was driven not by different patient characteristics, but by the small number of participating units.

CLABSI incidence rates are assumed to vary randomly over the year, without a seasonal pattern.[16] Thus, as the monthly CLABSI incidence rate pattern may change over the years, it becomes problematic for surveillance programs to impose when participants should collect data. As shown in our non-random simulation scenarios for a regional/provincial surveillance program, options that worked relatively well in 2007-2008 did not have the same performance in 2008-2009 and vice-versa. Moreover, the validity of the results of non-random scenarios also seemed to be associated to sample size. Yet, despite presenting better results when used for the larger national surveillance program dataset, non-random strategy results were more unstable overall when compared to those produced by random scenarios. Therefore, we do not recommend its use for either small or large surveillance programs.

Our study has several limitations. First, the lack of a national CLABSI surveillance database where ICUs continuously participate throughout the year obliged us to simulate such a dataset. The use of the SPIN database to model the expected number of ICU CLABSI and CVC-days decreased the precision of our simulated results for PICUs and NICUs as shown by the random mean square error values for these units. This is due to the small number of pediatric and neonatal units participating in SPIN (4 and 6, respectively), and may partly explain the better performance in some of the scenarios of the real provincial database over our simulated one. However, as our objective was to simulate a range of plausible CLABSI incidence rates for adult, pediatric and neonatal units, we were more interested in generating rates with low bias relative to the original SPIN rates, which was achieved, rather than with low variability. Also, for the random scenarios, we assumed that ICUs randomly chose when to send data to the surveillance program, which may not be completely true. Due to feasibility issues common to all hospitals, it is possible that different ICUs will choose to avoid sending data during the same periods, e.g., summer (reduced staffing due to vacations) or winter (infection control teams busy with respiratory tract infection outbreaks), a phenomenon that was not accounted for in our model. Finally, due to the different sizes and ICU population characteristics of different provincial and national surveillance programs, our results may not be widely generalizable.

Nevertheless, our study makes an important contribution to clarify the appropriateness of eliminating the continuous participation requirement from multicenter CLABSI surveillance programs. Overall, although this strategy

certainly decreases the financial burden of surveillance and therefore facilitates the recruitment and retention of participating hospitals, shortening the duration of surveillance performed per year may negatively impact the validity of the obtained results. To our knowledge, this is the first study that evaluates the effect of different surveillance programs' participation requirements on the validity of CLABSI incidence rate benchmarks. In the future, we plan to assess the participation requirements for surveillance programs with different sizes, as well as for scenarios in which CLABSI rates change over the years, due to random variation, outbreaks or implementation of new infection control practices.

CONCLUSIONS

The elimination of a continuous participation requirement may be a suitable alternative for large surveillance programs for ICU CLABSI if data submitted are randomly collected. However, minimum participation cut-offs should be based on the number of participants, with smaller programs requiring longer participations. To decrease the risk of generating biased benchmarks, small surveillance programs for ICU CLABSI such as regional/provincial ones, should opt for continuous participation. Further research is needed to determine the cut-offs for different size programs.

ACKNOWLEDGEMENTS

The authors thank Dr. Jesse Papenburg for his thoughtful review of this manuscript and Luc Villandré for his statistical guidance.

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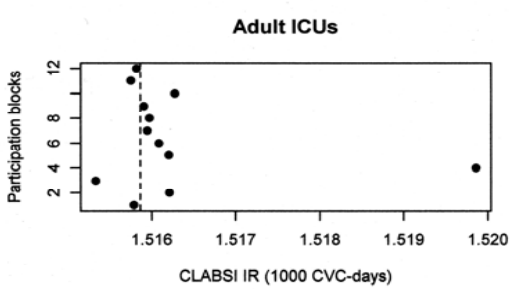
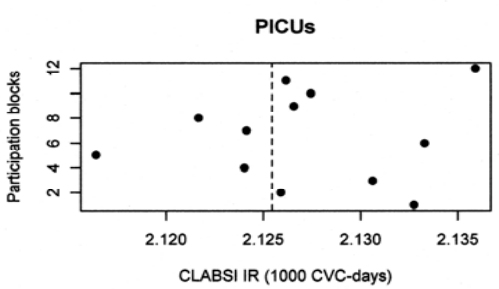
Figure 7.2.1 – Graphic representation of the bias of the central line-associated bloodstream infection incidence rate estimates obtained for the random scenarios with equal intensive care unit participation

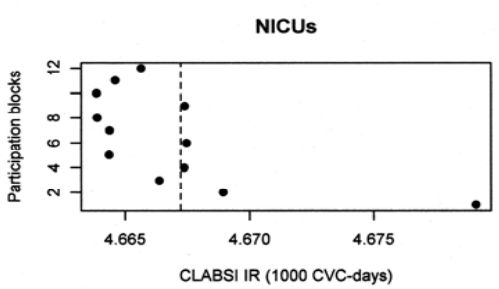
Figure 7.2.2 – Graphic representation of the bias of the central line-associated bloodstream infection incidence rate estimates obtained for the random scenarios with unequal intensive care unit participation

Figure 7.2.3 - Graphic representation of the bias of the central line-associated bloodstream infection incidence rate estimates obtained for the non-random scenarios

National







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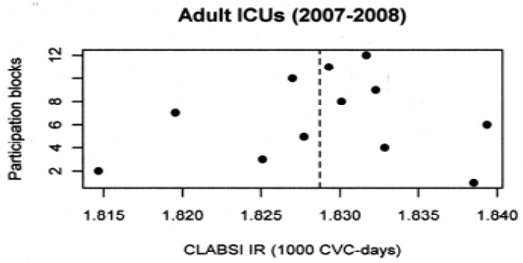

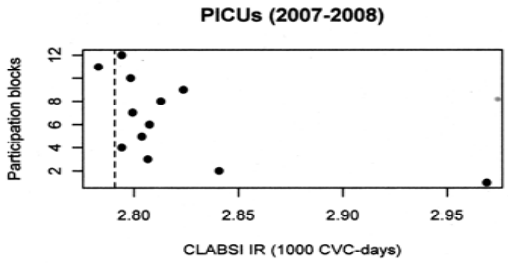

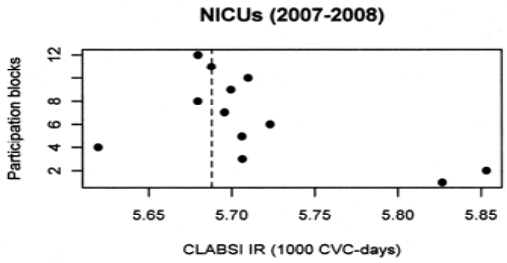

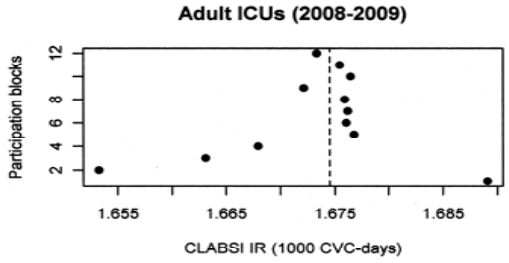

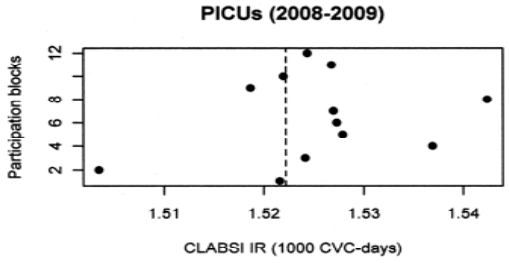

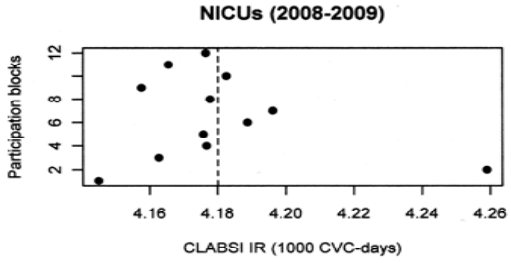

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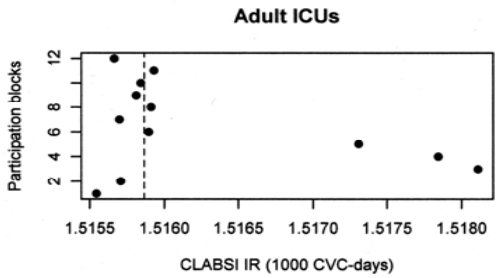

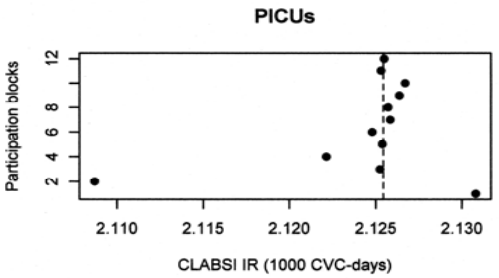

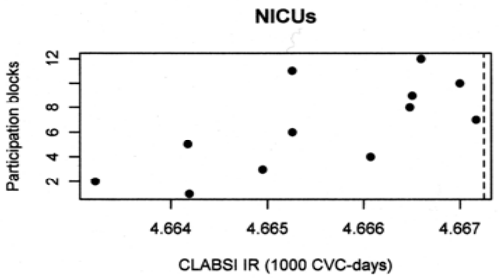

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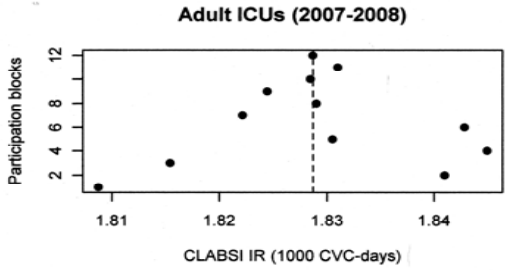

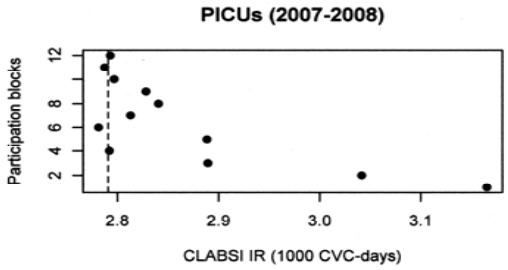

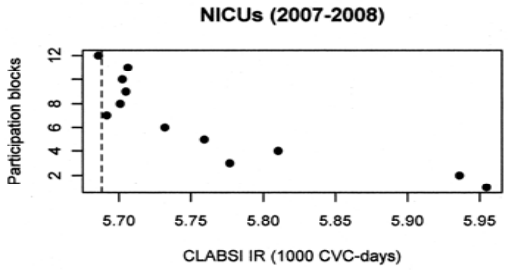

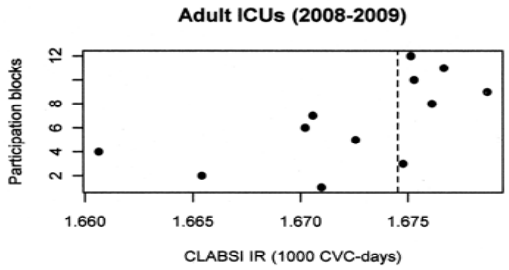

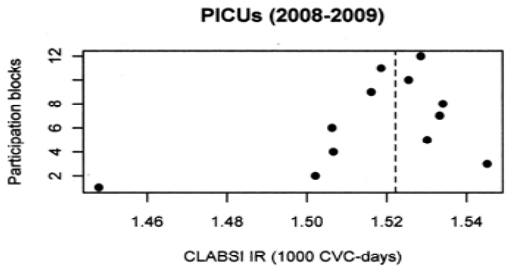

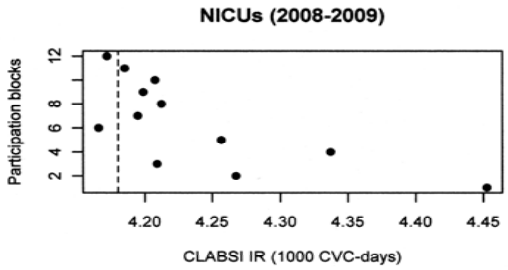

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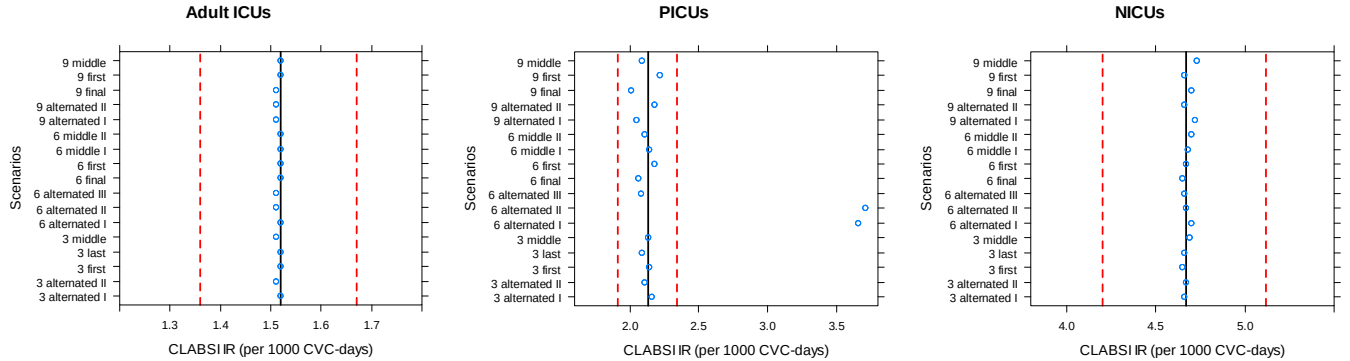

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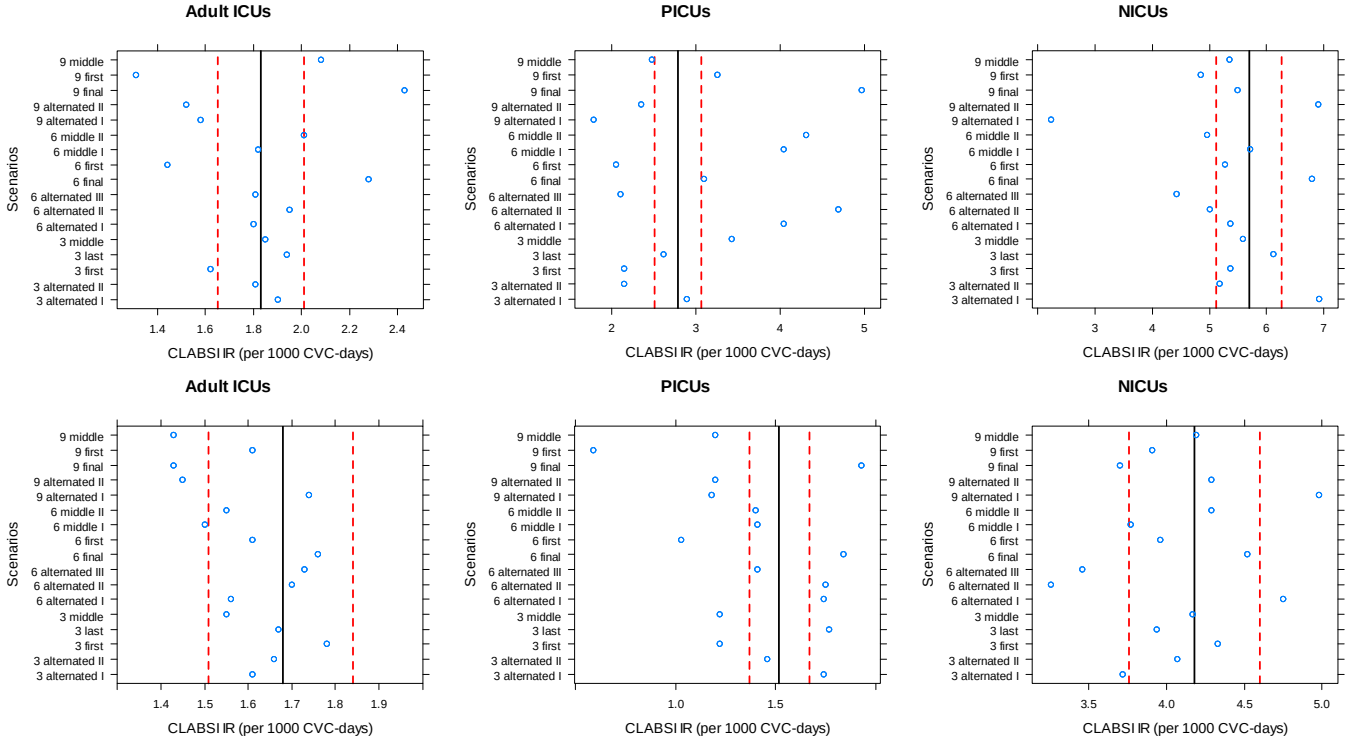

APPENDIX A - Simulation involving a national CLABSI surveillance program

Data sources

Two main data sources were used for modelling ICU population structure and individual ICU characteristics and annual CLABSI incidence rate:

- The ***Surveillance Provinciale des Infections Nosocomiales (SPIN)*** program database was used to provide data on the ICU population characteristics and on the expected number of CLABSI and CVC-days.[1-4] This is a provincial CLABSI surveillance program, which was launched in 2003 by the *Institut National de Santé Publique du Québec* and currently has 62 participating ICUs. Variables contained in this database include ICU type (adult, pediatric – PICU - and neonatal -NICU), number of beds, academic profile ("teaching" and "non-teaching units"), and annual number of CLABSI cases and CVC-days divided in 13 4-week surveillance periods. For this study, we used SPIN data for the period from April 2007 to March 2009, after participation in the program was determined to be mandatory for Quebec ICUs with ≥10 beds and the participating ICU population became more stable.

- The ***National Nosocomial Infections Surveillance (NNIS) System*** and the ***National Healthcare Safety Network (NHSN)*** were used to provide data on the characteristics of hospitals participating in a national CLABSI

surveillance program. NNIS was the largest monitoring system for hospital-acquired infections in the U.S. until 2006, when it was replaced by the NHSN. In 2001, the NNIS group conducted a survey of a sample of 229 participating hospitals (81% of the total number of participants) in which the characteristics of hospitals, such as academic profile, were recorded.[5] The structure of the simulated ICU population regarding number of participating units and ICU type was derived from the 2006 NHSN report.[6]

Modelling simulated ICU characteristics

We simulated data collected by a countrywide ICU CLABSI surveillance program containing 600 ICUs (80% adult, 8% PICU and 12% NICUs) during a one-year period. Regarding academic profile, 60% of the simulated units were classified as "teaching ICUs", defined as ICUs whose hospitals to which they belong are part of a teaching and research program of a medical school.[1] All simulation procedures were performed using R 2.11.1. We used the command "rbinom" to perform the random number generation for the binomial distribution of the variables "ICU type" and "academic profile" for each simulated ICUs, with the parameters size and probability.[7]

To determine the number of beds of the simulated units, we built a multivariate linear regression model using SPIN data for 2007-2009, which

included the variables “academic profile” and “ICU type” The fitted equation used to model the ICU number of beds was:

ICU number of beds = 10.129 + 4.340*academic profile - 3.669*PICU + 10.103*NICU

Consequently, we used the command “rpois” to perform the random generation of numbers for the Poisson distribution of the variable “ICU number of beds”, with parameter lambda, i.e., a vector of non-negative means.[8]

Modelling number of CLABSI cases and CVC-days

Initially, using data from the SPIN database, we created a random effects Poisson model to model the number of CVC-days that would be observed in different ICUs in each of the 13 4-week surveillance blocks throughout a year. The model included the variables “academic profile”, “number of ICU beds”, and “ICU type”, and had random slopes for “surveillance blocks” and “ICU”. The command “rpois” was used to perform the random generation of values for the variable “CVC-days” for each of the 13 simulated surveillance blocks, and stored the results in a temporary vector.[8] The fitted equation used to predict the number of CVC-days for each simulated surveillance block was:

CVC-days = exp (3.10547 + 0.79459*academic profile - 1.31578*PICU - 1.21487*NICU + 0.07784*ICU beds)

Subsequently, we created a random effects Poisson regression model to predict the number of CLABSI cases that the simulated ICUs would present in each of the 13 surveillance blocks. The variables included in this second model were “academic profile”, “ICU type”, “number of ICU beds”, and the simulated variable “CVC-days”, this latter used as the offset. Again, the command “rpois” was used to randomly generate the values for the variable “CLABSI” for each of the 13 surveillance blocks. All results were stored in a temporary vector. The fitted equation used to model the CLABSI number per simulated surveillance block was:

CLABSI = exp (-6.69841 + 0.28540*academic profile + 0.33162*PICU + 1.11861*NICU - 0.00123*ICU beds) * CVC-days

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CHAPTER 8 - THE IMPACT OF TARGETED SURVEILLANCE ON CENTRAL LINE-ASSOCIATED BLOODSTREAM INFECTION INCIDENCE RATES IN INTENSIVE CARE UNITS

8.1. Preamble

In addition to the use of surveillance results for the monitoring of trends and as benchmarks, surveillance may also be employed as an intervention to reduce HAI rates. Briefly, the dissemination of surveillance results would lead to the improvement of infection control practices and a consequent decrease in HAI rates.[14, 60]

Nevertheless, the magnitude of the effect of targeted surveillance on ICU CLABSI incidence rates has yet to be determined. This would allow public health officers and infection control teams to establish achievable goals regarding the reduction of CLABSI rates. Earlier studies showed a wide range of effect sizes, which may be due to confounding, as none of these before-after studies performed any sort of statistical adjustment.[17-22] Also, it is possible that the effect of targeted surveillance on CLABSI rates will vary according to ICU characteristics.

The third objective of this thesis was to determine the effect of a targeted surveillance program (SPIN-BACC) on CLABSI incidence rate in Quebec ICUs. In this manuscript, we evaluated the impact of the dissemination of targeted surveillance results on the CLABSI incidence rates of 56 ICUs after their first

year of participation in the SPIN-BACC program. Differently from earlier studies, we performed a comparison of rates before and after the dissemination of results while accounting for ICU-level potential confounding factors. In addition, we also explored the existence of interaction between the dissemination of results (intervention) and ICU participating characteristics. Finally, we identified ICU-level variables associated with higher CLABSI incidence rates.

This manuscript was prepared for submission.

8.2 - Effect of targeted surveillance on central line-associated bloodstream infection incidence rates in intensive care units

Authors

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Keywords:

Surveillance, cross-infection, healthcare associated infection, central venous catheterizations.

Conflicts of interest:

None to report.

ABSTRACT

Introduction: The magnitude of decrease in central line-associated bloodstream infections (CLABSI) incidence rates in intensive care units (ICUs) associated with targeted surveillance is still uncertain and may vary with ICU characteristics.

Objectives: To determine the effect of a targeted surveillance program (SPIN-BACC) on the CLABSI incidence rate in Quebec ICUs and ICU-level risk factors for higher CLABSI incidence rates.

Methods: Before-after study including 56 ICUs that continuously participated in SPIN-BACC for 3 years between 2003 and 2011. The change in CLABSI incidence rate after the first dissemination of annual surveillance results (intervention) and risk factors for higher CLABSI incidence rates were estimated using Poisson regression models adjusted for ICU-level confounders. Moreover, we studied if the intervention effect would be modified by ICU academic profile and previous exposure to surveillance.

Results: There was no evidence of an overall effect of targeted surveillance (rate ratio - RR - 1.08; 95%CI 0.84-1.40). We observed a clinically significant 31% reduction in the CLABSI incidence rate of ICUs that joined SPIN-BACC after participation became mandatory, a surrogate for not having performed surveillance before (RR 0.69; 95%CI 0.33-1.44). The adjusted CLABSI incidence rate reduction for non-teaching ICUs was 27% (RR 0.73; 95%CI 0.28-1.92). Both neonatal units (RR 1.67; 95%CI 1.08-2.60) and ICUs that joined SPIN-BACC after participation became mandatory (RR 1.57; 95%CI 1.12-2.21) were associated with higher CLABSI incidence rates.

Conclusions: Targeted surveillance may lead to a larger reduction in CLABSI incidence rate in "surveillance-naïve" and non-university affiliated ICUs. Furthermore, neonatal and "surveillance-naïve" units are associated with high CLABSI rates. Intensified infection control efforts should be directed towards these units.

INTRODUCTION

Healthcare associated infections (HAI) surveillance programs were initially developed to monitor rates and changes in trends over time. However, these programs are also implemented with the objective to reduce HAI incidence rates. As demonstrated in the SENIC study, this might be achieved by a transitory Hawthorne effect, which would increase the compliance of healthcare professionals with infection control measures while observed, but, most importantly, following the dissemination of surveillance results, which may trigger changes in the infection control programs that ultimately lead to a reduction in HAI rates.[1]

The SENIC study showed that the use of high quality, hospital-wide surveillance and infection control programs by hospitals not previously exposed to surveillance was associated with a 35% decrease in bloodstream infections incidence rates.[2] In the last decades, the use of hospital-wide surveillance was replaced by targeted surveillance programs. In the specific case of central line-associated bloodstream infections (CLABSI), these programs target ICU patients.

The magnitude of the effect of targeted surveillance on CLABSI incidence rate in ICU is still uncertain. Earlier single-ICU studies estimated a reduction of CLABSI incidence rate of 13% and 69%, 1 year and 3.5 months after the first dissemination of results, respectively.[3, 4] Studies evaluating multicenter ICU CLABSI surveillance programs also reported a wide range of results. Gastemeier

et al observed a 19% (95%CI and p value not reported) reduction in the CLABSI incidence rate in ICUs that participated in the national German program (*Krankenhaus Infektions Surveillance System* - KISS) for 3 years. However, over the same period of time, L'Heriteau et al reported a 59% (95% CI and p value not reported) decrease in the CLABSI incidence rate in ICUs participating in the REACAT program in France. [5, 6]

From a public health perspective, knowing the effect size associated to CLABSI targeted surveillance in ICUs would be extremely useful when implementing such programs, as it would allow the setting of realistic objectives. We hypothesize that the effect of targeted surveillance is modified by ICU characteristics, such as teaching hospital and previous exposure to surveillance – explaining the wide range of observed effects. Thus, we performed a study that aims to determine the effect of a targeted surveillance program (SPIN-BACC) on the CLABSI incidence rate in Quebec ICUs, as well as identify ICU-level risk factors for higher CLABSI incidence rates.

METHODS

Study design and population

We performed a before-after study within a retrospective cohort that included 56 ICUs (88% of the total number of units) that continuously participated in the *Surveillance Provinciale des Infections Nosocomiales – Bactériémies Associées aux Cathéters Centraux* (SPIN-BACC) program in the

Province of Quebec, Canada, for 3 years between 2003 and 2011. A detailed description of the SPIN-BACC surveillance methods has been already published.[7] This study was approved by the McGill University Institutional Review Board.

Outcomes

Our primary outcome was the rate ratio of CLABSI incidence rate, comparing the year prior and the 2 years after the first dissemination of surveillance results, which happened at the end of the first SPIN-BACC participation year. Our secondary outcome was the association between ICU-level variables and CLABSI incidence rate.

Study variables

The ICU-level variables retrieved from the SPIN-BACC database included university affiliation, ICU type (adult, pediatric, or neonatal), monthly number of CLABSI cases, central venous catheter-days (CVC-days), and patient-days, monthly central venous catheter utilization ratio (CVCUR), and volunteer status. ICUs were classified as "teaching" units if the majority of the hospital's clinical services to which it belonged were part of a medical school teaching and research program at the undergraduate and post-graduate levels.[7]

Monthly CVCUR is a measure of the intensity of CVC use in ICUs and is calculated by dividing CVC-days by patient-days.[8] Patient-days are defined as the sum of patients present in the ICU at a given time point daily over a 28-day period.[7, 9] Finally, "volunteer ICUs" were defined as units that joined the

surveillance program while participation was still voluntary, while "non-volunteer ICUs" were units that joined SPIN-BACC as of January 2007, when participation became mandatory for all Quebec ICUs with 10 or more beds. The "non-volunteer" status is considered a surrogate for not having performed surveillance before, as the most common reason given by ICUs for not joining SPIN-BACC was lack of infection control resources to perform surveillance.

Statistical analysis

Descriptive statistics including mean and standard deviation (SD), median and interquartile range (IQR), and proportions were used. Monthly CLABSI incidence rate was calculated following the National Healthcare Safety Network (NHSN) standards:[8]

Monthly CLABSI incidence rate = (Σ CLABSI cases / Σ CVC-days) in a month

To test the hypothesis that the effect of targeted surveillance on CLABSI incidence rate is modified by volunteer status, we initially calculated a rate ratio (RR) for "non-volunteer" and "volunteer" units for each of the 39 surveillance months. Consequently, we compared the 13 pre-intervention monthly rate ratios with the 26 corresponding post-intervention ones. We used a logistic regression model to estimate the post-intervention change in the rate ratios, in which the sum of monthly CLABSI in the 2 comparison groups ("non-volunteer" vs. "volunteer") was used as the binomial denominator and the sum of monthly CLABSI in "non-volunteer" units was used as the numerator. The complement of

the post-intervention rate ratio was interpreted as the percentage reduction in CLABSI incidence rate of "non-volunteer" ICUs associated with targeted-surveillance. The same logistic regression model was used to test if "academic profile" modified the effect of the targeted surveillance on CLABSI incidence rate.

We also built Poisson regression models to adjust the effect of targeted-surveillance on "non-volunteer" and "non-teaching" ICUs for potential confounders. The models had a binary categorical term indicating if observations had happened before or after the first dissemination of surveillance results (intervention) and 2 other binary terms that indicated the volunteer status and the academic profile of the ICUs. Also, interaction terms between volunteer status and intervention, and academic profile and intervention were included to test for a possible modification of the effect of targeted-surveillance on CLABSI incidence rate by these 2 variables, which allowed us to estimate the overall effect of targeted-surveillance on "non-volunteers" and "non-teaching" ICUs. The total sum of monthly CVC-days was used as the model offset (that is, entered into the model with a coefficient of 1.0, to account for varying denominators). Adjusted models included potential confounders and variables known to affect variation in CLABSI incidence rate. In addition to ICU type, a potential confounder, we included the variable "patient-days". As CVCUR did not vary according to comparison groups and during pre- and post-intervention periods, this variable was not included in the model.

Finally, for the identification of risk factors for higher CLABSI incidence rates, we built a Poisson regression model using data from the first year of SPIN participation, i.e., before the intervention. ICU-level variables included in the model were ICU type, volunteer status, academic profile, and patient-days.

All 95% confidence intervals (CI) were calculated using Huber-White estimated standard errors, which account for heteroscedasticity.[10] All the analyses were performed using R version 2.13.0 and the packages sandwich and lmtest.[11]

RESULTS

We analyzed a total of 285,697 CVC-days from 56 ICUs (44 adult, 5 pediatric and 7 neonatal units) during the first 3 years (39 28-day surveillance blocks) of their participation in the SPIN-BACC program. During this period, 652 CLABSI cases were identified. Table 8.2.1 shows the distribution of CLABSI cases, CVC-days, patient-days, and CVCUR for the periods before and after the intervention for all ICUs and stratified according to volunteer status and academic profile.

Effect modification by volunteer status and academic profile

Unadjusted models

There was no evidence of a crude effect of the intervention on all ICUs (RR 0.97; 95%CI 0.76-1.25). However, after the first dissemination of annual surveillance results, we observed a 47% decrease in the non-volunteer group's

CLABSI incidence rate compared to the volunteer ICUs rates (RR 0.53; 95%CI 0.35-0.81). Similarly, non-teaching ICUs showed a 42% (RR 0.58; 95%CI 0.36-0.92) decline in their CLABSI incidence rate. The evolution of the monthly rate ratios for these 2 subgroups is shown in Figure 8.2.1.

Adjusted models

As ICU groups' composition differed in terms of type and variation in patient-days during the before and after periods, we used Poisson regression models to adjust for these variables. The overall intervention's adjusted effect was small (RR 1.08; 95%CI 0.87-1.35). Nevertheless, the interaction term for non-volunteer ICUs (RR 0.64; 95%CI 0.42-0.96), and for non-teaching units (RR 0.67; 95%CI 0.39-1.16) both suggested reduced rates.

When estimating the effect that the first dissemination of targeted surveillance results had in non-volunteer and non-teaching ICUs, we observed a 31% decline in the CLABSI incidence rate in non-volunteer units compared to volunteer units, but the confidence interval reflected significant uncertainty (RR 0.69; 95%CI 0.33-1.44). The adjusted CLABSI incidence rate reduction for non-teaching ICUs was 27%, but again, the confidence interval was wide (RR 0.73; 95%CI 0.28-1.92).

Risk factors for higher CLABSI incidence rates

The ICU-level variables evaluated as potential risk factors for higher CLABSI incidence rates included ICU type, volunteer status, and academic

profile. Non-volunteer ICUs were associated with a 57% increase in CLABSI incidence rate (RR 1.57; 95%CI 1.12-2.21), while neonatal ICUs were associated with a 67% increase (RR 1.67; 95%CI 1.08-2.60).

DISCUSSION

We showed that the first dissemination of targeted surveillance results tends to decrease CLABSI incidence rate more markedly in non-teaching units and for non-volunteer ICUs, a surrogate for not having been previously exposed to surveillance. In both cases, moderate and clinically significant declines in the CLABSI incidence rate were detected (27% and 31% after adjustment, respectively), but our limited sample size was reflected in substantial uncertainty and wide confidence intervals. Furthermore, non-volunteer and neonatal ICUs were associated with higher CLABSI incidence rates.

The seminal SENIC study evaluated the effect of the implementation of hospital-wide surveillance and infection control programs in hospitals never previously exposed to this intervention. According to its conceptual model, dissemination of surveillance results would lead to changes in infection control practices with a consequent reduction in HAI rates.[1, 2] After an initial decrease in rates, hospitals would tend to reach a plateau, driven by non-preventable HAI cases. Most of the ICUs that joined the SPIN-BACC program while participation was still voluntary belonged to hospitals where surveillance and infection control programs had already been established for many years. Despite the absence of

Canadian benchmarks, these hospitals were using international benchmarks, such as the NHSN results.[9, 12] Consequently, the initial decrease in rates following implementation of surveillance happened prior to SPIN-BACC's inception and data reported to the program belonged to their plateau phase. As these "volunteer" units represent the majority of SPIN-BACC ICUs, and thus, the majority of ICUs included in this study (46 out of 56 units), the observation of an overall non-significant effect of targeted-surveillance on CLABSI incidence rate was not unexpected.

This finding differs significantly from the results obtained by the NHSN national ICU CLABSI surveillance program. Gaynes et al reported overall reductions in CLABSI rates of ICUs participating in the NHSN program that ranged from 31% to 44% (no p values or 95%CI provided) for the period between 1990 and 1999.[13] These results may be partly explained by a change in the American healthcare system, which shifted away from hospital-based care during this period, as well as by the non-continuous participation of ICUs in the program, which may have diluted the initial rates.[13]

However, when comparing our results with those from studies that only included ICUs that continually participate in multicenter surveillance programs, there were some similarities. L'Heriteau et al reported a 58.6% decrease in the CLABSI incidence rate of 35 adult ICUs that continuously participated in REACAT over a 3-year period (from 5.99 to 2.48 CLABSI/1000 CVC-days; p value not calculated).[6] However, the catheter-related infection definition used by

REACAT included both CLABSIs and localized infections at the catheter insertion site, without bloodstream infection. According to data published in the REACAT annual reports for the first 3 years of surveillance, CLABSI rates dropped by 32% (from 1.5 to 1.0 cases/1,000 CVC-days; no p value or 95%CI provided).[14] Zuschneid et al studied a group of 84 ICUs that continuously participated in KISS for 2 years and showed a 28.7% decrease in the CLABSI incidence rate (from 2.1 to 1.5 CLABSI/1,000 CVC-days; p 0.04), which was mainly observed in small non-teaching hospitals.[15] This result is similar to our findings, especially because it is possible that a substantial number of KISS participating ICUs were "surveillance-naïve", as the authors mentioned that the training of infection control nurses was directed to the supervision of "procedures, equipments and facilities" rather than towards surveillance.[15]

We hypothesized that the strongest effect of SPIN-BACC, and of any other targeted-surveillance program, would be observed among "surveillance naïve" ICUs, as well as among non-teaching units, which tend to have a different case-mix and a less structured surveillance and infection control programs compared to teaching hospitals.[16] Our "surveillance naive" ICUs were those that initially declined to join SPIN-BACC claiming insufficient infection control resources and only joined in 2007, when participation became mandatory in Quebec. For both "non-volunteer" and "non-teaching" units, our point estimates indicated that the effect of targeted surveillance on CLABSI incidence rate is larger in these two ICU subgroups. However our results did not reach statistical significance because of small sample size (e.g., only 10 non-volunteer ICUs),

which generated high standard errors and, consequently, wide confidence intervals.

Therefore, as pointed above, our small sample size is the main limitation of this study. In defining the SPIN-BACC program as our source population, we were limited to only include the ICUs participating in it, as recruiting units participating in other programs that use difference surveillance methods would impair the comparability of the results. Furthermore, we were not able to adjust our results for other variables that may have influenced CLABSI incidence rate during the before and after study periods, such as changes in ICUs case-mix or nurse-patient ratio, as these data were not available. Finally, as previously explained, some ICUs had already performed CLABSI surveillance in their ICUs prior to SPIN-BACC. Ideally, data for the period before intervention should have been collected during the first year of CLABSI surveillance for all ICUs. However, this would have introduced important bias, as the surveillance methods used prior to SPIN-BACC were not standardized and the first year of ICU CLABSI surveillance for some of the ICUs occurred more than 15 years ago.

Nevertheless, our study has important strengths. By including 56 of the 64 ICUs eligible to participate in SPIN-BACC (88%), we reduced the risk of selection bias. In addition, there were no major changes in the Quebec healthcare system or in the infection control practices during the study period, decreasing the risk for confounding. Finally, this is the first study on CLABSI incidence rate and impact of surveillance that adjusted for potential confounders.

We also demonstrated that neonatal and non-volunteer ICUs were associated with higher CLABSI incidence rates. Neonates have an immature immune system and limited number of neutrophil precursors and weaker defense barriers, as their skin is more fragile and consequently more permeable to microbes.[17, 18] Moreover, these premature babies lack normal flora and are often colonized with ICU flora, making them more susceptible to infections.[19] Finally, premature babies often need CVCs for long periods of time to receive medication and parenteral nutrition while in NICUs, which increases their CLABSI risk.[19] Higher rates in non-volunteer ICUs can be explained by the fact that lack of previous HAI monitoring did not allow for the evaluation of the magnitude of the CLABSI problem and the effectiveness of infection control measures.

Our study mainly contributes by generating the hypothesis that targeted surveillance for CLABSI may be more effective in decreasing rates in surveillance naïve and non-teaching ICUs. Therefore, the overall decrease in CLABSI rates after the implementation of a regional or national targeted surveillance program may vary depending on the number of "surveillance-naïve" and non-teaching participating ICUs. In addition, the identification of neonatal and "surveillance-naïve" units as ICUs that present high CLABSI rates may help infection control teams and public health officers to focus CLABSI prevention efforts on these subgroups.

CONCLUSIONS

The implementation of targeted surveillance may lead to a more important reduction in CLABSI incidence rate in "surveillance-naïve" and non-teaching ICUs. Furthermore, neonatal and "surveillance-naïve" units are associated with high CLABSI rates. Intensified infection control efforts should be directed towards these units.

ACKNOWLEDGMENTS

We would like to thank Dr. Jesse Papenburg for the critical revision of this manuscript, and Dr. Annie Hoen and Dr. Dana Teltsch for their guidance on the statistical models.

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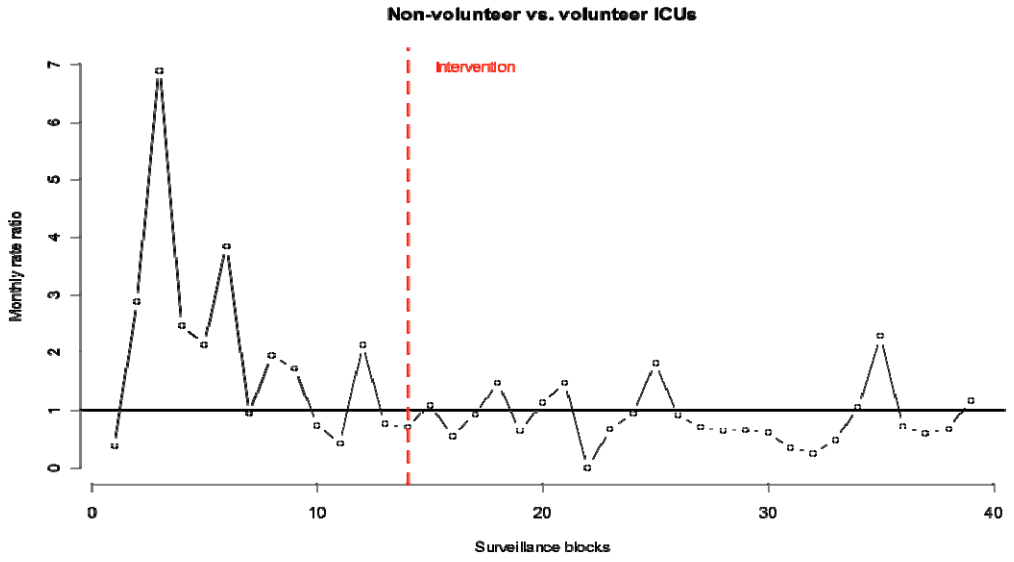
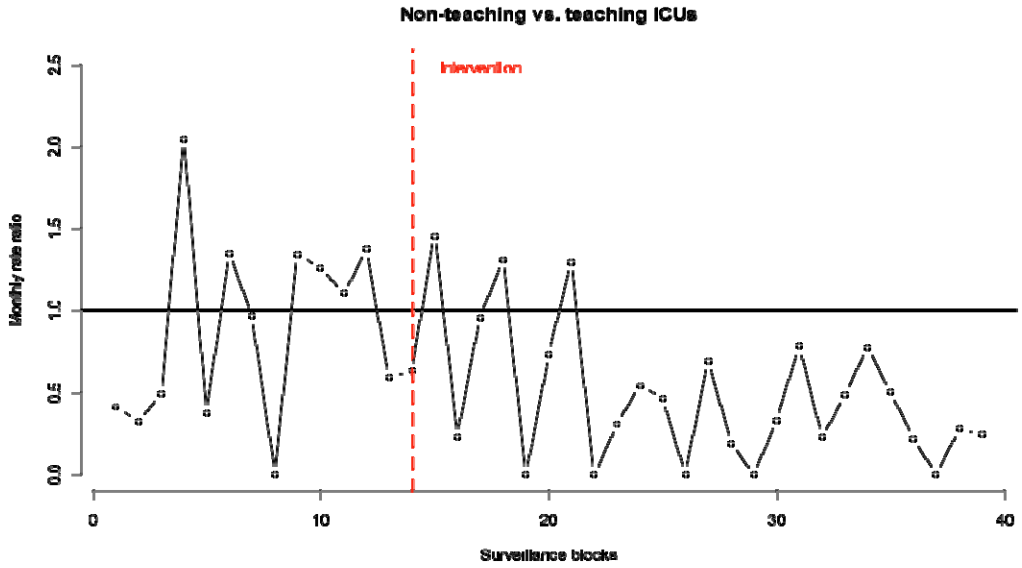
Table 8.2.1 – Distribution of central line-associated bloodstream infection cases, central venous catheter-days, patient-days and central venous catheter utilization ratios in the intensive care units before and after the first dissemination of the annual surveillance results

Period relative to the first 3 years of SPIN-BACC participation	**Total (N=56)**		**Volunteers (N=46)**		**Non-volunteers (N=10)**		**Teaching (N=36)**		**Non-teaching (N=20)**	
	Before	After	Before	After	Before	After	Before	After	Before	After
CLABSI	193	459	146	385	47	74	198	383	28	43
CVC-days	82,913	202,784	68,334	166,325	14,474	36,564	67,598	167,118	16,756	34,225
Patient-days	183,243	468,751	160,559	381,512	28,243	81,680	136,433	352,659	49,927	112,975
CVCUR	0.45	0.43	0.46	0.47	0.45	0.35	0.46	0.46	0.44	0.39

CLABSI = central line-associated bloodstream infection, CVC-days = central venous catheter-days, CVCUR = central venous catheter utilization ratio, SD = standard deviation, IQR = interquartile range

Figure 8.2.1 – Monthly rate ratios in non-volunteer vs. volunteer intensive care units and non-teaching vs. teaching units


Non-volunteer vs. volunteer ICUs
Intervention
Monthly rate ratio
0
1
2
3
4
5
6
7
0
10
20
30
40
Surveillance blocks


Non-teaching vs. teaching ICUs
Intervention
Monthly rate ratio
0.0
0.5
1.0
1.5
2.0
2.5
0
10
20
30
40
Surveillance blocks

CHAPTER 9 - SUMMARY AND CONCLUSIONS

In this dissertation, I explored the different applications of CLABSI surveillance data. First, I described the CLABSI problem in Quebec ICUs, and how provincial rates compare to Canadian and U.S. benchmarks. In the subsequent manuscript, I focused on the use of surveillance data for benchmarking. The potential problem of lack of continuity in data collection was discussed and recommendations were made. Finally, in the last study, I investigated the effect of targeted surveillance on the CLABSI incidence rate in ICUs, as well as its modification by ICUs' previous exposure to surveillance and academic profile. The important burden of disease of CLABSI in the ICU patient population and the potential use of surveillance results for its prevention are the reasons I have chosen to focus on this topic in this thesis.

In the first manuscript, entitled "Epidemiology of central line-associated bloodstream infections in Quebec intensive care units: a 6-year review", I showed that CLABSIs are an important problem Quebec ICUs, but that incidence rates have declined since 2007. However, due to the inclusion of a considerable number of ICUs in 2007, once participation in SPIN-BACC became mandatory for all Quebec ICUs with 10 beds or more, it is still premature to interpret this decrease as a trend. In addition, the methicillin-resistant *Staphylococcus aureus* proportion in Quebec ICU has remained below 40% since 2006, which is considerably lower than U.S. results. To determine the sustainability of both these changes, it is essential to maintain continuous surveillance.

The interpretation of the descriptive data was associated with many different challenges. The original group of ICUs that joined SPIN-BACC at its inception included many hospitals where surveillance and infection control had been performed for many years. Therefore, this group was aware of the importance of such a program and had a special interest in participating in it. This self-selection of participants may have led to a selection bias that initially impaired the representativeness of the SPIN-BACC results. While the implementation of mandatory participation was essential to improve the generalizability of the results, the inclusion of new participating ICUs, which had CLABSI incidence rate significantly higher compared to the old participants, had an important impact on benchmarks provided by the program. Consequently, we must continue to follow the SPIN-BACC CLABSI incidence rate over time to detect trends.

Another challenge was comparing SPIN-BACC and NHSN CLABSI incidence rates. The choice of NHSN as the comparison for SPIN-BACC was the most appropriate because these programs have nearly identical surveillance methods. However, SPIN-BACC and NHSN CLABSI definitions present slight differences. For instance, we demonstrated the important impact of excluding CLABSI cases caused by skin contaminants and diagnosed by only 1 positive blood culture – as per the NHSN case definition used in 2006-2008– on CLABSI incidence rate, and thus, on the ability to compare results between surveillance programs. The exclusion of these cases, initially included in the calculation of SPIN-BACC rates, reduced our adult, pediatric, and neonatal CLABSI incidence rates by 26, 15, and 35%, respectively. The recent change towards laboratory-

based definitions that require at least 2 positive blood cultures for skin contaminants to classify a bloodstream infection as CLABSI was made to improve the specificity of CLABSI diagnosis. Nevertheless, this creates a problem for special patient populations, such as premature babies, for whom it is frequently not feasible to obtain a second blood sample due to venous access difficulties.

Despite adjusting for differences in CLABSI definitions, incidence rates in Quebec were still lower compared with the U.S. As pointed by Coello et al, a comparison between hospitals or surveillance systems is not complete if differences in the case-mix are not accounted for.[10] For example, surveillance for surgical site infections are adjusted for case-mix by stratifying results by procedures, and, within the procedure categories, by procedure duration, wound class, and the America Society of Anesthesiology score.[96] We attempted to proceed in a similar manner for CLABSI by stratifying results according to ICU type and using SIR. However, this variable does not permit complete case-mix adjustment for CLABSI surveillance, as very different CLABSI incidence rates can be observed among same ICU types.[97] Furthermore, we cannot rule out that differences in healthcare practices and healthcare systems may not have affected the CLABSI rates in both programs.[10, 97, 98]

In the second manuscript, entitled "Effect of surveillance program participation requirements on the validity of benchmarks for central line associated bloodstream infections incidence rates in intensive care units", we

investigated, through simulation, the ability of national and provincial/regional surveillance programs to generate valid estimates of the true annual pooled CLABSI incidence rate for adult, pediatric, and neonatal ICUs depending on their different participation requirements. We demonstrated that reducing participation requirements might be suitable for large, e.g., national, ICU CLABSI surveillance programs, if data are randomly collected. However, regional/provincial programs, which have small ICU subgroups, should opt for continuous participation to decrease the risk of generating biased benchmarks.

Despite the fact that the continuity of data collection might not be a prerequisite to obtain valid benchmarks at a countrywide level, we strongly advocate for continuous CLABSI surveillance throughout the year in all hospitals. At the hospital-level, annual CLABSI rates are very unstable because of the small number of CLABSI events and CVC-days. Therefore, missing 1 or 2 months of data can have a substantial impact on the annual rate, and cause important bias. In addition, one of the reasons for doing surveillance is to ensure the detection of outbreaks, something that is only achieved if rates are monitored in a continuous fashion.

Problems arising from the generation of biased benchmarks are many. First, they will mislead public health officers and infection control teams, who will not be able to correctly identify the priorities regarding CLABSI prevention and control.[99] In a time when public reporting of HAI has become very popular, a bias towards higher CLABSI incidence rate may worry the public and

stakeholders about hospitals' performance from a province or country.[100] Nonetheless, the major problem arises from a bias towards lower CLABSI incidence rate, which is associated with the false belief in the success of the current infection control and healthcare practices in preventing CLABSI.

Our results are based on the assumption that the choice of when to collect data was made randomly by the ICUs. In the real setting, this could be achieved by defining *a priori*, i.e., at the beginning of a surveillance year or block, when data would be sent to the surveillance program. Nevertheless, even when we use this strategy, it is still possible to predict the occurrence of factors that might influence CLABSI incidence rate. For example, hospitals may choose not to send data during the summer months because they expect to have a reduction in the nurse-patient ratio due to summer vacation, which would tend to increase HAI risks. Similarly, university-affiliated hospitals might avoid the summer months because the academic year of most residency programs begins in July, a time when a high number of inexperienced doctors will be learning to insert CVCs in their ICUs, which would tend to increase CLABSI risks.

We intend to expand our simulation models to include the presence of outbreaks. Despite the fact that only 5 to 10% of HAI occur in outbreaks, we would like to study their impact on participation cut-offs and on the validity of ICU CLABSI incidence rate benchmarks.[101] In addition, we want to investigate the participation requirements for ICU CLABSI surveillance programs of different sizes, as the number of participating ICUs seems to be a determinant for

the cut-offs. We expect that our current and future results will help in the design of more effective ICU CLABSI surveillance programs and in the reassessment of provincial/regional multicenter programs that eliminated the continuous participation requirement.

In the third manuscript, entitled "Effect of targeted surveillance on the central line-associated bloodstream infection incidence rates in intensive care units", we tested the hypothesis that targeted surveillance for CLABSI may be more effective in decreasing rates in "surveillance naïve" and non-teaching ICUs. Moreover, we wanted to identify ICU-level variables associated with higher CLABSI incidence rates. While there were clinically significant reductions in the CLABSI incidence rate of SPIN-BACC non-volunteer ICUs (31%), a surrogate for not having performed surveillance before, and in non-university affiliated units (27%), these results could not be proven statistically significant, partly due to our limited sample size. Neonatal ICUs and non-volunteer units were significantly associated with higher CLABSI incidence rates.

So far, studies regarding the impact of targeted surveillance on CLABSI incidence rate have assumed that its effect is homogeneous among ICUs. However, as explained in our manuscript, we believe that the reduction in CLABSI incidence rate might be more pronounced among hospitals not previously exposed to surveillance, which, because they were surveillance naïve, were not aware of the magnitude of their CLABSI problem and/or the effectiveness of their infection control measures. A more pronounced effect

would also occur on non-university affiliated ICUs, but probably due to their case-mix and the absence of infection control programs as structured as in teaching hospitals.[90]

Surveillance programs act on preventable CLABSIs, which are CLABSI cases that are associated to the use of patient-care practices that are not in agreement with infection control standards.[60] It is possible that non-teaching ICUs have a higher number of preventable CLABSI compared to university-affiliated units as, in the latter, an important proportion of CLABSI cases is due to the presence of non-modifiable patient characteristics that are associated with a higher risk of CLABSI, such as immunosupression.[102, 103] Therefore, it would not be unreasonable to expect a stronger effect of targeted surveillance on the CLABSI incidence rate of non-teaching units.

When studying effect modification or interaction, we estimate the effect of the intervention or exposure on different subgroups. Consequently, unless each subgroup has a sufficient sample size, the study will be underpowered to statistically detect significant results. The major limitation of our study was the small number of non-volunteer ICUs (10 units), which contributed to our inconclusive results. Nonetheless, our study adds to the current literature by generating the hypothesis that the effect of targeted surveillance on ICU CLABSI incidence rate is not homogeneous, and that public health officers should take this into account when planning regional and/or national surveillance programs.

Last, it is important to discuss the impossibility of dissociating the effects of surveillance and infection control programs on CLABSI incidence rates in ICUs. As showed by the SENIC study, a reduction in rates will be more significant when surveillance results are disseminated to healthcare professionals, leading to a change in clinical practice, AND used to tailor infection control measures.[14, 60] As a future project, we plan to send a survey to all SPIN-BACC ICUs regarding the infection control measures used before and after they joined the program, in order to identify which interventions were more successful in reducing CLABSI incidence rates.

In the last years, a call for the elimination of CLABSI and other HAIs has been proposed in the U.S.[104] This call is based on the success achieved by some local and regional infection control programs, which reported 60-70% overall decreases of CLABSI incidence rates in ICUs.[105] In addition, investments in HAI prevention have been done at the federal, state, and local levels, which provides momentum for such an initiative.[106] However, as mentioned earlier in this thesis, HAIs can be classified as "preventable" and "non-preventable". Non-preventable HAIs are mainly driven by non-modifiable patient characteristics that increase the risk of such infections, e.g., age. Therefore, it is possible that, despite all the efforts, the objective of eliminating CLABSI and other HAI will not be met. As pointed by O'Grady et al in the "2011 Guidelines for the prevention of intravascular catheter-related infections", sustained elimination of CLABSI should be the ultimate goal, but the proposed preventive measures aim to reduce

CLABSI incidence rates to a minimum taking into account the patient population, environment and limitations of the current infection control strategies.[31]

In conclusion, in this thesis I demonstrated some applications of CLABSI surveillance data. Our descriptive study showed that CLABSI causes a significant burden on ICU patients in Quebec. Based on the results obtained, problematic areas were detected and infection control interventions were planned in Quebec ICUs. The use of surveillance data as benchmarks was addressed in our simulation study, which suggested that continuous surveillance should be performed by small and medium sizes programs in order to reduce the risk of generating biased benchmarks. Finally, we suggested that reductions in ICU CLABSI incidence rate associated with targeted surveillance may be more pronounced among "surveillance-naïve" and non-university affiliated ICUs. There are also other potential applications for these data that we expect to explore in the near future, such as their use for building CLABSI prediction models or for the study of antimicrobial resistance patterns, with the ultimate objective of improving patient safety.

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