OPEN

The Return on Investment of a Province-Wide Quality Improvement Initiative for Reducing In-Hospital Sepsis Rates and Mortality in British Columbia, Canada

Asif Raza Khowaja, PhD[1]
Alexander J. Willms, MSc[2,3]
Christina Krause, MSc[2,4]
Sarah Carriere, MScN[2]
Ben Ridout, MHA[2]
Colleen Kennedy, MHA[2]
Eric Young, BSc[2]
Craig Mitton, PhD[4,5]
Niranjan Kissoon, FRCPC, MD, FAAP, MCCM[6]
David D. Sweet, MD FRCP(C)[2,7,8]

OBJECTIVES: Sepsis is a life-threatening medical emergency. There is a paucity of information on whether quality improvement approaches reduce the in-hospital sepsis caseload or save lives and decrease the healthcare system and society's cost at the provincial/national levels. This study aimed to assess the outcomes and economic impact of a province-wide quality improvement initiative in Canada.

DESIGN: Retrospective population-based study with interrupted time series and return on investment analyses.

SETTING: The sepsis cases and deaths averted over time for British Columbia were calculated and compared with the rest of Canada (excluding Quebec and three territories).

PATIENTS: Aggregate data were obtained from the Canadian Institute for Health Information on risk-adjusted in-hospital sepsis rates and sepsis mortality in acute care sites across Canada.

INTERVENTIONS: In 2012, the British Columbia Sepsis Network was formed to reduce sepsis occurrence and mortality through education, knowledge translation, and quality improvement.

MEASUREMENTS AND MAIN RESULTS: A return on investment analysis compared the financial investment for the British Columbia Sepsis Network with the savings from averted sepsis occurrence and mortality. An estimated 981 sepsis cases and 172 deaths were averted in the post-British Columbia Sepsis Network period (2014–2018). The total cost, including the development and implementation of British Columbia Sepsis Network, was $449,962. Net savings due to cases averted after program costs were considered were $50.6 million in 2018. This translates into a return of $112.5 for every dollar invested.

CONCLUSIONS: British Columbia Sepsis Network appears to have averted a greater number of sepsis cases and deaths in British Columbia than the national average and yielded a positive return on investment. Our findings strengthen the policy argument for targeted quality improvement initiatives for sepsis care and provide a model of care for other provinces in Canada and elsewhere globally.

KEY WORDS: critical illness; economic impact; quality improvement; return on investment; sepsis

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection (1, 2). In 2017, 48.9 million new cases of sepsis and 11 million sepsis deaths were estimated, representing 19.7% of all global deaths (3). A disproportionate burden exists where inequity in access and quality of care exists, and Canada is no exception. There is scant information on the burden of sepsis in Canada, and recognition of

DOI: 10.1097/CCM.0000000000005353

the importance of sepsis led to sepsis being a focus of the *Canadian Medical Association Journal* in 2017 (4). Apart from sepsis deaths, about 40% of sepsis survivors may be readmitted to hospital (5–7), as well as higher odds of disabilities among sepsis survivors (8–10). Additionally, sepsis is more common in the elderly, and it is likely to increase substantially as the population ages (11, 12). Furthermore, the burden in acute care facilities, as well as long-term convalescent care due to sepsis, will be increased markedly due to severe coronavirus disease 2019. Postsepsis syndrome creates high stress and care needs that consume valuable resources from many, including patients (8, 10), families (13) and society (14).

Sepsis is often challenging to diagnose, yet early identification and rapid administration of key supportive measures are needed to ensure the best outcomes (15). Thus, the implementation of sepsis screening tools and sepsis protocols is paramount to rapid identification and treatment (16). These goals may be best achieved by a provincial quality improvement (QI) initiative, which maximizes efficiency and the program's effectiveness. To facilitate the implementation of sepsis tools provincially and support knowledge translation, the British Columbia Patient Safety & Quality Council (BCPSQC) formed the British Columbia Sepsis Network (BCSN) in June 2012. Its mandate is to support the early identification and rapid treatment of new infections, prevent the development of sepsis, and treat sepsis and septic shock; this is done through a model of distributed leadership to share resources, improve care, disseminate innovation, and collaborate for knowledge translation (17). As of 2020, the Network has grown to over 36 hospitals, including 300 members. It has diverse representation, including patient partners, allied healthcare frontline staff, physicians from various medical specialties, QI experts, and hospital administrators. The genesis and structure of the BCSN are outlined in **Supplementary Figure S1** (http://links.lww.com/CCM/G873), which summarizes the programs and activities of the largest and most active interconnected sepsis community within Canada dedicated to improved diagnosis and management of early severe infections, including sepsis and septic shock. As the mandate is to aggressively identify and treat significant infections in the emergency department (ED) and hospital wards, we propose that the program reduced the occurrence of patients progressing to develop in-hospital sepsis and reduce the mortality of those in whom sepsis develops. In the policy context, health system planners and decision-makers need evidence surrounding clinical effectiveness, costs, and benefits of QI interventions to allocate scarce resources for scale-up and sustainability. This study aimed to assess the clinical and economic impact of the BCSN in terms of cost savings from reducing the in-hospital sepsis occurrence and mortality across BC.

MATERIALS AND METHODS

This study used a retrospective population-based design. We determined the clinical and economic impact of the BCSN using the disease-specific occurrence of sepsis and sepsis case-fatality rates from a baseline of 2011–2013; this included a 1-year period prior to the formation of the network as well as the initial 2 years of the network. We calculated case reduction, mortality, and the return on investment (ROI) up to and including 2018.

The BCSN

The BCSN was based upon a model of inclusive membership, reflecting the full team involved in improving sepsis care, including administrative, clinical, and QI leaders. Overall, the Network formation and implementation occurred in three overlapping phases: 1) the development of resources, 2) identification of local champions, and 3) institutional capacity enhancement through engagement and access to shared resources. In the initial formation of the Network, there were in-person meetings to develop resources and create a shared purpose for the Network itself. There were a number of campaigns that were run in the initial stages of the BCSN. The intent of the campaigns was to raise awareness of the new guidelines, to engage staff in clinical practice change, and to provide opportunities for shared learning. During this period of time, the distributed leadership model allowed for interhospital communication and sharing to promote QI. Following this, the focus shifted to online connections through educational webinars on a monthly basis. The role of the Network was to support the self-identified personnel (i.e., physicians, nurses, pharmacists, QI leaders, and administrative staff) to lead change at their local site, rather than the Network trying to be the one reaching into each site themselves. However, the clinical

lead would commonly reach out to individual sites to discuss and support their local QI. The care providers conducted team huddles, clinical rounds, case presentations, and site-specific monitoring and evaluation at the hospital level. All participants were provided evidence-based resources, including clinical guidelines, flow sheets, sample protocols, and educational posters. The Network participants were further engaged through a number of strategies including lanyards, lanyard cards with sepsis guidelines, poster presentations, and a gamified campaign to engage other staff in practice change. In a 2016 study that assessed the distributed leadership and interconnectivity of the BCSN, members of the network identified high levels of trust, indicating a positive working environment and effective leadership within the BCSN. Furthermore, survey respondents attributed network success to a clear understanding of shared goals, collective decision-making, informal relationships bridging different areas of the network, sharing resources, free-flowing exchange of information and ideas, opportunities to meet and form relationships, and diversity in stakeholder groups (18). The success of the gamification campaign is attributable to the culture created within the network. The gamification campaign included participants from 31 EDs across BC, with the overall goal of avoiding mortality for, or "saving," 150 lives by treating 750 sepsis patients (number-needed-to-treat = 5) through evidence-based protocolized care (19). The gamification campaign implemented practice change in participating facilities through: 1) app-based data collection on sepsis patient information and clinical course; 2) distribution of resources and learning modules to encourage participation in the campaign and inform on evidence-based, protocolized sepsis care; and 3) game design that incentivized participation in the campaign. By the end of the campaign, the BCSN had grown by 52%, and 756 evidence-informed sepsis protocols were used for patients with severe infections in the ED, translating to 151 "lives saved" (19). More details regarding the BCSN initiative and activities are illustrated in Supplementary Figure S1 (http://links.lww.com/CCM/G873).

Setting and Population

This study used retrospective data for all in-hospital sepsis cases and sepsis mortality in nine Canadian provinces, including Alberta, British Columbia (BC), Manitoba, New Brunswick, Newfoundland, Nova Scotia, Ontario, Prince Edward Island, and Saskatchewan. Data from Quebec and three territories were not available. The study population included all adults 18+ years old with a diagnosis of sepsis identified after hospital admission. By comparing the number of patients with diagnosed in-hospital sepsis, this study focuses on how our clinical interventions aim to prevent deterioration of infection to sepsis or septic shock. In-hospital sepsis was defined using the following codes from the *International Statistical Classification of Diseases and Related Health Problems*, the Canadian version of the 10th revision: A40, A41, B37.7, R65.1, R57.2 as type-2, sepsis as a postprocedural complication, and sepsis in obstetric patients (20, 21). The data points for annual in-hospital sepsis cases, deaths, and hospital discharges for BC and a sum of Canadian provinces, excluding Quebec and three territories for the period starting from 2011 to 2018, are provided in **Supplementary Table S1** (http://links.lww.com/CCM/G874).

Data Sources

Epidemiologic data were obtained from the Canadian Institute for Health Information (CIHI) based on information from the hospital Discharge Abstract Database. The annual background mortality rates for BC and Canada were extracted from Statistics Canada (22). The BCSN operational costs were obtained from BCPSQC's financial reports, which included costs of staff compensation/benefits, training, educational material, and travel. The average cost of sepsis hospitalization was extracted from CIHI's Patient Cost Estimator that combines direct and indirect costs for a typical hospital stay (23). The average cost of posthospital discharge follow-up care (i.e., readmissions, ambulatory care visits, and physician claims) for three subsequent years was extracted from a previously conducted longitudinal study of sepsis survivors in Alberta, Canada (24). The average cost of in-hospital death and burial costs to the family were identified from the gray literature in the Canadian context (25, 26).

Epidemiologic Data and Cases Averted

The interrupted time series (ITS) analysis was performed in two steps. First, sequential plots were created to compare pre-and-post-BCSN in-hospital sepsis occurrence and hospital standard sepsis mortality

between BC and the Canadian average excluding BC. Second, we ran four autoregressive integrated moving average models to test the causal effect of BCSN on changes in in-hospital sepsis rates and hospital standard sepsis mortality. Specifically, we modeled time (i.e., yr), QI initiative (i.e., pre BCSN = 0 and post BCSN = 1) and the interaction term between time and QI initiative. The ITS analyses were conducted in IBM SPSS Statistics Version 27.0 (Armonk, NY). We justify the inclusion of the first 2 years of BCSN implementation within the baseline period (i.e., 2011–2013) based on historical data that large-scale sepsis QI initiatives tend to experience a significant change in outcome measures approximately 2 years following implementation. These outcome measures include hospital cost-saving, hospital site compliance to multicenter initiatives, and mortality related to sepsis (27–29). Additionally, we applied a disease modeling-based approach to calculate the number of in-hospital sepsis cases averted. The concept of modeling cases averted in a disease modeling-based approach involves a comparison between an "expected" or baseline epidemic with an "estimated" one (30). We used the average baseline occurrence (i.e., 2011–2013) as a reference point for future comparisons. The difference in the number of new in-hospital sepsis cases implied by the occurrence rate was taken as the number of cases averted.

Costs Data and ROI Calculations

This study used a broad perspective incorporating inpatient admission costs for the average hospital length of stay, the average follow-up costs of sepsis survivors, the average cost of death in the hospital, the average out-of-pocket cost of burial-related expenses for the family, and BCSN implementation costs. **Table 1** represents various model inputs and sources of information. The base case values were drawn from CIHI, which already factored other hospitalization costs for a case mix group. In the ROI analysis, we modeled an incremental cost (i.e., hospitalization expenses resulting from in-hospital sepsis minus the cost of standard hospital stay). For example, the average cost of a standard hospital stay in BC is CAD$6,103 for a patient without the diagnosis of sepsis. At the same time, the cost of managing a case of sepsis in BC hospitals is CAD$23,229. So, we assumed that a patient hospitalized for pneumonia or urinary tract infection, receiving good fluid resuscitation, receiving early antibiotics, and preventing the development of sepsis will have avoided an incremental cost of CAD$17,126 (i.e., $23,229–$6,103). The number of estimated sepsis cases averted were multiplied by an average inpatient hospitalization cost per sepsis to calculate savings from averted sepsis cases. Similarly, the number of estimated sepsis deaths averted were multiplied by an average burial cost per death to calculate savings from averted deaths. The annual net savings were calculated as the difference in the total savings from averted in-hospital sepsis cases and deaths minus the total BCSN investment. All costs were adjusted using the Canadian Consumer Price Index for Health and are reported in Canadian dollars as of 2020. An annual discount rate of 1.5% was applied to both savings and investment (31). One-way sensitivity analysis was applied to address potential uncertainties by varying the costs and occurrence variables. The ROI analyses were conducted using Microsoft Excel for Mac Version 16.37 (Microsoft, Redmond, WA).

Human Ethics

This study was undertaken as part of a QI initiative, and as such, Institutional Review Board or local ethics committee approval was not applicable.

RESULTS

Since the launch of BCSN, there has been a substantial reduction in in-hospital sepsis cases and sepsis mortality in the province of BC. **Figure 1** represents the occurrence of in-hospital sepsis and hospital standard mortality observed in BC and the Canadian average, excluding BC, Quebec, and three territories from 2011 to 2018. In the first 3 years (2011–2013), the average occurrence rate of in-hospital sepsis was relatively higher in BC (4.5 per 1,000 discharges) compared with the Canadian average, excluding BC (4.1 per 1,000 discharges). In 2018, the in-hospital sepsis cases notably decreased by 24.7% in BC compared with an average of 2.2% reduction in the rest of Canada, excluding BC, Quebec, and three territories. The annual in-hospital sepsis mortality rates have consistently remained lower throughout the study period in BC compared with the Canadian averages.

Our hypothesis that the rate of change in in-hospital sepsis occurrence, as well as hospital standard sepsis mortality, would vary over time was supported. Specifically, BC's mortality estimate was lower (i.e., 0.189) than the rest of the Canadian average, excluding BC, where it was 0.235. These findings were statistically

TABLE 1.
Model Input Variables

Variable	Base Value	References
Baseline period, 2011–2013		
Average occurrence rate of in-hospital sepsis		Calculated, Canadian Institute for Health Information (20, 21)
BC	0.0045	
Canada excluding BC	0.0041	
Average in-hospital sepsis mortality rate		
BC	0.1752	
Canada excluding BC	0.2237	
Endline period, 2018		
Occurrence rate of in-hospital sepsis		Calculated, Canadian Institute for Health Information (20, 21)
BC	0.0034	
Canada excluding BC	0.0040	
In-hospital sepsis mortality rate		
BC	0.1705	
Canada excluding BC	0.2032	
Average background mortality rate		Statistics Canada (22)
BC	0.0075	
Canada excluding BC	0.0074	
Average costs, in Canadian dollar		
Hospitalization, per case		Calculated, Patient Cost Estimator, Canadian Institute for Health Information (23)
BC	17,126	
Canada excluding BC	18,069	
Follow-up care, per case		Lee et al (24)
Year 1	20,855	
Year 2	7,139	
Year 3	7,091	
Death in the hospital, per death	12,000	Priest (25)
Burial expenses for family, per death	8,000	Lee (26)
BC Sepsis Network initiative, per annum	71,341	British Columba Patient Safety and Quality Council Financials (17)
Annual discount rate, %	1.5	Canadian Agency for Drugs and Technology in Healthcare (31)

BC = British Columbia.

significant ($p < 0.0001$). However, the interaction between time and BCSN on occurrence and mortality indicated declining trends but were not statistically significant ($p > 0.05$). Considering that we have fewer observations, we found wider CIs for the predicted values in the model (**Table 2**).

In the base case analysis, a total of 981 in-hospital sepsis cases were averted in BC compared with the Canadian average of 611 cases averted throughout the study period. In that same time period, a larger number of deaths were averted in BC (172 in BC vs 127 in the rest of the Canadian average). In 2017, approximately

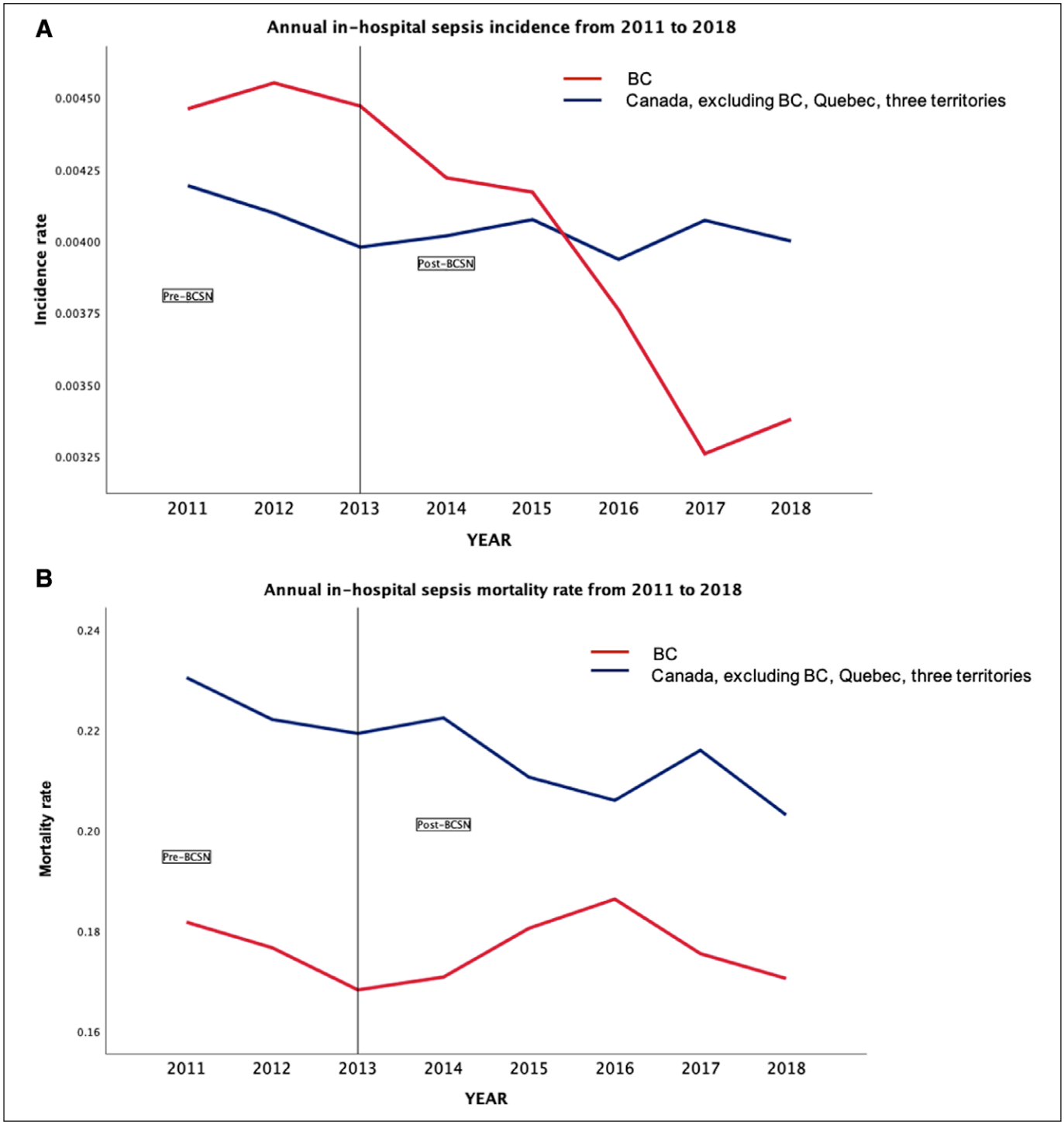

Figure 1. Annual in-hospital sepsis occurrence and hospital standard sepsis mortality. **A**, Annual in-hospital sepsis occurrence from 2011 to 2018. **B**, Annual in-hospital sepsis mortality rate from 2011 to 2018. BC = British Columbia, BCSN = BC Sepsis Network.

331 in-hospital sepsis cases and 58 deaths were averted in BC compared with the rest of the Canadian average of 30 cases and seven deaths averted (**Supplementary Fig. S2**, http://links.lww.com/CCM/G875: In-hospital sepsis cases and deaths averted). The financial analysis shows that BCPSQC invested a cumulative $449,962 in the BCSN, targeting efforts to improve sepsis care in the province from 2012 to 2018. Of this total, nearly 70% of funds ($314,973) were used for clinical leadership and 25% ($112,490) on staffing. The Canadian average, excluding BC, indicates a gradual increase in societal cost avoidance, and it was approximately $31.4 million in 2018. Although BC did not yield cost avoidance until 2012/2013, there was an exponential increase in societal cost avoidance from 2014/2015 onwards, reaching almost $51 million in 2018.

TABLE 2.
Autoregressive Integrated Moving Average Variables, In-Hospital Sepsis, and Hospital Standard Sepsis Mortality 2011–2018

Variable	Estimate	SE	*t* Statistics	Significance
Model 1: in-hospital sepsis in BC				
In-hospital sepsis (rate)	0.004	0.000	17.855	0.000
Time (yr)	5.000E-6	0.000	0.043	0.968
Pre-and-post	3.667E-5	0.000	0.160	0.880
Time interaction pre-and-post	0.000	0.000	–2.073	0.107
Model 2: hospital standard sepsis mortality in BC				
Hospital standard sepsis mortality	0.189	0.010	18.411	0.000
Time (yr)	–0.007	0.005	–1.418	0.229
Pre-and-post	0.010	0.009	1.030	0.361
Time interaction pre-and-post	0.006	0.005	1.186	0.301
Model 3: in-hospital sepsis in Canada[a]				
In-hospital sepsis (rate)	0.004	8.750E-5	49.182	0.000
Time (yr)	0.000	4.050E-5	–2.638	0.058
Pre-and-post	4.912E-5	7.964E-5	0.617	0.571
Time interaction pre-and-post	0.000	4.437E-5	2.319	0.081
Model 4: hospital standard sepsis mortality in Canada[a]				
Hospital standard sepsis mortality (rate)	0.235	0.009	26.439	0.000
Time (yr)	–0.006	0.004	–1.352	0.248
Pre-and-post	0.003	0.008	0.395	0.713
Time interaction pre-and-post	0.002	0.005	0.497	0.645

[a]Excluding British Columbia, Quebec, and three territories.

Table 3 shows the cumulative ROI per year by types of cost savings from averted cases of in-hospital sepsis and deaths. In the post-BCSN period (2014–2018), a lower occurrence of in-hospital sepsis and mortality translated into a societal savings of $50.6 million (i.e., ~$49,000 per case averted, and ~$18,000 per death averted). This represents a return of $112.5 for every dollar invested in BCSN. A vast majority of savings are related to the follow-up care ($31 million; 61%) and acute management of in-hospital sepsis cases ($17 million; 33%). Subtracting the Canadian average from the total in-hospital sepsis cases averted in BC, there were 370 cases averted (i.e., 981 – 611), indicating a 61% case reduction potentially attributable to BCSN. Similarly, approximately 45 sepsis deaths (i.e., 172 – 127) were potentially averted from BCSN. Under these assumptions, the cumulative savings decreased to $18.9 million, generating a return of $42 for every dollar invested in BCSN. The one-way sensitivity analysis revealed that in-hospital sepsis's annual occurrence introduces the highest level of uncertainty in the ROI findings. For example, when the occurrence rate was hypothetically increased by 10%, the benefit-to-cost ratio declined to $56 for every dollar invested in BCSN. Furthermore, the yearly cost of follow-up visits and in-hospital sepsis management cost had a smaller influence on ROI results (**Fig. 2**).

DISCUSSION

This study demonstrated a significant reduction in the occurrence of in-hospital sepsis and sepsis deaths in the post-BCSN period compared with the baseline. The financial spending in BCSN yielded a substantial clinical benefit for patients and their families and a monetary ROI for the health system. These findings illustrate the efficiency of a province-wide QI initiative that aimed to educate a large number of health workers

TABLE 3.
British Columbia Sepsis Network Return on Investment for the Financial Year 2011–2018

Variables	2014	2015	2016	2017	2018
Types of costs avoided					
Health system: in-hospital cases	$958,578	$2,231,049	$5,439,221	$11,502,445	$16,983,992
Health system: follow-up care	$2,216,841	$4,927,836	$11,100,510	$21,553,472	$31,003,624
Health system: deaths	$128,607	$294,808	$685,307	$1,307,856	$1,854,941
Out-of-pocket for families: deaths	$85,738	$196,539	$456,871	$871,904	$1,236,627
Societal (all inclusive)	$3,389,764	$7,650,232	$17,681,909	$35,235,677	$51,079,184
Cumulative investment					
BCSN program costs	$243,144	$308,507	$376,880	$412,826	$449,962
Return on investment					
Societal savings, minus BCSN investment	$3,146,620	$7,341,725	$17,305,029	$34,822,851	$50,629,222
Benefit-cost ratio (societal savings/BCSN investment)	$12.9	$23.8	$45.9	$84.4	$112.5

BCSN = British Columbia Sepsis Network.

on early identification and appropriate management of significant infections and sepsis in BC.

Although the BCSN and its successes are unique across Canada, some similar programs exist globally. Of studies that have been published, we found a similar QI initiative in terms of the approach but on a small scale (i.e., limited to one tertiary hospital setting) in Germany since January 2008. This program uses quarterly training, conferences for ICU and emergency health workers, lecturers, and educational tools similar to strategies used by the BCSN in an effort to address the impact of sepsis (32). In 2017, the researchers reported significant: 1) reductions in 90-day severe sepsis and septic shock mortality (19.8% reduction; $p < 0.001$), 2) reductions in hospital length of stay (8 d reduction; $p < 0.05$), and 3) increases in antibiotic therapy initiation within the first hour of sepsis onset (25.8% increase; $p < 0.001$). Another popular QI strategy is the implementation and maintenance of care management "bundles" originally developed by the Institute of Health improvement (IHI) and Surviving Sepsis Campaign Guidelines (33). When measuring adherence to these bundles, a large number of QI sepsis initiatives across Latin America and the United States

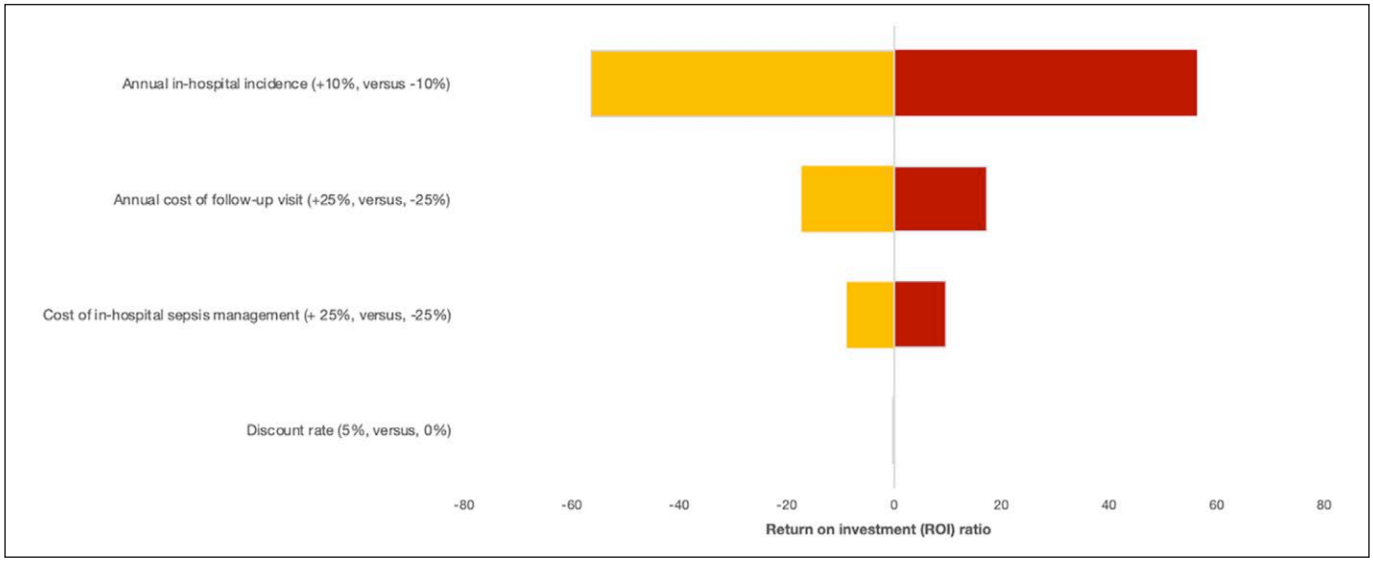

Figure 2. One-way sensitivity analysis, return on investment.

illustrated that improved compliance to these bundles is associated with improvements in mortality, cost of care, length of stay, and patient's quality of life related to sepsis (34, 35). These QI initiatives are limited to selected hospital settings. Therefore, the magnitude of impact can vary due to external factors such as the hospital's size, funding model, and ease of implementation. We strongly advocate that having an organization with a provincial mandate like the BCPSQC is much more efficient to drive change at scale than targeting one hospital at a time. These findings illustrate the need for further action and investment in QI and sepsis educational programs across Canada and internationally.

Despite the existence of other sepsis initiatives across Canada, the BCSN is the first of its kind. Examples of other initiatives in Canada include the following: 1) the Alberta Sepsis Network (36), 2) the Manitoba-based Translating Emergency Knowledge for Kids (37), and 3) "Sepsis Intervention" by Canadian Patient Safety Institute (38). Guided by our field observations and informal communications with the subject experts, we found that many of these QI programs in other provinces have been inactive for years, and none used QI strategies, learning networks, or otherwise, to address sepsis. The BCSN builds off the network model applied by the IHI throughout North America, as well as other provincial clinical QI initiatives supported by the BCPSQC, such as the Type 2 Diabetes Network and the Surgical Quality Action Network (SQAN) (39, 40). By implementing this model of distributed province-wide leadership, the BCSN improved patient outcomes and reduced costs related to sepsis and ensured sustainability and ongoing engagement.

Although the observational findings illustrate an association between the existence of the BCSN and improved sepsis mortality and economic burden over time, no causal relationship can be determined. We recognize that other provincial QI programs, also supported by BCPSQC, may have indirectly influenced the reduction of in-hospital sepsis cases. These include catheter-associated urinary tract infections (CAUTIs) (41), National Surgical QI Program (NSQIP) (42), SQAN (40), and various ventilation-associated pneumonia (VAP) reduction projects (43). However, although the global reduction in sepsis mortality over time is well recognized (44), this factor cannot fully explain our findings. Indeed, our decrease in cases has been steeper, and nearly all provinces have instituted programs similar to or participated in NSQIP, VAP, SQAN, and CAUTI initiatives. As such, although the reduction in sepsis mortality and associated costs may have been multifactorial, there were no novel advancements in the field of sepsis care to influence these outcome measures during this time period. Importantly, however, there was a significant improvement in lactate measurement by time goal and in sepsis-related mortality during the BCSN and BCPSQC-led 150 Lives Campaign at participating facilities (18). This illustrates the direct improvement in sepsis-related care as a result of a BCSN initiative. In a study conducted by Seymour et al (45), investigators initiated a sepsis protocol within 6 hours after the patient presented in the ED, as well as implemented a bundle of care (inclusive of testing blood culture, use of broad-spectrum antibiotics, and lactate measurement) within 12 hours. This study highlighted that delays in the initiation of sepsis protocol and bundle approach result in higher risk-adjusted hospital mortality (odds ratio, 1.04 per hour; 95% CI, 1.02–1.05; $p < 0.001$). However, the mortality estimates in that study were primarily drawn from patients diagnosed with severe sepsis and septic shock. Although this study's findings strengthen our argument for early identification and treatment of in-hospital sepsis through QI initiatives, the studies are not directly comparable in that we analyzed secondary, aggregate-level data for all in-hospital sepsis and in-hospital sepsis mortality, and hence, granular data regarding differing severity (i.e., severe versus non-severe) were not available. Lack of severity is an important limitation of the secondary aggregate-level data, and we recommend conducting sepsis subgroup analyses using primary data in future economic studies.

The QI teams, including physicians, nurses, and paramedical staff in the participating acute care facilities in BC, were engaged throughout the improvement period. Despite the programmatic efforts to maximize the reach for province-wide information dissemination, there were operational challenges related to geographical location (i.e., rural vs urban), hospital size (i.e., large vs small), and staffing levels (i.e., new hiring and turnover). More research is needed to qualitatively understand the programmatic challenges, mitigation strategies, and the varying level of support for participating sites across the province. However, because data aggregation was done at the province level, it was not feasible to identify acute care facilities (no identifiers were revealed for facility name, location, staffing levels, and bed capacity). We recognize the potential clustering effect, which could

have benefited specific sites (high performing) than others, but it is another limitation of the provincial-level aggregate analysis. Furthermore, the health authority-level costs for implementing clinical guidelines in respective hospital settings were not available. We assumed that the cost of healthcare personnel responsible for implementing sepsis care was represented in the patient hospitalization cost. Finally, efforts that do not directly target sepsis prevention, such as regional, provincial, and national Infection Prevention and Control and antimicrobial stewardship programs, could indirectly reduce in-hospital sepsis occurrence.

CONCLUSIONS

The BCSN appears to have resulted in a significant reduction of in-hospital sepsis cases, sepsis mortality, and yielded a positive ROI. This study's findings strengthen a policy argument for large-scale sepsis QI initiatives and provide a model of sepsis care both in the local and global context. Future studies should explore the relevance of QI strategies used by the BCSN and determine how they may be applied to reduce the burden of in-hospital sepsis cases and sepsis mortality.

ACKNOWLEDGMENTS

We thank British Columbia Patient Safety & Quality Council staff (Analytics and Strategic Initiatives team and Health System Improvement team) for ongoing support, data request submission, office space, and analytical software access. We thank Shawna Nichol for helping with the data analysis software and Chelsea Hochfilzer for proof editing the article.

1 *Department of Health Sciences, Brock University, St. Catharines, ON, Canada.*

2 *BC Patient Safety & Quality Council, Vancouver, BC, Canada.*

3 *Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada.*

4 *School of Population & Public Health, Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada.*

5 *Centre for Clinical Epidemiology and Evaluation Vancouver, Vancouver, BC, Canada.*

6 *Children's and Women's Global Health University of British Columbia and BC Children's Hospital, BC Children's Hospital Research Institute, Global Sepsis Alliance, Vancouver, BC, Canada.*

7 *Department of Emergency Medicine, University of British Columbia, Vancouver, BC, Canada.*

8 *Division of Critical Care Medicine, Vancouver General Hospital, Vancouver, BC, Canada.*

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (http://journals.lww.com/ccmjournal).

Supported, in part, by the Canadian Institutes of Health Research, Institute of Health Services and Policy Research, the Michael Smith Foundation for Health Research, and British Columbia Patient Safety & Quality Council (grant number: award number: 18164).

Dr. Khowaja received support for article research from the Michael Smith Foundation for Health Research (18164). Ms. Krause received funding from the University of British Columbia. Mr. Ridout and Ms. Kennedy disclosed they are employees of the British Columbia Patient Safety & Quality Council. Mr. Young disclosed government work. The remaining authors have disclosed that they do not have any potential conflicts of interest.

For information regarding this article, Email: akhowaja@brocku.ca

REFERENCES

1. Singer M, Deutschman CS, Seymour CW, et al: The third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA* 2016; 315:801–810
2. Angus DC, van der Poll T: Severe sepsis and septic shock. *N Engl J Med* 2013; 369:2063
3. Rudd KE, Johnson SC, Agesa KM, et al: Global, regional, and national sepsis incidence and mortality, 1990-2017: Analysis for the Global Burden of Disease study. *Lancet* 2020; 395:200–211
4. Kelsall D, Kissoon N: Sepsis, one of CMAJ's four new areas of focus. *CMAJ* 2017; 189:E1127
5. Chang DW, Tseng CH, Shapiro MF: Rehospitalizations following sepsis: Common and costly. *Crit Care Med* 2015; 43:2085–2093
6. Mayr FB, Talisa VB, Balakumar V, et al: Proportion and cost of unplanned 30-day readmissions after sepsis compared with other medical conditions. *JAMA* 2017; 317:530–531
7. Prescott HC, Langa KM, Iwashyna TJ: Readmission diagnoses after hospitalization for severe sepsis and other acute medical conditions. *JAMA* 2015; 313:1055–1057
8. Herridge MS, Tansey CM, Matté A, et al; Canadian Critical Care Trials Group: Functional disability 5 years after acute respiratory distress syndrome. *N Engl J Med* 2011; 364:1293–1304
9. Linder A, Guh D, Boyd JH, et al: Long-term (10-year) mortality of younger previously healthy patients with severe sepsis/septic shock is worse than that of patients with nonseptic critical illness and of the general population. *Crit Care Med* 2014; 42:2211–2218
10. Linder A, Lee T, Fisher J, et al: Short-term organ dysfunction is associated with long-term (10-yr) mortality of septic shock. *Crit Care Med* 2016; 44:e728–e736
11. Liang SY: Sepsis and other infectious disease emergencies in the elderly. *Emerg Med Clin North Am* 2016; 34:501–522
12. Rowe TA, McKoy JM: Sepsis in older adults. *Infect Dis Clin North Am* 2017; 31:731–742
13. Angus DC, Linde-Zwirble WT, Lidicker J, et al: Epidemiology of severe sepsis in the United States: Analysis of incidence,

outcome, and associated costs of care. *Crit Care Med* 2001; 29:1303–1310

14. Herridge MS, Moss M, Hough CL, et al: Recovery and outcomes after the acute respiratory distress syndrome (ARDS) in patients and their family caregivers. *Intensive Care Med* 2016; 42:725–738
15. Rezende E, Silva JM Jr, Isola AM, et al: Epidemiology of severe sepsis in the emergency department and difficulties in the initial assistance. *Clinics (Sao Paulo)* 2008; 63:457–464
16. Weiss SL, Peters MJ, Alhazzani W, et al: Surviving Sepsis Campaign international guidelines for the management of septic shock and sepsis-associated organ dysfunction in children. *Pediatr Crit Care Med* 2020; 21:e52–e106
17. British Columbia Patient Safety and Quality Council: BC Sepsis Network. Available at: https://bcpsqc.ca/improve-care/bc-sepsis-network/. Accessed September 25, 2020
18. Gorley C, Lindstrom RR, McKeown S, et al: Exploring distributed leadership in the BC sepsis network. In: Healthcare Management Forum. Vol. 29. XXXLos Angeles, CA, SAGE Publications, 2016, pp 63–66
19. McKeown S, Krause C, Shergill M, et al: Gamification as a strategy to engage and motivate clinicians to improve care. *Healthc Manage Forum* 2016; 29:67–73
20. Canadian Institute for Health Information: In-Hospital Sepsis. Available at: http://indicatorlibrary.cihi.ca/display/HSPIL/In-Hospital+Sepsis. Accessed September 25, 2020
21. Canadian Institute for Health Information: ICD-10-CA| CCI. Available at https://secure.cihi.ca/free_products/CodingStandards_v2018_EN.pdf. Accessed September 25, 2020
22. Statistics Canada: Deaths and Mortality Rates, by Age Group. Available at: https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1310071001. Accessed September 25, 2020
23. Canadian Institute for Health Information: Cost of a Standard Hospital Stay. Available at: https://yourhealthsystem.cihi.ca/hsp/inbrief?lang=en#!/indicators/015/cost-of-a-standard-hospital-stay/;mapC1;mapLevel2;/. Accessed September 25, 2020
24. Lee H, Doig CJ, Ghali WA, et al: Detailed cost analysis of care for survivors of severe sepsis. *Crit Care Med* 2004; 32:981–985
25. Priest L: How Much Does Dying Cost Canadians? The Global and Mail, 2011. Available at: https://www.theglobeandmail.com/life/health-and-fitness/how-much-does-dying-cost-canadians/article554853/. Accessed September 25, 2020
26. Lee R: Burial Plots, Funeral Services and More – This Is How Much It Costs to Die in Canada. Available at: https://www.lowestrates.ca/blog/burial-plots-funeral-services-and-more-how-much-it-costs-die-canada. Accessed September 25, 2020
27. Afshar M, Arain E, Ye C, et al: Patient outcomes and cost-effectiveness of a sepsis care quality improvement program in a health system. *Crit Care Med* 2019; 47:1371–1379
28. Levy MM, Evans LE, Rhodes A: The Surviving Sepsis Campaign bundle: 2018 update. *Intensive Care Med* 2018; 44:925–928
29. van Zanten AR, Brinkman S, Arbous MS, et al; Netherlands Patient Safety Agency Sepsis Expert Group: Guideline bundles adherence and mortality in severe sepsis and septic shock. *Crit Care Med* 2014; 42:1890–1898
30. Heaton LM, Komatsu R, Low-Beer D, et al: Estimating the number of HIV infections averted: An approach and its issues. *Sex Transm Infect* 2008; 84(Suppl 1):i92–i96
31. Canadian Agency for Drugs and Technology in Healthcare: Guidelines for the Economic Evaluation of Health Technologies: Canada (4th Edition). Available at: https://www.cadth.ca/sites/default/files/pdf/CADTH_Economic_Guidelines-3rd_vs_4th_Editions.pdf. Accessed September 25, 2020
32. Scheer CS, Fuchs C, Kuhn SO, et al: Quality improvement initiative for severe sepsis and septic shock reduces 90-day mortality: A 7.5-year observational study. *Crit Care Med* 2017; 45:241–252
33. Institute for Healthcare Improvement: Severe Sepsis Bundles. Available at: http://www.ihi.org/resources/Pages/Tools/SevereSepsisBundles.aspx. Accessed September 25, 2020
34. Thompson MP, Reeves MJ, Bogan BL, et al: Protocol-based resuscitation bundle to improve outcomes in septic shock patients: Evaluation of the Michigan Health and Hospital Association keystone sepsis collaborative. *Crit Care Med* 2016; 44:2123–2130
35. Machado FR, Ferreira EM, Sousa JL, et al; Latin American Sepsis Institute Network: Quality improvement initiatives in sepsis in an emerging country: Does the institution's main source of income influence the results? An analysis of 21,103 patients. *Crit Care Med* 2017; 45:1650–1659
36. University of Calgary: Alberta Sepsis Network. Available at: https://www.ucalgary.ca/albertasepsisnetwork/. Accessed September 25, 2020
37. University of Manitoba: Translating Emergency Knowledge for Kids – TREKK. Available at: https://www.nce-rce.gc.ca/NetworksCentres-CentresReseaux/NCEKM-RCEMC/TREKK-TRACE_eng.asp. Accessed September 25, 2020
38. Canadian Patient Safety Institute: Infection Prevention and Control (IPAC). Available at: https://www.patientsafetyinstitute.ca/en/Topic/Pages/Infection-Prevention-and-Control.aspx. Accessed September 25, 2020
39. British Columbia Patient Safety and Quality Council: Type 2 Diabetes Network. Available at: https://bcpsqc.ca/improve-care/diabetes-network/. Accessed September 25, 2020
40. British Columbia Patient Safety and Quality Council: Surgical Quality Action Network. Available: https://bcpsqc.ca/improve-care/surgical-improvement/sqan/. Accessed September 25, 2020
41. Centers for Disease Control and Prevention: Catheter-Associated Urinary Tract Infection (CAUTI). Available: https://www.cdc.gov/hai/ca_uti/uti.html. Accessed September 25, 2020
42. British Columbia Patient Safety and Quality Council: National Surgical Quality Improvement Program. Available at: https://bcpsqc.ca/improve-care/surgical-improvement/national-surgical-quality-improvement-program/. Accessed September 25, 2020
43. Muscedere J, Dodek P, Keenan S, et al; VAP Guidelines Committee and the Canadian Critical Care Trials Group: Comprehensive evidence-based clinical practice guidelines for ventilator-associated pneumonia: Prevention. *J Crit Care* 2008; 23:126–137
44. Kaukonen KM, Bailey M, Suzuki S, et al: Mortality related to severe sepsis and septic shock among critically ill patients in Australia and New Zealand, 2000-2012. *JAMA* 2014; 311:1308–1316
45. Seymour CW, Gesten F, Prescott HC, et al: Time to treatment and mortality during mandated emergency care for sepsis. *N Engl J Med* 2017; 376:2235–2244