

Methicillin-resistant *Staphylococcus aureus*: A public health issue with economic consequences

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BACKGROUND: Methicillin-resistant *Staphylococcus aureus* (MRSA) has become endemic worldwide in hospitals, and community-associated MRSA is spreading into the community at large.

OBJECTIVES: To estimate the current cost of MRSA in Canada and to assess the magnitude of this public health issue.

METHODS: An extensive review of the literature was conducted to gather epidemiology, health care resource utilization and cost data for MRSA in Canadian settings. The current MRSA burden was estimated using available cost data and the most recent epidemiology data.

RESULTS: The rate of MRSA in Canadian hospitals increased from 0.46 to 5.90 per 1000 admissions between 1995 and 2004, while community-associated MRSA continued to spread into the community. Patients harbouring MRSA required prolonged hospitalization (average 26 days of isolation per patient), special control measures, expensive treatments and extensive surveillance. Total cost per infected MRSA patient averaged \$12,216, with hospitalization being the major cost driver (81%), followed by barrier precautions (13%), antimicrobial therapy (4%) and laboratory investigations (2%). The most recent epidemiological data, combined with available cost data, suggest that direct health care cost attributable to MRSA in Canada, including cost for management of MRSA-infected and -colonized patients and MRSA infrastructure, averaged \$82 million in 2004 and could reach \$129 million in 2010.

CONCLUSION: MRSA is a costly public health issue that needs to be tackled if the growing burden of this disease in Canadian hospitals and in the community is to be limited.

Key Words: Costs; Methicillin-resistant *Staphylococcus aureus*; Review

Staphylococcus aureus, on the skin or in the nasopharynx of humans, has colonized 30% to 50% of the population (1). The global SENTRY Antimicrobial Surveillance Program, a network of approximately 100 sentinel hospitals in Canada, the United States (US), Latin America, Europe and the West Pacific, demonstrated that *S aureus* was the most prevalent cause of nosocomial and community-acquired bloodstream infections, skin and soft tissue infections (SSTIs) and pneumonia in almost all geographic areas (2). Although conflicting and inconsistent results have been reported, recent data suggest that patients with methicillin-resistant *S aureus* (MRSA) infections have worse clinical and economic outcomes than patients with methicillin-susceptible *S aureus* (MSSA) infections (3-5).

MRSA is endemic worldwide in hospitals, and community-associated MRSA (CA-MRSA) is spreading into the community at large (6). Rates of MRSA ranging from 5.7% in Canada

Le staphylocoque doré méthicillino-résistant : Un problème de santé publique ayant des conséquences économiques

HISTORIQUE : Le staphylocoque doré méthicillino-résistant (SARM) est devenu endémique dans les hôpitaux du monde entier, tandis que le SARM non nosocomial se répand dans l'ensemble de la population.

OBJECTIFS : Évaluer le coût actuel du SARM au Canada et l'importance de ce problème de santé publique.

MÉTHODOLOGIE : On a mené une analyse approfondie des publications scientifiques pour colliger des données d'épidémiologie, d'utilisation et de coût des ressources de santé pour le SARM dans le contexte canadien. On a estimé le fardeau actuel du SARM au moyen des données relatives aux coûts et des données épidémiologiques les plus récentes.

RÉSULTATS : Le taux de SARM dans les hôpitaux canadiens est passé de 0,46 à 5,90 cas sur 1 000 hospitalisations entre 1995 et 2004, tandis que le SARM non nosocomial a continué de se propager dans la collectivité. Les patients atteints du SARM ont dû subir une hospitalisation prolongée (moyenne de 26 jours d'isolement par patient), des mesures de contrôle spéciales, des traitements coûteux et une surveillance étroite. Le coût total par patient infecté par le SARM était d'une moyenne de 12 216 \$, l'hospitalisation étant le principal inducteur de coût (81 %), suivi des précautions antibiorésistantes (13 %), de la thérapie antimicrobienne (4 %) et des enquêtes de laboratoire (2 %). D'après les données épidémiologiques les plus récentes, combinées aux inducteurs de coût disponibles, les coûts de santé directs attribuables au SARM au Canada, y compris le coût de prise en charge des patients infectés et colonisés par le SARM et de l'infrastructure du SARM, atteignaient une moyenne de 82 millions de dollars en 2004 et pourraient atteindre 129 millions de dollars en 2010.

CONCLUSION : Le SARM est un problème de santé publique coûteux auquel il faut s'attaquer pour limiter le fardeau croissant de cette maladie dans les hôpitaux canadiens et dans la collectivité.

to 34.2% in the US to 45.3% in Chile were reported in 2001 (2). Since 1995, the Canadian Nosocomial Infection Surveillance Program (CNISP), a collaboration involving sentinel hospitals across the country, has released surveillance data showing a 10-fold increase in the incidence of MRSA in Canadian hospitals between 1995 and 2003 (7-9).

CA-MRSA is an emerging cause of morbidity and mortality among healthy people (10-12). A meta-analysis of 10 surveys, including more than 8000 patients on three continents, reported a CA-MRSA colonization rate of 1.3% (95% CI 1.04 to 1.53), with significant heterogeneity among study populations (13). In Canada, although CA-MRSA was associated with only specific populations when it was first described (such as First Nations communities), it has since been associated with pediatric populations and the general population (12-20).

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TABLE 1
Characteristics of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) versus health care-associated MRSA

	MRSA	CA-MRSA
Groups at risk, and risk factors	Prolonged hospitalization, intensive care unit admission, hemodialysis or peritoneal dialysis, intravascular catheter, diabetes, residents in long-term care institutions	Children, prisoners, military personnel, amateur or professional competitive athletes, selected ethnic populations (First Nations communities), intravenous drug users, men who have sex with men
Clinical syndromes	Wide variety of infections: nosocomial pneumonia, wound infections, prosthesis infections, surgical site infections, catheter-associated bacteremias (urinary tract, bloodstream)	Specific syndrome of skin manifestations (folliculitis, abscesses), severe infections such as necrotizing pneumonia, necrotizing fasciitis and sepsis
Antimicrobial resistance	Multidrug resistance	Beta-lactam resistance alone
Presence of exotoxin (Panton-Valentine leukocidin toxin)	Rare	Frequent
Type of chromosomal element carrying the methicillin-resistant gene (<i>SCCmec</i>)	Types IV and V	Types I, II and III

Data from references 1, 10 and 31

Although the Canadian rate of MRSA is much lower than that observed in many other countries, its continuing spread will contribute to an increasing financial burden on Canadian health care resources (9). MRSA can be present in sputum, wounds and the bloodstream of infected patients, but also on apparently healthy skin, requiring extensive and costly barrier precautions to limit transmission (21). Several Canadian studies have explored resource utilization and costs associated with the management of MRSA patients (22-27). In the early 2000s, the MRSA financial burden in Canada ranged from \$40 to \$59 million (22,24). The objectives of the present study were to estimate the current burden and cost of MRSA in Canada, and to assess the magnitude of this public health issue.

METHODS

In an extensive review of the literature, MEDLINE and databases from the Centre for Reviews and Dissemination <www.york.ac.uk/inst/crd/crddatabases.htm> were searched for the following key words: methicillin-resistant *S aureus*, community-acquired, epidemiology, outbreaks, CNISP, SENTRY, PROTEKT, treatment patterns, clinical guidelines, recommendations, cost, burden and Canada. Searching by prominent authors in the field was also carried out. Selected journals, including *The Canadian Journal of Infectious Diseases & Medical Microbiology*, *The Journal of the American Medical Association* and *The New England Journal of Medicine*, were also searched. In addition, retrieved bibliographies were screened. Web sites were also searched, including the Public Health Agency of Canada <www.phac-aspc.gc.ca>, Health Canada <www.hc-sc.gc.ca>, the Canadian Committee on Antibiotic Resistance <www.ccar-ccra.com> and the Canadian Institute for Health Information <www.cihi.ca>.

Numbers of MRSA colonization or infection cases in Canada were obtained by multiplying the MRSA rate per 1000 admissions from the CNISP (Dr Andrew Simor, personal communication) (9) by the corresponding annual number of hospitalizations (28,29).

Canadian costs for MRSA were collected from the literature. The total direct cost per infected MRSA patient included hospitalization, antimicrobial treatment, laboratory investigations and barrier precautions. Lost revenue from hospital rooms used for isolation was not considered. A range for cost per infected MRSA patient was estimated using minimum and maximum costs for each component.

Costs to the Canadian health care system included hospital costs for MRSA patients (infected or colonized) and costs for

MRSA infrastructure. Hospital costs were obtained by multiplying the estimated cost per patient by the number of MRSA cases. Annual costs for MRSA colonization and infection were projected to 2010 using separate linear regression models based on historical calculated costs, with cost as the dependent variable and year as the independent variable. Hospital admission rates for the corresponding time period were projected using the same methodology.

Canadian dollar estimates retrieved in the literature were adjusted for inflation using the Consumer Price Index (30). Currency years were assumed to be the same as the year of publication. All analyses were performed using Microsoft Excel (Microsoft Corporation, USA).

RESULTS

Types of MRSA and epidemiology in Canada

CA-MRSA strains differ from other nosocomial strains in clinically relevant ways, including a propensity to cause SSTIs and necrotizing pneumonia (Table 1) (1,10,31). Patients at risk for CA-MRSA are generally younger and in better health than patients at risk for MRSA (10). Unlike multidrug-resistance patterns that typify nosocomial strains, CA-MRSA often expresses resistance to beta-lactams alone (1,10,31). CA-MRSA is characterized by the presence of the Panton-Valentine leukocidin toxin and by the chromosomal element carrying the methicillin-resistant gene (1).

Recent studies from the CNISP have reported MRSA infection rates, determined using standard definitions (32), and MRSA colonization rates, defined as the presence of MRSA without signs or symptoms of infection (9). The most recent data from the CNISP indicate a combined increased incidence of MRSA infections and colonization in Canadian hospitals of approximately 12-fold between 1995 and 2004, from 0.46 to 5.90 per 1000 admissions (Dr Andrew Simor, personal communication) (9). Most of this occurred in Ontario and Quebec. During the same time period, MRSA infection incidence alone increased from 0.25 to 1.73 per 1000 admissions. In 2004, MRSA infection accounted for 34% of all MRSA cases (colonization and infection). The mean age of MRSA patients was 66 years. MRSA strains were resistant to multiple classes of antibiotics, but susceptibility to vancomycin was maintained (9). According to 2004 CNISP data, 72% of MRSA cases likely were acquired in hospital, 3% in long-term care facilities, 14% in the community and 10% from an undetermined origin. For

community-originated MRSA, this represents a 1.75-fold increase over 2003 data (9). Recently, in the Canadian National Intensive Care Unit (CAN-ICU) study, which involved 20 sites across the country, MRSA accounted for 21.2% of *S aureus* isolates in Canadian intensive care units (ICUs) (33). The SENTRY Antimicrobial Surveillance Program, initiated in 1997 as a global network for longitudinal tracking of antimicrobial resistance, reported an overall MRSA rate in Canada of 5.7% from bloodstream isolates of nosocomial and community-onset origins (2).

In Canada, CA-MRSA was reported to be endemic in First Nations and Métis communities in northern Saskatchewan (34). Between 1990 and 1992, First Nations patients accounted for 62% of those MRSA-positive on hospital admission (35). Crowding, lack of good quality running water and heavy antibiotic use may have accounted for this (34). Several reports have also highlighted CA-MRSA spread in pediatric and general populations (12-20). The emergence of two different strains of MRSA was recently reported in Saskatchewan (19). In Manitoba, 40% of MRSA isolates collected by the provincial health laboratory were community acquired (18). CA-MRSA outbreaks were recently reported in a Canadian correctional facility in southern Ontario (20). In British Columbia, CA-MRSA is on the rise, with the proportion of isolates of community origin ranging from 25% to 70% (15). The first outbreak of severe CA-MRSA USA₃₀₀ infections was reported recently in Alberta in marginalized populations (16,36). One study, which included 50 nursing homes in the US and Canada, reported that 33% of *S aureus* isolates were MRSA (14). CA-MRSA was present in 10.9% of patients with community-acquired respiratory tract infections in Canada, versus 28.5% in the US (17).

Although MRSA rates in Canada are still lower than in the US and elsewhere, its continued spread is concerning and is impressing a growing burden on Canadian health care resources, in hospitals and in the community.

The management of MRSA and its associated costs

A meta-analysis indicated that, compared with MSSA patients, MRSA patients are at increased risk for mortality (OR=1.93) (3). Differences in morbidity do not appear to be related to virulence, similar in both strains, but perhaps to the lesser efficacy of vancomycin used for MRSA than that of beta-lactams used for MSSA, and to the longer time until appropriate therapy is found for MRSA patients (4). MRSA strains are resistant to multiple antimicrobial agents, and treatment options are limited (37). Current guidelines in Canada recommend vancomycin as the treatment of choice for serious or invasive MRSA infection (37). Alternative treatments such as clindamycin, trimethoprim-sulfamethoxazole, minocycline, quinupristin-dalfopristin or linezolid are considered for susceptible organisms (37). The first MRSA strain with reduced susceptibility to vancomycin was recently reported in Alberta (38), emphasizing a pressing need for appropriate use of vancomycin and new options in the management of MRSA patients.

Canadian guidelines for CA-MRSA are underway, and a consensus conference was held on October 2006. US guidelines and a recent Canadian practitioner guide for the management of CA-MRSA SSTIs recommended oral antimicrobial therapy for patients with moderate infections (10,39,40); for more severe cases, hospitalization and parenteral antimicrobials were preferred. Patients with CA-MRSA pneumonia

should be treated in consultation with infectious disease and critical care specialists (10).

Treatment patterns in Canada were explored in a retrospective analysis of MRSA patients with SSTIs treated in teaching hospitals from three distinct geographical areas (41). Considerable variation in treatment patterns was observed, with a mean (\pm SD) duration of anti-infective treatment of 22.4 \pm 21 days and mean duration of hospitalization of 28.9 \pm 20.8 days (Table 2). Controlling MRSA infection can be expensive and labour intensive, and can cause considerable disruption of clinical services (42). Several Canadian studies have investigated health care resource utilization and the direct medical costs associated with MRSA infection (22,24-27). Substantial variation was observed among studies in methodologies used and depth of analyses, as well as in their measures of health care utilization, resources included in estimates, cost per component and total cost per patient (Table 2). Patients harbouring MRSA required prolonged hospitalization, varying from 14 to 36 days per patient in isolation (average 26 days). Cost per day of hospitalization also varied from \$84 to \$917, depending on the perspective considered. For example, Papia et al (25) considered only the portion paid by the hospital deducted from the reimbursable portion from patients with private insurance. Total hospitalization cost per patient ranged from \$3,024 to \$12,835.

The cost of antimicrobial therapy was included in only two studies, and varied between \$325 and \$574 (Table 2). Components of barrier precautions were detailed in two studies, while global costs were reported in three, ranging from \$806 to \$2,086 per patient. Nursing time, as well as the cost of gowns, gloves and masks, were the major components of cost for barrier precautions. Cost estimates for laboratory investigations varied considerably, with a minimum of \$125 and a maximum of \$315.

Based on available data, low and high estimates of cost per hospitalized patient infected with MRSA were calculated, including hospitalization, barrier precautions, antimicrobial therapy and laboratory investigations. For hospitalization cost, the full daily cost of \$210 reported by Papia et al (25) was used, including any portion reimbursable by private insurance. For total costs, using the minimum cost for each component, the low estimate amounted to \$6,878 per patient; the high estimate was \$17,553 per patient. Minimum and maximum costs for each component were averaged, and the total average cost per infected MRSA patient amounted to \$12,216, with hospitalization the major cost driver (81%), followed by barrier precautions (13%), antimicrobial therapy (4%) and laboratory investigations (2%) (Figure 1).

Estimating the cost of MRSA to the Canadian health care system

Low and high estimates for the total cost of MRSA to the Canadian health care system was calculated considering MRSA infection, MRSA colonization and MRSA infrastructure for surveillance (Table 3). Low and high estimates for cost per patient with MRSA infection (estimated above) were used. For MRSA colonization, only one estimate was available in the literature. Published estimates for MRSA infrastructure varied between \$3,000 and \$7,000. After adjusting with the Consumer Price Index, cost data combined with epidemiological data suggested that the direct health care cost attributable to MRSA in Canada ranges from \$54 million to \$110 million annually.

TABLE 2
Health care utilization and associated costs for the management of methicillin-resistant *Staphylococcus aureus* (MRSA) patients in Canada

Study	Health care resource	Unit	Quantity	Unit cost	Cost per patient
Conly, 2003 (41) • Tertiary care hospitals • British Columbia, Ontario and Quebec • Skin and soft tissue infections only	Hospitalization	Days	28.9	Not applicable	Not applicable
	Antimicrobial therapy	Days	22.4	Not applicable	Not applicable
	Intravenous vancomycin	Days	19.5	Not applicable	Not applicable
Kim et al, 2001 (22) • Tertiary care hospitals • Ontario	Hospitalization	Days	14	\$916.83*	\$12,835.60*
	Antimicrobial therapy	–	–	–	\$574.40*
	Laboratory investigations	Specimen	–	\$8.34	\$143.60*
	Barrier precautions	Contact	60/day	\$0.96	\$806.40*
	MRSA surveillance	Specimen	–	\$5.50	–
	Total cost/MRSA infection	–	–	–	\$14,360.00
	Total cost/MRSA colonization	–	–	–	\$1,363.00
Canada Communicable Disease Report, 2002 (24) • General hospitals • Ontario	Hospitalization	Days	28	\$185.00	\$5,180.00
	Laboratory investigations	Specimen	21	\$15.00	\$315.00
	Total barrier precautions*	–	–	–	\$1,727.00
	Added nursing time	Days	1.12	\$576.00	\$645.00
	Gowns and masks	Each	50×28	\$0.40	\$560.00
	Examination gloves	Each	28	\$7.00	\$196.00
	Mupirocin ointment masks	Each	3	\$15.00	\$45.00
	Chlorhexidine gluconate	Bottle	4	\$2.35	\$9.00
	Environmental cleaning	Days	15.25	\$17.82	\$272.00
	Total cost to hospital (antimicrobials not included)	–	–	–	\$7,222.00
	Papia et al, 1999 (25)	Hospitalization†	Days	36	\$210.00
Laboratory investigations		Specimen	15	\$8.34	\$125.00
Total barrier precautions*		–	–	–	\$2,086.00
Added nursing time		Min	60×36	\$0.36	\$778.00
Gowns and gloves		Each	60×36	\$0.60	\$1,296.00
2% mupirocin		–	–	–	\$7.40
4% chlorhexidine gluconate		–	–	–	\$5.04
Total cost to hospital (antimicrobials not included)		–	–	–	\$9,771.00
Rosner et al, 2004 (26) • Model based on data from tertiary care hospitals • British Columbia, Ontario, Quebec • Skin and soft tissue infections only	Hospitalization	Days	21.4–23.4	\$401.00	\$6,191.00–\$6,979.00
	Antimicrobial therapy	Days	21.1–20.8	–	\$325.00–\$358.00
	Professional fees	–	–	–	\$509.00–\$984.00
	Outpatient intravenous antimicrobial	–	–	–	\$74.00–\$370.00
	Outpatient oral antimicrobial	–	–	–	\$0–\$378.00
	Home intravenous care service	–	–	–	\$12.00–\$227.00
	Total cost to Ministry of Health and Long-term Care	–	–	–	\$7,693.00–\$8,444.00
Bryce et al, 2000 (27) • Tertiary care hospital • British Columbia	Hospitalization	–	–	–	\$6,500.00
	Laboratory investigations and barrier precautions	–	–	–	\$4,345.00
	Total cost to hospital (antimicrobial not included)	–	–	–	\$10,845.00
Gardam et al, 2001 (23) • University-affiliated laboratory • Ontario	Total cost – protocol MSA-4	Specimen	–	–	\$3.83
	Laboratory cost	Specimen	–	–	\$1.33
	Laboratory technologist cost	Specimen	–	–	\$2.50
	Total cost – protocol M-SAM	Specimen	–	–	\$8.05–\$9.30
	Laboratory cost	Specimen	–	–	\$4.31
Laboratory technologist cost	Specimen	–	–	\$3.74–\$4.99	

*Numbers calculated from data available in published document; †Daily cost per room was \$210; costs included in the estimate by Papia et al were only those incurred by the hospital (\$84), assuming that 60% were recovered from the patient. M-ASM Broth-containing protocol as recommended by the American Society for Microbiology; MSA-4 Mannitol-salt agar containing 4 µg/mL of oxacillin

Trends in the annual cost of MRSA infection and colonization were estimated for the past 10 years using the average cost per patient of \$12,216, derived from the literature (Figure 2). Between 1995 and 2004, annual costs of MRSA infection and colonization increased from \$10.6 million to \$76.4 million (in 2005 dollars) (Figure 2). This increasing

economic burden was attributable to a continuous rise in the incidence of MRSA over 10 years, approximately 20-fold for colonization and sevenfold for infection. The cost increase was observed despite an 11.3% decrease in hospital admissions, from 3,140,659 in 1994 to 2,786,545 in 2004. Projected costs based on historical data suggest that the annual cost of MRSA

TABLE 3
Annual cost estimate of methicillin-resistant *Staphylococcus aureus* (MRSA) to the Canadian health care system – 2004

	Rate/1000 admissions*	Number of hospitalizations†	Number of cases	Cost per patient‡ (2005 dollars)		Cost in Canada (2005 dollars)		Average
				Minimum	Maximum	Minimum	Maximum	
MRSA infection	1.73	2,786,545	4821	\$6,878	\$17,553	\$33,157,558	\$84,619,546	\$58,888,552
MRSA colonization	4.17	2,786,545	11,620	\$1,506	\$1,506	\$17,499,558	\$17,499,558	\$17,499,558
MRSA infrastructure§						\$3,191,860	\$7,736,842	\$5,464,351
Total cost						\$53,848,977	\$109,855,947	\$81,852,462

*Unpublished data; †Data from reference 29; ‡Estimated from minimum and maximum for each cost component published in the literature (see Table 2) and adjusted for inflation with the Consumer Price Index; §Data from references 22 and 24

infection and colonization may reach \$123.6 million in 2010 (Figure 2). Assuming a constant cost for MRSA infrastructure, the total MRSA cost will amount to \$129 million in 2010.

DISCUSSION

The rate of MRSA in Canadian hospitals increased more than 10-fold between 1995 and 2004, while CA-MRSA continued to spread in the community. Patients harbouring MRSA required prolonged hospitalization (26 days on average), special control measures, expensive treatments and extensive surveillance, resulting in an average total cost per MRSA-infected patient of \$12,216. The direct health care cost attributable to MRSA in Canada, including management of MRSA-infected and -colonized patients and MRSA infrastructure, averaged \$82 million in 2004 and may reach \$129 million in 2010.

Although MRSA rates in Canada have increased sharply over the past 10 years, they remain below that observed in the US and other countries. In 2003 in the US, MRSA accounted for 59.5% of *S aureus* isolates in ICUs, 46% in non-ICU inpatient areas and 31.1% in outpatient areas (43). Important differences in MRSA rates observed across countries are likely related to variations in antimicrobial use and infection control practices (2). There is some controversy regarding the feasibility and usefulness of barrier precautions in hospitals (44). Programs that have been effective at reducing transmission of MRSA have included active surveillance cultures of high-risk patients, contact precautions, hand hygiene and treatment of health care workers implicated in transmission (21). Although decolonization of colonized MRSA patients has been used to reduce the reservoir of MRSA during outbreaks, current Canadian guidelines for the management of MRSA do not support the routine use of antimicrobial therapy for eradicating MRSA colonization in hospitalized patients (37). This is not advisable because eradication cannot be guaranteed and there is a risk of developing resistance to decolonization agents (44). Measures to limit the spread of MRSA in the community include antimicrobial stewardship, personal and caregiver hygiene measures, environmental and organizational control measures, and health care-initiated measures (10,15,39).

The present review indicated that Canadian patients infected with MRSA required prolonged hospitalization (average 26 days, range 14 to 36 days), comprising, on average, 81% of the total cost. Several studies have indicated that appropriate switching of MRSA patients from intravenous to oral treatment could reduce the length of hospital stay and cost per infected patient (26,41,45), suggesting that oral therapy may be one strategy to reduce the economic impact of MRSA. Cost estimates in the literature have varied from \$7,222 to \$14,630 per infected MRSA patient in Canada. Such variations across studies may be

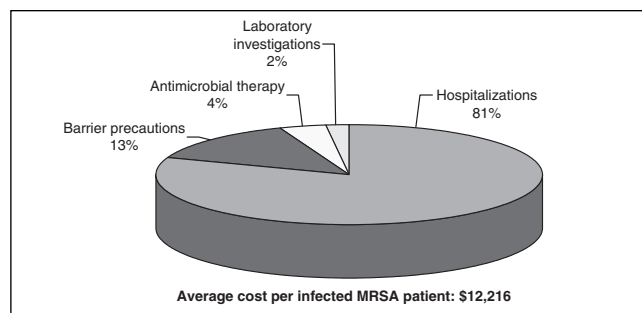


Figure 1 Breakdown of costs for the management of a patient hospitalized with a methicillin-resistant *Staphylococcus aureus* (MRSA) infection

attributable to differences in disease management, health care utilization, costing methodology and complexity of cases.

The average cost of \$12,216 per hospitalized MRSA patient presented in this study is in the lower range of those reported in other countries (4,5). Several US studies have reported total costs between US\$16,575 and US\$39,400 per MRSA patient (4,5,46-48). A French study reported a mean cost per MRSA infected patient of US\$9,275 (49). Another US study reporting cost by type of infection found total costs per MRSA patient of US\$23,616 for SSTIs, US\$26,446 for bacteremia, US\$48,925 for infective endocarditis and US\$48,945 for hospital-acquired pneumonia (50). Some studies also compared the cost of MRSA infection with that of MSSA infection and reported a 1.4- to 2.8-fold increase in cost per patient, highlighting the increased burden associated with resistance (4,5,46,47).

In the present study, the total cost to the Canadian health care system ranged from \$54 million to \$110 million annually, with MRSA infection only ranging from \$33.2 to \$84.6 million (4821 cases, with a cost per patient of \$6,878 to \$17,553). Previous estimates in Canada reported a range from \$40 million to \$59 million (22,24). One recent US study estimated the annual cost of treating patients hospitalized with MRSA infections to be between US\$3.2 billion and US\$4.7 billion (120,000 cases, with a cost per patient of US\$27,083 to US\$34,900) (48). Although MRSA rates and overall costs are still much lower in Canada than in the US, continuously increasing rates have resulted in a significant increase of burden to Canadians. Projected costs based on historical data suggest that the average total cost of MRSA, estimated at \$82 million in 2004, may reach \$129 million in 2010.

Cost estimates in the present paper underestimate the global cost of MRSA, because they do not include the costs of

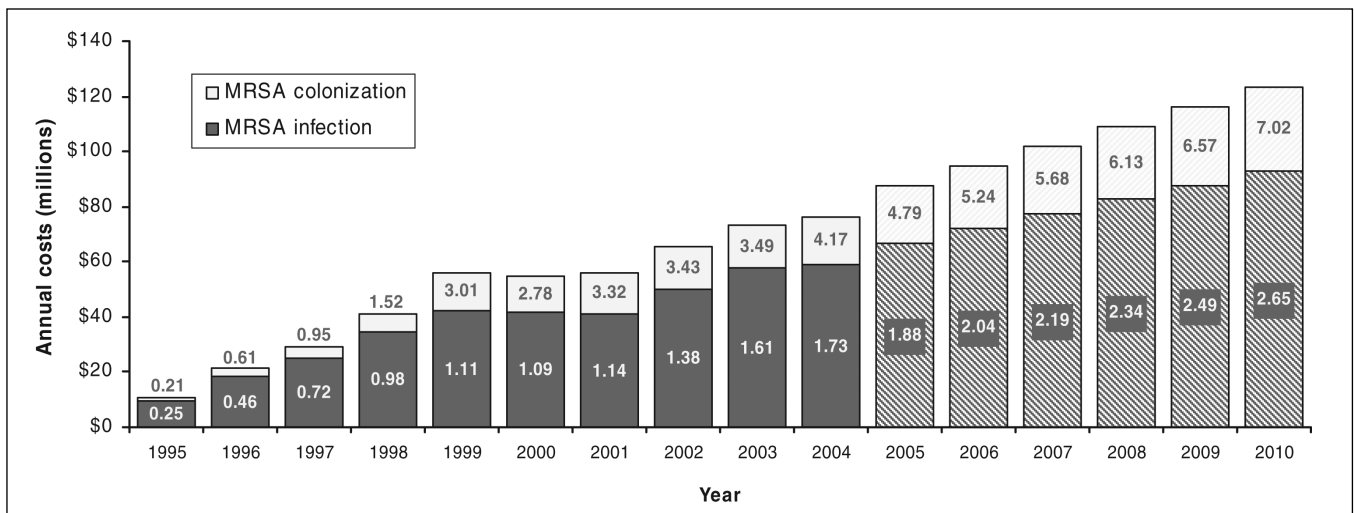


Figure 2) Estimated annual cost of methicillin-resistant *Staphylococcus aureus* (MRSA) infection and colonization in Canada – 1995 to 2010. Numbers in graph indicate incidence of MRSA (rate per 1000 admissions); hatched bars indicate projected annual costs based on historical data. Costs based on the Canadian dollar in 2005

CA-MRSA, the costs of outbreak management (in addition to the cost of managing infection, such as cost of service disruption, etc) or indirect costs. There are limited countrywide data on CA-MRSA incidence or on the cost of CA-MRSA in Canada. However, the rising number of CA-MRSA infections associated with severe soft tissue infections and necrotizing pneumonia (16,51,52) is likely to have a significant human and financial impact. There were insufficient published data to quantify cost of outbreaks in terms of disruption of clinical activity. In the Netherlands, the cost to bring an outbreak of MRSA under control was approximately US\$250,000, including closing ICUs, postponing operations, laboratory investigations and other unspecified measures; no breakdown was available to estimate the contribution of each component (53). Several other studies have reported outbreak cost, but they either represented costs already covered in our analysis or did not sufficiently detail the contribution of other cost components. An outbreak in Australia was estimated to cost AUS\$90,000 (54); outbreak cost varied from US\$13,000 to US\$144,000 (55,56) in the US, and from £13,000 to £80,000 in the United Kingdom (57,58).

Limited data exist on indirect costs of MRSA. One Canadian study reported that patients who have suffered drug-resistant infections endure physical, emotional, financial and psychological harm, but no dollar value was assigned to these human costs (24). Given the required isolation, the long-term nature of some infections and the need for outpatient treatment for wound care or intravenous treatment (24), the toll on quality of life and productivity is likely to be significant, especially for CA-MRSA affecting younger people in good general health.

The limitations of those cost estimates should be considered. Although we attempted to account for variations between studies by averaging extreme values, most data were from tertiary care hospitals and not necessarily representative of Canadian hospitals. Only one source of incidence data was used (CNISP), and it has been suggested that it may underestimate MRSA rates (22). The cost of intravenous therapy was underestimated, because most of the studies that were reviewed considered only acquisition cost of antimicrobials, not administration. A US study reported that when costs for material, preparation, administration, monitoring, adverse events and therapeutic failure

were included, the cost of using vancomycin was three to five times that of its acquisition (50). Cost of treatment failure was not assessed, although current treatment options for MRSA patients are of limited efficacy (59). In this respect, new generations of broad-spectrum antimicrobials, such as tigecycline, the first-in-class glycylcycline that overcomes major resistance mechanisms (ribosomal protection and active drug efflux), and the cephalosporin ceftobiprole, promise more efficacious management of MRSA patients (59-62).

CONCLUSIONS

The present study describes MRSA as a costly public health issue that needs to be tackled if the growing burden of this disease is to be limited. No simple solution exists to prevent escalation to those rates observed in the US and elsewhere. Coordinated leadership, compliance with barrier precautions, use of efficacious, first-line antimicrobials and guidelines for proper use of new antimicrobials are some available avenues. The feasibility of community control of CA-MRSA is debatable, highlighting the pressing need for effective agents against MRSA and rational use of antibiotics to limit resistance.

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