Financial impact of health care-associated infections: When money talks

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According to the Canadian Institute for Health Information, health spending in Canada was projected to reach $211 billion in 2013 (versus $207 billion in 2012), corresponding to $5,988 per person (1). Overall, this represents 11.2% of Canada's gross domestic product. Approximately 60% of total health spending is directed to hospitals (30%), drugs (16%) and physicians (15%). Although it is difficult to estimate, the proportion of this spending attributed to the management of nosocomial infections, overuse and/or misuse of antimicrobials, and infections due to multidrug-resistant bacteria is significant. Despite the availability of efficient strategies targeting each of these aspects, large-scale progress has not been demonstrated.

In a recent meta-analysis, Zimlichman et al (2) included 26 studies and used incidence estimates from the National Healthcare Safety Network of the Centers for Disease Control and Prevention, formerly known as the National Nosocomial Infections Surveillance (NNIS). They estimated the costs and excess length of stay (xLOS) associated with significant health care-associated infections (HAIs). On a per-case basis, central line-associated bloodstream infections (CLABSIs) were found to be the most costly (US$45,814 [2012]; xLOS 10.4 days), followed by ventilator-associated pneumonia (US$40,144; xLOS 13.1 days) and surgical site infections (US$20,785; xLOS 11.2 days). When caused by methicillin-resistant *Staphylococcus aureus* (MRSA), both the cost and xLOS of surgical site infections increased by 105%; CLABSI cost increased by 22% and CLABSI xLOS increased by 51%. These results highlight the importance of strategies to control bacterial antibiotic resistance.

The three most significant antibiotic-resistant bacteria found in Canadian centres are MRSA, vancomycin-resistant enterococci (VRE) and extended-spectrum beta-lactamase (ESBL)-producing organisms. A summary of a literature review is shown in Table 1. Most studies were from different states in the United States (US), and used retrospective cohorts from administrative databases and various analyses with various levels of sophistocation.

Very few cost assessments were found for Canada: according to a systematic review (3), MRSA infection cost the Canadian health system between $54 million and $110 million (2005 CAD$) (direct attributable health care cost per year) including infection, colonization and infrastructure. The average cost per patient for MRSA infection was estimated to be $12,216 (range $6,878 to $17,553) (3). In a conference publication, Muller et al (4) showed that $10 million in expenses were needed to control an MRSA outbreak in Toronto (Ontario) in 2006 to 2007, increasing hospital cost per patient by 35%. In studies from the US, Filice et al (5) estimated adjusted mean cost of medical services for MRSA in patients with low Charlson's score (0 to 3) to be $51,252 (2007 US$) (95% CI $46,041 to $56,464) versus $30,158 (95% CI $27,092 to $33,225) for methicillin-sensitive *Staphylococcus aureus*, and up to $84,436 (95% CI $79,843 to $89,029) versus $59,245 (95% CI $56,016 to $62,473) for a high Charlson's score (≥4). Shorr et al (6) did not find significant differences between MRSA and methicillin-sensitive *Staphylococcus aureus* in a crude analysis, but estimates of cost were both high ($70,028 versus $71,186).

Only one study assessed the cost of VRE; performed in Vancouver, British Columbia (7), it involved a large sample (n=1292) and showed that this infection would increase mean costs by 62% to reach as high as $17,949 per patient (95% CI $13,949 to $21,464). Using the Nationwide Inpatient Sample database, Nguyen et al (8) found that VRE infection would increase the adjusted average cost of inflammatory bowel disease by 127%.

We did not find any studies evaluating the financial impact of ESBL-producing organisms in Canada. Only one US study investigating ESBL-producing organisms was found (9). This small, matched-cohort study (n=42) was performed in an 810-bed community hospital (Hartford, Connecticut, USA). It compared patients infected with ESBL-producing *Escherichia coli* or *Klebsiella* species at a site other than the urinary tract with control patients infected with a non-ESBL-producing organism. The total mean infection-related costs were $41,353 (2004 US$) for cases of infections with ESBL-producing organisms and $24,902 for controls (P=0.034). Infection-related xLOS was prolonged in patients infected with ESBL compared with controls (21 days versus 11 days; P=0.006); most of the difference in cost was directly related to the xLOS.

Another major HAI is *Clostridium difficile* infection (CDI). No recent national estimation of incidence is available in Canada and the latest estimation of cost, in 2008 US$, was found in a systematic review (10): the mean total cost for a primary case of CDI would be $12,099. According to the US NNIS incidence data, CDIs represent 30% of nationwide annual HAIs, with a cost of approximately $1.5 billion (2). Lipp et al (11) estimated the annual cost of health care-associated CDI (2007 to 2008) extrapolated to all nonfederal US hospitals to be $792 million, and a mean cost per case of $11,285 ($9,118 to $13,574) (2). Three studies investigating CDI cost completed in different US states and a simulation model were retrieved and are shown in Table 1. The results of the study by Campbell et al (12) highlight the higher total costs in patients exposed to concurrent antibiotics compared with elderly patients or those with renal impairment: $17,015 (2010 US$) (95% CI $9,575 to $24,456) were needed per case of CDI.

Several intervention studies have shown a positive association between antimicrobial stewardship and a decrease in the incidence of MRSA and CDI, either alone or as a component of a bundle (13-16). Fewer studies are available to support the same relationship with ESBL-producing organisms (17-20), but it is reasonable to assume that decreasing overuse and misuse of antimicrobials should have a positive effect on most hospital antibiotic-resistant pathogens. Interventions associated with a decrease in antimicrobial consumption are inevitably linked with a decrease in antimicrobial costs as well, making these strategies even more interesting from the payers' and providers' perspectives. In addition, many different infection-control strategies have also been shown to decrease the incidence of HAIs, CDI and multidrug-resistant bacteria (21). These strategies have been evaluated alone or as part of multifaceted approaches, mainly on modifiable risk factors for HAI acquisition. The key strategies are hand hygiene, isolation of cases, education programs and compliance with good practice guidelines.

Nosocomial infections are associated with major burden of illness and use of health care resources. The massive expenditures of limited

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health care dollars required to manage these infections, as outlined in the present note, are neither new nor surprising. Considering an annual discount rate of 5% in health economic evaluations (22), the future trends are not likely to be decreasing soon. We believe that these data are needed to convince health care administrators to prioritize infection prevention and control resourcing according to the magnitude of this problem. In our personal experiences, funding of infection prevention and control efforts occurs at a small fraction of the cost likely incurred by nosocomial infections, while in some jurisdictions worldwide, use of funding penalties has been implemented in an attempt to motivate health care institutions to reduce nosocomial infection incidence. However, such an approach potentially results in minimizing funds to health care institutions with the greatest need for resources to control nosocomial infections. Perhaps an alternative would be to centrally and specifically fund infection prevention control programs at all health care institutions at the level that we are currently paying to deal with these infections. This would allow generous funding of programs that would stimulate enhanced and innovative preventive efforts. Effective institutions would inevitably have money 'left over' following successful prevention of infection that, in turn, could be used to benefit other areas within the hospital, or perhaps be even used as cash incentives to staff to enhance performance. Audits of hand-washing compliance of physicians and health care workers typically demonstrate dismal results despite repeated efforts to do so. Would physicians and health care workers improve these and other preventive efforts if we specifically paid them to do this?

TABLE 1
Cost of infections in published studies (PubMed, 2003–2013)

Study	Setting, year of data	Methods*	Perspective; temporal horizon; cost adjustment	n	Main results
Methicillin-resistant *Staphylococcus aureus* (MRSA)					
Labreche 2013 (23)	South Texas, USA 13 primary care clinics administrative database, 2009–2011	Prospective cohort of adults with SSTI; 90-day follow-up MRSA moderate or complicated vs mild or uncomplicated	Health insurance payer; 32-month study period; 2011 US$	265	Mean additional cost of treatment failure/case: $1,933; $1,255 in mild or uncomplicated, $2,093 in moderate or complicated
Filice 2010 (5)	Minneapolis, Minnesota, USA Veterans Affairs database, 2004–2006	Retrospective cohort, patients with *S aureus* disease MRSA vs MSSA Semilogarithmic least-squares multivariate model	Hospital, society; 2007 US$	725/ 355:390	Unadjusted median health care cost: $34,657 (range: $11,517–$98,287) Overall median inpatient median cost: $26,274 (range $4,531–$86,974) vs $6,748 for MSSA (P<0.001) Overall median outpatient median cost: $4,322 (range $1,395–$9,438) vs $4,495 (P=0.30)
Shorr 2010 (6)	Detroit, Michigan, USA 903-bed tertiary care center database, 2005–2008	Retrospective cohort, inpatients with pneumonia and blood or respiratory culture of *S aureus* MRSA vs MSSA	Hospital; study period; not indicated	142/ 55:87	Median total charges $70,028 vs $71,186 MSSA (P=NS)
Weigelt 2010 (24)	Marlborough, Massachusetts, USA 97 acute care hospitals clinical research database, 2003–2007	Retrospective cohort, postoperative infection and positive surgical site culture MRSA vs other organisms Multivariate logistic regression	Hospital; not indicated	8302	Adjusted attributable cost vs other non-MRSA monomicrobial infections: $1,157 (95% CI $641–$1,644); P<0.0001 Median raw cost (mono and polymicrobial): $7,036 (IQR $4,024–$11,989)
Vancomycin-resistant enterococci (VRE)					
Lloyd-Smith 2013 (7)	Vancouver, British Columbia Urban hospital database, 2008–2009	Retrospective cohort, inpatients with VRE colonization or infection; VRE colonization or infection vs inpatients without VRE General linear model	Hospital; not indicated	1292/ 217:1075	Mean total cost of care: $46,924/case vs $13,069; Absolute mean attributable cost/days: $17,949 (95%CI $13,949–$21,464); Relative attributable cost 61.9% (95%CI 42.3–84.3) greater than total hospital cost/patient without VRE
Butler 2010 (25)	Missouri, USA Academic hospital database, 2002–2003	Retrospective cohort, nonsurgical patients with first-episode enterococcal BSI; VRE BSI and VSE BSI vs never BSI; Standard GLS regression, propensity score-weighted regression and propensity score-matched pairs	Hospital; study period; 2007 US$	276/ 94:182 controls 20,150	Crude median hospital cost (IQR) for VRE: $42,106 ($16,310–$93,870); VSE: $20,895 ($11,263–$41,879); controls: $8,192 ($5,615–$13,495) Adjusted mean cost (95% CI): Using GLS: $4,479 ($3,500–$5,732) for VRE BSI, $2,250 ($1,758–$2,880) for VSE BSI; Using GLS + probability weighting: $4,036 ($3.0170–$5,140) and $2,023 ($1,588–$2,575); Using matched pairs: $9,949 ($1,579–$24,693) and $5,282 ($2,042–$8,043)
Nguyen 2011 (8)	Nationwide Inpatient Sample database of acute care hospitals 1998–2004	Retrospective cohort, IBD inpatients; Discharge diagnosis ulcerative colitis or Crohn's disease vs non-IBD GI disorder χ^2, multivariate adjustment	Hospital; not indicated 2005 US$	116,842: 919,408	Crude total hospital charges $63,517 vs $21,918 for no VRE; P<0.001 Crude average charges/day: $3,272 vs $3,124 for no VRE; P=0.546; Adjusted average total charges 127% higher with VRE (95% CI 85%–177%)

TABLE 1 – CONTINUED
Cost of infections in published studies (PubMed, 2003–2013)

Study	Setting, year of data	Methods*	Perspective; temporal horizon; cost adjustment	n	Main results
***Clostridium difficile* infection (CDI)**					
Campbell 2013 (12)	Kansas City, Missouri, 74 hospitals, electronic health record database 2005–2011	Retrospective cohort, adult inpatients, five high-risk patient groups: ≥65 years of age, renal disease, cancer, IBD, concurrent antibiotic use Propensity matching: HA-CDI vs non-CDI Multivariate adjustment	Hospital; Study period 2010 US$	4521	Difference in total costs HA-CDI vs non-CDI (95% CI): Age ≥65 years: $6,906 ($3,942–$9,871) Concurrent antibiotics : $17,015 ($9,575–$24,456) Renal impairment : $4,604 ($1,025–$8,182)
Tabak 2013 (26)	Pennsylvania, six hospitals, administrative database 2007–2008	Retrospective cohort, adult inpatients with primary HA-CDI Propensity score matching: HA-CDI vs non-CDI; Random-effects model	Hospital; Not indicated	255 vs 765	Increase in attributable cost/year: $6,117 (95% CI $1,659–$10,574) Mean (± SD) cost/case: $32,237±43,036 Median cost/case $20,804 (IQR $11,059–$38,429)
Lipp 2012 (11)	New York State All nonfederal acute care hospitals administrative database 2007–2008	Retrospective cohort of HA-CDI General linear model	Hospital and state; Study period (two years); Cost/charge ratios; Medicare hospital cost report	4,853,800	Average cost per infection: $29,000; Annual cost in state: $55 million
McGlone 2011 (27)	United States hospitals Computational simulation model	HA-CDI ≥65 years; mild or severe CDI; Recurrence and progression to fulminant colitis accounted for	Hospital, third-party payer and societal; 2010 US$ 3% discount/year	1000/ simulation	Median cost (95% CI) of lost hospital bed days/first occurrence and 6-day LOS: $7,511 ($6,868–$8,210); 14-day LOS: $9,539 ($8,342–$10,994); 3rd party direct costs: $8,237 ($7,563–$9,014); Direct and indirect costs/CDI and 6-day LOS: $14,726 ($10,491–$20,724)

**Methods: Design, population, cases and comparison group, and analysis. BSI Bloodstream infection; GI Gastrointestinal; GLS Generalized least-squares; HA-CDI Hospital-acquired CDI; IBD Inflammatory bowel disease; IQR Interquartile range; LOS Length of stay; MSSA Methicillin-sensitive* S aureus*; SSTI Skin and soft tissues infection; vs Versus; VSE Vancomycin-sensitive enterococci*

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