Antimicrobial Stewardship Programs Must Apply to All •
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Source: *Infection Control and Hospital Epidemiology*, Vol. 30, No. 2 (February 2009), pp. 205-207
Published by: The University of Chicago Press on behalf of The Society for Healthcare Epidemiology of America
Stable URL: http://www.jstor.org/stable/10.1086/593209

LETTERS TO THE EDITOR

Serological Survey of Mumps Immunity Among Healthcare Workers in Connecticut, December 2006–May 2007

To the Editor—Mumps is a highly contagious acute viral disease transmitted by oral and respiratory secretions. In unvaccinated persons, unilateral or bilateral parotitis occurs in approximately half of patients. The incubation period of the virus is 16–18 days. Although mumps is usually self limited, adults are more likely than children to develop severe symptoms and complications, such as orchitis, aseptic meningitis, and meningoencephalitis.[1]

The 2006–2007 mumps epidemic in the United States involved 6,584 cases of mumps in different midwestern states. Of patients who had a known vaccination status for measles, mumps, and rubella (hereafter collectively referred to as MMR) and who lived in 8 highly affected Midwestern states, 63% had received 2 doses, 25% had received 1 dose, and 13% had received no vaccine. The national incidence of mumps during this resurgence was 2.2 cases per 100,000 people, with the highest incidence among people 18–24 years of age.[2]

In the United States, the Jeryl Lynn strain of mumps vaccine, currently in use, was introduced in 1967. The combination vaccine for MMR was licensed in 1971 but routinely administered only after 1977.[3] The incidence of mumps began to decline after 1977, when all 1-year-olds were vaccinated. The recommendation for 2 inoculations of the mumps vaccine for children entering school was instituted by the Centers for Disease Control and Prevention in the 1990s. As a result, after 1989, the incidence of mumps decreased further. In 1994, the requirement for entering the public school system was 1 dose of MMR vaccine. In 2001, 2 doses of MMR vaccine became a mandatory requirement. From 2001 through 2003, fewer than 300 cases of mumps were reported in the United States, a decline of more than 99% from the 185,691 cases in 1968.[4]

Reports of transmission of mumps in healthcare settings are rare; however, during community outbreaks, exposure of unprotected healthcare workers (HCWs) to mumps is common, both in hospital and community settings.

In June 2007, the Advisory Committee on Immunization Practices approved the adult immunization schedule for October 2007 to September 2008. This update tightened requirements for "presumptive evidence of immunity" to mean 2 doses of MMR vaccine, or serologic evidence, or physician-documented mumps infection.[5]

Although there were, at the time, no reported cases of mumps in the state of Connecticut, we assessed the baseline mumps serology status of all HCWs who joined the University of Connecticut Health Center, during preplacement evaluation. Our goals were to immunize susceptible HCWs to prevent risk of future mumps transmission, to document the proportion of HCWs who were seronegative for mumps when they joined our institution, and to guide the development of our institution's protection against mumps.

All newly hired HCWs are required to provide evidence of 2 MMR vaccinations (one of the vaccinations must have occurred after 1980). We conducted a cross-sectional study, from December 2006 to May 2007, that included all HCWs who underwent preplacement or immunization screening at our employee health service clinic. The study was approved by the institutional review board.

A total of 209 employee health records were reviewed during the study period. Data were deidentified. Data on age, sex, and vaccination status and/or history were recorded. Specific immunoglobulin G (IgG) antibodies against mumps virus were measured using enzyme-linked immunosorbent assays (ELISAs), at the time of the health center visit. Tests were conducted according to the standard protocol for ELISAs. IgG index values of at least 1.10 were considered positive results; lower levels were considered negative results. According to previous studies, the ELISA is simple, rapid, and ideally suited to large-scale mumps serosurveys.[6] The sensitivity and specificity of mumps IgG antibody testing by ELISA are 93% and 87%, respectively.[7]

During the study period, 209 HCWs underwent preplacement screening; all had received 2 doses of MMR vaccination. Most (119) of the HCWs were women. Negative antibody titer results were reported for 16 (8%) of the 209 HCWs. The Table presents the distribution of HCWs across different age groups; there were 108 (52%) aged 20–29 years, and 8 of these had negative antibody titer results. Susceptible HCWs (ie, those with negative antibody titer results) received an MMR booster dose.

The US mumps outbreak occurred because of crowded campus environments that facilitated transmission of respiratory and oral secretions. During the outbreak, a high proportion of the individuals had a documented history of 2 MMR vaccine doses. The effectiveness of 1 dose of mumps

TABLE. Results of Titers for Immunoglobulin G Antibodies Against Mumps Virus for 209 Healthcare Workers (HCWs) With a History of 2 Doses of Vaccine for Measles, Mumps, and Rubella (MMR), by Age Group

Result	HCWs aged 20–29 years	HCWs aged 30–39 years	HCWs aged ⩾40 years	All HCWs
Negative	8 (4)	6 (3)	2 (1)	16 (8)
Positive	100 (48)	43 (21)	50 (24)	193 (92)
Total	108 (52)	49 (23)	52 (25)	209 (100)

NOTE. Data are no. (%) of HCWs.

vaccine has been reported as approximately 80%, which is considered inadequate to provide population protection. Previous studies have shown that the effectiveness of 2 doses of vaccine is from 88% to 95%.[8,9] The estimated herd immunity threshold for mumps ranges from 88% to 92%.[10]

Although there was no single explanation for this outbreak, multiple factors may have contributed; these factors include waning immunity, vaccine failure, high population density and high contact rates in colleges, and incomplete vaccine-induced immunity to the wild virus. The relatively advanced age of the majority of infected patients points toward the waning immunity hypothesis. However, more research is needed to study the long-term vaccine effectiveness.

In our study, all the subjects had received 2 doses of MMR vaccine, and yet 16 HCWs were found to be seronegative. In a recent measles outbreak, an unvaccinated HCW became infected in a hospital. Of 64 people with confirmed cases of measles, 17 became infected while visiting the healthcare facility.[11]

A limitation of our study is the small sample size; we did not include all the HCWs employed. Therefore, the results may underestimate the number of susceptible HCWs already employed.

Mumps should be considered a reemerging yet vaccine-preventable disease, with transmission occurring in both healthcare and community settings. Future studies should include all HCWs, to better assess mumps seroprevalence in healthcare institutions. In view of the possible waning immunity, it is essential to carry out periodic serological surveillance and to vaccinate susceptible HCWs.

ACKNOWLEDGMENTS

Potential conflicts of interest. All authors report no conflicts of interest relevant to this article.

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Presented in part: American Occupational Health Conference; New York, New York; April 13, 2008 (Poster 114).

Infect Control Hosp Epidemiol 2009; 30:202-203

 0899-823X/2009/3002-0018$15.00. DOI: 10.1086/593966

REFERENCES

1. Caplan CE. Mumps in the era of vaccines. *CMAJ* 1999; 160:865-856.
2. Dayan GH, Quinlisk MP, Parker AA, et al. Recent resurgence of mumps in the United States. *N Engl J Med* 2008; 358:1580-1589.
3. Mumps vaccine. *MMWR Morb Mortal Wkly Rep* 1977; 26:393-394.
4. Centers for Disease Control and Prevention (CDC). Update: multistate outbreak of mumps—United States, January 1–May 2, 2006. *MMWR Morb Mortal Wkly Rep* 2006; 55:559-563.
5. Advisory Committee on Immunization Practices. Recommended adult immunization schedule: United States, October 2007– September 2008. *Ann Intern Med* 2007; 147:725-729.
6. Van den Hof S, Beaumont MTA, Berbers GAM, de Melker HE. Antibodies against mumps in the Netherlands as assessed by indirect ELISA and virus neutralization assay. *Epidemiol Infect* 2003; 131:703-709.
7. Tischer A, Andrews N, Kafatos G, et al. Standardization of measles, mumps, and rubella assays to enable comparisons of seroprevalence data across 21 European countries and Australia. *Epidemiol Infect* 2007; 135: 787-797.
8. Schaffzin JK, Pollock L, Schulte C, et al. Effectiveness of mumps vaccine in a summer outbreak. *Pediatrics* 2007; 120:e862-e868.
9. Harling R, White JM, Ramsay ME, Macsween KF, van den Bosch C. The effectiveness of the mumps component of the MMR vaccine: a case control study. *Vaccine* 2005; 23:4070-4074.
10. Anderson RM, May RM. Vaccination and herd immunity to infectious diseases. *Nature* 1985; 318:323-329.
11. Centers for Disease Control and Prevention (CDC). Measles—United States, January 1–April 25, 2008. *MMWR Morb Mortal Wkly Rep* 2008; 57:494-498.

Reduction of Hospital-Acquired Methicillin-Resistant *Staphylococcus aureus* Infection by Cohorting Patients in a Dedicated Unit

To the Editor—One of the risk factors for methicillin-resistant *Staphylococcus aureus* (MRSA) acquisition is proximity to MRSA-colonized or MRSA-infected patients who are not receiving care that includes isolation precautions.[1] Increased numbers of preventable adverse events in patients placed under barrier precautions have been reported recently.[2–4] These factors may adversely affect the nosocomial infection rates and length of hospital stay (LOS) for patients with MRSA infection. We describe our experience creating a dedicated MRSA infection unit and the implementations that helped reduce the rate of hospital-acquired MRSA infection and average LOS in the medical and surgical units at Crouse Hospital (Syracuse, NY).

Crouse Hospital has 506 acute care beds. In 1999, Crouse Hospital had an outbreak of MRSA infection in the intensive care unit (ICU) during which 1 patient died. Patient beds were situated in close proximity to each other and were separated by curtains. To control the outbreak, all patients in the ICU were screened for MRSA; if they tested positive, they were cohorted to one side of the unit, were placed under contact precautions, and were assigned dedicated staff. The

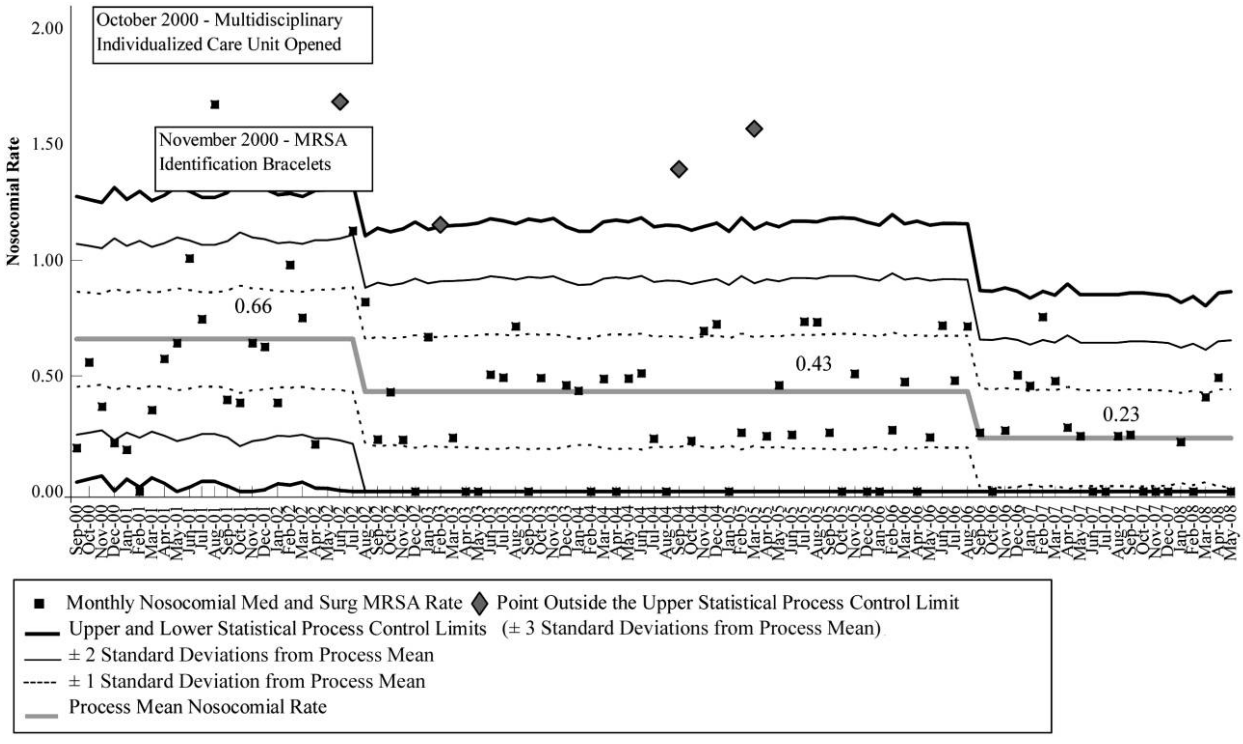

FIGURE. Methicillin-resistant *Staphylococcus aureus* (MRSA) nosocomial infection rate per 1,000 patient-days in medical and surgical (med and surg) units at Crouse Hospital, September 2000–May 2008, after establishment of a dedicated MRSA unit.

intervention was successful in preventing further spread of MRSA colonization and infection in the ICU.

The Crouse infection-control policy and procedure for MRSA-colonized and MRSA-infected patients at that time included MRSA screening (as defined by the Centers for Disease Control and Prevention[5] and the Hospital Infection Control Practices Advisory Committee[6]) and placement under contact precautions in a private room. This created problems with regard to bed availability for other patients—especially those in the emergency department—and a decreased census, and had financial repercussions. Healthcare providers found it difficult to care for these patients because of the time constraints associated with using isolation precautions. The perception of patients, administration, and infection-control personnel was that patients who were colonized or infected with MRSA were getting a lower level of care because of the time required for healthcare providers to use gowns and gloves.

A unit with 17 private rooms, each with a bathroom, became available. Hospital administration and the medical and surgical unit staff endorsed the idea of a self-contained unit capable of providing all aspects of care, including rehabilitation, required by patients colonized or infected with MRSA. The designated staff (voluntarily assigned) would not have to gown on entering the unit, although they would still practice hand hygiene and wear gloves. A gown would be worn only for patients colonized with other drug-resistant organisms. Staff not assigned to the unit would practice hand hygiene, would don a gown on entering the unit, and would change gloves after contact with each patient. Gowns would be removed when leaving the unit and changed only in between examining patients who had infections with other resistant organisms. Patients who were coinfected or colonized with other resistant organisms were cohorted with similar patients at one end of the unit. Patients and their families would be able to ambulate in the hallways without gowning and wearing gloves. Space was available for physical therapy and whirlpool treatments. The unit opened in October 2000. A policy was created in 2003 to never remove MRSA status once a patient had a culture positive for MRSA, and a computer entry system was initiated to alert staff of the patient's MRSA status on readmission to the hospital.

Six years of data were extracted from infection-control records. Crouse Hospital monitors MRSA infection rates (no. of infections per 1,000 patient-days) through use of statistical process-control charts. A pattern ("runs rule") of 11 of 15 points below the process average is used to detect a decrease in the process average. Three different process averages were detected, during September 2000–July 2002, August 2002–August 2006, and September 2006–February 2008. Crouse's hospital-acquired MRSA infection rates decreased from 0.66 infections per 1,000 patient care days (during September 2000–July 2002) to 0.43 infections per 1,000 patient-days

(during August 2002–August 2006) and then decreased to 0.23 infections per 1,000 patient-days (during September 2006–February 2008) (Figure). There was also a significant decrease in the mean LOS in the MRSA unit, in comparison of 2002 with 2003-2006, from 23.9 days to 12 days ($P = .009$).

Patient benefits include the freedom to ambulate in the hall and lounge area. Physical therapy is available for gait training and stair walking in the unit's mini–physical therapy room. Patients have verbalized how important this is, in contrast to isolation for their entire hospitalization. Patients are frequently assigned the same nursing personnel during their stay and on readmission. The level of visitor emotional stress, compared with seeing loved ones placed "in isolation," decreased because visitors no longer had to wear gowns or gloves; this new ward allowed for a closer relationship to develop among family, visitor, and nurse during this and possible subsequent hospitalizations. Crouse Hospital was able to decrease costs because fewer gowns were used and the LOS for patients with MRSA infection or colonization decreased, which represented a cost savings of $1.5 million. Bed placement in the general and medical and surgical unit population has eased because of the decreased need to isolate beds.

Just cohorting staff to care for patients has been reported as an effective way of reducing transmission of infection in hospitals.[7] The rate of hand-washing compliance on this designated unit exceeds 90%; the staff is more likely to comply because they are aware that the unit patients are colonized or infected with a resistant organism. The rates of MRSA-colonized or MRSA-infected patients may have decreased because patients are considered "once positive, always positive" and are no longer rescreened on subsequent hospitalizations. A small census with fewer staff members makes it easier to care for unit patients and to attend to their needs. This could explain why the average LOS has decreased significantly.

Cohorting patients on this dedicated MRSA unit has been a challenging and successful intervention. Creation of this designated unit has helped reduce both the rate of hospital-acquired MRSA infection in the medical and surgical units and the LOS in the MRSA unit.

ACKNOWLEDGMENTS

Potential conflicts of interest. All authors report no conflicts of interest relevant to this article.

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Infect Control Hosp Epidemiol 2009; 30:203-205

 0899-823X/2009/3002-0019$15.00. DOI: 10.1086/593968

REFERENCES

1. Crossley KB, Landesman, Zaske D. An outbreak of infections caused by strains of *Staphylococcus aureus* resistant to methicillin and aminoglycosides. II. Epidemiologic studies. *J Infect Dis* 1979; 139:280-287.
2. Kirkland KB, Weinsein JM. Adverse effects of contact isolation. *Lancet* 1999; 354:1177-1178.
3. Evans JL, Shaffer MM, Hughes MG et. al. Contact isolation in surgical patients: a barrier to care? *Surgery* 2003; 134:180-188.
4. Saint S, Higgins LA, Nallamothu BK, Chenoweth C. Do physicians examine patients in contact isolation less frequently? A brief report. *Am J Infect Control* 2003; 31:354-356.
5. Centers for Disease Control and Prevention. National Nosocomial Infections Surveillance System (NNIS) semi-annual reports, 2002. http://www.cdc.gov/ncidod/dhqp/nnis_pubs.html. Accessed December 29, 2008.
6. Garner JS. Guideline for isolation precautions in hospitals. The Hospital Infection Control Practices Advisory Committee. *Infect Control Hosp Epidemiol* 1996; 17:53-80.
7. Beggs CB, Noakes CJ, Shepherd SJ, Kerr KG, Sleigh PA, Banfield K. The influence of nurse cohorting on hand hygiene effectiveness. *Am J Infect Control* 2006; 34:621-626.

Antimicrobial Stewardship Programs Must Apply to All

To the Editor—We read with great interest the letter from Kenichi Nomura, MD, PhD,[1] from the Department of Oncology and Hematology of Kyoto, Japan, in the May issue of the journal, that questioned the utility of antimicrobial stewardship programs that apply to all clinicians. First of all, we agree that there is plenty of evidence of the benefits of antimicrobial stewardship programs worldwide. The structure for antimicrobial stewardship programs has been published by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America.[2] A multidisciplinary team is needed, and, although there is no agreement about which is the best approach, a combination of education, the need for a preapproval order (ie, a "front-end approach"), and a postprescription review of the case and streamlining of the prescription process (ie, a "back-end approach") might be a good option.

Furthermore, to prevent the emergence of drug resistance, an intervention combining antibiotic stewardship programs with other infection control practices, such as isolation precautions and adherence to hand hygiene practices, is even more important.[3] The Centers for Disease Control and Prevention has published a 12-step program to reduce resistance, and one part of the program is to use antimicrobials wisely.

Wise use means to practice antimicrobial control, to stop treatment when the patient is cured, to say no to vancomycin, to treat infection not colonization, to treat infection not contamination, and to use local data.[4]

Nomura[1] cited a study by Singer et al.[5] about an intervention that was unsuccessful in reducing resistance and questioned the utility of an antibiotic stewardship program. At the same time, a recent systematic review found that 12 of 16 studies had interventions (ie, antibiotic stewardship programs) that reduced the incidence of antimicrobial drug resistance.[6] In the study by Singer et al.,[5] the use of education and an active intervention to stop vancomycin use resulted in a statistically significant 22% decrease in its use, but most of the indications of vancomycin use did not meet published guidelines. The conclusion by Singer et al.[5] was that more aggressive interventions are needed to change prescribing patterns. The point is: the intervention used was not broad enough to meet the goal of reduction of antimicrobial drug resistance. A systematic review and meta-analysis showed that the risk of acquiring methicillin-resistant *Staphylococcus aureus* infection or colonization was increased not only by the use of glycopeptides but also by the use of fluoroquinolones, cephalosporins, and other β-lactams.[7]

The problem of antagonism between the infection control team and the hematologist and the role played by febrile neutropenia guidelines were addressed by Zuckerman et al.[8] Adherence to a local data protocol for the management of febrile neutropenia was tested in a hematology ward. The rate of full compliance with this protocol was very low (21.6%). The use of standardized practices in protocols has been shown to improve patient outcomes. A critical component of the management of febrile neutropenia is an infection control team, which should help the clinicians in the decision-making process, save them time and labor, and share their responsibilities in relation to the final decision.

In our institution, a 250-bed surgical hospital for cardiology patients, we initiated, in 2005, an antibiotic stewardship program based on education, a back-end approach, and a front-end approach. This intervention reduced significantly the total consumption of antibiotics, mostly carbapenems. The trends of increasing resistance also stabilized during the 5-year study period. The program resulted in a reduction of more than 80% in antibiotic costs, without an increase in patient mortality. Our program is addressed to all our clinicians, irrespective of knowledge, specialty, number of years of practice, or position in the hospital; and the mean rate of acceptance of our recommendations was 58.7%, which was considered high. Most of the recommendations were to stop therapy (49.6%); to change antibiotic therapy (35.5%); to switch to oral therapy (13.9%); and to change the dose (1.1%). The most prepared clinician, even the hematologist who is familiar with antibiotics, is not necessarily aware of trends in hospital or community resistance. It is the role of the infection control team to provide colleagues with information on trends of resistance and on the best option for therapy in each hospital, on the basis of local data. Most physicians underestimate the true degree of antimicrobial resistance in their own institution.[9] The question is not who has the accountability for the outcome; both the clinician and the infection control team must work for the patient's well-being, but from different perspectives. The infection control practitioner has a broader view, in terms of local resistance trends, and his or her decisions must take into account both the problem of resistance and the benefits of aggressive early therapy. The clinician has responsibilities to an individual patient, and, for him, antimicrobial resistance is rated as the least important factor, in terms of antibiotic choice.[10]

The final recommendation by Nomura,[1] about education for clinicians who do not have sufficient knowledge about antibiotics, seems awkward. Studies on the passive dissemination of information for behavior change have shown a low rate of effectiveness.[11] Besides, with which physician or specialty would one choose to start a focused educational antibiotic program? One study found that inappropriate antibiotic prescribing increased with time in practice. Physicians with a high practice volume, compared with those with a low practice volume, were more likely to prescribe antibiotics for viral respiratory infections (relative risk [RR], 1.27 [95% confidence interval {CI}, 1.09–1.48]) and to prescribe second- and third-line antibiotics as first-line treatment (RR, 1.20 [95% CI, 1.06–1.37]).[12]

Antibiotic stewardship programs must apply to all clinicians in a hospital. We can not preclude clinicians from using this important component of quality improvement and patient safety in their decision-making process.

ACKNOWLEDGMENTS

Potential conflicts of interest. All authors report no conflicts of interest relevant to this article.

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Infect Control Hosp Epidemiol 2009; 30:205-207

 0899-823X/2009/3002-0020$15.00. DOI: 10.1086/593209

REFERENCES

1. Nomura K. Should infection control teams enforce an antimicrobial stewardship program for all clinicians? *Infect Control Hosp Epidemiol* 2008; 29:468-469.
2. Dellit TH, Owens RC, McGowan JE, et al. Infectious Diseases Society

of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis* 2007; 44:159-177.
3. Aldeyab MA, Monnet DL, López-Lozano JM, et al. Modelling the impact of antibiotic use and infection control practices on the incidence of hospital-acquired methicillin-resistant *Staphylococcus aureus:* a time-series analysis. *J Antimicrob Chemother* 2008; 62:593-600.
4. Brinsley K, Sinkowitz-Cochran R, Cardo D, CDC Campaign to Prevent Antimicrobial Resistance Team. An assessment of issues surrounding implementation of the Campaign to Prevent Resistance in Healthcare Settings. *Am J Infect Control* 2005; 33:402-409.
5. Singer MV, Haft R, Barlam T, Aronson M, Shafer A, Sands KE. Vancomycin control measures at a tertiary care hospital: impact of interventions on volume and patterns of use. *Infect Control Hosp Epidemiol* 1998; 19:248-253.
6. Davey P, Brown E, Fenelon L, et al. Systematic review of antimicrobial drug prescribing in hospitals. *Emerg Infect Dis* 2006; 12:211-216.
7. Tacconelli E, De Angelis G, Cataldo MA, Pozzi E, Cauda R. Does antibiotic exposure increase the risk of methicillin-resistant *Staphylococcus aureus* (MRSA) isolation? a systematic review and meta-analysis. *J Antimicrob Chemother* 2008; 61:26-38.
8. Zuckermann J, Moreira LB, Stoll P, Moreira LM, Kuchenbecker RS, Polanczyk CA. Compliance with a critical pathway for the management of febrile neutropenia and impact on clinical outcomes. *Ann Hematol* 2008; 87:139-145.
9. Giblin TB, Sinkowitz-Cochran RL, Harris PL, et al. Clinicians' perceptions of the problem of antimicrobial resistance in health care facilities. *Arch Intern Med* 2004; 164:1662-1668.
10. Wester CW, Durairaj L, Evans AT, Schwartz DN, Husain S, Martinez E. Antibiotic resistance: a survey of physician perceptions. *Arch Intern Med* 2002; 162:2210-2216.
11. Grimshaw JM, Shirran L, Thomas R, et al. Changing provider behavior: an overview of systematic reviews of interventions. *Med Care* 2001; 39(8 Suppl 2):II2-45.
12. Cadieux G, Tamblyn R, Dauphinee D, Libman M. Predictors of inappropriate antibiotic prescribing among primary care physicians. *CMAJ* 2007; 177:877-883.