Trends in nosocomial bloodstream infections following health care restructuring in Alberta between 1999 and 2005

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OBJECTIVE: A previous study at the University of Alberta Hospital/Stollery Children's Hospital in Edmonton, Alberta, revealed an increase in hospital-acquired bloodstream infection (BSI) rates associated with an increase in patient acuity during a period of public health care delivery restructuring between 1993 and 1996. The present study assessed trends in BSIs since the end of the restructuring.

DESIGN: Prospective surveillance for BSIs was performed using Centers for Disease Control and Prevention (USA) criteria for infection. BSI cases between January 1, 1999, and December 31, 2005, were reviewed. Available measures of patient volumes, acuity and BSI risk factors between 1999 and 2005 were also reviewed from hospital records.

SETTING: The University of Alberta Hospital/Stollery Children's Hospital (617 adult and 139 pediatric beds, respectively).

PATIENTS: All pediatric and adult patients admitted during the above-specified period with one or more episodes of BSIs.

RESULTS: There was a significant overall decline in the BSI number and rate over the study period between 1999 and 2005. The downward trend was widespread, involving both adult and pediatric populations, as well as primary and secondary BSIs. During this period, the number of hospital-wide and intensive care unit admissions, intensive care unit central venous catheter-days, total parenteral nutrition days and number of solid-organ transplants were either unchanged or increased. Gram-positive bacterial causes of BSIs showed significant downward trends, but Gram-negative bacterial and fungal etiologies were unchanged.

CONCLUSIONS: These data imply that, over time, hospitals can gradually adjust to changing patient care circumstances and, in this example, control infectious complications of health care delivery.

Key Words: Bloodstream infections; BSI; Health care delivery; Health care restructuring; Infection control; Trends

Hospital-acquired (nosocomial) infections are the most common complication of health care delivery (1). Bloodstream infections (BSIs) are especially serious, and, because they are readily detectable through prospective surveillance, they are useful markers of long-term trends in infection rates. Occurrences of health care-acquired infections are known to be sensitive to processes of care (2,3). The 1993 to 1996 restructuring era of public health care delivery in the province of Alberta involved a dramatic budgetary funding cut for existing health care services, and a significant shifting of certain types of patients from acute tertiary hospitals to community-based hospital settings. This also resulted in a significant reduction in the operational budget of the University of Alberta Hospital and the Stollery Children’s Hospital (located within the University of Alberta Hospital) in Edmonton, Alberta, and a marked concomitant increase in patient acuity and in primary and secondary BSI rates (4).

In the present follow-up study, we sought to analyze the trends of both hospital activity and patient acuity as well as BSIs during the subsequent seven years following the previous report (4).

PATIENTS AND METHODS

The present study was conducted at the University of Alberta Hospital and Stollery Children’s Hospital – a hospital complex with 139 pediatric and 617 adult beds, with over 700,000 patients treated annually from western and northern Canada. This is the principal teaching facility of the University of Alberta’s Faculty of Medicine and Dentistry. A full range of diagnostic and treatment services are offered including cardiac surgery, neurosurgery and...
neurology, general surgery, internal medicine and its subspecialty services, renal dialysis, emergency and solid-organ transplant (SOT) for both the pediatric and the adult population. Obstetrics/gynecology and ophthalmology services are not included. There are seven intensive care units (ICUs — coronary, adult cardiac surgery, adult neurosurgery, adult medical-surgical, burns, pediatric and neonatal), which make up 14.4% of rated beds. No change in services provided occurred during the study period.

Hospital volume and acuity
To assess the trends in hospital patient care volume, the number of annual patient-days (overall) and admissions in both hospitals and in the seven ICUs were obtained. To assess changes in the prevalence of risk factors for BSI, facility-wide days-of-use of total parenteral nutrition (TPN) supplied by the hospital pharmacy (5,6), central venous catheter (CVC) days-of-use by ICUs (excluding neonatal ICUs) (7-9) and annual number of all on-site SOTs (kidney, liver, heart, lung and heart-lung) were determined. Data on the number of hemodialysis runs performed annually by the hemodialysis unit, the extent of mechanical ventilation use in the ICUs or CVC days-of-use outside of the ICUs for the period of the current study were not available for use as additional indicators of acuity.

Hospital-acquired BSIs and rates
Prospective surveillance for hospital-acquired BSIs in all units has been performed in the facility since 1986 (except 1998) by prospective monitoring of clinical microbiology laboratory reports as well as review of patient charts by the hospitals’ infection control practitioners, as previously described (10,11). The Centers for Disease Control and Prevention (USA) criteria for infection are used (12,13). Infection rates are calculated using patient-days, patient admissions and catheter-days as denominators where applicable – all supplied by the hospitals’ information systems department and the respective ICUs. ICU CVC-associated BSI rates were calculated using CVC line-days as denominators, which were supplied by the ICU departments (9,14). Primary BSIs are attributable to CVCs only, which may include a small number of transient in-ICU hemodialysis and peripherally inserted central catheter lines, and are exclusive of all peripheral lines. Secondary BSIs are attributable to all other body sources and exclusive of all intravenous devices – central or peripheral. Infections and infection rates occurring in the seven years (1999 to 2005) following the end of the 1993 to 1996 Alberta health care restructuring were analyzed.

Statistical calculations
To detect any significant monotonic, linear temporal trends in the rates, a nonparametric Mann-Kendall test (15) was performed. In the Mann-Kendall test, a negative (positive) value of S, where S is the Kendall trend score, indicates a downward (upward) trend. The magnitude of the linear trend in terms of slope Q was then estimated using a nonparametric Sen’s method (15). P value shows statistical significance of the trend analysis. The calculations were performed using an Excel (Microsoft Corporation, USA) macrotemplate MAKESENS (Mann-Kendall test for trend and Sen’s slope estimates [16]).

RESULTS
Hospital volume and acuity (Table 1)
Over the 10 years following the restructuring era, there was a steady rise in the number of total admissions at the University

| TABLE 1 |
| Hospital volume and activity by year (1999 to 2005) |

|          | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 |
|----------|------|------|------|------|------|------|------|
| Admissions, n |
| Total    | 31,186 | 30,155 | 30,327 | 31,724 | 33,285 | 34,826 | 35,986 |
| Adult    | 26,701 | 25,592 | 25,376 | 25,634 | 26,569 | 28,097 | 29,050 |
| Pediatric | 4485  | 4563  | 4951  | 6090  | 6716  | 6729  | 6936  |
| Patient-days, n |
| Total    | 237,145 | 226,365 | 251,350 | 251,530 | 266,607 | 276,443 | 281,259 |
| Adult    | 205,092 | 202,880 | 221,943 | 217,151 | 228,600 | 236,397 | 241,829 |
| Pediatric | 32,053 | 23,485 | 29,407 | 34,379 | 38,007 | 40,046 | 41,340 |
| ICU admissions, n |
| Total    | 921 | 951 | 822 | 611 | 814 | 793 | 979 |
| Adult    | 677 | 612 | 579 | 422 | 603 | 573 | 749 |
| Pediatric | 244  | 339  | 243  | 189  | 211  | 220  | 231  |
| ICU patient-days, n |
| Total    | 29,655 | 25,791 | 27,212 | 29,373 | 30,449 | 32,396 | 32,877 |
| Adult    | 26,878 | 22,775 | 23,849 | 25,308 | 26,250 | 27,776 | 28,389 |
| Pediatric | 2777  | 3016  | 3363  | 4065  | 4199  | 4620  | 4488  |
| ICU central venous catheter line-days, n |
| Total    | 15,293 | 15,273 | 13,260 | 17,976 | 18,806 | 20,275 | 22,276 |
| Adult    | 10,824 | 11,618 | 9140 | 13,438 | 14,542 | 15,385 | 16,209 |
| Pediatric | 4469  | 3655  | 4120  | 4538  | 4264  | 4890  | 6067  |
| Total parenteral nutrition days, n |
| Total    | 17,352 | 14,883 | 14,634 | 16,003 | 15,664 | 17,177 | 17,867 |
| Adult    | 11,618 | 10,688 | 10,126 | 10,606 | 10,480 | 11,251 | 11,733 |
| Pediatric | 5734  | 4195  | 4508  | 5397  | 5184  | 5926  | 6134  |
| Transplant procedures (solid organ), n | 181 | 209 | 228 | 235 | 191 | 221 | 269 |

ICU Intensive care unit
The incidence of bloodstream infections following health care restructuring of Alberta/Stollery Children’s Hospitals, in proportion with an 18.5% population growth in the city of Edmonton. Incidence rates of new admissions per unit of patient time at risk were comparable through time (data not shown). This was also paralleled by an increasing number of patient-days spent in the hospital and in the ICUs annually. Additionally, within the hospital’s five adult and one pediatric ICUs (neonatal ICU excluded), the annual use of CVCs showed considerable upward trend over the study period, with a lesser nonsignificant upward trend observed in the adults’ and pediatrics’ inpatient TPN use. The number of SOTs (both children and adult) at the site rose from 181 cases in 1999 to 269 cases in 2005.

**Hospital-acquired primary BSIs and rates (Table 2)**

From 1999 to 2005, there were a total of 475 episodes of ICU-acquired primary BSIs, which occur largely as a complication of intravascular catheterization. A steady and significant downward trend was observed in the rate of primary BSIs in the adult population (S=–13; P=0.033), which fell from 4.25 episodes per 1000 catheter-days in 1999 to 3.15 episodes per 1000 catheter-days by 2005. The overall trend within the pediatric population remained largely unchanged over our study period despite a seeming nonsignificant upward trend peaking in 2002.

**Hospital-acquired secondary BSIs and rates (Table 3)**

Although the rate of secondary BSIs in the adult and pediatric groups of patients each showed a positive downward trend during this study period (S=–11; P=0.06 for both; Q slope=–0.04 and –0.10, respectively), they did not reach statistical significance individually. The combined rate resulted, however, in a significant downward trend overall (S=–15; Q=–0.03; P=0.016). The rates of pneumonia-related BSI displayed a significant reduction over the duration of the study period (S=–15; P= 0.017).

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**Table 2**

|                      | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | Total | P    |
|----------------------|------|------|------|------|------|------|------|-------|------|
| All primary BSI      |      |      |      |      |      |      |      |       |      |
| Total number of ICU CVC lines infected | 63   | 75   | 51   | 83   | 75   | 65   | 63   | 475   | –    |
| Total central line-days | 15,293 | 15,273 | 13,260 | 17,976 | 18,806 | 20,275 | 22,276 | 123,159 | –    |
| Rate per 1000 catheter-days | 4.12 | 4.91 | 3.85 | 4.62 | 3.99 | 3.21 | 2.83 | 3.86 | 0.033* |
| Pediatric            |      |      |      |      |      |      |      |       |      |
| Total number of ICU CVC lines infected | 17   | 15   | 14   | 23   | 18   | 21   | 12   | 120   | –    |
| Total central line-days | 4,469 | 3,655 | 4,120 | 4,538 | 4,264 | 4,890 | 6,067 | 32,003 | –    |
| Rate per 1000 catheter-days | 3.80 | 4.10 | 3.40 | 5.07 | 4.22 | 4.29 | 1.98 | 3.75 | 0.50  |
| Adult                |      |      |      |      |      |      |      |       |      |
| Total number of ICU CVC lines infected | 46   | 60   | 37   | 60   | 57   | 44   | 51   | 355   | –    |
| Total central line-days | 10,824 | 11,618 | 9,140 | 13,438 | 15,442 | 16,209 | 16,209 | 91,156 | –    |
| Rate per 1000 catheter-days | 4.25 | 5.16 | 4.05 | 4.46 | 3.92 | 2.86 | 3.15 | 3.89 | 0.033* |

*Total central line-days’ and ‘rate per 1000 catheter-days’ are both based on intensive care unit (ICU) central venous catheter (CVC) days only. P value assesses trends in rates. *P<0.05

|                      | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | Total | S   | Q   | P   |
|----------------------|------|------|------|------|------|------|------|-------|-----|-----|-----|
| All secondary BSI    |      |      |      |      |      |      |      |       |     |     |     |
| Total BSIs, n        | 181  | 213  | 180  | 189  | 153  | 172  | 1240 | –     |      |     |     |
| Total patient-days   | 237,145 | 226,365 | 251,350 | 251,530 | 266,607 | 276,443 | 281,259 | 1,790,699 | –   |     |     |
| Rate per 1000 patient-days | 0.76 | 0.94 | 0.72 | 0.67 | 0.57 | 0.62 | 0.61 | 0.69 | –15 | 0.03 | 0.016* |
| Pediatric            |      |      |      |      |      |      |      |       |     |     |     |
| Total BSIs, n        | 29   | 34   | 27   | 38   | 28   | 36   | 211  | –     |      |     |     |
| Total patient-days   | 32,053 | 23,485 | 29,407 | 34,379 | 38,007 | 40,046 | 39,430 | 236,807 | –   |     |     |
| Rate per 1000 patient-days | 0.90 | 1.45 | 0.92 | 1.11 | 0.74 | 0.90 | 0.89 | 0.89 | –11 | 0.10 | 0.060 |
| Adult                |      |      |      |      |      |      |      |       |     |     |     |
| Total BSIs, n        | 152  | 179  | 153  | 131  | 125  | 136  | 153  | 1029 | –   |     |     |
| Total patient-days   | 205,092 | 202,880 | 221,943 | 217,151 | 228,600 | 236,397 | 241,829 | 1,553,892 | –   |     |     |
| Rate per 1000 patient-days | 0.74 | 0.88 | 0.69 | 0.60 | 0.55 | 0.58 | 0.63 | 0.66 | –11 | 0.04 | 0.060 |

**Secondary source BSI adult rates**

|                      | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | Total | S   | Q   | P   |
|----------------------|------|------|------|------|------|------|------|-------|-----|-----|-----|
| Urinary tract infection source |      |      |      |      |      |      |      |       |     |     |     |
| Total BSIs, n        | 30   | 18   | 15   | 28   | 22   | 27   | 34   | 174   |     |     |     |
| Rate per 1000 patient-days | 0.15 | 0.09 | 0.07 | 0.13 | 0.10 | 0.11 | 0.14 | 0.11  | 3   | 0.004 | 0.728 |
| Pneumonia source      |      |      |      |      |      |      |      |       |     |     |     |
| Total BSIs, n        | 37   | 55   | 38   | 38   | 38   | 27   | 31   | 264   |     |     |     |
| Rate per 1000 patient-days | 0.18 | 0.27 | 0.17 | 0.17 | 0.17 | 0.11 | 0.13 | 0.17  | –15 | 0.013 | 0.017* |
| Superficial skin infection source |      |      |      |      |      |      |      |       |     |     |     |
| Total BSIs, n        | 2    | 3    | 1    | 4    | 2    | 2    | 7    | 21    |     |     |     |
| Rate per 1000 patient-days | 0.010 | 0.015 | 0.006 | 0.018 | 0.009 | 0.008 | 0.029 | 0.014 | 3   | 0.002 | 0.728 |

*P value assesses trends in rates. *P<0.05
unchanged over this time. Microorganisms, including Staphylococcus aureus and all other Gram-negative organisms, remained unchanged over this time.

The rate of infection involving other BSI-implicated species (Q=–0.0063) infection rates also showed a downward trend. The rate of infection involving other BSI-implicated species (Q=–0.015) and (Q=–0.031) all showed a downward trend. The fall in the primary BSIs, particularly among adults and occurring in most circumstances as a complication of intra-vascular catheterization, was reflected by the marked decline in Gram-positive bacteremia, and particularly Enterococcus species.

In the present study, we have found that the overall combined BSI rates, both primary and secondary, among adult and pediatric populations served by the University of Alberta Hospital/Stollery Children's Hospital fell significantly following the end of the restructuring era between 1993 and 1996. By 2005, the hospitals' BSI rate had returned to the baseline rate seen immediately before the restructuring era (analysis data not shown). The fall in the primary BSIs, particularly among adults and occurring in most circumstances as a complication of intravascular catheterization, was reflected by the marked decline in Gram-positive bacteremia, and S. aureus in particular, while bacteremia involving other common pathogens remained mostly unchanged. Over the same period, the hospital's patient volume, length of stay (expressed in patient-days), and BSI risk factors such as CVC use, TPN use and number of SOTs, increased substantially.

| Pathogens                              | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | Mean | S    | Q     | P    |
|----------------------------------------|------|------|------|------|------|------|------|------|------|-------|------|
| Candida species                        |      |      |      |      |      |      |      |      |      |       |      |
| Total, n                               | 29   | 25   | 23   | 17   | 22   | 16   | 29   | 23   |      |       |      |
| Rate per 1000 patient-days             | 1.09 | 0.98 | 0.91 | 0.66 | 0.83 | 0.57 | 1.00 | 0.86 | –11  | –0.011| 0.064|
| Coagulase-negative Staphylococcus      |      |      |      |      |      |      |      |      |      |       |      |
| Total, n                               | 135  | 105  | 130  | 117  | 108  | 123  | 105  | 118  |      |       |      |
| Rate per 1000 patient-days             | 5.06 | 4.10 | 5.12 | 4.56 | 4.06 | 4.38 | 3.61 | 4.40 | –13  | –0.035| 0.030*|
| Enterococcus species                   |      |      |      |      |      |      |      |      |      |       |      |
| Total, n                               | 67   | 66   | 51   | 47   | 46   | 52   | 55   | 55   |      |       |      |
| Rate per 1000 patient-days             | 2.51 | 2.58 | 2.01 | 1.83 | 1.73 | 1.85 | 1.89 | 2.05 | –11  | –0.015| 0.064|
| Staphylococcus aureus                  |      |      |      |      |      |      |      |      |      |       |      |
| Total, n                               | 81   | 75   | 73   | 70   | 44   | 56   | 51   | 64   |      |       |      |
| Rate per 1000 patient-days             | 3.03 | 2.93 | 2.88 | 2.73 | 1.66 | 1.99 | 1.76 | 2.41 | –17  | –0.031| 0.007*|
| Pseudomonas species                    |      |      |      |      |      |      |      |      |      |       |      |
| Total, n                               | 17   | 20   | 18   | 16   | 15   | 12   | 19   | 17   |      |       |      |
| Rate per 1000 patient-days             | 0.64 | 0.78 | 0.71 | 0.62 | 0.56 | 0.43 | 0.65 | 0.63 | –13  | –0.0063| 0.036*|
| All other Gram-negative organisms      |      |      |      |      |      |      |      |      |      |       |      |
| Total, n                               | 26   | 21   | 23   | 28   | 20   | 25   | 28   | 24   |      |       |      |
| Rate per 1000 patient-days             | 0.97 | 0.82 | 0.91 | 1.09 | 0.75 | 0.89 | 0.96 | 0.91 | 1    | 0.0001| 0.50  |
| Others                                 |      |      |      |      |      |      |      |      |      |       |      |
| Total, n                               | 3    | 5    | 0    | 0    | 4    | 3    | 3    | 3    |      |       |      |
| Rate per 1000 patient-days             | 0.11 | 0.20 | 0.00 | 0.00 | 0.15 | 0.11 | 0.10 | 0.10 | –4   | –0.0004| 0.319 |
| Total adult patient admission, n        | 26,701| 25,592| 25,376| 25,634| 25,669| 28,097| 29,050| 26,717|      |       |      |

P assesses trends in rates. *P<0.05

Hospital-acquired BSIs by organisms (Table 4)
Table 4 shows organism-specific trends for the seven most common microorganisms implicated in BSIs reported in the hospital. Between 1999 and 2005, a steady decline in Gram-positive organisms as agents of BSIs was observed. Specifically, coagulase-negative Staphylococcus (Q=–0.035), Enterococcus species (Q=–0.015) and Staphylococcus aureus (Q=–0.031) all showed downward trends and, with the exception of Enterococcus species, all reached statistical significance (Table 4). Pseudomonas species (Q=–0.0063) infection rates also showed a downward trend. The rate of infection involving other BSI-implicated microorganisms, including Candida species, Corynebacterium species, anaerobes and all other Gram-negative organisms, remained unchanged over this time.

**DISCUSSION**

In the present study, we have found that the overall combined BSI rates, both primary and secondary, among adult and pediatric populations served by the University of Alberta Hospital/Stollery Children's Hospital fell significantly following the end of the restructuring era between 1993 and 1996. By 2005, the hospitals' BSI rate had returned to the baseline rate seen immediately before the restructuring era (analysis data not shown). The fall in the primary BSIs, particularly among adults and occurring in most circumstances as a complication of intravascular catheterization, was reflected by the marked decline in Gram-positive bacteremia, and S. aureus in particular, while bacteremia involving other common pathogens remained mostly unchanged. Over the same period, the hospital's patient volume, length of stay (expressed in patient-days), and BSI risk factors such as CVC use, TPN use and number of SOTs, increased substantially.

Our current findings are counter to the trends observed during the restructuring period in Alberta (1993 to 1996), which saw a period of rapid health care downsizing and shifting care and resources from acute tertiary hospitals to community-based hospital settings (4). During that era, bed numbers at the University of Alberta Hospital/Stollery Children's Hospital fell by 10%, and volumes declined following a 19% drop in the annual number of admissions and a 17% drop in the annual patient-days parameter. Acuity soared concomitantly. Markers of hospital acuity such as ICU use of CVCs, number of TPN days, and number of hemodialysis runs reflected that trend, with increases seen at 41%, 25% and 9%, respectively (4). Concurrently, some services within tertiary centres saw a marked increase in patient-days (neurosurgery 49%, nephrology 30%, orthopedic surgery 24% and general surgery 16%). During this same period, hospital-acquired BSIs saw a dramatic increase such that toward the end of the restructuring period, there was an annual 31% increase in the number of hospital-acquired BSIs and a 60% increase in BSI rate compared with that observed in the pre-restructuring era.

In spite of the soaring of facility volumes and acuity since the end of the restructuring era, the present study shows that BSI rates have steadily declined in the 10 years that followed to near pre-restructuring baseline. During the same period, Census Canada data revealed that the city of Edmonton saw a steady population growth of 18.5%, 8.1% of which occurred before the beginning of the current study. Such concomitant population growth before and during our study may have accounted for the increased hospital activity and volume we have observed. In contrast, it is unlikely that a technological improvement in care is solely responsible for the decline in BSI rates. Improved care of CVC lines and the introduction of antibiotic-impregnated catheters (which
occurred midpoint of the study period) may have accounted for some of the observed trend, especially in the decline of the primary BSI rate. However, introduction of antimicrobial-impregnated catheters would be expected to have a single-step effect on BSI rate rather than a gradual downward trend. No systematic institution-wide process to improve the quality of catheter care was implemented during the study period. Furthermore, the reductions seen were widespread, involving pediatric and adult patient groups, and secondary and primary BSIs. Thus, a single change in the process of care is unlikely to have resulted in such widespread and progressive decline in BSI rates. Rather, the most likely explanation for our observed BSI rate decline, considering all observations gathered, would be that a collection of potentially heterogeneous health care process improvements occurred within the University of Alberta Hospital/Stollery Children’s Hospital during our study period. Examples of such care processes would include improved CVC care and use, mouth care, skin antisepsis and hand hygiene, among others. Unlike BSIs involving Gram-positive organisms, BSIs with *Pseudomonas aeruginosa* very infrequently involve CVCs as primary sources (17,18). Rather, bacteremia with *Pseudomonas aeruginosa* is often secondary, originating most commonly from primary sites such as the respiratory system (eg, ventilator-associated pneumonia), and, to a lesser extent, urinary and surgical wound sites (17). This offers a plausible explanation for the concurrent decline in the rates of *Pseudomonas aeruginosa* BSIs and that of pneumonia-derived secondary BSI source in the present study. Although multifactorial in cause, enhanced quality of care through improved oral hygiene and ICU-assisted respiratory support would invariably account for the observed reduction in pneumonia rates at our site over the study period.

**REFERENCES**

1. Leape LL, Brennan TA, Laird N, et al. The nature of adverse events in hospitalized patients. Results of the Harvard Medical Practice Study II. N Engl J Med 1991;324:377-84.
2. Siegel J, Rhinehart E, Jackson M, Chiarello L; the Healthcare Infection Control Practices Advisory Committee. Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings. Atlanta, Georgia: Centers for Disease Control and Prevention, 2007.
3. Pittet D, Donaldson L. Challenging the world: Patient safety and health care-associated infection. Int J Qual Health Care 2006;18:4-8.
4. Taylor GD, McKenzie M, Kirkland T, Buchanan-Chell M, Wiens R. The impact of health care restructuring on nosocomially acquired bloodstream infections. Can J Infect Dis 2000;11:29-32.
5. Buchman AL. Catheter-related complications of total parenteral nutrition. Am J Clin Nutr 1993;12:379-85.
6. Marra AR, Opilla M, Edmond MB, Kirby DF. Epidemiology of bloodstream infections in patients receiving long-term total parenteral nutrition. J Clin Gastroenterol 2002;36:118-23.
7. Fricklin SK, Welbel SF, Weinstein RA. Magnitude and prevention of nosocomial infections in the intensive care unit. Infect Control Hosp Epidemiol 1991;11:479-96.
8. Gastmeier P, Sohr D, Oeffers C, Behnke M, Riiden H. Risk factors for death due to nosocomial infection in intensive care unit patients: Findings from the Krankenhaus Infections Surveillance System. Infect Control Hosp Epidemiol 2007;28:466-72.
9. Jarvis WR, Edwards JR, Culver DH, et al. Nosocomial infection rates in adult and pediatric intensive care units in the United States. National Nosocomial Infections Surveillance System. Am J Med 1991;91(2B):185S-91S.
10. Taylor GD, Buchanan-Chell M, Kirkland T, McKenzie M, Wiens R. Nosocomial Gram-negative bacteremia. Int J Infect Dis 1997;1:202-5.
11. Taylor GD, McKenzie M, Buchanan-Chell M, Cabillo L, Chui L, Kowalewska-Grochowska K. Central venous catheters as a source of hemodialysis-related bacteremia. Infect Control Hosp Epidemiol 1998;19:643-6.
12. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. Am J Infect Control 1988;16:128-40.
13. Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG. CDC definitions of nosocomial surgical site infections, 1992: A modification of CDC definitions of surgical wound infections. Am J Infect Control 1992;20:271-4.
14. Gaynes RP, Solomon S. Improving hospital-acquired infection rates: The CDC experience. Jt Comm J Qual Improv 1996;22:457-67.
15. Gilbert RO. Statistical methods for environmental pollution monitoring. New York: Van Nostrand Reinhold Co, 1987.
16. Satlin T, Mänttä A, Aamila P, Paasiku-Airola T, Amnell T. Detecting Trends of Annual Values of Atmospheric Pollutants by the Mann-Kendall Test and Sen's Slope Estimates – The Excel Template Application MAKSENS. Helsinki: Finnish Meteorological Institute, 2002.
17. Sherertz RJ, Sarabji FA. A three-year study of nosocomial infections associated with *Pseudomonas aeruginosa*. J Clin Microbiol 1983;18:160-4.
18. Tullu MS, Deshmukh CT, Baveja SM. Bacterial profile and antimicrobial susceptibility pattern in catheter related nosocomial infections. J Postgrad Med 1998;44:7-13.
19. World Alliance for Patient Safety. Global Patient Safety Challenge. Geneva, Switzerland: World Health Organization, 2005.
