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Secular trends of healthcare-associated infections at a teaching hospital in Taiwan, 1981–2007

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SUMMARY

The National Taiwan University Hospital (NTUH) adopted international guidelines for surveillance and control of healthcare-associated infection (HCAI) in 1981. This report describes the secular trends in HCAI at the NTUH over the past 27 years according to site of infection, aetiological agents and control measures. Clinical and microbiological data were collected by infection prevention and control nurses using a standardised case-record form. Specific control programmes were implemented and/or intensified as needed. Poisson or negative binomial regression analysis was used to quantify time trends of the incidence of HCAI. The annual number of discharges increased from 25 074 to 91 234 with a parallel increase in the Charlson comorbidity index. Active HCAI surveillance and periodic feedback were associated with a marked decrease in surgical site infections from 1981 to 2007 (2.5 vs 0.5 episodes per 100 procedures, $P < 0.0001$). On the other hand, there was a 4.8-fold increase in bloodstream infections (BSIs) (0.39 vs 1.88 episodes per 100 discharges, $P < 0.0001$). The average annual increase of pathogen-specific HCAI incidence during 1981–2007 was 11.4% for methicillin-resistant *Staphylococcus aureus* (MRSA), 75.4% for extensively drug-resistant *A. baumannii* (XDRAB), and 7.5% for *Candida albicans* ($P < 0.0001$, respectively). The infection prevention and control programme was upgraded in 2004 by implementing annual, intensive, project-based control programmes, and decreases in rates of HCAI, BSI, MRSA and XDRAB were observed. This long term study demonstrates the need to couple surveillance of HCAI with focused control programmes. Hospitals must invest in adequate manpower to accomplish these goals.

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Introduction

Ongoing surveillance of healthcare-associated infection (HCAI) is an essential component of hospital infection control programmes. The goals are to assess the burden of infectious diseases, identify important problems, monitor the efficacy of specific interventions and support rational hospital policies.¹ The National Nosocomial

Infections Surveillance System was established in the 1980s. HCAs were reported to be significantly decreased in hospitals that adopted surveillance programmes.^{2,3} Hospital-wide surveillance programmes are highly labour intensive and tend to divert resources needed to implement control measures and prevention activities. Consequently, they are often of minimal interest to hospital policymakers except during major outbreaks such as severe acute respiratory syndrome (SARS). It has become increasingly apparent that hospital support for surveillance programmes needs to be justified by improved outcomes. To accomplish these goals they must be closely linked to effective interventional strategies.

The first infection prevention and control hospital-wide HCAI surveillance programme in Taiwan, based on international

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guidelines, was established at the National Taiwan University Hospital (NTUH) in 1981. A vigorous hospital-wide hand hygiene programme was initiated in 2004. This report describes the secular trends in HCAI at the NTUH during the past 27 years (1981–2007) according to site of infection, aetiological agents and control measures.

Methods

Hospital setting

The NTUH is a 2200-bedded teaching hospital located in Taipei, Taiwan. It provides both primary and tertiary medical care, and served approximately 2000 inpatients, 7000 outpatients, and 300 emergency department visits daily in 2007. There are 220 intensive care unit (ICU) beds, 1866 beds in other acute care units, and 160 beds in a psychiatric day care unit. Among the acute care units are the following beds: 700 on medical wards, 800 on surgical wards, 200 on paediatric wards, 130 on gynaecology wards, and 100 on oncology wards. There are 68 negative pressure isolation rooms.

Infection prevention and control programme

The NTUH Infection Control Team currently consists of 10 full-time infection control nurses (ICNs), two full-time technicians and is supervised by two infection disease physicians. Prospective, hospital-wide on-site surveillance of HCAI was conducted by weekly visits of ICNs to all patient units. Hospital charts were reviewed to identify patients with HCAs according to definitions of the Centers for Disease Control and Prevention with the help of infectious disease physicians at weekly meetings.^{4–6} The data were collected on standardised data collection forms (Appendix 1) and incorporated into the computer database by manual entry. The unit-specific incidences of HCAI (episodes per 100 discharges) including overall and site-specific infection rates were analysed monthly and compared with historical data. Feedback was provided to each service to stimulate intervention measures.

Infection prevention and control events and interventions

Multiple special infection prevention and control events and interventions occurred during the study period. Prevention and control measures for surgical site infection (SSI) included intensified surveillance of SSI with feedback to the surgeons during 1988–1990, monitoring the timing and choice of prophylactic antibiotics, reinforcement of aseptic procedures, amelioration and monitoring ventilation in the operation rooms since 1991, and enhanced environmental cleaning in 1992. Organism-specific isolation precautions for methicillin-resistant *Staphylococcus aureus* (MRSA) were initiated in 1990 and this was augmented in 1993 for extensively drug-resistant *Acinetobacter baumannii* (XDRAB) in 2001 and SARS-specific precautions during March to June 2003.^{7–9} The infection control guideline for XDRAB requiring contact isolation (single room cohort) was introduced in 2001. This was reinforced the following year by requiring ICNs to inform staff to isolate patients with XDRAB. Hospital-wide surveillance of HCAs was interrupted temporarily during the SARS epidemic because the ICNs were fully occupied with containing SARS. The infection prevention and control programme was upgraded in 2004 by implementing annual, intensive, project-based control programmes. The hospital-wide hand hygiene programme was instituted in April 2004 and has continued as an annual campaign. Targeted surveillance and control for device-associated infections in ICUs (e.g. urinary catheters, central venous catheters, and ventilators) and SSI for selected surgical procedures were initiated

in 2000 and intensified since 2005. Data were analysed and compared with national and international data and feedback every quarter.

Microbiological studies

Culture data were obtained from computer-generated reports issued by the hospital clinical microbiology laboratory.¹⁰ The *in vitro* susceptibility of *Acinetobacter* isolates was determined by disc diffusion method.^{8,10} The following antibacterial agents were tested: cephalosporins (ceftazidime and cefepime), extended-spectrum penicillins (piperacillin-tazobactam), carbapenems (imipenem), aminoglycosides (gentamicin and amikacin), fluoroquinolones (ciprofloxacin), sulbactam and colistin. *In vitro* susceptibility testing of colistin was begun in July 2006. XDRAB was defined as *A. baumannii* isolates that were resistant to five or more classes of antibacterial agents.

Statistical analysis

Poisson regression was used to model the secular trends of the annual incidence (episodes per 100 discharges) of HCAs during 1981–2007.¹¹ The Poisson regression model form is written as

$$\log(Y) = \beta_0 + \beta_1 \times \text{time} + \log(PY)$$

where Y is the number of HCAI cases at time t , PY is the number of patient-years discharged at time t , β_0 represents the baseline level of HCAI rate (HCAI rate in 1981), β_1 represents the annual change of HCAI, and 'time' indicates the linear trend of HCAI, denoted as time in year from 1981. Estimated average annual changes during 1981–2007 were calculated by $(e^{\beta_1} - 1) \times 100\%$. The negative binomial regression was applied while the number of HCAI cases was overdispersed, i.e. the variance was greater than the mean.¹² $P < 0.05$ was considered to be significant. Statistical analyses were performed using SAS 9.1.3 (SAS Institute, Cary, NC, USA).

Results

The annual number of discharges and the severity of underlying diseases on admission, as defined by Charlson comorbidity index, are shown in Figure 1A.¹³ The number of acute care beds was 1846 in 1999 and 2212 in 2007. The number of discharges was 25 074 in 1981 and 91 234 in 2007. The average length of patient stay decreased from 11.3 in 1993 to 7.3 days in 2007. This was accompanied by an increasing proportion of patients admitted with multiple underlying conditions.

Secular trends in annual rates of overall infections

The annual infection rates increased slowly (average 0.3% per year, range –0.1% to 0.7%, $P = 0.16$) during 1981–2007 and fluctuated around 4.5 episodes per 100 discharges (Figure 1B). The major exception was an abrupt increase during 1989–1990 in HCAI with microbiological documentation and those cases without (Figure 1C). This was attributed to more intensive surveillance following adoption of the 1988 Centers for Disease Control (CDC, Atlanta, GA, USA) criteria.⁶

Secular trends in the distribution of infections according to site

The major sites of HCAs over the entire study period are shown in Figure 1D. The average annual change (95% confidence interval) for bloodstream infection (BSI) was 6.4% (5.5% to 7.4%, $P < 0.0001$); urinary tract infection (UTI), 1.9% (1.2% to 2.5%, $P < 0.0001$);

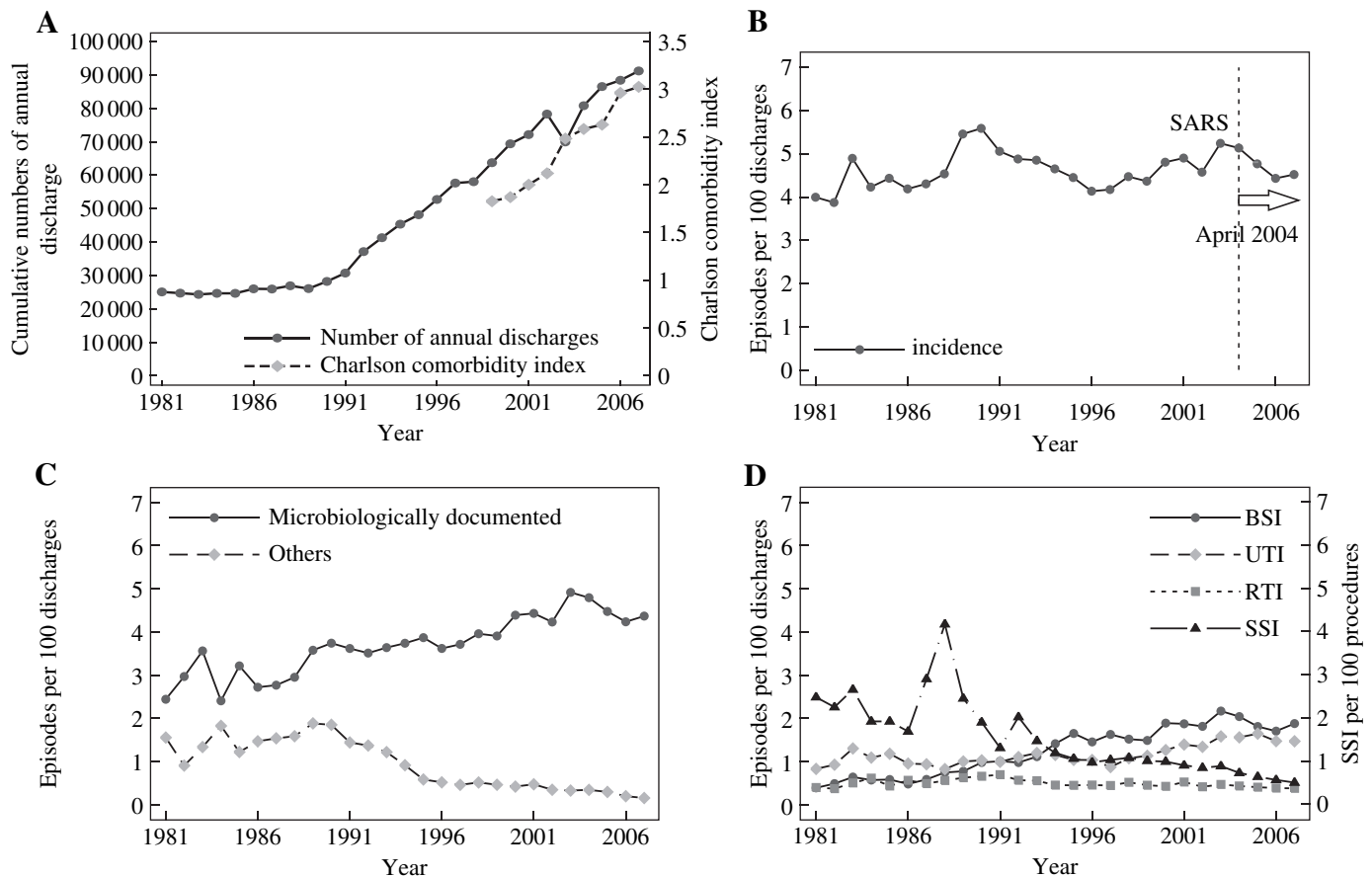


Figure 1. (A) Trends in annual discharges and Charlson comorbidity index of patients hospitalised at the National Taiwan University Hospital from 1981 to 2007 (data of Charlson comorbidity index are available from 1999 onwards). (B) The hospital-wide annual incidence (per 100 discharges) of healthcare-associated infections during 1981–2007. Dashed line/arrow: Reorganisation of infection control team, increase in manpower and hospital-wide hand hygiene programme. SARS, severe acute respiratory syndrome. (C) Time trends of the incidences of microbologically documented and other infections. (D) Hospital-wide annual incidence (per 100 discharges) of healthcare-associated infections by site during 1981–2007. BSI, bloodstream infection; RTI, respiratory tract infection; SSI, surgical site infection; UTI, urinary tract infection.

respiratory tract infection (RTI), -1.0% (-1.7% to -0.3% , $P = 0.0083$); and SSI, -6.1% (-7.2% to -5.0% , $P < 0.0001$). The differences in the incidence and proportion of the major sites contributing to HCAIs in 1981 and 2007 are shown in Table I. SSI was the leading cause of HCAI during 1981–1993. A peak in SSI was noted during 1988 to 1990. This was attributed to more intensive surveillance but without post-discharge surveillance (PDS). The incidence of SSI decreased sharply after intensified infection control programmes. BSI gradually increased over the study period. There was a 4.8-fold rise in BSI from 1981 to 2007 ($P < 0.0001$). BSI was the leading HCAI site during 1994–2007, accounting for 41.6% of HCAI in 2007. The incidence of UTI increased 1.8-fold ($P < 0.0001$).

Changes in the distribution of pathogens

The proportions of infections by pathogens in 1981 and 2007 are shown in Table I. Gram-negative bacteria were about twice as common as Gram-positives during both time periods. There was an 8.7-fold increase in fungal infections (mainly *Candida* spp.) from 1981 to 2007 ($P < 0.0001$). Rate of *C. difficile* infection increased from 0.004 episodes per 100 discharges in 1983 to 0.037 in 2007 ($P = 0.008$).

Secular trends in the major pathogens

Annual percentage changes in the incidences of pathogens causing all HCAI during 1981–2007 are shown in Table II. The

average annual increase of pathogen-specific HCAI incidence during 1981–2007 was 11.4% for MRSA, 7.5% for *C. albicans*, and 75.4% for XDRAB ($P < 0.0001$, respectively).

The incidences for all BSI pathogens increased significantly (Table III). The secular trends of pathogen-specific BSI rates closely mirrored the overall rates of HCAIs, except for anaerobes. The secular trends of the major pathogens causing BSI are shown in Figure 2A. Fungi (mainly *Candida* spp.) were rare in the 1980s and increased rapidly in later years. Note the decrease in BSI caused by *S. aureus*, *Acinetobacter* spp., and *C. albicans*, but not *Escherichia coli* after the implementation of a hand hygiene programme.

Secular trends for *S. aureus* infections

The secular trends of the annual incidence of *S. aureus* and MRSA are shown in Figure 2B. *S. aureus* steadily increased over the study period, peaked in 2001 and fell thereafter (year 2003 vs 2007; $P < 0.0001$). The incidence of MRSA paralleled that of all *S. aureus* infections and accounted for 69.2% of *S. aureus* infections at their peak in 2000.

Secular trends for *Acinetobacter* infections

The secular trends of the annual incidence of *Acinetobacter* and XDRAB are shown in Figure 2C. XDRAB began to appear in 1999, increased rapidly and peaked in 2005. XDRAB markedly decreased

Table I
Incidence of healthcare-associated infections and the proportion by site and pathogen at the National Taiwan University Hospital, 1981–2007

Parameters	1981	2007	Average annual change, % (95% CI)	P-value ^a
Total no. of discharges	25 074	91 234		
Total no. of infections	1002	4125		
Total no. of pathogens	1181	5081		
Overall incidence, per 100 discharges	4.00	4.52	0.3 (–0.1 to 0.7)	0.1621
Site-specific infection				
Surgical site				
No. of episodes	374	279		
Incidence, per 100 procedures	2.5	0.5	–6.1 (–7.2 to –5.0)	<0.0001
Proportion (%)	37.3	6.8		
Urinary tract				
No. of episodes	208	1340		
Incidence, per 100 discharges	0.83	1.47	1.9 (1.2 to 2.5)	<0.0001
Proportion (%)	20.8	32.5		
Respiratory				
No. of episodes	100	347		
Incidence, per 100 discharges	0.40	0.38	–1.0 (–1.7 to –0.3)	0.0083
Proportion (%)	10.0	8.4		
Bloodstream				
No. of episodes	98	1714		
Incidence, per 100 discharges	0.39	1.88	6.4 (5.5 to 7.4)	<0.0001
Proportion (%)	9.8	41.6		
Others				
No. of episodes	222	445		
Incidence, per 100 discharges	0.89	0.49	–3.6 (–5.1 to –2.1)	<0.0001
Proportion (%)	22.2	10.8		
Pathogens				
Gram-positive aerobic bacteria				
Incidence, per 100 discharges	0.91	1.25	1.1 (0.5 to 1.7)	0.0006
Proportion (%)	21.8	24.6		
Gram-negative aerobic bacteria				
Incidence, per 100 discharges	2.01	2.63	0.8 (0.3 to 1.2)	0.0018
Proportion (%)	65.5	57.5		
Anaerobic bacteria				
Incidence, per 100 discharges	0.34	0.16	–4.9 (–6.3 to –3.6)	<0.0001
Proportion (%)	10.5	3.1		
Fungi				
Incidence, per 100 discharges	0.09	0.79	7.0 (5.5 to 8.5)	<0.0001
Proportion (%)	1.9	14.6		

CI, confidence interval.

^a Negative binomial regression was used to model the secular trends of the annual incidence.

in association with the hand hygiene programme and possibly with other interventions between 2003 and 2007 ($P < 0.0001$).

Changes in the distribution of the five most common pathogens

There were modest place changes of the leading pathogens causing any HCAI, BSI and UTI during five-year intervals from 1981

Table II
Time trends of pathogen-specific healthcare-associated infections at the National Taiwan University Hospital, 1981–2007

Pathogen	Incidence (per 100 discharges)		Average annual change, % (95% CI)	P-value ^a
	1981	2007		
<i>Staphylococcus aureus</i>	0.199	0.404	3.1 (1.9 to 4.3)	<0.0001
Meticillin-resistant	0.028	0.272	11.4 (8.3 to 14.6)	<0.0001
Meticillin-susceptible	0.164	0.132	–2.8 (–3.9 to –1.7)	<0.0001
<i>Enterococcus</i> spp.	0.004	0.452	0.2 (–1.8 to 2.2)	0.8463
<i>Escherichia coli</i>	0.634	0.650	–0.2 (–1.3 to 0.9)	0.719
<i>Klebsiella</i> spp.	0.447	0.552	0.5 (–0.6 to 1.5)	0.3683
<i>Enterobacter</i> spp.	0.299	0.356	0.0 (–0.6 to 0.6)	0.9234
<i>Pseudomonas aeruginosa</i>	0.538	0.516	–1.7 (–2.4 to –1.0)	<0.0001
<i>Acinetobacter</i> spp.	0.227	0.393	2.4 (1.4 to 3.4)	<0.0001
Extensively drug-resistant	0.000	0.105	75.4 (46.9 to 109.3)	<0.0001
<i>Candida albicans</i>	0.016	0.272	7.5 (5.5 to 9.6)	<0.0001

CI, confidence interval.

^a Negative binomial regression was used to model the secular trends of the annual incidence.

to 2007. The leading pathogen causing BSI was *Klebsiella* spp. (18.6%) in 1981, *E. coli* (20.9%) in 1986, *Candida* spp. and other yeasts (18.6%) in 1996, *S. aureus* (12.7%) in 2001, and *Klebsiella* spp. (11.0%)

Table III
Time trends of pathogen-specific healthcare-associated bloodstream infections at the National Taiwan University Hospital during 1981 and 2007

Pathogen	Incidence (per 100 discharges)		Average annual change, % (95% CI)	P-value ^a
	1981	2007		
Gram-positive aerobic bacteria	0.092	0.617	8.4 (7.0 to 9.8)	<0.0001
<i>Staphylococcus aureus</i>	0.024	0.203	10.3 (8.1 to 12.5)	<0.0001
Meticillin-resistant	0.000	0.138	23.4 (16.9 to 30.2)	<0.0001
Meticillin-susceptible	0.020	0.066	3.0 (1.2 to 4.8)	0.0009
<i>Enterococcus</i> spp.	0.000	0.180	7.85 (6.3 to 9.3)	<0.0001
Gram-negative aerobic bacteria	0.291	1.137	5.4 (4.7 to 6.1)	<0.0001
<i>Escherichia coli</i>	0.048	0.180	3.3 (2.3 to 4.3)	<0.0001
<i>Klebsiella</i> spp.	0.076	0.246	5.8 (4.6 to 7.0)	<0.0001
<i>Enterobacter</i> spp.	0.048	0.166	5.2 (3.7 to 6.8)	<0.0001
<i>Pseudomonas aeruginosa</i>	0.016	0.153	4.0 (2.9 to 5.0)	<0.0001
<i>Acinetobacter</i> spp.	0.040	0.217	7.7 (6.3 to 9.1)	<0.0001
Extensively drug-resistant	0.000	0.045	62.1 (37.7 to 90.8)	<0.0001
Anaerobic bacteria	0.004	0.052	2.3 (1.0 to 3.6)	0.0005 ^b
Fungi	0.008	0.213	15.0 (9.9 to 20.4)	<0.0001
<i>Candida albicans</i>	0.000	0.105	13.5 (8.7 to 18.4)	<0.0001

^a Negative binomial regression.

^b Poisson regression.

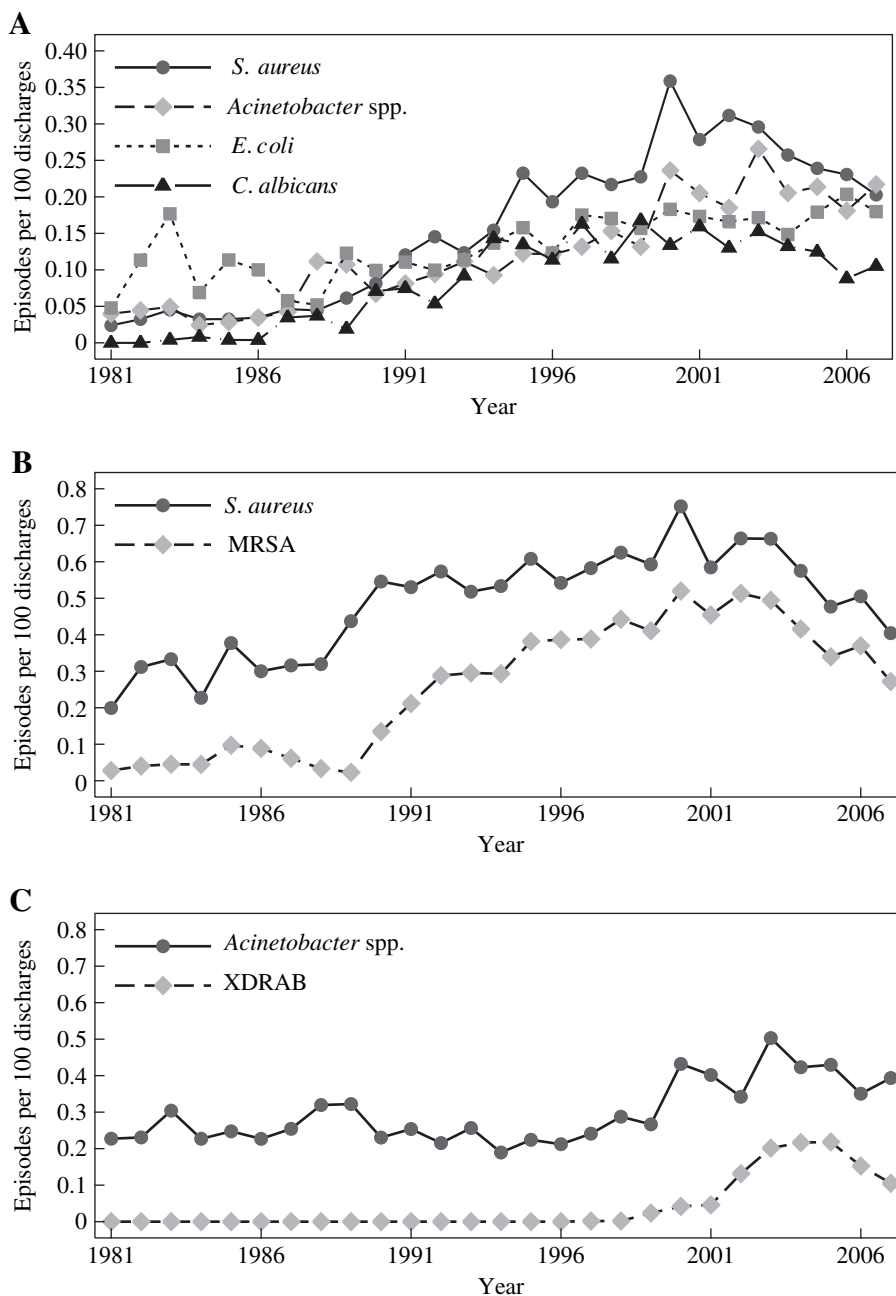


Figure 2. (A) Annual incidence (per 100 discharges) of the major pathogens causing healthcare-associated bloodstream infections during 1981–2007. (B) Annual incidence (per 100 discharges) of healthcare-associated infections due to *Staphylococcus aureus* and methicillin-resistant *S. aureus* (MRSA) during 1981–2007. (C) Annual incidence (per 100 discharges) of healthcare-associated infections due to *Acinetobacter* spp. and extensively resistant *Acinetobacter baumannii* during 1981–2007. XDRAB, extensively drug-resistant *A. baumannii*.

in 2007. Gram-negative bacilli accounted for 60% of healthcare-associated BSI in 2007. Among the leading five pathogens causing UTI, *E. coli* was the first or second most common pathogen followed by *C. albicans* and other yeasts, *Enterococcus* spp., *Enterobacter* spp., *Pseudomonas aeruginosa* and *Klebsiella* spp..

Discussion

This report describes the secular trends of HAIs over the course of a 27 year prospective hospital-wide surveillance programme in a large university hospital in Taiwan. The major findings are similar to those in tertiary care hospitals in western countries.^{3,14–16} There was a gradual increase in admissions of patients with severe

underlying disease. The overall rate of the HCAI increased slowly and has fluctuated at approximately 4.5 episodes per 100 discharges. This is in the high range reported by other tertiary care facilities.^{17–20} The time trend of overall infection rates tended to obscure the substantial changes in SSI rates, a 4.8-fold increase in BSI, an increase in UTI, the appearance of XDRAB and MRSA, and an 8.7-fold increase in fungal infections.

The remarkable decrease in SSI may result from improvements in surgical prophylaxis, active surveillance and periodic feedback, and changes in surgical practice including the increasing shift to 'day surgery' which led to decreased detection of SSIs in a system which depended on ICNs going through inpatient charts. However, there was no PDS apart from those patients readmitted for

postoperative complications. Changes in HCAs may be due to multiple factors (e.g. implementation of targeted surveillance, SARS outbreak, multidrug-resistant organism outbreaks, active surveillance, etc.), and the rates of HCAI may fluctuate over time. We instituted several focused control programmes to deal with the increasing occurrence of MRSA and XDRAB. These consisted of more intense surveillance, strict isolation procedures for patients with XDRAB and a hand hygiene programme to control multidrug-resistant organisms.

A notable decrease was observed in the overall HCAI rates since 2004 when a hospital-wide hand hygiene programme was launched. However, due to a limited postintervention period, it is not possible to attribute the decrease to the hand hygiene programme. Therefore further analysis is required by expanding the follow-up periods which might make the formal statistical inference possible.

Regarding pathogens causing healthcare-associated BSI, a multicentre study in the USA [Surveillance and Control of Pathogens of Epidemiological importance (SCOPE)] from 1995 to 2002 showed that Gram-positive organisms accounted for 65% of cases and the leading pathogens were coagulase-negative staphylococci, *S. aureus*, and enterococci.²¹ Furthermore, the proportion of healthcare-associated BSI due to Gram-positive cocci increased gradually.^{21–23} Most of the studies showed coagulase-negative staphylococci were the leading cause of healthcare-associated BSI.^{21,24–28} However, in this study, Gram-negative bacilli accounted for 60% of healthcare-associated BSI in 2007, and the leading pathogen was *Klebsiella* spp., which is very unusual in Europe and North America. Therefore when considering HCAs, regional factors should be considered. Despite these achievements we have not as yet been able to achieve our goal to reduce overall infection rates below 4.5%. It may be impossible to reduce the rate in a structurally and immunocompromised patient population that requires aggressive antimicrobial therapy for endogenous infections. A third of patients had one or more malignancies. This hospital also maintains very active organ and bone marrow transplantation programmes and ICUs. Rates of infection are more meaningful when adjusted for major underlying diseases and disease severity, such as the Charlson comorbidity index, the McCabe–Jackson criteria and Acute Physiological Assessment and Chronic Health Evaluation (APACHE) score.^{13,29,30} It is apparent from these observations that there needs to be a major shift in hospital infection prevention and control measures from passive surveillance to focused control programmes of proven efficacy.⁵ The CDC 12-step campaign to prevent antimicrobial resistance in healthcare settings provides a good start. Some of the key measures optimise conditions that prevent infections, e.g. removing an unnecessary device, minimising broad spectrum antibiotics, avoiding long term antimicrobial prophylaxis, treating infection rather than colonisation, and preventing transmission. Our major successes were achieved when we adopted some of these measures.

Time-trend analysis performed in this study can be considered a screening tool to decide whether a more intensive investigation into underlying causes is justified. Also regression analysis allows us to state the annual changes in HCAI rates. However, there are limitations to this study from the methodological viewpoint. This study has demonstrated that changes in HCAs were due to multiple factors which occurred in different time periods. Thus, the underlying trend might not be continuously increasing or decreasing. Also, the time trends might not be the same for overall HCAI rate, site-specific or pathogen-specific HCAI rates. The model used in our study to quantify the linear trend could not account for other variations such as possible serial correlation. However, a longer time period of one

year was used in our analysis, to minimise the correlations between adjacent periods.¹²

In conclusion, this long term prospective hospital-wide surveillance study indicates what needs to be addressed to prevent and control HCAI. There needs to be a shift in the paradigm from surveillance with feedback to implementation of proven, control measures using focused surveillance to monitor efficacy. This will require a greater investment on the part of hospitals, if we want to reduce HCAI to the minimum and thus improve the quality and safety of patient care.

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Conflict of interest statement

None declared.

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Appendix. Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.jhin.2010.05.001.

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