Clinical Infectious Diseases

SUPPLEMENT ARTICLE

Prevalence of Healthcare-Associated Infections and Antimicrobial Use Among Adult Inpatients in Singapore Acute-Care Hospitals: Results From the First National Point Prevalence Survey

Yiying Cai,[1,2] Indumathi Venkatachalam,[3] Nancy W. Tee,[4] Thean Yen Tan,[5] Asok Kurup,[6] Sin Yew Wong,[7] Chian Yong Low,[8] Yang Wang,[9] Winnie Lee,[1] Yi Xin Liew,[1] Brenda Ang,[10] David C. Lye,[10] Angela Chow,[11,12] Moi Lin Ling,[13] Helen M. Oh,[14] Cassandra A. Cuvin,[9] Say Tat Ooi,[15] Surinder K. Pada,[16] Chong Hee Lim,[17] Jack Wei Chieh Tan,[18] Kean Lee Chew,[19] Van Hai Nguyen,[20] Dale A. Fisher,[21,22] Herman Goossens,[23] Andrea L. Kwa,[1,2,24] Paul A. Tambyah,[21,22] Li Yang Hsu,[10,12] and Kalisvar Marimuthu[10,22]

[1]Department of Pharmacy, Singapore General Hospital, [2]Department of Pharmacy, National University of Singapore, [3]Department of Infectious Diseases, Singapore General Hospital, [4]Department of Pathology and Laboratory Medicine, KK Women's and Children's Hospital, [5]Department of Laboratory Medicine, Changi General Hospital, [6]Infectious Diseases Care, Mount Elizabeth (Orchard) Hospital, [7]Infectious Disease Specialists, Gleneagles Hospital, [8]Novena Medical Specialists, Mount Elizabeth (Novena) Hospital, [9]Division of Nursing, Raffles Hospital, Departments of [10]Infectious Diseases and [11]Clinical Epidemiology, Institute of Infectious Diseases and Epidemiology, Tan Tock Seng Hospital, [12]Saw Swee Hock School of Public Health, National University of Singapore, [13]Infection Control, Singapore General Hospital, [14]Division of Infectious Diseases, Changi General Hospital, [15]Department of General Medicine, Khoo Teck Puat Hospital, [16]Department of Infectious Diseases, Ng Teng Fong General Hospital, [17]Department of Cardiothoracic Surgery, National Heart Center, [18]Department of Cardiology, National Heart Center, [19]Department of Laboratory Medicine, National University Hospital, Singapore; [20]School of Pharmacy, Memorial University, St John's, NL, Canada; [21]Division of Infectious Disease, National University Hospital, and [22]Yong Loo Lin School of Medicine, National University of Singapore, Singapore; [23]Laboratory of Medical Microbiology, University of Antwerp, Belgium; and [24]Emerging Infectious Diseases, Duke-NUS Medical School, Singapore

Background. We conducted a national point prevalence survey (PPS) to determine the prevalence of healthcare-associated infections (HAIs) and antimicrobial use (AMU) in Singapore acute-care hospitals.

Methods. Trained personnel collected HAI, AMU, and baseline hospital- and patient-level data of adult inpatients from 13 private and public acute-care hospitals between July 2015 and February 2016, using the PPS methodology developed by the European Centre for Disease Prevention and Control. Factors independently associated with HAIs were determined using multivariable regression.

Results. Of the 5415 patients surveyed, there were 646 patients (11.9%; 95% confidence interval [CI], 11.1%–12.8%) with 727 distinct HAIs, of which 331 (45.5%) were culture positive. The most common HAIs were unspecified clinical sepsis (25.5%) and pneumonia (24.8%). *Staphylococcus aureus* (12.9%) and *Pseudomonas aeruginosa* (11.5%) were the most common pathogens implicated in HAIs. Carbapenem nonsusceptibility rates were highest in *Acinetobacter* species (71.9%) and *P. aeruginosa* (23.6%). Male sex, increasing age, surgery during current hospitalization, and presence of central venous or urinary catheters were independently associated with HAIs. A total of 2762 (51.0%; 95% CI, 49.7%–52.3%) patients were on 3611 systemic antimicrobial agents; 462 (12.8%) were prescribed for surgical prophylaxis and 2997 (83.0%) were prescribed for treatment. Amoxicillin/clavulanate was the most frequently prescribed (24.6%) antimicrobial agent.

Conclusions. This survey suggested a high prevalence of HAIs and AMU in Singapore's acute-care hospitals. While further research is necessary to understand the causes and costs of HAIs and AMU in Singapore, repeated PPSs over the next decade will be useful to gauge progress at controlling HAIs and AMU.

Keywords. healthcare-associated infections; antimicrobial prescribing practices; point prevalence survey.

Healthcare-associated infections (HAIs) are a major public health problem, contributing to increased healthcare costs worldwide [1, 2]. In a 2012 meta-analysis, the annual costs of 5 major HAIs in the United States were estimated at US$9.8 billion [2]. Of additional concern, HAIs caused by antimicrobial-resistant organisms have emerged as a global crisis, exacerbated by the dwindling antimicrobial development pipeline [3]. Studies have demonstrated a link between antimicrobial consumption and resistance emergence, suggesting that reducing inappropriate antimicrobial prescribing practices may curb the development of antimicrobial resistance [4].

To establish priorities and strategies for HAI prevention and appropriate antimicrobial use (AMU), baseline prevalence and factors driving HAIs and AMU are needed [5]. To date, accurate estimates of the national burden of HAIs and AMU

Correspondence: K. Marimuthu, Department of Infectious Diseases, Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng, Singapore 308433 (kalisvar_marimuthu@ttsh.com.sg).

Clinical Infectious Diseases® 2017;64(S2):S61–7

DOI: 10.1093/cid/cix103

are not available in Singapore. While the Ministry of Health, Singapore (MOH) requires regular surveillance of various device-associated and postsurgical HAIs and a few sentinel studies have explored the HAI burden at the institutional level, these data cannot be generalized to estimate the national burden due to the limited information, variability in study design, and heterogeneity in patient and hospital profiles [6, 7].

Various surveillance strategies exist for enumerating HAIs and AMU burden and to evaluate the impact of control interventions [8]. Prospective longitudinal surveillance is considered the gold standard method, but such national studies are resource-intensive [8]. Repeated point prevalence surveys (PPSs) are a practical alternative, and presently, the literature is replete with national PPSs conducted in different countries [9–12]. A major challenge encountered when interpreting the results of PPSs is the variability in study designs and definitions employed across different studies [8]. Hence, in 2011, the European Centre for Disease Prevention and Control (ECDC) published a standardized methodology for PPSs on HAIs and AMU [13]. The protocol was developed and tested extensively with reliable outcomes, has been administered across 29 European countries, and has been adopted in PPSs in several non-European countries [14–16].

In light of the current knowledge gap in the local epidemiology of HAIs and AMU, MOH commissioned the conduct of the first national PPS on HAIs and AMU among Singapore acute-care hospitals based on the ECDC protocol [13]. The objective of this report was to determine the (1) prevalence and distribution of HAIs, (2) prevalence of systemic AMU, and (3) factors associated with HAIs in Singapore acute-care hospitals.

METHODS

Study Period and Setting

The PPS was conducted in 13 general and specialty acute-care hospitals in Singapore from July 2015 to February 2016. These hospitals accounted for 86.3% of all adult inpatient acute beds in Singapore hospitals in 2014 (2 acute-care private hospitals and 1 mental health institute were excluded).

Study Design and Inclusion Criteria

The PPS protocol was based on the patient-based protocol published by the ECDC, and adapted to the local setting [13]. Ten modifications to the ECDC protocol were made based on advice from an expert advisory team (Supplementary Table 1). For ambiguities encountered in the ECDC protocol or definitions, advice was sought from key ECDC PPS study members [14].

We included inpatients ≥18 years old admitted to the wards before 8:00 AM on the survey date and not discharged at the time of the survey. Patients admitted to the emergency department, day-case wards, and long-term-care wards were excluded. Data collection in each ward was completed within the same day. The total data collection time frame for each hospital did not exceed 1 month, a modification made from the original ECDC protocol because of the large size of several participating hospitals.

Training, Data Collection, and Validation

The PPS data collection team consisted of 5 research assistants and 2 survey leaders (1 infectious diseases [ID] physician and 1 ID pharmacist). Prior to PPS initiation, the research assistants received 2 months of training in data collection procedures and definitions, followed by competency assessments and a pilot survey with cross-checking by the survey leaders.

We collected hospital-level data, patient-level denominator data, and HAI- and AMU-specific details (Supplementary Table 2), and entered them into the Research Electronic Data Capture (REDCap) software, which incorporated branching rules based on definitions of HAI and AMU [17]. To ensure the validity and reliability of the data collected, a same-day data validation was performed for at least 50% of the patients surveyed. Validation of entered data was further done by the survey leaders upon completion of a PPS in an institution. Corrections (if any) were made, subsequent to verification and discussion with the survey leaders (Supplementary Table 3).

Definitions

The definitions employed in the PPS were listed in Supplementary Table 2 [13, 18]. In brief, active HAI required (1) symptoms of infection present on the survey date, or if signs and symptoms were present previously and the patient was receiving treatment on the survey date, and (2) the HAI met the ECDC surveillance criteria for HAI. Active AMU was defined as (1) the presence of any systemic antibiotic or antifungal surgical prophylaxis within a 24-hour period before the survey date, or (2) the presence of any systemic antibiotic or antifungal medication on the survey.

Statistical Analysis

All data were analyzed using Stata/MP version 14.0 (StataCorp, College Station, Texas); 95% confidence intervals (CIs) were calculated for HAI and AMU prevalences and distributions. For data validation, the percentage of patients with discordant data and the sensitivity and specificity of determining the presence of HAIs and AMU were tabulated [13]. To identify independent factors associated with HAIs, patients with and without HAIs were first compared using univariate logistic regression. Covariates with P values ≤.05 in the univariate analysis or with clinical plausibility were entered into a multiple logistic regression model. Statistical significance was defined as a P value of ≤.05.

Ethical Considerations

This study was approved by the ethics review boards of National Health Group Singapore and Singapore Health Services (reference number: 2014/01307), Parkway Pantai Hospitals (reference number: PIEC/2015/011), and Raffles Hospital (reference number: 2015/007), which waived informed consent for all patients.

RESULTS

Hospital-Level Data

Of the 13 hospitals that participated in the PPS, 4 (30.8%) hospitals had <250 acute beds, 3 (23.0%) had 250–499 acute beds, 4 (30.8%) had 500–999 beds, and 2 (15.4%) had ≥1000 acute beds. The median intensive care unit (ICU) bed number was 24 (interquartile range [IQR], 16–41). The median number of admissions and inpatient bed-days for each hospital in 2014 was 24 546 patients (IQR, 16 475–56 986 patients) and 101 012 inpatient-days (IQR, 63 434–280 879 inpatient-days), respectively. The median number of infection prevention nurses per 250 beds was 2.09 (IQR, 1.62–2.45) for public hospitals and 1.09 (IQR, 0.79–1.39) for private hospitals. All public hospitals had an established antimicrobial stewardship program, whereas none of the private hospitals had one.

Patients and Data Validation

A total of 5432 patients were identified in the PPS; 17 patients were excluded for incomplete data entry. Hence, 5415 patients were included in the final analysis. Cross-validation was completed for 3562 (65.8%) patients, with 484 discordant data points in 397 (11.1%) patients (Supplementary Table 4). All discordant data were reconciled after verification by the survey leaders. The overall sensitivity and specificity of detecting and reporting an HAI was 97.3% and 99.7%, respectively: the overall sensitivity and specificity of detecting and reporting an AMU was 99.3% and 99.6%, respectively.

Patient Baseline Characteristics

The demographics and clinical characteristics of the cohort are summarized in Table 1. The median age was 65.8 (IQR, 52.5–77.0) years and 273 (5.0%) patients resided in an ICU on the survey date. Of the patients surveyed, 1404 (25.9%) had at least 1 surgery since admission, of which 685 (48.8%) had major surgeries as defined by the ECDC criteria. Six hundred eighty-nine (12.7%) patients had 1 or more central venous catheters (CVCs), with 45 (6.5%) patients having a catheter inserted via the femoral vein.

Prevalence and Distribution of HAIs

A total of 727 active HAIs were identified in 646 patients (11.9%; 95% CI, 11.1%–12.8%), in whom 571 (88.4%) had 1 HAI, 69 (10.7%) had 2 HAIs, and 6 (0.9%) had 3 concurrent HAIs. The prevalence of HAIs was markedly higher in the ICU (37.0%; 95% CI, 31.2%–42.8%) than in the general wards (10.6%; 95%

Table 1. Baseline Characteristics and Risk Factors for Healthcare-Acquired Infections

Characteristics	Patients Without HAI (n = 4769)	Patients With HAI (n = 646)	Unadjusted OR (95% CI)	*P* Value	Adjusted OR[a] (95% CI)	*P* Value
Hospital and ward type						
Public hospital[b]	4369 (91.6)	604 (93.5)	1.31 (.95–1.83)	.10		
Residing in ICU on survey date[c]	172 (3.6)	101 (15.6)	4.95 (3.81–6.43)	<.01	1.24 (.81–1.91)	.32
Patient demographics						
Male sex	2415 (50.6)	409 (63.3)	1.68 (1.42–1.99)	<.01	**1.52 (1.27–1.82)**	**<.01**
Age, y, median (IQR)	65.6 (51.5–77.0)	67.2 (56.1–76.5)	1.01 (1.00–1.01)	<.01	**1.01 (1.00–1.02)**	**.04**
Ethnicity						
Chinese	3259 (68.3)	440 (68.1)	Ref	Ref		
Indian	433 (9.1)	48 (7.4)	0.82 (.60–1.12)	.22		
Malay	634 (13.3)	88 (13.6)	1.03 (.80–1.31)	.82		
Others	443 (9.3)	70 (10.8)	1.17 (.89–1.53)	.26		
Time at risk, d, median (IQR)[d]	5 (3–9)	8 (4–19)	1.00 (1.00–1.01)	<.01	1.00 (1.00–1.00)	.08
Comorbidities and instrumentation						
Charlson index, median score (IQR)	5 (2–7)	5 (3–7)	1.05 (1.02–1.08)	<.01	1.02 (.97–1.07)	.42
Surgery since admission[e]	1131 (23.7)	273 (42.3)	2.35 (1.99–2.79)	<.01	**1.81 (1.49–2.19)**	**<.01**
Presence of CVC[f]	457 (9.6)	232 (35.9)	5.29 (4.38–6.38)	<.01	**3.54 (2.82–4.46)**	**<.01**
Presence of PVC	3627 (76.1)	437 (67.6)	0.66 (.55–0.79)	<.01	0.96 (.78–1.18)	.67
Presence of indwelling urinary catheter	1144 (24.0)	309 (47.8)	2.90 (2.46–3.44)	<.01	**1.92 (1.58–2.33)**	**<.01**
Presence of endotracheal intubation	92 (1.9)	74 (11.5)	6.58 (4.78–9.04)	<.01	1.36 (.83–2.24)	.23

Data are presented as No. (%) unless otherwise indicated. Factors in bold—significant ($P \leq .05$) in the multivariable model.

Abbreviations: CVC, central venous catheter; CI, confidence interval; HAI, healthcare-associated infection; ICU, intensive care unit; IQR, interquartile range; OR, odds ratio; PVC, peripheral vascular catheter.

[a]Variables with a *P* value of <.05 in univariate analysis or with clinical plausibility were included in the multivariable model.

[b]Public hospitals were compared with private hospitals.

[c]Patients in ICU were compared with patients in the general ward.

[d]Time from admission to date of onset of HAI for patients with HAI and time from admission to date of point prevalence survey for patients without HAI.

[e]Surgeries include major (National Health Safety Network [NHSN]) and minimally invasive (non-NHSN) surgery, with or without implants [13].

[f]CVCs include peripherally inserted central catheter, dialysis catheter, Hickman cathether, and other general catheter type (patients may have 1 or more types).

CI, 9.8%–11.5%). The most common HAI was unspecified sepsis (Table 2). Device-associated HAIs accounted for 12.6% of all HAIs—ventilator-associated pneumonia made up 27.7% of all healthcare-associated pneumonia, indwelling catheters (IDCs) were present in 59.2% of all urinary tract infections, and 20.6% of the bloodstream infections were catheter-related.

Causative Organisms and Antimicrobial Resistance

There were 480 identified pathogens in 331 of the 727 (45.5%) HAIs (Table 2). The most common pathogens were *Staphylococcus aureus* (12.9%) and *Pseudomonas aeruginosa* (11.5%). Overall, 37.7% of all Enterobacteriaceae were nonsusceptible to third-generation cephalosporins and 7.0% were nonsusceptible to carbapenems (Supplementary Table 5). Nonsusceptibility to carbapenems was present in 71.9% of all *Acinetobacter* species, 23.6% of all *P. aeruginosa*, and 7.0% of all Enterobacteriaceae.

Factors Associated With HAIs

Patients who were male, were older, had higher Charlson scores, were in the ICU, had surgery, or had a CVC, IDC, or endotracheal tube in place were at an increased risk of HAIs in the

Table 2. Prevalence of Each Healthcare-Associated Infection Type and Reported Causative Microorganisms

	All Infections[a]	Unspecified Sepsis	Pneumonia	Surgical Site Infection	Bloodstream	Skin/Soft Tissue Infection	Urinary Tract Infection	Other Infections[b]
No. of HAIs	727	185	180	126	63	52	49	72
Distribution of each HAI type, % (95% CI)	…	25.5 (22.4–28.7)	24.8 (21.7–28.0)	17.3 (14.7–20.3)	8.7 (6.8–10.9)	7.2 (5.5–9.3)	6.7 (5.1–8.8)	9.9(7.9–12.3)
No. of pathogens[c]	480	0	113	137	74	37	56	63
Gram-positive bacteria								
Enterococcus spp	28 (5.8)	0 (0)	1 (0.9)	12 (8.8)	3 (4.1)	2 (5.4)	5 (8.9)	5 (7.9)
Staphylococcus aureus	62 (12.9)	0 (0)	12 (10.6)	24 (17.5)	12 (16.2)	10 (27.0)	2 (3.6)	2 (3.2)
Streptococcus spp	15 (3.1)	0 (0)	1 (0.9)	7 (5.1)	4 (5.4)	2 (5.4)	0 (0)	1 (1.6)
Other gram-positive bacteria[d]	18 (3.8)	0 (0)	2 (1.8)	9 (6.6)	3 (4.1)	1 (2.7)	0 (0)	3 (4.8)
Gram-negative bacteria								
Acinetobacter spp	32 (6.7)	0 (0)	10 (8.8)	6 (4.4)	4 (5.4)	3 (8.1)	3 (5.4)	6 (9.5)
Escherichia coli	50 (10.4)	0 (0)	5 (4.4)	13 (9.5)	12 (16.2)	2 (5.4)	17 (30.4)	1 (1.6)
Klebsiella spp	49 (10.2)	0 (0)	17 (15.0)	4 (2.9)	15 (20.3)	2 (5.4)	7 (12.5)	4 (6.3)
Enterobacter spp	28 (5.8)	0 (0)	11 (9.7)	10 (7.3)	3 (4.1)	1 (2.7)	0 (0)	3 (4.8)
Other Enterobacteriaceae	24 (5.0)	0 (0)	3 (2.7)	9 (6.6)	4 (5.4)	2 (5.4)	4 (7.1)	2 (3.2)
Pseudomonas aeruginosa	55 (11.5)	0 (0)	12 (10.6)	20 (14.6)	5 (6.8)	3 (8.1)	9 (16.1)	6 (9.5)
Stenotrophomonas maltophilia	16 (3.3)	0 (0)	9 (8.0)	2 (1.5)	1 (1.4)	0 (0)	0 (0)	4 (6.3)
Other gram-negative bacteria[e]	22(4.6)	0 (0)	8 (7.1)	6 (4.4)	4 (5.4)	2 (5.4)	1 (1.8)	1 (1.6)
Anaerobic bacteria								
Clostridium difficile	18 (3.8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	18 (28.6)
Other anaerobic bacteria	8 (1.7)	0 (0)	0 (0)	4 (2.9)	0 (0)	3 (8.1)	0 (0)	1 (1.6)
Fungi								
Candida albicans	13 (2.7)	0 (0)	5 (4.4)	4 (2.9)	0 (0)	1 (2.7)	1 (1.8)	2 (3.2)
Candida tropicalis	6 (1.3)	0 (0)	2 (1.8)	3 (2.2)	0 (0)	1 (2.7)	0 (0)	0 (0)
Candida glabrata	5 (1.0)	0 (0)	0 (0)	0 (0)	1 (1.4)	2 (5.4)	1 (1.8)	1 (1.6)
Other *Candida* spp	16 (3.3)	0 (0)	7 (6.2)	3 (2.2)	2 (2.7)	0 (0)	4 (7.1)	0 (0)
Other fungi	14 (2.9)	0 (0)	8 (7.1)	1 (0.7)	1 (1.4)	0 (0)	2 (3.6)	2 (3.2)
Viruses								
Influenza A virus	1 (0.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.6)

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: CI, confidence interval, HAI, healthcare-associated infection.

[a]A total of 727 HAIs were identified in 646 patients.

[b]Other infections were lower respiratory tract infection, gastrointestinal tract infection, bone/joint infection, central nervous system infection, cardiovascular or endovascular infection, and ear, nose, throat infection.

[c]A total of 480 pathogens were reported for 331 of the 727 (45.5%) infections. No pathogens were reported for the remaining 396 (54.5%) infections.

[d]Other gram-positive bacteria included nonspecified gram-positive cocci (n = 4), *Bacillus* spp (n = 3), *Lactobacillus* spp (n = 2), and *Corynebacterium* (n = 1).

[e]Other gram-negative bacteria include nonspecified gram-negative bacilli (n = 7), *Burkholderia cepacia* (n = 5), *Aeromonas* spp (n = 3), *Haemophilius influenzae* (n = 3), *Achromobacter* spp (n = 2), and nonspecified gram-negative cocci (n = 2).

unadjusted analysis (Table 1). Multivariable regression analysis showed that patients who were male, were older, had surgery during current admission, or had a CVC or IDC in place had an increased risk of HAI (Table 1).

Antimicrobial Use

A total of 3611 antimicrobials were administered in 2762 (51.0%; 95% CI, 49.7%–52.3%) patients, for whom 2046 (74.1%) received 1 agent, 613 (22.2%) received 2 agents, and 103 (3.7%) received ≥3 antimicrobial agents. Amoxicillin/clavulanate and piperacillin/tazobactam were the top-ranked prescribed systemic antimicrobial agents (Table 3). A total of 2997 (83%) antimicrobial agents were prescribed for treatment, and the most common anatomic site recorded for treatment was the respiratory tract (24.3%). In 414 (12.6%) treatment antimicrobial courses, no suspected or confirmed anatomic site was identifiable.

DISCUSSION

This study describes the 2015–2016 national point prevalence estimates for HAIs and AMU among adult inpatients in Singapore. The major finding of this study was that 1 in every 9 inpatients had at least 1 HAI, and 1 in every 2 inpatients was on at least 1 systemic antimicrobial agent on any given day. Factors that were independently associated with increased HAI risk among adult inpatients were male sex, older age, surgery in current admission, and the presence of a CVC or IDC.

More than a quarter of all hospital-acquired pneumonia, half of all urinary tract infections, and 20% of all bloodstream infections were device-associated. This represents a key target intervention area for reducing the HAI prevalence in Singapore, as device-associated HAIs are considered to be largely preventable [19]. Evidence-based interventions, such as the use of prevention bundles, should form the foundation for the prevention of device-associated HAIs [19]. Upon subanalysis of patients meeting the ECDC definition of unspecified sepsis, which was the most common HAI in our study, we found that 86% had a fever but not hypotension or oliguria [13]. Two important points can be surmised. First, as fever can also arise due to noninfectious inflammatory causes, the ECDC definition for unspecified sepsis is nonspecific and can lead to an overestimation of HAI prevalence [20, 21]. Second, a large number of patients in Singapore acute-care hospitals are prescribed antibiotics for fever in the absence of other symptoms, which represents a target for intervention to reduce unnecessary antibiotic prescriptions.

The predominant families of microorganisms (gram-positive cocci, gram-negative nonfermenters, and Enterobacteriaceae) were similar to Europe and Southeast Asia but differed from the United States [9, 12, 14]. Approximately one-third of all Enterobacteriaceae were nonsusceptible to third-generation cephalosporins, which was higher than reported in previous

Table 3. Antimicrobial Use: Distribution, Route, Indication for Prescription, and Anatomical Site Diagnoses

Use	No. (%)
Route of administration (Total No. of antimicrobials = 3611)	
Parenteral	2130 (59.0)
Oral	1477 (40.9)
Others[a]	4 (0.1)
Distribution of antimicrobials[b] (Total No. of antimicrobials = 3611)	% (95% CI)
Amoxicillin/clavulanate (J01CR02)	24.6 (23.2–26.0)
Piperacillin/tazobactam (J01CR05)	9.2 (8.3–10.2)
Ceftriaxone (J01DD04)	7.7 (6.9–8.6)
Ciprofloxacin (J01MA02)	7.1 (6.3–8.0)
Cefazolin (J01DB04)	7.0 (6.2–7.9)
Metronidazole (J01XD01)	6.1 (5.4–7.0)
Meropenem (J01DH02)	5.4 (4.7–6.2)
Vancomycin (J01XA01/A07AA09)	4.5 (3.8–5.2)
Sulfamethoxazole/trimethoprim (J01EE01)	2.5 (2.0–3.0)
Clarithromycin (J01FA09)	2.1 (1.7–2.6)
Other antimicrobials	23.9 (22.5–25.3)
Indications for prescription[c] (Total No. of indications = 3611)	No. (%)
Treatment	2997 (83.0)
Surgical prophylaxis	462 (12.8)
Single dose or 1 day	158 (4.4)
>1 day	304 (8.4)
Medical prophylaxis	119 (3.3)
Reasons other than prophylaxis/ treatment (eg, erythromycin for prokinetic)	17 (0.5)
No reason stated in patient notes	16 (0.4)
Systemic antimicrobials indicated for treatment: anatomic site diagnoses[d] (Total No. of diagnoses = 3276)[e]	No. (%)
Respiratory	797 (24.3)
Skin and soft tissue	557 (17.0)
Upper and lower urinary tract	372 (11.4)
Suspected or confirmed bloodstream infections	249 (7.6)
Intra-abdominal site other than GI tract	239 (7.3)
Gastrointestinal tract	233 (7.1)
Bone and joint	131 (4.0)
Ear, nose, throat, larynx, and mouth	122 (3.7)
Febrile neutropenia	53 (1.6)
Central nervous system	45 (1.4)
Cardiovascular and endovascular	35 (1.1)
Reproductive tract	29 (0.9)
No anatomic site stated	414 (12.6)

Abbreviations: CI, confidence interval; GI, gastrointestinal.

[a]Other systemic antibiotics included intraperitoneal route (n = 3) and intrathecal (n = 1) route.

[b]Antimicrobials were classified in accordance to the Anatomical Therapeutic Chemical classification system of the World Health Organization Collaborating Centre for Drug Statistics Methodology [18].

[c]Indications for antimicrobial use describes the physicians' intention for antimicrobial prescription and were classified by data collectors as treatment, surgical prophylaxis, medical prophylaxis, and other reasons (eg, erythromycin for prokinetic use).

[d]Anatomical site diagnoses describes the physicians' diagnosis for the suspected or confirmed site of infection for antimicrobial prescription, as stated in the patient's notes.

[e]No. of anatomical sites recorded was more than the number of antimicrobials employed for treatment, as each antimicrobial may be prescribed for the treatment of infections in >1 anatomical site.

local surveillance studies [4]. Resistance rates to carbapenems among Enterobacteriaceae, which appeared to be increasing locally in the past 5 years, was 7.0% [22]. High prevalence of carbapenem resistance, comparable to the United States, was observed in gram-negative nonfermenters [23]. To combat these high resistance rates, targeted prevention strategies that take into account the risk factors associated with the acquisition of antibiotic-resistant organisms in our local setting should be implemented [6, 24, 25].

More than half of all patients surveyed were on at least 1 systemic antimicrobial agent; broad-spectrum β-lactam antibiotics accounted for approximately half of all antimicrobials prescribed. This AMU prevalence is surprisingly high, considering that our HAI prevalence was 11.9%, and brings into question the appropriateness of the antimicrobial prescriptions. Unfortunately, we were unable to assess antimicrobial appropriateness, as the accurate assessment of antimicrobial appropriateness required extensive clinical interpretation and was deemed to be beyond the scope of this PPS. More than half of the surgical prophylactic antimicrobial courses were administered beyond 24 hours—this non-evidence-based practice presents a target for quality improvement, as it may be associated with increased surgical site infection risk [26, 27]. The anatomical site of infection could not be identified in 13% of the antimicrobials prescribed for treatment. This represents another target area for quality improvement, as documentation of intention of treatment should be considered the rule instead of the exception [28, 29].

The prevalence of HAI in Singapore appears to be higher compared to Europe (overall HAI prevalence, 6%; country range, 2%–11%) and other Southeast Asian countries (pooled HAI prevalence, 9%); similarly, the prevalence of AMU appears to be higher than in most European countries (overall AMU prevalence, 35%; country range, 21%–55%) [12, 14]. However, we caution against such direct comparison of prevalence figures, as several reasons can account for the observed difference between countries. First, differences in HAI and AMU prevalence between different countries may be contributed by differences in the case-mix, including severity, comorbidities, and length of stay. Second, the prevalence of HAIs in Singapore may have been overestimated due to the large proportion of patients with unspecified sepsis. If these patients were excluded from the analysis, the prevalence of the other HAIs appeared to be similar to the ECDC data [14]. Last, the higher HAI and AMU prevalence observed in our study may be attributable to a prolonged duration of antimicrobial use, since PPSs are subjected to overestimation of prevalence if there were a preponderance of long duration cases [8].

Our study has some limitations. For feasibility purposes, each PPS in a hospital could be conducted for up to a month. The long time span between surveys in different hospitals could potentially affect the interinstitutional comparability of HAI rates [30]. Next, we did not derive the local HAI incidences from our prevalence results, as the routine applicability of the Rhame and Sudderth formulae has been not been established [31, 32].

In conclusion, we provided an insight into the burden of HAIs and AMU among Singapore acute-care hospitals, and highlighted several priority areas and targets for quality improvement. While further research is necessary to understand the causes and costs of HAIs and AMU in Singapore, our study findings can serve to direct any national effort aimed at reducing HAIs and antimicrobial resistance. Moving forward, the PPS should be repeated at periodic intervals to elucidate HAI and AMU trends and to gauge the impact of interventions in Singapore.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Acknowledgments. We thank the following people: Dr Tang Chien Her from MOH Singapore, Professor Mike Sharland, and Dr Ying Fen Hsia from St Georges University, Ann Versporten from the University of Antwerp, Professor Peter Zarb from Mater Dei Hospital, and Dr Piotr Chlebicki from Singapore General Hospital for their expert advice; the data collection team (Fathinah Bt. Mohd Jaffar, Huan Xiao Wei, Zaw Linn Kyaw, See Pei Shi, and Bindu Karunakaran) for their dedication; Soh Siew Hwa for her support in the project logistics; the Singapore Infectious Diseases Initiative for support of the study; the infection prevention control units of all participating institutions; the clinical research units of Changi General Hospital, Ng Teng Fong General Hospital, Khoo Teck Puat Hospital, Parkway Hospitals, and Mount Alvernia Hospital; and the SingHealth REDCap team.

Disclaimer. The funders had no role in study design, data collection, or interpretation of the work for publication.

Financial support. This study was supported by the Communicable Diseases—Public Health Research Grant awarded by the Ministry of Health, Singapore (award number CDPHRG-CS/0002/2014).

Supplement sponsorship. This article appears as part of the supplement "Infection Prevention in Asia Pacific," sponsored by the Infectious Diseases Association of Thailand (IDAT).

Potential conflicts of interest. All authors: No potential conflicts. The authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Klevens RM, Edwards JR, Richards CL Jr, et al. Estimating health care-associated infections and deaths in U.S. hospitals, 2002. Public Health Rep **2007**; 122:160–6.
2. Zimlichman E, Henderson D, Tamir O, et al. Health care-associated infections: a meta-analysis of costs and financial impact on the US health care system. JAMA Intern Med **2013**; 173:2039–46.
3. Boucher HW, Talbot GH, Bradley JS, et al. Bad bugs, no drugs: no ESKAPE! An update from the Infectious Diseases Society of America. Clin Infect Dis **2009**; 48:1–12.
4. Hsu LY, Tan TY, Tam VH, Kwa A, Fisher DA, Koh TH; Network for Antimicrobial Resistance Surveillance (Singapore). Surveillance and correlation of antibiotic prescription and resistance of gram-negative bacteria in Singaporean hospitals. Antimicrob Agents Chemother **2010**; 54:1173–8.
5. Wilson AP, Kiernan M. Recommendations for surveillance priorities for health-care-associated infections and criteria for their conduct. J Antimicrob Chemother **2012**; 67:i23–8.
6. Ling ML, Tee YM, Tan SG, et al. Risk factors for acquisition of carbapenem resistant Enterobacteriaceae in an acute tertiary care hospital in Singapore. Antimicrob Resist Infect Control **2015**; 4:26.
7. Vasudevan A, Memon BI, Mukhopadhyay A, Li J, Tambyah PA. The costs of nosocomial resistant gram negative intensive care unit infections among patients with

the systemic inflammatory response syndrome—a propensity matched case control study. Antimicrob Resist Infect Control **2015**; 4:3.
8. Llata E, Gaynes RP, Fridkin S. Measuring the scope and magnitude of hospital-associated infection in the United States: the value of prevalence surveys. Clin Infect Dis **2009**; 48:1434–40.
9. Magill SS, Edwards JR, Bamberg W, et al; Emerging Infections Program Healthcare-Associated Infections and Antimicrobial Use Prevalence Survey Team. Multistate point-prevalence survey of health care-associated infections. N Engl J Med **2014**; 370:1198–208.
10. Gravel D, Taylor G, Ofner M, et al; Canadian Nosocomial Infection Surveillance Program. Point prevalence survey for healthcare-associated infections within Canadian adult acute-care hospitals. J Hosp Infect **2007**; 66:243–8.
11. van der Kooi TI, Mannien J, Wille JC, van Benthem BH. Prevalence of nosocomial infections in the Netherlands, 2007–2008: results of the first four national studies. J Hosp Infect **2010**; 75:168–72.
12. Ling ML, Apisarnthanarak A, Madriaga G. The burden of healthcare-associated infections in Southeast Asia: a systematic literature review and meta-analysis. Clin Infect Dis **2015**; 60:1690–9.
13. European Centre for Disease Prevention and Control. Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals—protocol version 4.3. Stockholm, Sweden: ECDC, **2012**.
14. European Centre for Disease Prevention and Control. Point prevalence survey of healthcare associated infections and antimicrobial use in European acute care hospitals. Stockholm, Sweden: ECDC, **2013**.
15. Morioka H, Hirabayashi A, Iguchi M, et al. The first point prevalence survey of health care-associated infection and antimicrobial use in a Japanese university hospital: a pilot study. Am J Infect Control **2016**; 44:e119–23.
16. Phu VD, Wertheim HF, Larsson M, et al. Burden of hospital acquired infections and antimicrobial use in Vietnamese adult intensive care units. PLoS One **2016**; 11:e0147544.
17. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform **2009**; 42:377–81.
18. World Health Organization Collaborating Centre for Drug Statistics Methodology. The ATC/DDD system: International language for drug utilization research. Oslo, Norway: WHO Collaborating Centre for Drug Statistics Methodology, **2007**.
19. Cardo D, Dennehy PH, Halverson P, et al; HAI Elimination White Paper Writing Group. Moving toward elimination of healthcare-associated infections: a call to action. Am J Infect Control **2010**; 38:671–5.
20. Pittet D, Rangel-Frausto S, Li N, et al. Systemic inflammatory response syndrome, sepsis, severe sepsis and septic shock: incidence, morbidities and outcomes in surgical ICU patients. Intensive Care Med **1995**; 21:302–9.
21. Hersch EC, Oh RC. Prolonged febrile illness and fever of unknown origin in adults. Am Fam Physician **2014**; 90:91–6.
22. Teo J, Cai Y, Lim TP, Tan TT, Kwa AL. Carbapenem resistance in gram-negative bacteria: the not-so-little problem in the little red dot. Microorganisms **2016**; 4:pii: E13.
23. Weiner LM, Webb AK, Limbago B, et al. Antimicrobial-resistant pathogens associated with healthcare-associated infections: summary of data reported to the national healthcare safety network at the centers for disease control and prevention, 2011–2014. Infect Control Hosp Epidemiol **2016**: 37:1288–301.
24. Ng TM, Teng CB, Lye DC, Apisarnthanarak A. A multicenter case-case control study for risk factors and outcomes of extensively drug-resistant *Acinetobacter baumannii* bacteremia. Infect Control Hosp Epidemiol **2014**; 35:49–55.
25. Teo J, Cai Y, Tang S, et al. Risk factors, molecular epidemiology and outcomes of ertapenem-resistant, carbapenem-susceptible Enterobacteriaceae: a case-case-control study. PLoS One **2012**; 7:e34254.
26. Young B, Ng TM, Teng C, Ang B, Tai HY, Lye DC. Nonconcordance with surgical site infection prevention guidelines and rates of surgical site infections for general surgical, neurological, and orthopedic procedures. Antimicrob Agents Chemother **2011**; 55:4659–63.
27. Bratzler DW, Dellinger EP, Olsen KM, et al; American Society of Health-System Pharmacists (ASHP); Infectious Diseases Society of America (IDSA); Surgical Infection Society (SIS); Society for Healthcare Epidemiology of America (SHEA). Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surg Infect (Larchmt) **2013**; 14:73–156.
28. Ansari F, Erntell M, Goossens H, Davey P. The European surveillance of antimicrobial consumption (ESAC) point-prevalence survey of antibacterial use in 20 European hospitals in 2006. Clin Infect Dis **2009**; 49:1496–504.
29. Hansen S, Sohr D, Piening B, et al. Antibiotic usage in German hospitals: results of the second national prevalence study. J Antimicrob Chemother **2013**; 68:2934–9.
30. Richet H. Seasonality in gram-negative and healthcare-associated infections. Clin Microbiol Infect **2012**; 18:934–40.
31. Rhame FS, Sudderth WD. Incidence and prevalence as used in the analysis of the occurrence of nosocomial infections. Am J Epidemiol **1981**; 113:1–11.
32. Gbaguidi Haore H, Muller A, Talon D, Bertrand X. Estimation of the cumulative incidence of hospital-acquired bacteremia from prevalence data: a formula. Infect Control Hosp Epidemiol **2005**; 26:415–7.