Carbapenem susceptibilities of Gram-negative pathogens in intra-abdominal and urinary tract infections: updated report of SMART 2015 in China

Hui Zhang1, Haishen Kong2, Yunsong Yu3, Anhua Wu4, Qiong Duan5, Xiaofeng Jiang6, Shufang Zhang7, Ziyong Sun8, Yuxing Ni9, Weiping Wang10, Yong Wang11, Kang Liao12, Huayin Li13, Chunxia Yang14, Wenxiang Huang15, Bingdong Gui16, Bin Shan17, Robert Badal18, Qiwen Yang1* and Yingchun Xu1*

Abstract

Background: To evaluate the susceptibility rates of aerobic and facultative Gram-negative bacterial isolates from Chinese intra-abdominal infections (IAI) and urinary tract infections (UTI) focusing on carbapenems and comparing their effectiveness between 2014 and 2015.

Methods: A total of 2318 strains in 2015 (1483 from IAI and 835 from UTI) and 2374 strains in 2014 (1438 from IAI and 936 from UTI) were included in the analysis. Antimicrobial susceptibilities were determined at a central laboratory using CLSI broth microdilution and interpretive standards. Hospital acquired (HA) IAI and UTI were defined as isolates sampled > 48 h and community acquired (CA) as isolates sampled < 48 h after admission.

Results: The main species derived from IAI and UTI in 2015 were Escherichia coli (50.86%) and Klebsiella pneumoniae (19.20%). Susceptibilities of Escherichia coli IAI and UTI strains to imipenem (IPM) and ertapenem (ETP) were > 90% in 2014 and 2015, while the susceptibilities to IPM and ETP of Klebsiella pneumoniae IAI strains were > 80% in 2014 but dropped to ≤80% in 2015 for UTI strains. Susceptibilities of IAI Enterobacteriaceae strains to IPM and ETP in 2015 were lowest in the colon and abscesses, and Enterobacteriaceae susceptibilities of UTI and IAI isolates to IPM and ETP were lowest in medical, pediatric and surgery intensive care units (ICUs) in 2015.

Conclusions: IPM and ETP were effective in vitro against Enterobacteriaceae isolated from IAIs and UTIs in 2014 and 2015, but susceptibility to carbapenems in UTIs markedly decreased in 2015.

Keywords: Enterobacteriaceae, Carbapenem; ertapenem, Imipenem, Intra-abdominal infection, Urinary tract infection

Background

The Study for Monitoring Antimicrobial Resistance Trends (SMART)-CHINA is a surveillance program which monitors annually in vitro activities of antimicrobial agents against pathogens that cause intra-abdominal infections (IAI) and urinary tract infections (UTI). In a previous Chinese study it was reported that the incidence of Extended-Spectrum β-Lactamases (ESBL)-producing Escherichia coli (E. coli) strains derived from IAI had significantly increased between 2002 and 2011, while the percentages of ESBL-producing Klebsiella pneumoniae (K. pneumoniae) strains isolated from IAI remained relatively constant between 30.1 and 39.3%, but these two species were the major pathogens during the entire period [1]. However, Asia has been reported to have the world’s highest incidence of ESBL-producing E. coli, K. pneumoniae, Klebsiella oxytoca and Proteus mirabilis strains from IAIs and UTIs in 2011, reaching 40% to 45% [2], and a number of recent publications have noted that cephalosporins and fluoroquinolones were not suitable antibiotics for the empirical treatment of IAI and UTI in China [3, 4],
underlining the importance of monitoring susceptibilities to alternative antibiotics such as the carbapenems. Epidemiological and individual hospital drug susceptibilities are commonly used as a guide for selecting suitable antibiotics for empirical treatments. However, susceptibility analyses have been extended to weighted-incidence syndromic combination antibiograms (WISCA), which reflects the likelihood that regimens treat all relevant organisms in a patient with a given syndrome [5].

In the present study we developed organ-specific weighted incidence antibiograms (OSWIAs) to estimate the likelihood of an isolate from a specific organ being susceptible to a given antibiotic. IAI and UTI derived isolates and their susceptibilities to carbapenems, cephalosporins, fluoroquinolones, broad-spectrum penicillins combined with β-lactamase inhibitors, and an aminoglycoside were compared in different infected organs. In addition, the distribution of Enterobacteriaceae and non-Enterobacteriaceae infections isolated from HA and CA IAI and UTIs in different age subgroups as well as the susceptibility patterns of major pathogens in different medical departments were also analyzed.

Methods
Isolates from IAI and UTI infections
The Human Research Ethics Committee of Peking Union Medical College Hospital approved this study and waived the need for consent (Ethics Approval Number: S-K238). A total of 2318 aerobic and facultative Gram-negative bacterial strains (1483 from IAI and 835 from UTI) in 2015 and 2374 strains in 2014 (1438 from IAI and 936 from UTI) collected from 21 hospitals in 16 Chinese cities were retrospectively analyzed. The majority of the intra-abdominal specimens were obtained during surgery, with some paracentesis specimens. The UTI isolates were obtained from clean catch midstream urine, the urinary bladder, kidney and the prostate gland. All duplicate isolates (the same genus and species from the same patient) were excluded. Bacteria were identified by standard methods used in the participating clinical microbiology laboratories. Isolates were considered to be community-associated (CA) if they were recovered from a specimen taken <48 h after the patient was admitted to a hospital, or HA if the specimen was taken ≥48 h after admission, as previously described [6].

Antimicrobial susceptibility test methods
Minimum inhibitory concentrations (MIC) were determined by broth microdilution according to the Clinical and Laboratory Standards Institute (CLSI) [7] using panels purchased from ThermoFisher Scientific (Cleveland, OH, USA). Relative susceptibility interpretations were based on CLSI clinical breakpoints [8].

Twelve antimicrobial agents commonly used to treat IAI and UTI were tested: ampicillin-sulbactam (SAM), piperacillin-tazobactam (TZP), ceftriaxone (CRO), ceftaxime (CTX), ceftazidime (CAZ), cefoxitin (FOX), cefteme (FEP), ciprofloxacin (CIP), levofloxacin (LVX), amikacin (AMK), imipenem (IPM) and ertapenem (ETP). Reference strains E. coli ATCC (American Type Culture Collection) 25,922, Pseudomonas aeruginosa ATCC 27853, and K. pneumoniae ATCC 700603 (positive ESBL control), were used as quality control (QC) strains for each batch of MIC tests. Results were only included in the analysis when corresponding quality control isolate test results were in accordance with CLSI guidelines and therefore within an acceptable range.

Organ-specific weighted incidence antibiogram (OSWIA) calculation
In order to calculate bacterial sensitivities in various organs of the abdominal cavity OSWIAs were calculated using the following equation:

Weighted susceptibility of a certain antimicrobial drug in a certain organ = antimicrobial susceptibility of \(A \times \) the constituent ratio of \(A\) in the organ + antimicrobial susceptibility of \(B \times \) the constituent ratio of \(B\) in the organ + antimicrobial susceptibility of \(C \times \) the constituent ratio of \(C\) in the organ +... (where \(A\), \(B\) and \(C\) represent the pathogenic bacteria in a certain organ). For example when we calculated the OSWIA susceptibility of gall bladder isolates to ETP in 2015, first we extracted specific bacterial infection rates and then multiplied them by the specific bacterial susceptibilities to ETP in 2015. Isolates in 2015 from gall bladder were 241 Escherichia coli (50.1%), 87 Klebsiella pneumoniae (18.1%), 36 Enterobacter cloacae (7.5%).....until 1 Serratia odorifer (0.21%). The corresponding susceptibilities to ETP were 87.55% (Escherichia coli), 86.21% (Klebsiella pneumoniae), 66.67% (Enterobacter cloacae).....and 100% (Serratia odorifera). According to the above mentioned equation, the susceptibility of gall bladder to ETP was calculated as 50.1% × 87.55% + 18.1% × 86.21% + 7.5% × 66.67%......0.21% × 100% = 85.79%.

Statistical analysis
The susceptibility of all Gram-negative isolates combined was calculated using breakpoints appropriate for each species and assuming 0% susceptible for species with no breakpoints for any given drug. The 95% confidence intervals (CIs) were calculated using the adjusted Wald method; linear trends of ESBL rates in different years were assessed for statistical significance using the Cochran-Armitage test and comparison of ESBL rates were assessed using a chi-squared test. \(P\)-values < 0.05 were considered to be statistically significant.
Results

Distribution of Enterobacteriaceae isolates acquired from different organ groups of IAI and UTI in 2015

Enterobacteriaceae strains of IAIIs were mainly derived from gall bladder (33%), peritoneal fluid (28%), abscesses (14%) liver (7%), appendix (6%) and other organs (1–3%). Comparing Enterobacteriaceae strains acquired from HA (76.3%) and CA (23.6%) IAI, the percentages for peritoneal fluid, abscesses and liver-derived isolates were similar, but in HA-derived IAIIs, gall bladder isolates were collected more often (35% vs 26%), whereas appendix isolates were less frequently sampled (2% vs 20%) compared to CA isolates (Fig. 1). Similar distributions were found in 2014 (Additional file 1: Figure S1). From UTI pathogens, 99.4% of the strains were acquired from urine, with only 3 strains from the kidneys, and 1 strain each from the bladder and prostate gland. The distribution of HA and CA UTI isolates was 599 (71.9%) and 234 (28.1%) in 2015, and 58.1% and 40.9% in 2014, respectively.

Distribution of all isolates acquired from HA and CA IAI and UTI in 2015

There were 2318 strains collected in 2015, including 1483 strains from IAIIs and 835 strains from UTIs. The majority of infections were caused by E. coli and K. pneumoniae, accounting for 50.86% and 19.20% in 2015 (Table 1) as well as 46.3% and 17.3% in 2014 (Additional file 2: Table S1).

The distribution analysis of strains acquired from IAIIs and UTIs in HA and CA in different age groups revealed that E. coli was the major IAI pathogen in CA IAI in the 0–39 year age range (CA: 31.76%; HA: 9.01%) and in HA IAI in the 60–79 years age range (CA: 32.35%; HA: 47.38%), as well as in the HA UTI of > 80 year-old patients (CA: 5.56%; HA: 18.53%) (Fig. 2), which was similar in 2014 (Additional file 3: Figure S2).

Comparison of susceptibilities to 12 common antibiotics for E. coli and K. pneumoniae isolates (IAI and UTI) in 2014 and 2015

E. coli in IAI were highly susceptible to IPM, AMK and ETP (> 90%) in 2014, but the susceptibility to ETP showed a small decrease in 2015 (Fig. 3a) compared to 2014. K. pneumoniae from IAI was also highly sensitive to AMK, IPM and ETP (> 80%) in 2014–2015, but the susceptibility to these three antibiotics in 2015 was generally lower than in 2014 (Fig. 3c). More than 90% E. coli isolates from UTI were susceptible to IPM, AMK, ETP and TZP. In contrast, compared to 2014 susceptibilities of K. pneumoniae strains from UTIs decreased by 10% to AMK, IPM and ETP in 2015, which was a general trend also for all the other antibiotics tested (Fig. 3d). Susceptibilities to all other antibiotics were between 20 and 70% for E. coli and 30–75% for K. pneumoniae (Fig. 3). Corresponding MIC90 values of 12 antibiotics for E. coli and K. pneumoniae IAI and UTI isolates are presented in the Additional file 4: Table S2.

Comparison of the Enterobacteriaceae susceptibilities to carbapenem antibiotics (ETP and IPM) based on the OSWIA in different organs of IAI patients as well as isolates derived from IAI and UTI patients in different departments between 2014 and 2015

In general, besides abscesses and colon infections in 2015 as well as small intestine infections in 2014 to ETP, most included Enterobacteriaceae IAI isolates showed OSWIA susceptibilities to carbapenems of > 80% in 2014 and 2015 (Fig. 4a, Fig. 4b).

In 2015, carbapenem susceptibility rates of Enterobacteriaceae isolated from IAIIs and UTIs decreased below 80% in medical and surgery ICUs to ETP as well as in general pediatric departments and surgery ICUs in 2015 to IPM. The greatest decline in susceptibility to IPM and ETP was seen between 2014 and 2015 in pediatric ICUs (Fig. 4c, Fig. 4d). In general there was a trend of susceptibility reductions to ETP and IPM in HA, and susceptibility increases to ETP and IPM in CA-derived Enterobacteriaceae caused IAIIs between 2014 and 2015 (Fig. 4e, Fig. 4f).

Detailed information of MIC90 values from E. coli and K. pneumoniae for ETP and IMP in different organs, departments and HA vs CA infections in 2014 and 2015 are shown in Table 2 and indicate dramatically increased MIC90 values of IPM for E. coli isolates only in medicine ICUs in 2015, while the MIC90 values
for IPM of *K. pneumoniae* IAI isolates from abscesses, colon, peritoneal fluid and others were all > 32 in 2015, pointing out increasing IPM resistance of *K. pneumoniae* infections in 2015. In addition, the MIC\textsubscript{90} values of IPM for *K. pneumoniae* isolates derived from general surgery departments as well as from ICUs of medicine, pediatric and surgery became > 32 and also reflected in essentially increased HA MIC\textsubscript{90} values (Table 2), which showed that clinical relevant resistance of IAI derived *K. pneumoniae* isolates to IPM appeared in hospitals in 2015.

### Discussion

*Enterobacteriaceae* were the major pathogens in IAI and UTI, with *E. coli* and *K. pneumoniae* being the most commonly isolated strains, which is in accordance with recent studies in China and abroad [3, 9][10]. *E. coli* isolated from both UTI and IAI were < 40% susceptible to the tested fluoroquinolones that reflects an overuse of fluoroquinolones in China, which has also been reported for Europe and the US [11, 12]. In addition, in 2015 *E. coli* isolates were < 70% susceptible to all cephalosporins tested including cefoxitin whether they were obtained

### Table 1 Distribution of the IAI and UTI pathogens in China in 2015

| Pathogen              | IAI Total | UTI Total | UTI + IAI Total |
|-----------------------|-----------|-----------|-----------------|
| **Enterobacteriaceae**|           |           |                 |
| *Escherichia coli*    | 928 (79.7)| 287 (90.3)| 1216 (82.0)     |
| *Klebsiella pneumoniae*| 477 (41.0)| 170 (53.5)| 648 (43.7)      |
| *Enterobacter cloacae*| 262 (22.5)| 69 (21.7)| 331 (22.3)      |
| *Proteus mirabilis*   | 83 (7.1)  | 17 (5.4)  | 100 (6.7)       |
| *Citrobacter freundii*| 21 (1.8)  | 8 (2.5)   | 29 (2.0)        |
| *Enterobacter aerogenes*| 16 (1.4) | 3 (0.9) | 19 (1.3)        |
| **Non-Enterobacteriaceae**| | | |
| *Pseudomonas aeruginosa*| 104 (8.9)| 14 (4.4)| 118 (8.0)       |
| *Acinetobacter baumannii*| 103 (8.9)| 12 (3.8)| 115 (7.8)       |
| *Stenotrophomonas maltophilia*| 16 (1.4)| 3 (0.9)| 19 (1.3)        |
| **Other**             | 58 (5.0)  | 19 (6.0)  | 77 (5.2)        |
| **All**               | 1164 (100)| 318 (100)| 1483 (100)      |

\*32 isolates lacked partial demographic information and could not be identified as CA or HA

**Fig. 2** Distribution of *E. coli*, *K. pneumoniae* and other *Enterobacteriaceae* strains derived from HA and CA a) IAI and b) UTIs in different age groups in 2015. * P < 0.05, *** P < 0.001
Fig. 3 Comparison of E. coli and K. pneumonia isolate susceptibilities (IAI and UTI) to 12 common antibiotics between 2014 and 2015.  

- **a** E. coli isolated from IAI patients. 
- **b** E. coli isolated from UTI patients. 
- **c** K. pneumoniae isolated from IAI patients. 
- **d** K. pneumoniae isolated from UTI patients. 

Dotted lines show the indicated percentages throughout the columns for comparison.

Fig. 4 Susceptibility based on OSWIA in IAI isolates.  

- **a** OSWIA susceptibility of Enterobacteriaceae IAI to ETP. 
- **b** OSWIA susceptibility of Enterobacteriaceae IAI to IPM. 
- **c** Susceptibilities of Enterobacteriaceae UTI and IAI strains to ETP. 
- **d** to IPM. 
- **e** Enterobacteriaceae susceptibilities of HA and CA IAI and UTI to ETP. 
- **f** Enterobacteriaceae susceptibilities of HA and CA IAI and UTI to IPM. *** P < 0.001
from IAI or UTI, suggesting a high prevalence of ESBL production, which is an extension of the trend shown previously between 2002 and 2011 [1]. A similar but less dramatic pattern has been observed for *K. pneumoniae*, but in contrast to *E. coli*, *K. pneumoniae* showed a decreasing susceptibility to all tested antibiotics from 2014 to 2015 (Fig. 3). Though ESBL-producing *E. coli* and *K. pneumoniae* strains should be susceptible to cefoxitin, both species, whether found in IAI or UTI, were < 80% susceptible to cefoxitin, which suggests that besides ESBL production other resistance mechanisms may be on the rise [13]. In particular *K. pneumoniae* showed a decreasing susceptibility to carbapenems, which was more pronounced in UTI isolates and indicated that carbapenemases or other mechanisms of carbapenem resistance have developed in *K. pneumoniae* strains, which has also been previously noted since carbapenem resistant *K. pneumoniae* strains isolated in Shanghai between July 2014 and May 2015 harbored all or at least one of the ESBL genes plus mainly New Delhi metallo-β-lactamase-1 (NDM-1) and IMP-4 or *Klebsiella pneumoniae* carbapenemase (KPC)-2 [14].

However, data from 2015 showed *K. pneumoniae* IAI isolate susceptibilities between 80 and 90% to IPM and ETP in our study, which was much higher than the 43.24% susceptibility to IPM reported for *K. pneumoniae* IAI isolates from a Chinese tertiary-care hospital between 2012 and 2015 [15], but was in a similar range to Chinese isolates from abdominal trauma-associated IAI collected between 2010 to 2015, with susceptibilities of *K. pneumoniae* strains to IPM and ETP of 87.5–90.6% [16].

The distribution of *Enterobacteriaceae* IAI isolates were similar in peritoneal fluid, abscesses and the colon for HA and CA infections, but HA IAIIs manifested more in the gall bladder whereas CA infections occurred to a greater extent in appendicitis IAIIs in 2015 (Fig. 1), which is a fair finding since acute appendicitis is a common reason for hospital admissions worldwide [17]. In particular, colon IAI-derived strains showed an increased resistance to carbapenems, decreasing to 80% susceptibility to ertapenem and imipenem in 2015. Similarly, IAI strain susceptibilities from abscesses were about 80% to carbapenems in 2015, but the decrease compared to 2014 was less pronounced (Fig. 3). Apart from general pediatric departments, in 2015 lowered susceptibilities

| *K. pneumoniae* | ETP | IPM | ETP | IPM |
|-----------------|-----|-----|-----|-----|
| Abscesses       | > 4 | > 4 | > 8 | > 32|
| Appendix        | 1   | 0.06| 0.5 | 1   |
| Colon           | ≤ 0.03| > 4 | 0.25| > 32|
| Diverticulum    | ≤ 0.03| ≤ 0.03| ≤ 0.5|
| Gall Bladder    | 2   | > 4 | 2   | 8   |
| Liver           | 0.06| ≤ 0.03| 0.5 | 1   |
| Pancreas        | 0.25| 0.25| 8   | 1   |
| Peritoneal Fluid| > 4 | > 4 | > 8 | > 32|
| Rectum          | 0.12| 0.12| 0.12| 2   |
| Small Intestine | 4   | 0.12| ≤ 0.5|
| Stomach         | 0.25| 0.5 | 1   |
| Other           | > 4 | > 4 | > 8 | > 32|
| Emergency Room  | 1   | 0.5 | 2   | 2   |
| General Unspecified ICU | > 4 | 0.25 | > 8 | 1   |
| Medicine General| 0.5 | 4   | 1   | 2   |
| Medicine ICU    | > 4 | > 4 | > 8 | > 32|
| None Given      | ≤ 0.03| 0.06| 0.12| ≤ 0.5|
| Pediatric General| ≤ 0.03| ≤ 0.03| 0.25| ≤ 0.5|
| Pediatric ICU   | > 4 | > 4 | > 8 | > 32|
| Surgery General | > 4 | > 4 | 8   | 32  |
particularly to IPM were most obvious in ICUs, which is in agreement with previous studies, in which it was noted that patients infected with carbapenem-resistant *K. pneumoniae* strains were mainly elderly, possessed multiple co-morbidities, were frequently admitted from and discharged to post-acute care facilities, and experienced prolonged hospital stays [18]. In addition, for carbapenem-resistant Gram-negative pathogen infections, previous administration of carbapenems has been shown to be a major factor, particularly in ICUs [19], and isolation of patients harboring carbapenem-resistant *Enterobacteriaceae* and delayed application of alternative antibiotics has been proposed to lead to a spread of these pathogens in ICUs [20].

A limitation of the present study is the missing data about molecular mechanisms of resistances against the included antibiotics.

Conclusions

Susceptibilities of *E. coli* IAI and UTI strains to IPM and ETP were > 90% in 2014 and 2015, while susceptibilities to IPM and ETP of *K. pneumoniae* IAI strains were > 80% in 2014, but decreased to ≤ 80% in 2015, particularly for UTI strains. Susceptibilities of all IAI *Enterobacteriaceae* strains to IPM and ETP were lowest in the colon and abscesses and *Enterobacteriaceae* susceptibilities of both UTI and IAI isolates to IPM and ETP were lowest in medical, pediatric and surgery ICUs in 2015.

Susceptibilities rates of *E. coli* and *K. pneumoniae* strains to cephalosporins collected from UTIs ranged from 38.6 to 69.5% and for IAI strains from 33.18 to 67.7% in 2015, which suggests that cephalosporins should not be the first choice for empirical UTI and IAI antibiotic therapy.

Additional files

**Additional file 1:** Figure S1. Distribution of isolates acquired from IAI pathogens in different organ groups in 2014. (TIF 357 kb)

**Additional file 2:** Table S1. Distribution of the IAI and UTI pathogens in China in 2014. (DOCX 18 kb)

**Additional file 3:** Figure S2. Distribution of *E. coli*, *K. pneumoniae* and other *Enterobacteriaceae* strains in different age groups in 2014. *P < 0.05, ***P < 0.001.* (TIF 288 kb)

**Additional file 4:** Table S2. MIC90 values of *E.coli* and *K. pneumoniae* for the indicated antibiotics in 2014 and 2015. (DOCX 15 kb)

**Abbreviations**

AMK: amikacin; CA: community-associated; CAZ: ceftazidime; CIP: ciprofloxacin; Cls: confidence intervals; CLSI: Clinical and Laboratory Standards Institute; CRO: ceftriaxone; CTX: cefotaxime; E. coli: *Escherichia coli*; ETP: ertapenem; FEP: cephalaxin; FOX: cefoxitin; IAI: intra-abdominal infections; IPM: imipenem; K: *k pneumoniae*; Klebsiella pneumoniae; LVX: levofloxacin; MIC: Minimum inhibitory concentrations; OSWIA: organ-specific weighted incidence antibiograms; QC: quality control; SAM: ampicillin-sulbactam; SMART: Study for Monitoring Antimicrobial Resistance Trends; Tzp: piperacillin-tazobactam; UTI: urinary tract infections

**Funding**

This research was supported by Outstanding Talents Training Funding Project of Dongcheng District, Beijing (2017), The National Key Research and Development Program of China (SQ2018YFC120102), CAMS Innovation Fund for Medical Sciences (CIFMS) (Grant no. 2015-12M-1-014) and CAMS Initiative for Innovative Medicine (Grant no. 2016-12M-3-014). This study was supported by funding from Merck Sharp & Dohme (MSD; Whitehouse Station, NJ, USA).

**Availability of data and materials**

The data that support the findings of this study are directly available from MSD China Holding Co. Ltd., but the SMART database is not public. Data are also available from the authors upon reasonable request and with permission of MSD China Holding Co. Ltd.

**Authors’ contributions**

All authors have read and approved the manuscript. The authors were solely responsible for the conception and performance of the study and for writing this manuscript. Conceptualization: HZ, YXN, QWY, YCX. Data collection: HZ, HSK, YSY, AHW, QD, XFJ, SFZ, ZYS, YXN, WPW, YW, KL, HYL, CXY, WWH, BDG, BS, RB, QWY, YCX. Data analysis: HZ, YSY, AHW, QD, SFZ, BDG, WPW, RB, QWY, YCX. Writing original draft: HZ, YCX. Writing review & editing: HZ, HSK, YSY, AHW, QD, XFJ, SFZ, ZYS, YXN, WPW, YW, KL, HYL, CXY, WWH, BDG, BS, RB, QWY, YCX.

**Ethics approval and consent to participate**

The Human Research Ethics Committee of Peking Union Medical College Hospital approved this study and waived the need for consent (Ethics Approval Number: S-K238).

**Consent for publication**

Not applicable.

**Competing interests**

Robert Badal received financial support in the form of salaries from International Health Management Associates, who receive funding from MSD to administer the SMART program and for SMART-related travel and consultation expenses.

**Publisher’s Note**

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

**Authors**

1 Division of Microbiology, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences, No. 1 Shuifu, Wangfujing Street, Beijing 100730, China. 2 Department of Microbiology, The First Affiliated Hospital of Zhejiang University, Hangzhou 310003, China. 3 Department of Infectious Diseases, Sairun Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou 310016, China. 4 Infection Control Center, Xiangya Hospital, Central South University, Changsha 410008, China. 5 Microbiology Laboratory, Jilin Province People’s Hospital, Changchun 130021, China. 6 The Fourth Hospital of Harbin Medical University, No. 37 Yiyuan Road, Nangang District, Harbin, China. 7 Division of Microbiology, Haikou People’s Hospital, Haikou 570028, China. 8 Department of Laboratory Medicine, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China. 9 Division of Microbiology, Ruijin Hospital, School of Medicine, Shanghai Jiaotong University, Shanghai 200025, China. 10 Nanjing General Hospital, No. 305 Zhongshan Dong Road, Nanjing, China. 11 Department of Laboratory Medicine, Shandong Provincial Hospital Affiliated to Shandong University, Jinan 250021, China. 12 Division of Microbiology, The First Affiliated Hospital, Sun Yat-Sen University, Guangzhou 510080, China. 13 Zhongshan Hospital Affiliated to Fudan University, No. 180 Fenglin Road, Shanghai 200032, China. 14 Beijing Chao-yang Hospital, 8 Gongren Tiyuchang Nanlu, Chaoyang District, Beijing 100020, China. 15 Division of Microbiology, The First Affiliated Hospital of Chongqing Medical University, Chongqing 400016, China. 16 Clinical laboratory, The Second Affiliated Hospital of Nanchang University, Nanchang 330006, China. 17 First Affiliated Hospital of Kunming Medical University, No. 295 Xichang Road, Kunming 650032, China. 18 Division of Microbiology, International Health Management Associates, Schaumburg, IL 60173-3817, USA.
References

1. Yang Q, Zhang H, Wang Y, Xu Y, Chen M, Badal RE, Wang H, Ni Y, Yu Y, Hu B, et al. A 10 year surveillance for antimicrobial susceptibility of Escherichia coli and Klebsiella pneumoniae in community- and hospital-associated intra-abdominal infections in China. J Med Microbiol. 2013;62(Pt 9):1343–9.

2. Montrey I, Hackett M, Badal R, Bouchillon S, Hawser S, Biedenbach D. A review of ten of the study for monitoring antimicrobial resistance trends (SMART) from 2002 to 2011. Pharmaceuticals (Basel). 2013;6(11):1335–46.

3. Yang Q, Zhang H, Wang Y, Xu Z, Zhang G, Chen X, Xu Y, Cao B, Kong H, Ni Y, et al. Antimicrobial susceptibilities of aerobic and facultative gram-negative bacilli isolated from Chinese patients with urinary tract infections between 2010 and 2014. BMC Infect Dis. 2017;17(1):192.

4. Liao K, Chen Y, Wang M, Guo P, Yang Q, Ni Y, Yu Y, Hu B, Sun Z, Huang W, et al. Molecular characteristics of extended-spectrum beta-lactamase-producing Escherichia coli and Klebsiella pneumoniae causing intra-abdominal infections from 9 tertiary hospitals in China. Diagn Microbiol Infect Dis. 2017;87(1):45–8.

5. Hebert C, Ridgway J, Vekhter B, Brown EC, Weber SG, Robicsek A. Demonstration of the weighted-incidence syndromic combination antibiogram: an empiric prescribing decision aid. Infect Control Hosp Epidemiol. 2012;33(4):381–8.

6. Zhang S, Huang W. Epidemiological study of community- and hospital-acquired intraabdominal infections. Chin J Traumatol. 2015;18(2):84–9.

7. CLSI: Clinical and Laboratory Standards Institute (CLSI) M07-A10. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically; approved standard—tenth edition. Wayne: CLSI; 2015.

8. CLSI: Clinical and Laboratory Standards Institute (CLSI) M100-S25. Performance standards of antimicrobial susceptibility testing. Twenty-fifth informational supplement. Wyane: CLSI. 2015.

9. Lee S, Han SW, Kim KW, Song DY, Kwon KT. Third-generation cephalosporin resistance of community-onset Escherichia coli and Klebsiella pneumoniae bacteremia in a secondary hospital. Korean J Intern Med. 2014;29(1):49–56.

10. Kokal J, Yilmaz G, Unal S, Zaralolu P, Korten V, Mulazimoglu L, Tabak F, Mete B, Oguz VA, Gulay Z, et al. Epidemiology and susceptibility of pathogens from SMART 2011-12 Turkey: evaluation of hospital-acquired versus community-acquired urinary tract infections and ICU versus non-ICU-associated intra-abdominal infections. J Antimicrob Chemother. 2017;72(5):1364–72.

11. Redgrave LS, Sutton SB, Webber MA, Piddock LJ. Fluoroquinolone resistance: mechanisms, impact on bacteria, and role in evolutionary success. Trends Microbiol. 2014;22(8):438–45.

12. Werner NL, Hecker MT, Sethi AK, Donskey CJ. Unnecessary use of fluoroquinolone antibiotics in hospitalized patients. BMC Infect Dis. 2011;11:187.

13. Shi W, Li K, Ji Y, Jiang Q, Wang Y, Shi M, Mi Z. Carbapenem and cefotixin resistance of Klebsiella pneumoniae strains associated with porin OmpK36 loss and DHA-1 beta-lactamase production. Braz J Microbiol. 2013;44(2):435–42.

14. Zhang X, Chen D, Xu G, Huang W, Wang X. Molecular epidemiology and drug resistant mechanism in carbapenem-resistant Klebsiella pneumoniae isolated from pediatric patients in Shanghai, China. PLoS One. 2018;3(3):e0194000.

15. Liu Q, Ren J, Wu X, Wang G, Wang Z, Wu J, Huang J, Lu T, Li J. Shifting trends in bacteriology and antimicrobial resistance among gastrointestinal fistula patients in China: an eight-year review in a tertiary-care hospital. BMC Infect Dis. 2017;17(1):637.

16. Fan S, Wang J, Li Y, Li J. Bacteriology and antimicrobial susceptibility of ESBLs producers from pus in patients with abdominal trauma associated intra-abdominal infections. Eur J Trauma Emerg Surg. 2017;43(1):165–71.

17. Davies GM, Daskas ME, Teutsch S. The burden of appendicitis-related hospitalizations in the United States in 1997. Surg Infect. 2004;5(2):160–5.

18. Perez F, Erdiniari A, Ray AJ, Decker BK, Wallace CJ, Hujer KM, Ecker DJ, Adams MD, Toltsis P, Dul MJ, et al. Carbapenem-resistant Acinetobacter baumannii and Klebsiella pneumoniae across a hospital system: impact of post-acute care facilities on dissemination. J Antimicrob Chemother. 2017;62(8):1807–18.

19. Routsi C, Pratikakis M, Platsouka E, Sotropoulou C, Papas V, Pissolis T, Tsakris A, Nanas S, Roussos C. Risk factors for carbapenem-resistant gram-negative bacteremia in intensive care unit patients. Intensive Care Med. 2013;39(7): 1253–61.

20. Zurawski RM. Carbapenem-resistant enterobacteriaceae: occult threat in the intensive care unit. Crit Care Nurse. 2014;34(5):44–52.