Infection Control & Hospital Epidemiology (2018), **39**, 1237–1245
doi:10.1017/ice.2018.188

SHEA
The Society for Healthcare Epidemiology of America

Review

Antimicrobial stewardship for acute-care hospitals: An Asian perspective

Anucha Apisarnthanarak MD[1], Andrea Lay-Hoon Kwa PharmD[2,3,4], Cheng-Hsun Chiu MD[5], Suresh Kumar MRCP[6], Le Thi Anh Thu MD, PhD[7], Ban Hock Tan FRCP(UK)[8], Zhiyong Zong PhD[9], Yin Ching Chuang MD[10,11], Anis Karuniawati MD, PhD[12,13], Maria Fe Tayzon MD[14,15], Thomas Man-Kit So FRCP[16] and Lance R. Peterson MD[17,18]

[1]Division of Infectious Diseases, Faculty of Medicine, Thammasat University Hospital, Pathumthani, Thailand, [2]Department of Pharmacy, Singapore General Hospital, Singapore, [3]Emerging Infectious Diseases, Duke-National University of Singapore Medical School, Singapore, [4]Department of Pharmacy, Faculty of Science, National University of Singapore, Singapore, [5]Department of Pediatrics, Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Taoyuan, Taiwan, [6]Department of Medicine, Hospital Sungai Buloh, Sungai Buloh, Malaysia, [7]Department of Infection Control, Cho Ray Hospital, Ho Chi Minh City, Vietnam, [8]Department Infectious Diseases, Singapore General Hospital, Singapore, [9]Center of Infectious Diseases, West China Hospital, Sichuan University, Chengdu, China, [10]Department of Internal Medicine, Chi Mei Medical Center, Liouying, Taiwan, Taiwan, [11]Department of Medical Research, Chi Mei Medical Center, Tainan, Taiwan, [12]Department of Microbiology, Faculty of Medicine, Universitas Indonesia, [13]Cipto Mangunkusumo Hospital, Jakarta, Indonesia, [14]Hospital Infection Control and Epidemiology Center, The Medical City, Pasig City, Philippines, [15]Ateneo School of Medicine and Public Health, Manila, Philippines, [16]Infectious disease specialist in private practice, Hong Kong, [17]NorthShore University Health System, Evanston, Illinois, United States and [18]University of Chicago Pritzker School of Medicine, Chicago, Illinois, United States.

Abstract

Inappropriate use of antibiotics is contributing to a serious antimicrobial resistance problem in Asian hospitals. Despite resource constraints in the region, all Asian hospitals should implement antimicrobial stewardship (AMS) programs to optimize antibiotic treatment, improve patient outcomes, and minimize antimicrobial resistance. This document describes a consensus statement from a panel of regional experts to help multidisciplinary AMS teams design programs that suit the needs and resources of their hospitals. In general, AMS teams must decide on appropriate interventions (eg, prospective audit and/or formulary restriction) for their hospital, focusing on the most misused antibiotics and problematic multidrug-resistant organisms. This focus is likely to include carbapenem use with the goal to reduce carbapenem-resistant gram-negative bacteria. Rather than initially trying to introduce a comprehensive, hospital-wide AMS program, it would be practical to begin by pilot testing a simple program based on 1 achievable core intervention for the hospital. AMS team members must work together to determine the most suitable AMS interventions to implement in their hospitals and how best to put them into practice. Continuous monitoring and feedback of outcomes to the AMS teams, hospital administration, and prescribers will enhance sustainability of the AMS programs.

(Received 29 June 2018; accepted 11 July 2018)

Background

Antimicrobial resistance (AMR) has long been recognized as a major global health threat,[1,2] and it is now a particularly urgent issue in the Asia-Pacific region.[2–5] Indiscriminate use of antibiotics drives the rapid rate at which AMR is developing in this region.[2,6,7]

Antimicrobial stewardship (AMS) is a coordinated set of interventions designed to improve the appropriate use of antimicrobial agents by optimizing antimicrobial selection, dosage, duration of treatment, and route of administration.[8] Although effective hospital AMS programs and infection control are essential to reducing the threat of AMR,[8] the implementation of AMS programs has been inconsistent across countries and regions and is often inadequate in low- and middle-income economies common in Asia.[9–13]

International guidelines provide evidence-based recommendations for the implementation of a broad range of AMS interventions.[8,14,15] However, these guidelines are often incompatible with the practice and the infrastructure of many hospitals in Asia.[10,12,13,15] To guide the implementation of AMS programs in acute-care hospitals across Asia, a panel of regional experts developed a consensus statement that is the basis for this document. The goal is to provide practical, flexible recommendations for implementing AMS programs designed to suit the varying clinical needs and resources of hospitals across the region.

Consensus statement methods

Consensus generation

In November 2016, a panel of 11 expert infectious disease (ID) clinicians, researchers, and opinion leaders from Asia met to

Author for correspondence: Anucha Apisarnthanarak, Division of Infectious Diseases, Faculty of Medicine, Thammasat University Hospital, Pathumthani, Thailand 12120. E-mail: anapisarn@yahoo.com

Cite this article: Apisarnthanarak A, *et al.* (2018). Antimicrobial stewardship for acute-care hospitals: An Asian perspective. *Infection Control & Hospital Epidemiology* 2018, 39, 1237–1245. doi: 10.1017/ice.2018.188

discuss and formulate a consensus statement on AMS programs for acute-care hospitals in the Asian region. In a pre-meeting survey, the experts answered questions relating to AMS program goals and outcome measures, team structure, AMS interventions, the importance of information technology systems, the strategy of combining AMS and infection control, and stakeholder advocacy. At the 2-day meeting, the experts reviewed the available medical literature then discussed the results of the survey in relation to gaps and challenges in Asia. After the meeting, draft consensus statements based on this discussion were distributed to each panel member for review and comment, and these statements were revised accordingly. This process was repeated until final consensus was reached in November 2017.

Search strategy and selection criteria

A system adapted from the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used to rate the strength of recommendations for AMS program interventions and the quality of the supporting evidence (Table 1).[8] Evidence for these recommendations was primarily based on updated Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) guidelines and recent systematic reviews and meta-analyses of interventions, including from hospitals in the Asia-Pacific region.[8,16–18] We also searched PubMed for relevant English language articles using terms such as "antimicrobial resistance," "antimicrobial stewardship," and "Asia" from 2000 through August 2017.

Key findings and recommendations

Gaps and challenges facing implementation of AMS in Asia

The common gaps and challenges that can hinder implementation of AMS programs in Asia and potential solutions to overcoming them are listed in Table 2. A critical concern is the lack of routinely collected epidemiological AMR data in Asian countries, which makes planning difficult.[4–7] A paucity of epidemiological data contributes to low awareness of the scale of the problems associated with the misuse of antibiotics.[5]

Compounding the low awareness of AMS program benefits, hospital administrators and prescribers in overworked and overcrowded, resource-poor hospitals often do not prioritize AMS because they perceive themselves to have more immediate challenges, primarily patient care and potentially infection control.[2,9,11,12,19,20] The pharmaceutical industry can support discussion among the stakeholders, which occurred during the preparation of this document, but the industry is often seen as a negative influence, especially when financial incentives are offered for prescribing antibiotics.[2,11,12,19–21] Provider resistance is another important barrier to the widespread implementation of hospital AMS programs.[9,11,19]

Resource constraints pose a major barrier to the implementation of AMS programs in many Asian hospitals.[2,10,13,19,20,22] Ongoing training and education should encourage and emphasize the importance of AMS activities.[11,13,20,23] Strengthening microbiology laboratory and information technology capacity to deliver reliable and timely data on causative pathogens and antibiotic susceptibility is particularly important for implementation of AMS.[2,13]

As hospitals differ in terms of AMS program status, we recommend that each hospital assess the AMS gaps using an AMS assessment checklist (Supplementary Material S1) and prioritize actionable steps (Supplementary Material S2) to overcome the barriers.

AMS program goals

The primary objective of a hospital AMS program is to achieve best clinical outcomes related to antibiotic use while minimizing toxicity and limiting the selective pressure on bacterial populations that drive the emergence of AMR.[24]

AMS process and outcome measures

Before an AMS program is implemented, outcome measures need to be chosen that prospectively evaluate the efficiency of the AMS program in relation to its goals.[24,25] We recommend selecting a combination of commonly used process and outcome measures (Table 3) and accounting for data and resource availability.[26] Process measures, such as antibiotic consumption and appropriate antibiotic use, should be evaluated to confirm compliance with the AMS program. An effective AMS program can improve outcomes, such as length of hospital stay, rates of MDR bacterial infection or colonization, and treatment-related costs.[16–18,27,28]

Table 1. Grading System Used to Rate the Strength of Guideline Recommendations and Quality of Supporting Evidence[a]

Strength of Recommendation	Extent of Consensus
Strong	Most or all healthcare professionals would endorse the recommended course of action, and only a small proportion may not (eg, 9–11 panel members agree with the recommendation).
Weak	Most health care professionals would endorse the recommended course of action, and a proportion would not (eg, 6–8 panel members agree with the recommendation).
Quality of evidence	**Type of Evidence**
High	Randomized controlled trials (≥1)
Moderate	Well-designed nonrandomized controlled trials (>1); cohort or case-controlled studies (preferably from >1 center); multiple time-series; or large effect from uncontrolled studies
Low	A well-designed nonrandomized controlled trial (≥1); cohort or case-controlled studies (preferably from >1 center); multiple time series; or large effect from uncontrolled studies
Very low	Opinions of respected authorities, based on clinical experience, descriptive studies, or expert committee reports

[a]Based on the US Grading of Recommendations Assessment, Development and Evaluation (GRADE) system used in current IDSA/SHEA guidelines.[12]

https://doi.org/10.1017/ice.2018.188 Published online by Cambridge University Press

Table 2. Common Gaps and Challenges in Relation to Implementing AMS Programs in Hospitals in Asia

Common Gaps and Challenges in Implementing Hospital AMS Programs in Asia[a]	Potential Solutions to Overcoming Gaps in Hospital AMS Programs[b]
Lack of epidemiological data and surveillance systems	• Prioritize obtaining support for microbiology laboratory services for reliable culture-guided therapy, AMR surveillance and provision of hospital antibiograms
Lack of awareness of AMR	• Provide regular report of AMR data and AMS program performance to relevant hospital departments and hospital administration
Weak infrastructure	• If there is no infrastructure to set up IT systems to support a hospital AMS program, a paper-based system can be used in conjunction with syndrome-specific guidelines.
Insufficient education and training of hospital staff	• Obtain formal support from hospital administration for infectious disease and AMS training, and appropriate time commitment and remuneration for AMS providers based on the size of the hospital • Consider obtaining external infectious disease specialist advice and training from a more well-resourced hospital
Limited funding	• Provide hospital administrators with credible business case to persuade them that funding of an AMS program is beneficial to the hospital • Start small and build capacity over time; gradually introduce AMS interventions by hospital unit or ward
Prescriber resistance to AMS	• Provide regular feedback and education to prescribers in an easily interpreted format • Make efforts to understand the reasons for noncompliance to AMS recommendations and rectify the problems.
Poor infection control	• Include an infection control personnel in the AMS core team • AMS and infection control teams work together under the same leadership to achieve the goal of reducing the rate of multidrug-resistant infections.

Note. AMR, antimicrobial resistance; AMS, antimicrobial stewardship.
[a]See Supplementary Material S1 for an AMS program assessment checklist, for Asian hospitals to assess which aspects of the AMS programs are in place and what gaps need to be addressed.
[b]See Supplementary Material S2 for a flowchart of potential next steps and solutions to overcome gaps and challenges in AMS programs in Asian hospitals.

Table 3. Suggested Process-Related Measures and Outcome Measures for AMS Programs

Process-Related Measures
Antibiotic consumption
DOT or DDT
Prescription rates
Appropriate antibiotic use
Time to IV to oral switch
Duration of antibiotic therapy
Outcome Measures
Length of infection-related ICU or hospital stay
MDR bacterial infection and colonization rates
Changes in MDR patterns
Infection-related mortality
Readmission and reinfection rates
Antibiotic-associated toxicity
Treatment-related costs

Note. AMS, antimicrobial stewardship; DDT, defined daily dose; DOT, days of therapy; ICU, intensive care unit; IV, intravenous; MDR, multidrug resistant.

All AMS programs should focus on classes of antibiotics and MDR pathogens that are most relevant to their own region and hospital.[8] In Asian hospitals, this will include carbapenem consumption, with a focus on carbapenem-resistant *A. baumannii* and carbapenemase-producing, carbapenem-resistant *Enterobacteriaceae* infection.

How to build a multidisciplinary AMS team and define roles and responsibilities

In agreement with IDSA/SHEA guidelines,[8,24] we believe that AMS teams should include an ID specialist, clinical pharmacist (with ID training, if possible), a clinical microbiologist, an infection control specialist, and an information technology expert as core team members (Fig. 1). In this AMS team scenario, the ID specialist leads the team, and is responsible for implementation and evaluation of the program, and the clinical pharmacist/pharmacologist performs many daily AMS program tasks and supports the team leader. Clinical microbiologists, clinicians with expertise in infection control and epidemiology, and information technology experts should also have key roles in AMS teams.

Although AMS programs may be best led by ID physicians with additional AMS training,[8,24] many hospitals in Asia do not have adequate personnel to make up the AMS team.[19] In these cases, hospitals should work within their resources to create the most effective team possible.[25,29] For example, the team leader could be an interested clinician from another specialty or a clinical pharmacist.[10,30] External ID specialist advice and AMS training could be obtained from other hospitals to support the local AMS team.[31,32] The minimum personnel for an effective AMS team should include an interested clinician, a pharmacist, and a collaborating microbiologist.[29] However, because of the value ID training offers to hospital AMS programs,[33–35] we encourage all hospitals to commit to ID specialty training for AMS team members.

Several stages are involved in building and establishing a successful AMS team. First, a business plan should be developed, and formal approval and financial support should be obtained from hospital administration, followed by the appointment of a team leader and core team members with clearly defined roles and responsibilities (Table 4). The team should then start working within their budget and existing resources to decide on

https://doi.org/10.1017/ice.2018.188 Published online by Cambridge University Press

measurable clinical outcomes and feasible interventions that achieve short- and long-term AMS program goals. After implementing these interventions, the team should begin monitoring AMS program processes and outcomes. Regular team meetings must be scheduled to review AMS program activities and AMR data and to modify the program. One strategy is to incorporate serial plan-do-study-act (PDSA) cycles to evaluate the effects of AMS interventions and implement further changes as required to improve processes and achieve outcomes.[36]

AMS program interventions

A recent systematic review and meta-analysis of AMS programs in hospitals in Asia showed that AMS implementation was associated with reduced carbapenem and overall antimicrobial consumption, reduced antibiotic expenditure, and trends toward reductions in the incidence of MDR pathogens.[17] Many programs implemented bundled interventions, making it difficult to determine which individual interventions contributed to the success of the AMS program.[17] However, on the basis of these and other reports,[8,16,18] we recommend a range of AMS strategies (Table 5), any number of which can be selected to form AMS programs.

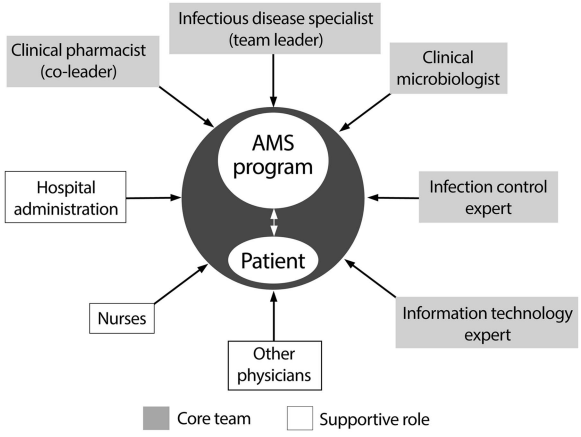

Fig. 1. An ideal hospital antimicrobial stewardship (AMS) program team structure.

Recommended physician-driven interventions

Implementation of local guidelines for surgical prophylaxis and empiric antibiotic therapy of common infection syndromes (strong recommendation, low-quality evidence). As has occurred in China and Vietnam, Asian countries should work toward establishing their own national or regional guidelines for antibiotic therapy.[13,37] Facility-specific guidelines for infection syndromes commonly treated in hospitals can be adapted from pre-existing national, regional, or international guidelines to suit the types of infection commonly seen at the local facility.[19,38,39]

Use of monotherapy instead of combination antibiotics (strong recommendation, high-quality evidence). For many common infections, monotherapy is often one of the most practical, straightforward approaches to reducing antibiotic consumption.[40–43] Evidence indicates that routine use of combination therapy is not superior to monotherapy in terms of outcome for sepsis, endocarditis, neutropenia, and gram-negative infections, or for preventing AMR, and that more toxicity is seen with combination therapy.[44–49] Where appropriate, guidelines should advocate monotherapy as a first-line option, especially for those who are not critically ill.

Use of antibiotic diversity (eg, multiple agents and classes) (strong recommendation, low-quality evidence). A quantitative relationship between the volume of antibiotics consumed and the development of AMR has been demonstrated; resistance to

Table 4. AMS Core Team Member Roles and Responsibilities

Team Member	Role	Responsibilities
Infectious disease specialist[a]	Team leader	• Development of clinical pathways and guidelines • Formulary choices • Reviewing antibiotic use data • Education
Clinical pharmacist	Coleader	• Assist team leader (guideline development and formulary choices) • Guiding optimal antibiotic dosing • Guiding switching from IV to oral • Identifying de-escalation opportunities • Compiling antibiotic use data • Education
Clinical microbiologist	Diagnostic support	• Guiding appropriate specimen collection, cultures and tests • Ensuring accurate pathogen identification and susceptibility testing • Ensuring timely reporting and clear interpretation of patient-specific culture results (including probable contamination or colonization) • Regular provision of antibiograms • Keeping abreast of new developments in the field of diagnostics
Infection control expert	Infection control support	• Monitoring and reporting outbreaks of MDR bacterial infections • Education
Information technology expert	Information technology support	• Developing and maintaining computerized AMS systems, including – Data collection and analysis – Prompts for action (ie, stops on antibiotic prescriptions requiring review; prescription review reminders) – Clinical decision support systems for antibiotic use

Note. AMS, antimicrobial stewardship; IV, intravenous; MDR, multidrug resistant.
[a]If no ID specialists are available, another physician or pharmacist with an interest in infectious diseases can assume responsibility for this role.

https://doi.org/10.1017/ice.2018.188 Published online by Cambridge University Press

Table 5. Recommended physician-, pharmacist- and microbiology-driven AMS program interventions.

Intervention	Strength of recommendation	Overall evidence quality[8,17,18]	Relevant studies from the Asia-Pacific region
Physician-driven			
Implementation of local guidelines for surgical prophylaxis and empiric antibiotic therapy of common infection syndromes	Strong	Low	China,[65,73] Hong Kong,[75] Indonesia,[22] Singapore[38,39]
Use of monotherapy instead of combination antibiotics as a standard approach to most infection treatments	Strong	High	China[76]
Use of antibiotic diversity (e.g. multiple agents and classes)	Strong	Low	Japan[77,78]
Formulary restriction and preauthorization and/or prospective audit and feedback	Strong	Moderate	China,[79] Hong Kong,[80] Malaysia,[10] Singapore,[39,54,48,62] Korea,[64] Thailand[33,55]
Education	Weak	Low	China,[81] Japan,[82] Korea,[56] Taiwan,[83] Thailand,[55] Singapore[54,57]
Pharmacist-driven			
De-escalation	Strong	Low	Thailand,[84] Singapore[58]
Dose optimization (using PK/PD models and therapeutic drug monitoring)	Strong	Low to moderate	Singapore[54,58]
IV to oral switching	Strong	Moderate	Korea,[85] Singapore[38]
Microbiology-driven			
Use of rapid diagnostic testing in addition to conventional diagnostic testing	Strong	Moderate	Australia[86]
Selective antibiotic susceptibility reporting	Strong	Low	NA
Site-specific hospital antibiograms with or without active surveillance	Strong	Low	Singapore[38,57]

AMS, antimicrobial stewardship; IV, intravenous; NA, not available; PK/PD, pharmacokinetic/pharmacodynamic

specific drugs increases when consumption of those drugs passes a critical threshold.[50,51] Therefore, strategies promoting antibiotic diversity should be encouraged, such as changing the first-line antibiotic in consecutive patients or prescribing according to patient characteristics.[52,53] In line with IDSA/SHEA guidelines,[8] we do not recommend antibiotic cycling as an AMS strategy.

Formulary restriction and preauthorization and/or prospective audit and feedback (strong recommendation, moderate-quality evidence). All AMS programs should include some form of prospective audit and/or formulary restriction. With restriction and preauthorization, approval of restricted agents must be granted by an ID expert or another authorized clinician (eg, if ID specialists are unavailable) before they can be prescribed. With prospective audit and feedback, which has similar effects to formulary restriction and preauthorization, the prescription is reviewed by appropriate staff members after empiric antibiotic therapy has been initiated, and recommendations are made based on factors such as hospital guidelines, potential for misuse (spectrum of antibiotic activity), hospital AMR patterns, and the availability of microbiologic test results. Many physicians in Asian countries practice social bedside medicine and like to be personally involved in patient care, so prospective audit and feedback is better suited to such prescribing culture than preauthorization.[27,54,55]

Formulary restriction and preauthorization can be conducted on a small scale by evaluating antimicrobial usage patterns and resistance trends, then devising interventions targeted at a single antibiotic agent or class thought to be misused. For example, an intervention focused on carbapenems in response to endemic carbapenem-resistant *A. baumannii* may be more practical than wide-ranging formulary restriction in many Asian hospitals.

Education (weak recommendation, low-quality evidence). Passive educational activities, such as quarterly or yearly lectures, should not be solely relied upon to improve antibiotic prescribing, but they should be used to complement other AMS activities. Presenting the positive impact of the hospital AMS program can encourage participation by all providers. An education program in combination with ongoing feedback as part of the audit/feedback process is an example of an inexpensive and highly effective AMS program that could be easily applied to many hospitals and is well suited to the Asian bedside prescribing culture.[54–57]

Recommended pharmacist-driven interventions

De-escalation (strong recommendation, low-quality evidence). With this approach, once the pathogen and its susceptibility are known, empiric prescribing should be changed to a narrow-spectrum, pathogen-directed treatment as soon as possible. Carbapenem de-escalation is an example of a beneficial strategy in settings of endemic gram-negative resistance and high rates of carbapenem prescription often found in Asian hospitals.[58]

Choice of antibiotics for de-escalation during empirical therapy should be based on hospital guidelines, while that for pathogen-

https://doi.org/10.1017/ice.2018.188 Published online by Cambridge University Press

directed therapy is based on microbiology results. However, as a caution, the prescriber needs to understand that microbiology results can be confusing as to whether the isolated pathogen is causing the infection or is just a contaminant or colonizer.[59]

Dose optimization (using pharmacokinetic/pharmacodynamic models and therapeutic drug monitoring) (strong recommendation, low-to-moderate–quality evidence). Dose optimization does not necessarily require therapeutic drug monitoring, and can be implemented on the basis of identifying deviations from recommended dosing schedules, making recommendations to optimize dosing based on pharmacokinetic/pharmacodynamic principles.[54,58] In patients who are critically ill, with fluctuating hemodynamic parameters, and with sepsis from infection caused by MDR pathogens, dose-optimization via therapeutic drug monitoring will help ensure adequacy of treatment.[60]

IV to oral switching (strong recommendation, moderate-quality evidence). Intravenous to oral conversion of the same antibiotic is a relatively simple intervention and applicable to many settings.[8] During the prospective audit process, pharmacists should encourage the appropriate use of oral formulations.

Recommended microbiology-driven interventions

Use of rapid diagnostic testing in addition to conventional diagnostic testing (strong recommendation, moderate-quality evidence). Delayed (≥72 hours) conventional bacterial culture and antimicrobial susceptibility testing results are barriers to optimizing therapy.[61] Few hospitals in Asia use rapid diagnostic testing, and many are not in a position to deliver accurate and reliable conventional pathogen-defining testing. It is essential to strive toward strengthening laboratory capacity that can deliver such services. In the meantime, early AMS review and prospective interventions, such as use of monotherapy, de-escalation, and IV-to-oral switch, can be implemented to help optimize empiric antibiotic therapy.[62]

Selective antibiotic susceptibility reporting (strong recommendation, low-quality evidence). Some evidence suggests an association between antibiotics listed in susceptibility reports and their prescription. When feasible, reporting susceptibility to broader-spectrum drugs only when isolates are resistant to narrow-spectrum agents may guide physicians to select the more appropriate narrow-spectrum drugs.[59,61] Although the practice of reporting susceptibility results for a limited number of antibiotics instead of all tested antibiotics may promote appropriate antibiotic use, it requires the specialized expertise of a clinical microbiologist and could be difficult to implement in many Asian hospitals. This reporting needs to be carefully monitored so that errors are not made (eg, no active antibiotic treatment is found in the laboratory report).

Site-specific hospital antibiograms with or without active surveillance testing (strong recommendation, low-quality evidence). Active surveillance testing and availability of hospital antibiograms can present unique susceptibility patterns that help AMS programs develop optimized treatment guidelines and recommendations for empiric treatment.[38,57] In resource-constrained settings, targeted and strategic surveillance testing (eg, point-prevalence surveys for resistant gram-negative bacteria) may be more feasible than continuous active surveillance of all bacterial isolates.

Use of computer systems to support AMS programs

As hospitals move toward adopting electronic health records, there are increasing opportunities to integrate surveillance and decision support into information technology systems.[25,63] A recent systematic review has shown that using information technology systems to streamline AMS program processes and guide prescribing decisions can help to improve appropriate antibiotic use in acute-care hospitals.[63]

Computer-assisted AMS strategies, ranging from computerized systems for data analysis and recording to online AMS systems and computerized decision support systems, are being implemented in various hospitals across Asia.[55,64–67] However, these can be costly and time-consuming to implement and maintain, and they may not be readily accepted.[67,68] If a hospital does not have the infrastructure to set up information technology systems to support an AMS program, a paper-based system can be used in conjunction with syndrome-specific guidelines.

How to combine AMS programs and infection control

Implementation of AMS programs alone may not reduce rates of MDR pathogens.[4,16,59,64,65,69] Infection control measures, including hand hygiene, contact precaution, environmental cleaning, and disinfection, are critical for controlling MDR pathogens in hospitals. Practices to prevent common healthcare-associated infections (eg, central-line–associated blood stream infection and catheter-associated urinary tract infection) are also important.[70,71] We strongly recommend that AMS and infection control teams work together under the same leadership to achieve the goal of reducing the rate of MDR infections.[24,70]

How can organizations and stakeholders work together to advocate for AMS?

The World Health Organization (WHO) is positioned to promote worldwide antimicrobial stewardship, and it acknowledges the roles of the Asia-Pacific Economic Cooperation (APEC) and the Association of Southeast Asian Nations (ASEAN) for successful implementation of AMS in the Asia-Pacific region.[5] The Vietnam Resistance Project (VINARES) is an example of a national project that addresses hospital-related priorities in the WHO policy package on antimicrobial resistance,[13] and a national campaign to enforce Ministry of Health regulations for the rational use of antibiotics has been conducted with a positive effect in China.[37,72,73] The VINARES project and Chinese Ministry of Health initiatives are models for similar healthcare settings.[2,37]

To operate successfully, AMS programs require buy-in from hospital administration and local stakeholders, and adequate financial support.[13,15,25,74] Formal statements of support for AMS should be given by organizational leadership.[15] AMS-related duties should be included in job descriptions, and staff should be given sufficient time and financial support to contribute to AMS activities.[15]

Making AMS programs sustainable

The foundation of a sustainable AMS program lies in starting small and progressively building capacity, with regular monitoring and reporting AMS program performance, modifying and adapting the AMS program, and continuing AMS education. Tracking of long-term trends of pre-specified AMS program process and outcome measures are as important as initial changes. A timeline for reporting progress toward AMS program goals should be specified to clarify expectations from stakeholders because some outcomes take longer to show noticeable changes from baseline.[25]

In conclusion, we also recommend that AMS team members stay up-to-date with the latest AMS guidelines from relevant

https://doi.org/10.1017/ice.2018.188 Published online by Cambridge University Press

professional societies and that they modify and/or add AMS program strategies as appropriate. The AMS team can test, evaluate, and modify interventions using a plan-do-study-act cycle.[31] Regular meetings should be scheduled with the AMS team and clinical staff most affected by the AMS program to make necessary changes to the program.[11,31]

Ongoing training and departmental feedback sessions are also important, where the purpose, evidence-based importance, and positive outcomes of the AMS program can be emphasized.[11,31] Finally, education about the AMS program should be provided as part of orientation for new staff, with regular updates to keep all staff informed about any changes to the antibiogram and the AMS program.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2018.188

Acknowledgments. The authors acknowledge the healthcare team from Weber Shandwick Hong Kong for their support in preparing the manuscript, which was funded by an unrestricted educational grant from Pfizer, Inc. The sponsor had no role in the preparation, review, or approval of the manuscript, or in the decision to submit for publication. The authors alone are responsible for the content and the recommendations, and the decision to submit for publication.

Financial support. The initial meeting held between the authors to discuss and prepare this manuscript was funded by an unrestricted educational grant from Pfizer, Inc.

Conflicts of interest. S.K. has received grant support from Pfizer, Inc. M.F. T. has been a committee member of the Pfizer Philippines Advisory Board. L. R.P received consultation fees from Pfizer, Inc, during the conduct of the study and has worked with several diagnostic companies (Cepheid, Becton-Dickinson, and Roche) as well as the National Institutes of Health (US) on the development of new infectious disease testing that in the future could be beneficial to antimicrobial stewardship. All other authors have nothing to declare.

References

1. O'Neill J. Tackling drug-resistant infections globally: final report and recommendations. Review on Antimicrobial Resistance website. https://amr-review.org/sites/default/files/160518_Final paper_with cover.pdf. Published May 2016. Accessed November 15, 2017.
2. Antimicrobial resistance in the Western Pacific Region: a review of surveillance and health systems response, 2015. World Health Organization website. http://apps.who.int/medicinedocs/documents/s22116en/s22116en.pdf. Published 2015. Accessed November 15, 2017.
3. Kang C-I, Song J-H. Antimicrobial resistance in Asia: current epidemiology and clinical implications. *Infect Chemother* 2013;45:22–31.
4. Lai C-C, Lee K, Xiao Y, *et al*. High burden of antimicrobial drug resistance in Asia. *J Glob Antimicrob Resist*. 2014;2:141–147.
5. Action agenda for antimicrobial resistance in the Western Pacific Region, 2015. World Health Organization website. http://www.wpro.who.int/entity/drug_resistance/documents/action_agenda.pdf. Published 2015. Accessed November 15, 2017.
6. Hsu L-Y, Apisarnthanarak A, Khan E, Suwantarat N, Ghafur A, Tambyah PA. Carbapenem-resistant *Acinetobacter baumannii* and Enterobacteriaceae in South and Southeast Asia. *Clin Microbiol Rev* 2017;30:1–22.
7. Suwantarat N, Carroll KC. Epidemiology and molecular characterization of multidrug-resistant gram-negative bacteria in Southeast Asia. *Antimicrob Resist Infect Control* 2016;5:15.
8. Barlam TF, Cosgrove SE, Abbo LM, *et al*. Implementing an antibiotic stewardship program: guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis* 2016;62:e51–e77.
9. Howard P, Pulcini C, Levy Hara G, *et al*. An international cross-sectional survey of antimicrobial stewardship programmes in hospitals. *J Antimicrob Chemother* 2015;70:1245–1255.
10. Sing DYF, Boo YL, Mukhlis R, Chin PW, Hoo FK. Antimicrobial stewardship program in a Malaysian district hospital: first year experience. *Pakistan J Med Sci* 2016;32:999–1004.
11. Teng CB, Lee W, Yeo CL, *et al*. Guidelines for antimicrobial stewardship training and practice. *Ann Acad Med Singapore* 2012;41:29–34.
12. Tiong JJL, Loo JSE, Mai C-W. Global antimicrobial stewardship: a closer look at the formidable implementation challenges. *Front Microbiol* 2016;7:1860.
13. Wertheim HFL, Chandna A, Vu PD, *et al*. Providing impetus, tools, and guidance to strengthen national capacity for antimicrobial stewardship in Viet Nam. *PLoS Med* 2013;10:e1001429.
14. Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use, August 2015. National Institute for Health and Care Excellence (NICE) website. https://www.nice.org.uk/guidance/ng15. Published 2015. Accessed November 15, 2017.
15. Pollack LA, Srinivasan A. Core elements of hospital antibiotic stewardship programs from the Centers for Disease Control and Prevention. *Clin Infect Dis* 2014;59 Suppl 3:S97–S100.
16. Baur D, Gladstone BP, Burkert F, *et al*. Effect of antibiotic stewardship on the incidence of infection and colonisation with antibiotic-resistant bacteria and *Clostridium difficile* infection: a systematic review and meta-analysis. *Lancet Infect Dis* 2017;17:990–1001.
17. Honda H, Ohmagari N, Tokuda Y, Mattar C, Warren DK. Antimicrobial stewardship in inpatient settings in the Asia Pacific Region: a systematic review and meta-analysis. *Clin Infect Dis* 2017;64:S119–S126.
18. Schuts EC, Hulscher MEJL, Mouton JW, *et al*. Current evidence on hospital antimicrobial stewardship objectives: a systematic review and meta-analysis. *Lancet Infect Dis* 2016;16:847–856.
19. Levy Hara G. Antimicrobial stewardship in hospitals: Does it work and can we do it? *J Glob Antimicrob Resist* 2014;2:1–6.
20. Nguyen K Van, Thi Do NT, Chandna A, *et al*. Antibiotic use and resistance in emerging economies: a situation analysis for Viet Nam. *BMC Public Health* 2013;13:1158.
21. Wang L, Zhang X, Liang X, Bloom G. Addressing antimicrobial resistance in China: policy implementation in a complex context. *Global Health* 2016;12:30.
22. Hadi U, Keuter M, van Asten H, van den Broek P, Study Group "Antimicrobial resistance in Indonesia: Prevalence and Prevention" (AMRIN). Optimizing antibiotic usage in adults admitted with fever by a multifaceted intervention in an Indonesian governmental hospital. *Trop Med Int Health* 2008;13:888–899.
23. Om C, Daily F, Vlieghe E, McLaughlin JC, McLaws M-L. "If it's a broad spectrum, it can shoot better": inappropriate antibiotic prescribing in Cambodia. *Antimicrob Resist Infect Control* 2016;5:58.
24. Dellit TH, Owens RC, McGowan JE, *et al*. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis* 2007;44:159–77.
25. Doron S, Davidson LE. Antimicrobial stewardship. *Mayo Clin Proc* 2011;86:1113–1123.
26. Akpan MR, Ahmad R, Shebl NA, Ashiru-Oredope D. A review of quality measures for assessing the impact of antimicrobial stewardship programs in hospitals. *Antibiotics* 2016;5.
27. Davey P, Marwick CA, Scott CL, *et al*. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database Syst Rev* 2017;2:CD003543.
28. Karanika S, Paudel S, Grigoras C, Kalbasi A, Mylonakis E. Systematic review and meta-analysis of clinical and economic outcomes from the implementation of hospital-based antimicrobial stewardship programs. *Antimicrob Agents Chemother* 2016;60:4840–4852.
29. Kim J, Craft DW, Katzman M. Building an Antimicrobial stewardship program: cooperative roles for pharmacists, infectious diseases specialists, and clinical microbiologists. *Lab Med* 2015;46:e65–e71.
30. Waters CD. Pharmacist-driven antimicrobial stewardship program in an institution without infectious diseases physician support. *Am J Health Syst Pharm* 2015;72:466–468.

31. Duguid M, Cruickshank M, eds. Antimicrobial stewardship in Australian hospitals 2011. Australian Commission on Safety and Quality in Health Care website. https://www.safetyandquality.gov.au/our-work/healthcare-associated-infection/antimicrobial-stewardship/book/. Published 2011. Accessed November 15, 2017.
32. Wu C-T, Chen C-L, Lee H-Y, *et al*. Decreased antimicrobial resistance and defined daily doses after implementation of a clinical culture-guided antimicrobial stewardship program in a local hospital. *J Microbiol Immunol Infect* 2017;50:846–856.
33. Apisarnthanarak A, Lapcharoen P, Vanichkul P, Srisaeng-Ngoen T, Mundy LM. Design and analysis of a pharmacist-enhanced antimicrobial stewardship program in Thailand. *Am J Infect Control* 2015;43:956–959.
34. Pulcini C, Botelho-Nevers E, Dyar OJ, Harbarth S. The impact of infectious disease specialists on antibiotic prescribing in hospitals. *Clin Microbiol Infect* 2014;20:963–972.
35. Schmitt S, McQuillen DP, Nahass R, *et al*. Infectious diseases specialty intervention is associated with decreased mortality and lower healthcare costs. *Clin Infect Dis* 2014;58:22–28.
36. Kanter G, Connelly NR, Fitzgerald J. A system and process redesign to improve perioperative antibiotic administration. *Anesth Analg* 2006;103:1517–1521.
37. Xiao Y, Zhang J, Zheng B, Zhao L, Li S, Li L. Changes in Chinese policies to promote the rational use of antibiotics. *PLoS Med* 2013;10:e1001556.
38. Loo LW, Liew YX, Lee W, Chlebicki P, Kwa AL-H. Impact of antimicrobial stewardship program (ASP) on outcomes in patients with acute bacterial skin and skin structure infections (ABSSSIs) in an acute tertiary care hospital. *Infect Dis Ther* 2015;4:15–25.
39. Liew YX, Lee W, Cai YY, *et al*. Utility and safety of procalcitonin in an antimicrobial stewardship program (ASP) in patients with malignancies. *Eur J Clin Microbiol Infect Dis*. 2012;31:3041–3046.
40. Gupta K, Hooton TM, Naber KG, *et al*. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis* 2011;52:e103–e120.
41. Kalil AC, Metersky ML, Klompas M, *et al*. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the Infectious Diseases Society of America and the American Thoracic Society. *Clin Infect Dis* 2016;63:e61–e111.
42. Lipsky BA, Berendt AR, Cornia PB, *et al*. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. *Clin Infect Dis* 2012;54:e132–e173.
43. Stevens DL, Bisno AL, Chambers HF, *et al*. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2014;59:e10–e52.
44. Falagas ME, Matthaiou DK, Bliziotis IA. The role of aminoglycosides in combination with a beta-lactam for the treatment of bacterial endocarditis: a meta-analysis of comparative trials. *J Antimicrob Chemother* 2006;57:639–647.
45. Bliziotis IA, Samonis G, Vardakas KZ, Chrysanthopoulou S, Falagas ME. Effect of aminoglycoside and beta-lactam combination therapy versus beta-lactam monotherapy on the emergence of antimicrobial resistance: a meta-analysis of randomized, controlled trials. *Clin Infect Dis* 2005;41:149–158.
46. Paul M, Dickstein Y, Schlesinger A, Grozinsky-Glasberg S, Soares-Weiser K, Leibovici L. Beta-lactam versus beta-lactam-aminoglycoside combination therapy in cancer patients with neutropenia. *Cochrane Database Syst Rev* 2013:CD003038.
47. Paul M, Lador A, Grozinsky-Glasberg S, Leibovici L. Beta lactam antibiotic monotherapy versus beta lactam-aminoglycoside antibiotic combination therapy for sepsis. *Cochrane Database Syst Rev* 2014;28:CD003344.
48. Tamma PD, Cosgrove SE, Maragakis LL. Combination therapy for treatment of infections with gram-negative bacteria. *Clin Microbiol Rev* 2012;25:450–470.
49. Falagas ME, Matthaiou DK, Karveli EA, Peppas G. Meta-analysis: randomized controlled trials of clindamycin/aminoglycoside vs. beta-lactam monotherapy for the treatment of intra-abdominal infections. *Aliment Pharmacol Ther* 2007;25:537–556.
50. Austin DJ, Kristinsson KG, Anderson RM. The relationship between the volume of antimicrobial consumption in human communities and the frequency of resistance. *Proc Natl Acad Sci U S A* 1999;96:1152–1156.
51. Peterson LR, Samia NI, Skinner AM, Chopra A, Smith B. Antimicrobial stewardship lessons from mupirocin use and resistance in methicillin-resitant *Staphylococcus aureus*. *Open Forum Infect Dis* 2017;4:ofx093.
52. Sandiumenge A, Lisboa T, Gomez F, Hernandez P, Canadell L, Rello J. Effect of antibiotic diversity on ventilator-associated pneumonia caused by ESKAPE organisms. *Chest* 2011;140:643–651.
53. Sandiumenge A, Diaz E, Rodriguez A, *et al*. Impact of diversity of antibiotic use on the development of antimicrobial resistance. *J Antimicrob Chemother* 2006;57:1197–1204.
54. Teo J, Kwa ALH, Loh J, Chlebicki MP, Lee W. The effect of a whole-system approach in an antimicrobial stewardship programme at the Singapore General Hospital. *Eur J Clin Microbiol Infect Dis* 2012;31:947–955.
55. Apisarnthanarak A, Danchaivijitr S, Khawcharoenporn T, *et al*. Effectiveness of education and an antibiotic-control program in a tertiary care hospital in Thailand. *Clin Infect Dis* 2006;42:768–775.
56. Song YJ, Kim M, Huh S, *et al*. Impact of an antimicrobial stewardship program on unnecessary double anaerobic coverage prescription. *Infect Chemother* 2015;47:111–116.
57. Teng CB, Ng TM, Tan MW, *et al*. Safety and effectiveness of improving carbapenem use via prospective review and feedback in a multi-disciplinary antimicrobial stewardship programme. *Ann Acad Med Singapore* 2015;44:19–25.
58. Lew KY, Ng TM, Tan M, *et al*. Safety and clinical outcomes of carbapenem de-escalation as part of an antimicrobial stewardship programme in an ESBL-endemic setting. *J Antimicrob Chemother* 2015;70:1219–1225.
59. Levy Hara G, Kanj SS, Pagani L, *et al*. Ten key points for the appropriate use of antibiotics in hospitalised patients: a consensus from the Antimicrobial Stewardship and Resistance Working Groups of the International Society of Chemotherapy. *Int J Antimicrob Agents* 2016;48:239–246.
60. Cotta MO, Roberts JA, Lipman J. Antibiotic dose optimization in critically ill patients. *Med Intensiva* 2015;39:563–572.
61. Morency-Potvin P, Schwartz DN, Weinstein RA. Antimicrobial Stewardship: How the microbiology laboratory can right the ship. *Clin Microbiol Rev* 2017;30:381–407.
62. Liew YX, Lee W, Tay D, *et al*. Prospective audit and feedback in antimicrobial stewardship: is there value in early reviewing within 48 h of antibiotic prescription? *Int J Antimicrob Agents* 2015;45:168–173.
63. Baysari MT, Lehnbom EC, Li L, Hargreaves A, Day RO, Westbrook JI. The effectiveness of information technology to improve antimicrobial prescribing in hospitals: a systematic review and meta-analysis. *Int J Med Inform* 2016;92:15–34.
64. Cheon S, Kim M-J, Yun S-J, Moon JY, Kim Y-S. Controlling endemic multidrug-resistant *Acinetobacter baumannii* in intensive care units using antimicrobial stewardship and infection control. *Korean J Intern Med* 2016;31:367–374.
65. Guo W, He Q, Wang Z, *et al*. Influence of antimicrobial consumption on gram-negative bacteria in inpatients receiving antimicrobial resistance therapy from 2008–2013 at a tertiary hospital in Shanghai, China. *Am J Infect Control* 2015;43:358–364.
66. Chen I-L, Lee C-H, Su L-H, Wang Y-CL, Liu J-W. Effects of implementation of an online comprehensive antimicrobial-stewardship program in ICUs: a longitudinal study. *J Microbiol Immunol Infect* 2018;51:55–63.
67. Chow AL, Ang A, Chow CZ, *et al*. Implementation hurdles of an interactive, integrated, point-of-care computerised decision support system for hospital antibiotic prescription. *Int J Antimicrob Agents* 2016;47:132–139.
68. Chow A, Lye DCB, Arah OA. Psychosocial determinants of physicians' acceptance of recommendations by antibiotic computerised decision support systems: a mixed methods study. *Int J Antimicrob Agents* 2015;45:295–304.
69. Apisarnthanarak A, Pinitchai U, Thongphubeth K, *et al*. A multifaceted intervention to reduce pandrug-resistant *Acinetobacter baumannii* colonization and infection in 3 intensive care units in a Thai tertiary care center: a 3-year study. *Clin Infect Dis* 2008;47:760–767.

https://doi.org/10.1017/ice.2018.188 Published online by Cambridge University Press

70. Nagel JL, Kaye KS, LaPlante KL, Pogue JM. Antimicrobial stewardship for the infection control practitioner. *Infect Dis Clin N Am* 2016;30:771–784.
71. Apisarnthanarak A, Ratz D, Greene MT, Khawcharoenporn T, Weber DJ, Saint S. National survey of practices to prevent health care-associated infections in Thailand: the role of prevention bundles. *Am J Infect Control* 2017;45:805–810.
72. Zhou W-J, Luo Z-N, Tang C-M, Zou X-X, Zhao L, Fang P-Q. Is there an improvement of antibiotic use in China? Evidence from the usage analysis of combination antibiotic therapy for type I incisions in 244 hospitals. *J Huazhong Univ Sci Technolog Med Sci* 2016;36:772–779.
73. Zou X, Fang Z, Min R, *et al*. Is nationwide special campaign on antibiotic stewardship program effective on ameliorating irrational antibiotic use in China? Study on the antibiotic use of specialized hospitals in China in 2011–2012. *J Huazhong Univ Sci Technolog Med Sci* 2014;34:456–463.
74. Trivedi KK, Kuper K. Hospital antimicrobial stewardship in the nonuniversity setting. *Infect Dis Clin N Am* 2014;28:281–289.
75. Ng CK, Wu TC, Chan WM, *et al.* Clinical and economic impact of an antibiotics stewardship programme in a regional hospital in Hong Kong. *Qual Saf Health Care* 2008;17:387–392.
76. Hou D, Wang Q, Jiang C, Tian C, Li H, Ji B. Evaluation of the short-term effects of antimicrobial stewardship in the intensive care unit at a tertiary hospital in China. *PLoS One* 2014;9:e101447.
77. Takesue Y, Nakajima K, Ichiki K, *et al.* Impact of a hospital-wide programme of heterogeneous antibiotic use on the development of antibiotic-resistant Gram-negative bacteria. *J Hosp Infect* 2010;75:28–32.
78. Chong Y, Shimoda S, Yakushiji H, *et al.* Antibiotic rotation for febrile neutropenic patients with hematological malignancies: clinical significance of antibiotic heterogeneity. *PLoS One* 2013;8:e54190.
79. Shen J, Sun Q, Zhou X, *et al.* Pharmacist interventions on antibiotic use in inpatients with respiratory tract infections in a Chinese hospital. Int *J Clin Pharm* 2011;33:929–933.
80. Cheng VC, To KK, Li IW, *et al.* Antimicrobial stewardship program directed at broad-spectrum intravenous antibiotics prescription in a tertiary hospital. *Eur J Clin Microbiol Infect Dis* 2009;28:1447–1456.
81. Shi Q, Ding F, Sang R, Liu Y, Yuan H, Yu M. Drug use evaluation of cefepime in the first affiliated hospital of Bengbu medical college: A retrospective and prospective analysis. *BMC Infect Dis* 2013;13:160.
82. Ikai H, Morimoto T, Shimbo T, Imanaka Y, Koike K. Impact of postgraduate education on physician practice for community-acquired pneumonia. *J Eval Clin Pract* 2012;18:389–395.
83. Lin YS, Lin IF, Yen YF, *et al.* Impact of an antimicrobial stewardship program with multidisciplinary cooperation in a community public teaching hospital in Taiwan. *Am J Infect Control* 2013;41:1069–1072.
84. Apisarnthanarak A, Bhooanusas N, Yaprasert A, Mundy LM. Carbapenem de-escalation therapy in a resource-limited setting. *Infect Control Hosp Epidemiol* 2013;34:1310–1313.
85. Park SM, Kim HS, Jeong YM, *et al.* Impact of intervention by an antimicrobial stewardship team on conversion from intravenous to oral fluoroquinolones. *Infect Chemother* 2017;49:31–37.
86. Davies J, Gordon CL, Tong SY, Baird RW, Davis JS. Impact of results of a rapid Staphylococcus aureus diagnostic test on prescribing of antibiotics for patients with clustered gram-positive cocci in blood cultures. *J Clin Microbiol* 2012;50:2056–2058.

https://doi.org/10.1017/ice.2018.188 Published online by Cambridge University Press