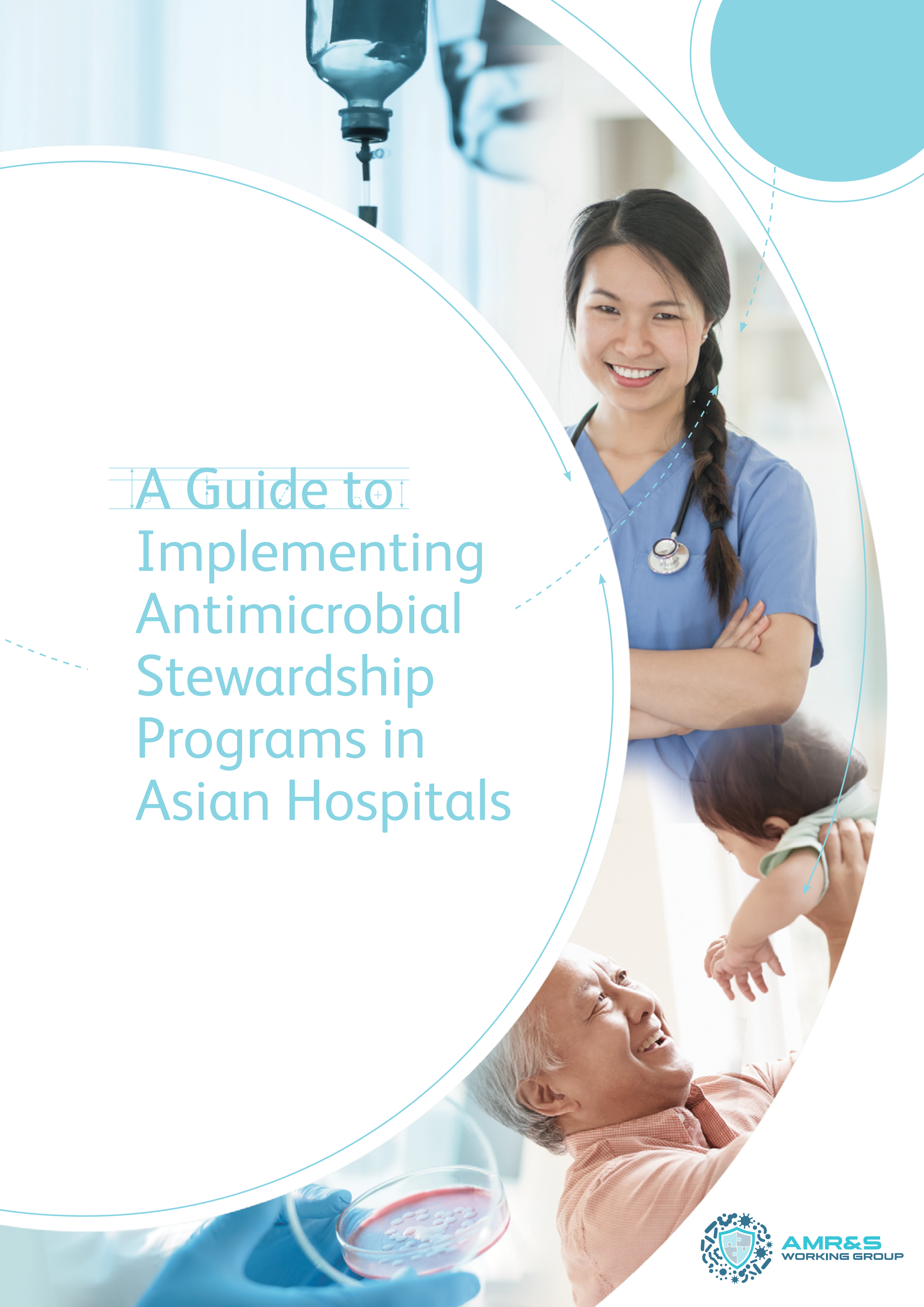


A Guide to Implementing Antimicrobial Stewardship Programs in Asian Hospitals

AMR&S
WORKING GROUP

A Guide to Implementing Antimicrobial Stewardship Programs in Asian Hospitals

This document is intended to provide a practical step-by-step guide to the implementation of antimicrobial stewardship (AMS) programs in Asian hospitals for AMS program leaders. The information contained in the guide is consistent with recommendations from influential internationally recognized organizations, primarily the US Centers for Disease Control and Prevention (CDC), and the Infectious Diseases Society of America (IDSA)/Society for Healthcare Epidemiology of America (SHEA).[1,2]

Many helpful AMS resources have been made freely available online. A table of links to useful guidelines and toolkits for the implementation of AMS programs is provided in Appendix 1. Case studies of successful AMS programs may also be useful to demonstrate different approaches to AMS and to help stimulate ideas for hospitals designing a new AMS program or improving an existing one. A selection of case studies in Asian hospitals can be found in Appendix 2. Additional case studies are available in a **report** from the Pew Charitable Trusts' **Antibiotic Resistance Project**.[3]

Key steps for implementing an AMS program

AMS program strategies depend on the needs and resources of individual hospitals,[4,5] but completion of the eight key steps outlined in this guide will ensure that your program incorporates all seven of the **core elements** of hospital AMS programs as recommended by the CDC (Figure 1).[2]

It is, however, not necessary to wait for all elements to be in place in your hospital before starting an AMS program.[6]

This content is independently developed and owned by the members of the Antimicrobial Resistance & Stewardship Working Group. In the dissemination of these materials, the group would like to acknowledge Pfizer's support which was limited to financial assistance only.

Figure 1

Key steps towards implementing the core components of AMS programs

Key steps for implementing an AMS program

Step 1
Perform a situation analysis

Step 2
Obtain approval for AMS activities

Step 3
Assemble an AMS team

Step 4
Set goals

Step 5
Select interventions

Step 6
Select key performance indicators

Step 7
Implement, educate and train

Step 8
Monitor and report progress

Core AMS program components[2]

Leadership commitment
Dedicate necessary human, financial and information technology resources

Accountability
Appoint a leader or co-leaders, such as a physician and pharmacist, responsible for program management and outcomes

Pharmacy expertise
Appoint a pharmacist, ideally as the co-leader of the AMS program, to help lead implementation efforts to improve antibiotic use

Action
Implement interventions, such as prospective audit and feedback or preauthorization, to improve antibiotic use

Tracking
Monitor antibiotic prescribing trends, impact of interventions, and important outcomes

Reporting
Regularly report information on antibiotic use and resistance to prescribers, pharmacists, nurses, and hospital leadership

Education
Educate prescribers, pharmacists, nurses and patients about adverse reactions from antibiotics, antibiotic resistance, and optimal prescribing

Step 1: Situation analysis

One of the first steps towards implementing an AMS program is to determine what policies, resources and systems are already in place to optimize antibiotic use and support AMS activities.[6,7] Use this **AMS checklist** to see how your hospital rates.

The availability of the following resources should be assessed:

- Interested and appropriately trained staff to contribute to a multidisciplinary AMS team and develop, implement and manage an AMS program (see Step 3)[4,6-8]
- Microbiology laboratory services for reliable culture-guided therapy, antimicrobial resistance (AMR) surveillance and provision of hospital **antibiograms**[4,6,8]
- Information technology (IT) systems to support AMS programs (eg, data entry and analysis systems, electronic medical records, computerized physician order entry)[4,6,7]

Poor laboratory infrastructure or support should not delay the initiation of an AMS program; extensive databases and sophisticated IT systems are NOT necessary for successful AMS programs[3,4,6,8]

Also assess the hospital's situation in relation to:

- Areas of antibiotic use most in need of improvement[4,6-8]
- The most prevalent multidrug-resistant (MDR) organisms[4,6-8]

For example, does your hospital have the following issues?

- Excessive carbapenem use?
- Poor intravenous (IV)-to-oral conversion?
- High rates of MDR Gram-negative bacteria?

The CDC has developed an **assessment tool** that describes generally accepted best practices in antibiotic prescribing.[9] This document may help you to identify problems with antibiotic prescribing in your hospital. Various other assessment tools for antibiotic use are available on the CDC's Antibiotic Prescribing and Use website (**www.cdc.gov/antibiotic-use/hcp/core-elements/hospital-implementation.html**). The World Health Organization (WHO) also provides resources on how to assess antibiotic use by defined daily dose (DDD) (**www.who.int/tools/atc-ddd-toolkit/about-ddd**) and point prevalence surveys (**www.who.int/publications/i/item/WHO-EMP-IAU-2018.01**).

Collect as much baseline antibiotic use and AMR data as practical, and if possible, identify pre-intervention trends over time. Such data will help you justify the need for an AMS program, decide where best to invest limited resources, build a business case for additional funding (see Step 2), and allow you to assess the impact of AMS interventions (see Step 8).[4,8]

Step 2: Obtain approval for AMS activities

Obtaining a formal statement of support and securing funding for AMS activities from hospital administration is crucial.[4] It is therefore important to provide hospital administrators with a credible business case to persuade them that funding for an AMS program is beneficial to the hospital.[4,10]

It has been suggested that inpatient AMS programs should have at least 1 combined physician and pharmacist full-time equivalents for every 100-250 beds, with a suggested physician-to-pharmacist ratio of 1:3[11,12]

Aim to get:

- Appropriate time commitment and remuneration for AMS providers based on the size of the hospital[4,13]
- Support for infectious disease (ID) and AMS training and education[4,13]
- Adequate microbiology and IT services to support AMS activities[4,13]

Some ideas for developing the business case:

- Emphasize the importance to the patient, hospital and society of making sure that antibiotics are used carefully[1,2]
- Point out any national regulations regarding implementation of AMS programs, and statements on the importance of AMS programs from organizations recognized by hospital administration, such as the CDC[1,2]
- Describe antibiotic and AMR problem areas within the hospital using data gathered during the situation analysis, or from local/regional hospitals if there is currently no hospital-specific data[14-16]

Problem areas in Asian hospitals often include high carbapenem use and high rates of carbapenem-resistant *Acinetobacter baumannii* and Enterobacteriaceae[4,14-18]

- Explain the processes that drive optimal antibiotic use (Figure 2)[19]
- Describe the purpose and proven benefits of AMS programs[1,20-22]
- Use the literature to describe successful AMS programs at similar hospitals in the region (these may range from focused unit-specific to comprehensive hospital-wide approaches)[20,21,23-45]

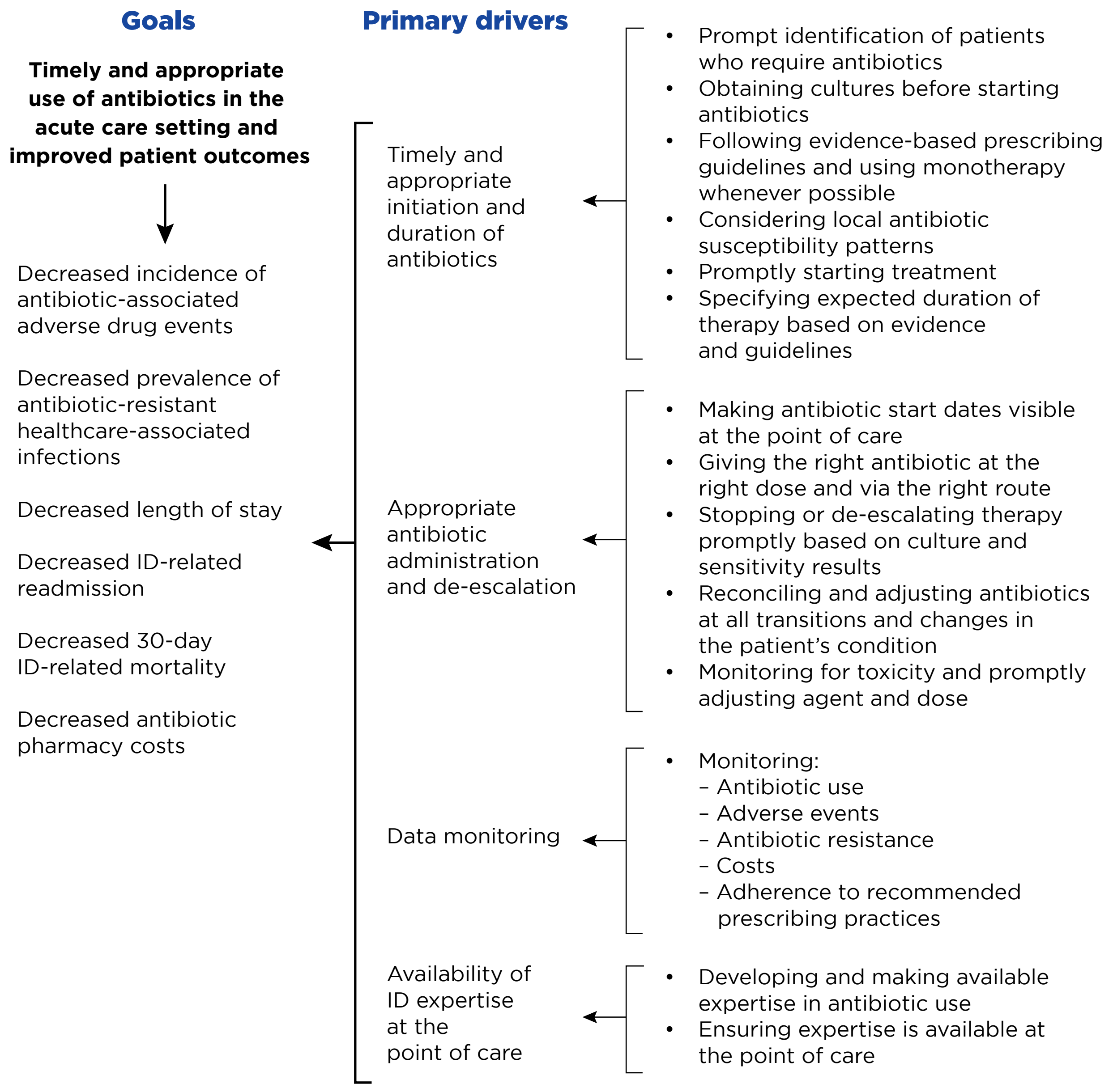
There is a growing body of evidence demonstrating the cost-saving benefits of AMS programs in the hospital setting, including a reduction in antimicrobial expenditure of up to 80% in Asian hospitals[20,21]

- Explain that AMS program savings will offset costs[7,10,19,46,47]
- Propose the most effective ways of implementing change using existing resources[8]
- Propose pilot-testing interventions that are easy or inexpensive to implement (see Step 5), focusing on only one or a few antibiotics or types of infections in one to two hospital units, with plans for expansion if success is demonstrated[4,8]

Business case sample slides can be found in Appendix 3.

Figure 2

Example of an AMS driver diagram[19]



Adapted from the Institute for Healthcare Improvement and CDC.

Step 3: Assemble an AMS team

Work within the hospital's budget and personnel constraints to create the most effective multidisciplinary AMS team available (Figure 3).[4,7,8,39]

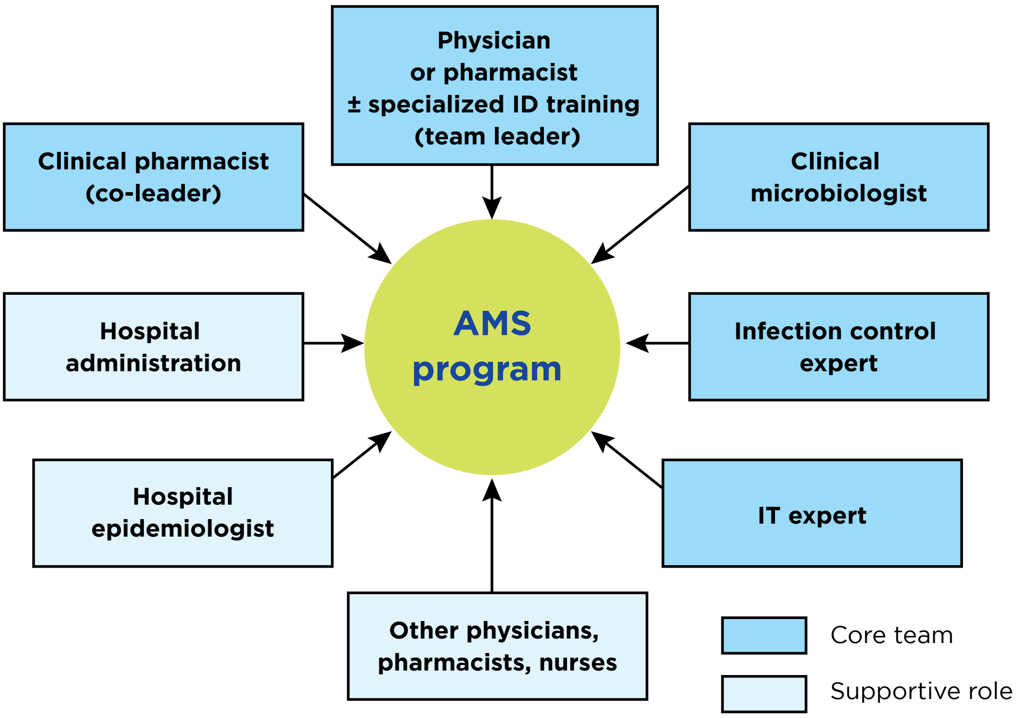
Although there is no set AMS team structure, the team will need a committed and influential leader with the authority to effect change (see **the leadership and communication guide** in this toolkit).[13] The AMS team leader would ideally be an **ID specialist physician**, assisted by an ID clinical pharmacist.[1,2] If there is no ID specialist to lead the team, the team leader could be an interested clinician from another speciality or a clinical pharmacist.[4,8] Infection control specialists, who already have a good understanding of many relevant issues, would be a logical leadership choice. You could also consider obtaining external ID specialist advice and training from a more well-resourced hospital to support the local AMS team.[40,45]

Close collaboration with microbiology laboratory, infection control and IT staff is especially helpful for a well-functioning AMS program.[7] When available, core AMS team members should therefore include clinical microbiologists, infection control experts and IT experts.[4,8] Also include representation from hospital administration, front-line prescribers and nurses to encourage widespread acceptance of the program.[2] In general, AMS team members and support can be recruited from a wide range of interested practitioners at your hospital.[4,7]

Once the roles and responsibilities of each team member have been clearly defined (Table 1), the team should start work on Steps 4 to 8.

Figure 3

Suggested hospital AMS team structure[4]



Adapted from Apisarnthanarak, et al. 2018.

Table 1

AMS core team member roles and responsibilities[4]

Team member	Role	Responsibilities
ID specialist (or physician with other speciality and experienced in infectious diseases or clinical pharmacist)	Team leader	• Developing syndrome-based prescription and treatment guidelines • Performing antibiotic audit and making formulary restriction choices • Reviewing and reporting antibiotic use data • Developing AMS education and training materials and programs • Active AMS education
ID clinical pharmacist (or general clinical pharmacist or staff pharmacist)	Co-leader	• Assisting the team leader • Guiding optimal antibiotic dosing • Guiding IV-to-oral switching • Identifying de-escalation opportunities • Compiling antibiotic use data • Active AMS education
Clinical microbiologist (or microbiology laboratory technician)	Diagnostic support	• Performing appropriate specimen collection, cultures and tests • Performing accurate pathogen identification and susceptibility testing • Timely reporting and clear interpretation of patient-specific culture results (including probable contamination or colonization) • Developing and maintaining antibiograms • Keeping informed of new developments in the field of diagnostics • Active diagnostic AMS education
Infection control physician (or nurse)	Infection control support	• Monitoring and reporting outbreaks of hospital-acquired infections and resistance • Active infection control education
IT expert	IT support	• Developing, implementing and maintaining computerized systems to support the AMS program, including: - Data collection and analysis (where possible, using electronic medical records and computerized physician order entry) - Prompts for action (ie, stops on antibiotic prescriptions requiring review; prescription review reminders) - Clinical decision support system tools

Based on expert opinion from the AMR&S Working Group.

Step 4: Set goals

Set manageable goals based on findings from the situation analysis (see Step 1).

The primary purpose of AMS is to encourage optimal antibiotic use, thereby improving patient outcomes and reducing the undesirable effects of antibiotics, including AMR.[1] While an AMS program is expected to reduce costs associated with inappropriate antibiotic use, the primary goal of the program should not be to reduce drug purchases and costs.[48]

Goals can be focused on[4,7,8]:

- Specific hospital units (eg, the intensive-care unit [ICU])
- Infection syndromes (eg, skin and soft tissue)
- Use of specific classes of antibiotics and resistant bacteria (eg, carbapenems and carbapenem-resistant *Acinetobacter baumannii)*
- Certain IV antibiotics (eg, conversion from IV to oral fluoroquinolones)

Goals can then be extended to include the whole hospital or a wider range of antibiotics and resistant bacteria (eg, all broad-spectrum antibiotics and MDR Gram-negative bacteria).[4,7,8] Implementing AMS programs with effective infection control measures increases the likelihood of achieving AMR-related goals.[27,47]

A ≥10% reduction of monthly carbapenem use and a ≥40% reduction in carbapenem-resistant *A. baumannii* infections at ≥1 year are examples of focused AMS program goals that may be manageable in Asian hospitals[20,26,27,47]

Step 5: Select interventions

There are many potential AMS interventions, any number or combination of which can be selected for use in AMS programs.[1,4,13] Decide which interventions will achieve AMS program goals (see Step 4), are most supported by clinical staff, and can be implemented using available resources (see Step 1). Recommended evidence-based AMS interventions are listed in Table 2.

If your goals are to reduce carbapenem use and carbapenem-resistant *A. baumannii* infections, implementing a carbapenem restriction/approval or audit/feedback system will help to achieve them[23,27,35,36]

It is recommended that all AMS programs are based on preauthorization or prospective audit or a combination of these two core strategies.[1] Prospective audit and feedback may be better suited to Asian prescribing culture than preauthorization, but the former is labor-intensive and must be adapted to suit the resources and workflow of the hospital.[4,40] Advantages and disadvantages of each strategy are outlined in Table 3. When available, computer-assisted strategies should be used to support these core interventions.[1,4]

Hospitals can use local data and knowledge of practices to determine which antibiotics should be subject to prospective audit and feedback and/or preauthorization.[2] The WHO Access, Watch, and Reserve (AWaRe) classification of antibiotics (**www.who.int/publications/i/item/2021-aware-classification**) is a useful tool which highlights antibiotics that could be key targets of AMS activities, and should be adapted according to local data and settings.

Table 2

A selection of evidence-based AMS interventions[1,4,48-50]

Interventions	Comments and recommendations
Core interventions	***Include one or both strategies in all AMS programs***
Preauthorization	• Certain antibiotics must be approved by an AMS physician or pharmacist before they can be prescribed
Prospective audit and feedback	• Prescriptions for audited antibiotics are reviewed by a clinical pharmacist or an ID physician after antibiotic therapy has started, with direct feedback and recommendations to continue, adjust, change or discontinue therapy
Standard interventions	***Use any of these strategies in conjunction with core interventions***
Facility-specific guidelines for common ID syndromes	• Help to standardize prescribing practices based on local AMR patterns, evidence-based guidelines and relevant clinical factors • Use to guide and assess empiric treatment choices, de-escalation and duration of therapy
IV-to-oral conversion	• Change antibiotics with good oral bioavailability from the IV to oral route as soon as possible • Relatively simple strategy applicable to many settings • Integrate into routine pharmacy activities
De-escalation	• Change empiric therapy to as narrow a spectrum treatment as possible, as soon as possible • Choice of antibiotics for de-escalation during empiric therapy can be based on hospital guidelines, while that for pathogen-directed therapy is based on microbiology results • Integrate into routine pharmacy activities
Pharmacokinetic monitoring and adjustment	• Integrate into routine pharmacy activities in relation to certain agents (ie, aminoglycosides and vancomycin)
Dose optimization	• Make recommendations to optimize dose based on patient characteristics, microorganism, site of infection and pharmacokinetic/pharmacodynamic principles of antibiotic agents • Integrate into routine pharmacy activities
Possible interventions	***Implement according to the level of available resources***
Rapid diagnostic testing	• Use when available and cost-effective, in addition to conventional culture and routine reporting
Procalcitonin-guided therapy	• Consider prioritizing for situations such as the following: - A physician is considering stopping antibiotic treatment, but needs reassurance - A patient is clinically deteriorating, and physicians need additional information about resolution of infection
Selective susceptibility reporting	• If implemented, this reporting needs to be carefully monitored so that errors are not made (eg, no active antibiotic treatment is found in the laboratory report)
Stratified antibiograms	• Use to expose differences in susceptibility (eg, by unit) and to complement non-stratified antibiograms
Computerized clinical decision support systems	• Only consider implementing if the required IT resources are readily available

Table 3

Comparison of preauthorization and prospective audit and feedback strategies for AMS programs[1]

Preauthorization	Prospective audit and feedback
Advantages	
• Reduces initiation of unnecessary/inappropriate antibiotics • Optimizes empiric choices based on hospital formulary and guidelines • Prompts review of clinical data/prior cultures at the start of therapy • Controls antibiotic use directly • Decreases use of high-cost antibiotics	• Direct interaction and feedback with prescribers can increase visibility of AMS programs and build working relationships between the AMS team and prescribers • Feedback can address empiric choice based on hospital guidelines as well as downstream treatment (IV-to-oral conversion, de-escalation and duration of therapy) • More clinical data available for recommendations • Greater flexibility in timing of recommendations • Frequency of audit can be adapted to suit clinical needs and resources (does not have to be done on a daily basis if resources are limited) • Maintains prescriber independence • Provides educational benefit to prescribers
Disadvantages	
• Only impacts use of certain/targeted antibiotics • Influences empiric use to a much greater extent than downstream use (eg, de-escalation, IV-to-oral conversion, duration of therapy) • Loss of prescriber independence • May delay therapy • Real-time resource intensive • May result in shift to other antibiotics and select for different AMR patterns	• Compliance with feedback recommendations is voluntary • Typically time-consuming and labor-intensive, thus may be difficult to perform frequently in resource-limited settings • Success depends on the manner in which feedback is delivered to prescribers • May take longer to achieve reductions in targeted antibiotic use

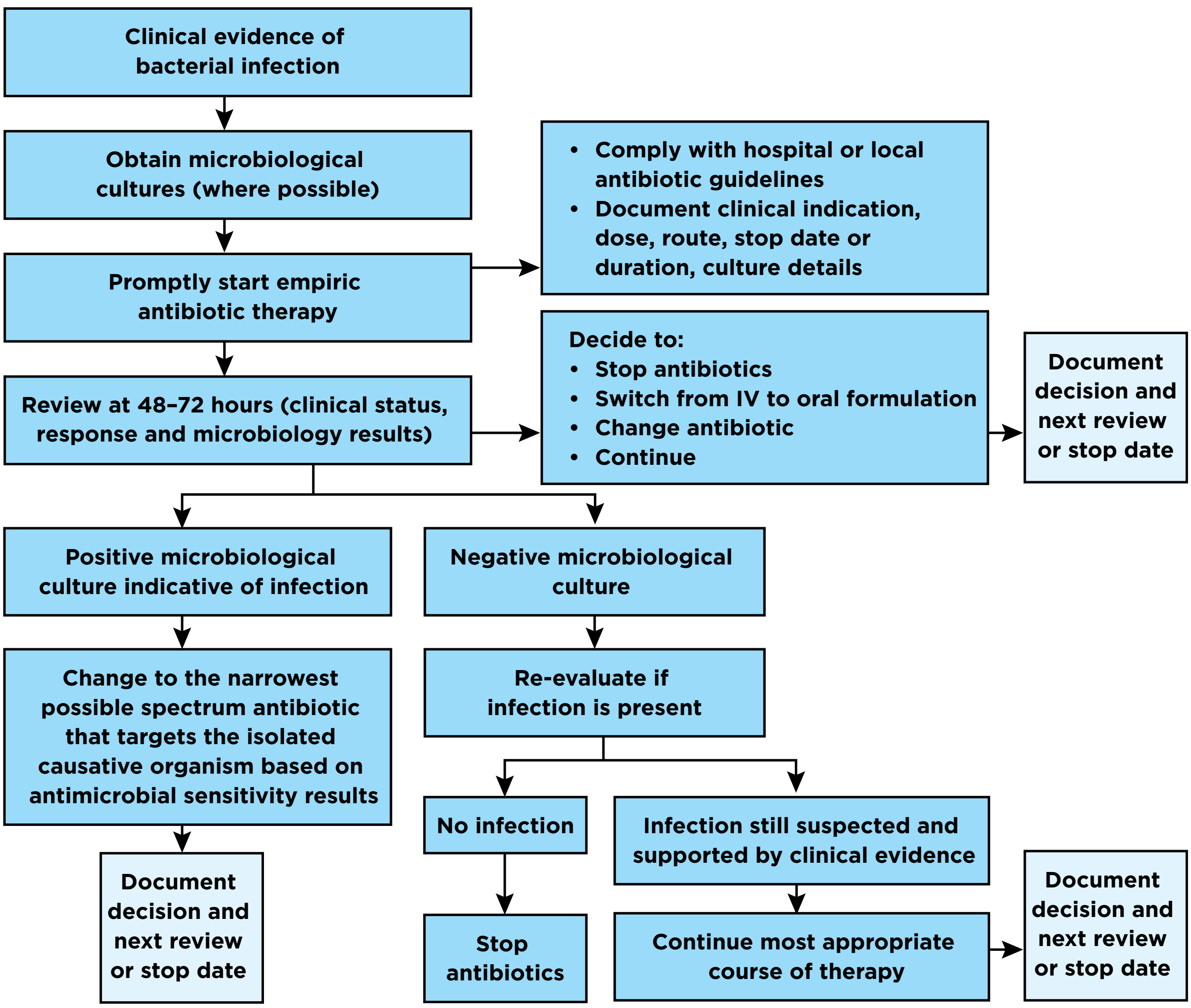
There are some general rules that should be adhered to when deciding on how to integrate core interventions into hospital workflow (Figure 4):

- In the absence of rapid diagnostic testing, aim to review prescriptions within 48 hours of the start of empiric therapy and again in relation to blood culture results (≥72 hours)[42,51-53]
- If daily approval of restricted agents is not feasible, initial doses can be dispensed while waiting for approval to be obtained, so that therapy is not delayed[25,52]

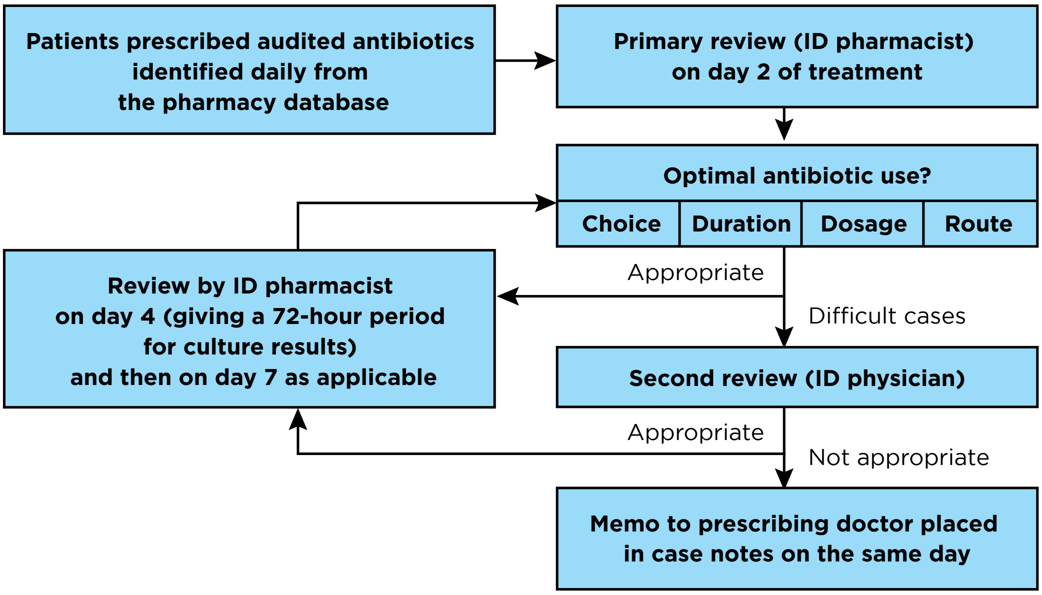
Figure 4

Diagrams of (a) general workflow into which AMS antibiotic approval or audit should be integrated[51,52] (b) a prospective audit and immediate feedback system implemented at Singapore General Hospital[40,53] and (c) a computerized approval system implemented at Chang Gung Memorial Hospital, Taiwan[25,42]

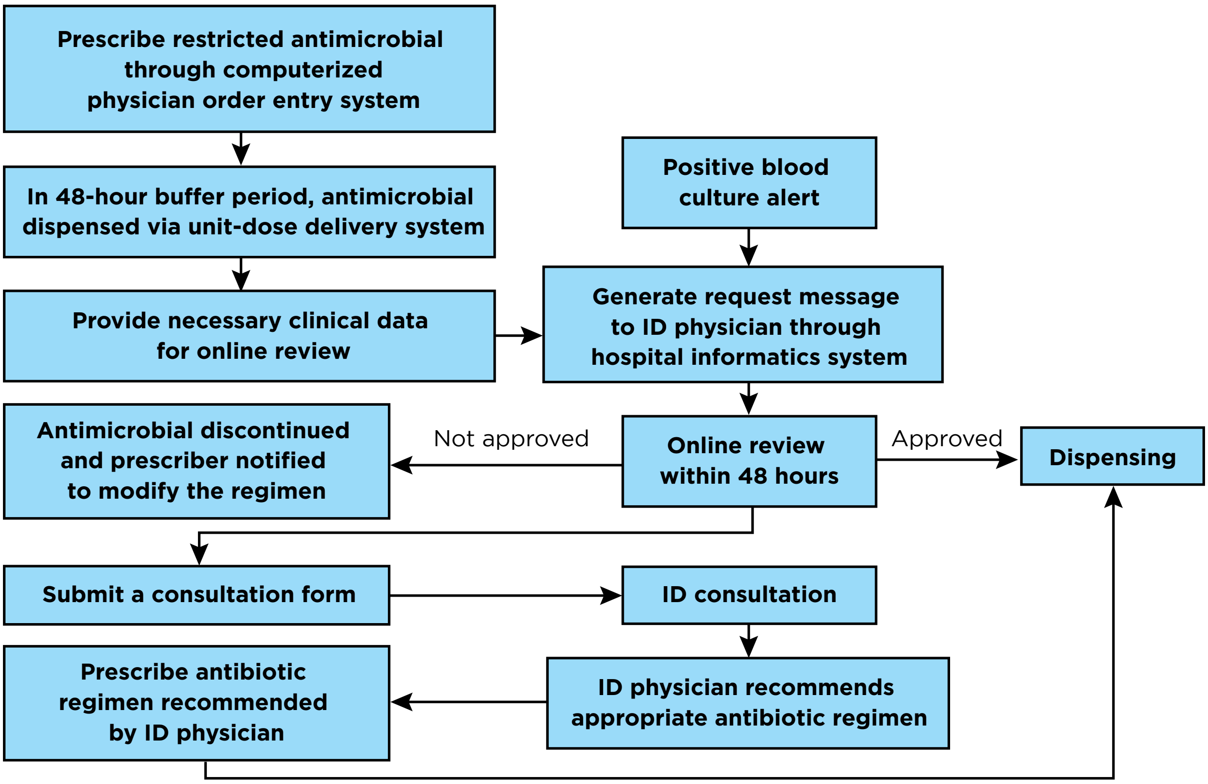
(a)



(b)


Patients prescribed audited antibiotics identified daily from the pharmacy database
Primary review (ID pharmacist) on day 2 of treatment
Optimal antibiotic use?
Choice
Duration
Dosage
Route
Review by ID pharmacist on day 4 (giving a 72-hour period for culture results) and then on day 7 as applicable
Appropriate
Difficult cases
Second review (ID physician)
Appropriate
Not appropriate
Memo to prescribing doctor placed in case notes on the same day

(c)


Prescribe restricted antimicrobial through computerized physician order entry system
In 48-hour buffer period, antimicrobial dispensed via unit-dose delivery system
Positive blood culture alert
Provide necessary clinical data for online review
Generate request message to ID physician through hospital informatics system
Antimicrobial discontinued and prescriber notified to modify the regimen
Not approved
Online review within 48 hours
Approved
Dispensing
Submit a consultation form
ID consultation
Prescribe antibiotic regimen recommended by ID physician
ID physician recommends appropriate antibiotic regimen

Three other strongly recommended interventions that can be easily implemented in association with core interventions are[1,4]:

- Antibiotic treatment **guidelines** adapted to the hospital **antibiogram**
- De-escalation
- IV-to-oral conversion

IV-to-oral conversion and de-escalation, as well as pharmacokinetic monitoring and dose optimization, can all be integrated into routine pharmacy activities (see the **pharmacist guide** to AMS in this toolkit).[1,4]

Step 6: Select key performance indicators

Before implementing the program, select measures (key performance indicators [KPIs]) to evaluate the effectiveness of the AMS program in relation to its goals and interventions (Table 4). Include process measures, such as antibiotic consumption, measured as DDD or days of therapy (DOT), and appropriate antibiotic use, to confirm that the AMS program is well implemented. Also consider assessing outcome measures, such as length of hospital stay (clinical), AMR trends (microbiological) and antibiotic expenditure (financial).[1,4,13] See the **guide to KPIs** in this toolkit for detailed guidance on selecting, calculating and tracking KPIs.

Table 4

A selection of potential performance indicators for AMS programs[1,4]

Process measures	Outcome measures
Quantity of antibiotic use • Defined daily dose • Days of therapy • Length of therapy	***Microbiological*** • MDR bacterial infection and colonization rates • *Clostridium difficile* infection rates
Quality of antibiotic use • Rate of appropriate antibiotic prescription in accordance with hospital guidelines • Rate of acceptance of interventions • Proportion of patients with revision of antibiotics based on microbiology data • Proportion of patients converted to oral therapy • Time to conversion to oral therapy	***Clinical*** • Length of hospital stay • Infection-related mortality • Readmission and reinfection rates ***Financial*** • Antibiotic cost per patient per day • Antibiotic cost per patient per admission

Step 7: Implement, educate and train

Strategize the rollout of interventions. Avoid making too many changes at once by gradually introducing interventions by unit or ward.[4]

A carbapenem restriction or audit program for the ICU in response to high carbapenem use and endemic ESBL-producing Gram-negative bacteria may be a more practical initial plan than wide-ranging formulary restriction or prospective audit[4,36]

Make sure treatment guidelines and hospital antibiograms are easily accessible. Consider using the **intranet, printed pocket guides, ward posters** and providing electronic summaries at workstations.

Ensure prescribers and other stakeholders are aware of new guidelines and procedures. Inform and educate prescribers and other stakeholders about AMS activities using avenues such as posters, leaflets, newsletters, lectures, electronic communication and the hospital intranet.[8,13] **AMS awareness materials** for prescribers are available in this toolkit.

Educational activities should not be relied upon to effect change on their own, but ongoing educational strategies can be used to complement other AMS activities.[1,4] Education on AMS and details of the hospital AMS program should routinely be provided as part of orientation for new staff, with regular (quarterly or yearly) updates to keep staff informed about any changes to the program.[4,8,13]

Make use of online educational resources and courses:

- The WHO offers training courses on AMS activities (**https://openwho.org/courses/policy-guidance-on-AMS**) and core competencies (**https://openwho.org/courses/AMR-competency**), and a practical toolkit for AMS programs in healthcare facilities in low- and middle-income countries (**https://openwho.org/courses/practical-toolkit-for-AMS**)
- The CDC's Antibiotic Prescribing and Use website (**www.cdc.gov/antibiotic-use/index.html**), SHEA website (**shea-online.org/antimicrobial-stewardship**) and the Center for Infectious Disease Research and Policy (CIDRAP) AMS website (**www.cidrap.umn.edu/asp**) provide excellent educational resources
- A free online AMS course is available at **www.futurelearn.com/courses/antimicrobial-stewardship**
- Making-a-Difference in Infectious Diseases (MAD-ID) is a US organization that offers online AMS training programs with discounts for participants from developing nations (visit **www.mad-id.org/training-programs** for more information)

An education program combined with a core intervention provides an example of an AMS program that could be easily implemented in many Asian hospitals[4,24,26]

Step 8: Monitor and communicate AMS program progress and success

After implementing chosen interventions, begin monitoring AMS program processes and outcomes to assess the impact of the implemented interventions and identify opportunities for improvement.[2] Instead of continuous surveillance, consider less resource-intensive point prevalence surveys to monitor antibiotic consumption and AMR in resource-constrained settings.[4]

Regular team meetings should be scheduled to review AMS program activities and data, and to modify the program as required, incorporating a Plan-Do-Check-Act (PDCA) cycle.[4] Aim for the AMS team to meet at least once a month to review KPIs. Deliver feedback to relevant departments regarding the appropriateness of antibiotic prescriptions and intervention acceptance rate, and recommended areas for improvement. Aim to do this on at least a quarterly basis.

Yearly progress reports should be prepared for hospital administration and other stakeholder groups. Use successes to obtain more resources to address more problem areas and demonstrate the importance of the AMS program, or explain why success was not possible (ie, poor compliance with interventions) and request help to provide solutions and overcome barriers.[8]

General advice

There is no 'one-size-fits-all' approach to implementing an AMS program, but some general rules should apply.[2,8]

Dos

- Design your program to fit the hospital's prescribing culture, clinical needs and resources
- Start small and aim to build capacity over time
- Implement an AMS program in conjunction with effective infection prevention and control measures
- Implement an AMS program that includes preauthorization and/or prospective audit of antibiotic use
- Monitor use of at least one class of antibiotic that is thought to be misused in at least one unit of the hospital
- Provide regular feedback to stakeholders to ensure continued support and increase the scope of the program

Don'ts

- Start if there is no commitment from hospital management
- Try to implement an intervention until you have sufficient resources to do it effectively
- Try to address every problem at once

Successful implementation of an AMS program will ultimately depend on strong leadership and a coordinated multidisciplinary team approach to planning and implementation.

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Appendices

Appendix 1: Online resources

These tables provide links to a selection of some of the most useful online resources to help with the implementation of hospital AMS programs.

Region	Organization	Resource
Global	WHO	AMS program toolkit in low- and middle-income countries (**https://apps.who.int/iris/handle/10665/329404**) and AMS practical guide (**https://apps.who.int/iris/handle/10665/340709**)
Asia-Pacific	ACSQHC	Hospital AMS program guidelines (**www.safetyandquality.gov.au/our-work/antimicrobial-stewardship/antimicrobial-stewardship-australian-health-care-ams-book**)
	KSAT, KSID, KSHSP	Guidelines on implementing AMS programs (**https://www.icjournal.org/DOIx.php?id=10.3947/ic.2021.0098**)
	MOH Malaysia	Hospital AMS program guidelines (**www.pharmacy.gov.my/v2/en/documents/protocol-antimicrobial-stewardship-program-healthcare-facilities.html**)
	DOH Philippines	Hospital AMS program guidelines (**https://pharma.doh.gov.ph/doh-program-on-combating-antimicrobial-resistance/**)
Europe	PHE	Start-smart-then-focus hospital AMS program toolkit (**www.gov.uk/government/publications/antimicrobial-stewardship-start-smart-then-focus**)
	NICE	AMS guidance (**www.nice.org.uk/guidance/ng15**)
	Biomerieux	Hospital AMS guide (**https://customer.theraconseil.com/bioMerieux/medical_affairs/5_Antimicrobial_Stewardship/#p=1**)

ACSQUC, Australian Commission on Safety and Quality in Health Care IDSA; DOH, Department of Health; KSAT, Korean Society for Antimicrobial Therapy; KSID, Korean Society of Infectious Diseases; KSHSP, Korean Society of Health-System Pharmacists; MOH, Ministry of Health; NICE, National Institute for Health and Care Excellence; PHE, Public Health England; WHO, World Health Organization.

Region	Organization	Resource
North America	CDC	CDC Antibiotic Prescribing and Use (**https://www.cdc.gov/antibiotic-use/index.html**)
		Core elements of hospital AMS programs (**https://www.cdc.gov/antibiotic-use/hcp/core-elements/index.html**)
		Core elements of AMS at small and critical access hospitals (**https://www.cdc.gov/antibiotic-use/hcp/core-elements/small-and-critical-access-hospitals.html**)
	CIDRAP	AMS resources website (**www.cidrap.umn.edu/asp**)
	IDSA/SHEA	Evidence-based hospital AMS program implementation guidelines (**www.idsociety.org/clinical-practice/antimicrobial-stewardship2/antimicrobial-stewardship/**)
	JCI	Hospital AMS program toolkit (**https://www.jointcommission.org/resources/patient-safety-topics/infection-prevention-and-control/antibiotic-stewardship/**)
	GNYHA	Hospital AMS toolkit (**www.uhfnyc.org/assets/1042**)
	PHO	AMS website (**www.publichealthontario.ca/en/health-topics/antimicrobial-stewardship**)
	SHEA	AMS website (**https://shea-online.org/antimicrobial-stewardship/**)
	SHS + UHN	AMS website (**www.antimicrobialstewardship.com**)

Infectious Diseases Society of America; CDC, Centers for Disease Control; CIDRAP, Center for Infectious Disease Research and Policy; GNYHA, Greater New York Hospital Association; JCI, Joint Commission International; PHO, Public Health Ontario; SHEA, Society for Healthcare Epidemiology of America; SHS + UHN, Sinai-Health System + University Health Network.

Appendix 2: Case examples of AMS programs in Asian hospitals

Nara Prefecture General Medical Center, Japan[34]

Setting

- 15-bed NICU of a community hospital with no pediatric ID specialist

AMS team

- NICU neonatologists

Interventions

- Antimicrobial treatment protocol*
- On request, blood culture results returned at 9.00 a.m. on the weekend or holidays
- Ordering antimicrobials in advance for the next day discouraged

Measures of program effectiveness

- Antibiotic use (DOT per 1,000 patient-days)
- Protocol compliance rate
- Methicillin-resistant rate of *Staphylococcus aureus*
- Length of stay
- Culture-positive sepsis and culture-negative sepsis

*If a neonate has any signs of sepsis, sepsis score ≥2 or maternal chorioamnionitis, then blood cultures should be obtained and the neonate should receive antimicrobial therapy; If a neonate has a positive blood culture, then the neonate should be treated with appropriate antibiotics for the proper duration of antimicrobial treatment; If a neonate had resolved symptoms within 24 h, sepsis score <2, and a negative blood culture result for 48 h without clinical suspicion of sepsis, then antimicrobials should be stopped within 48 h; each case with controversial antimicrobial management to be discussed with all neonatologists at a daily unit round

Hospital Enche' Besar Hajjah Khalsom, Malaysia[39]

Setting

- 268-bed district hospital

AMS team

- Medical specialists (no available ID physician, but an ID physician at a remote tertiary institution served as an off-site consultant when required)
- Residents
- Pharmacists
- Clinical microbiologist
- Infection control-linked nurses

Interventions

- Antibiotic restriction and approval (preauthorization)
- Prospective audit and feedback, with a monthly single-ward AMS round in accordance with hospital capacity and human resources (evolved from inclusion of restricted antibiotics only to all systemic antibiotics) and referrals during the interval between rounds
- Regular AMS education sessions
- Provision of more advanced training for AMS core team members through attachment to AMS rounds with ID physicians at other teaching institutions

Measures of program effectiveness

- Number of recommended interventions
- Rate of acceptance of recommendations
- Adherence to authorization policy

Thammasat University Hospital, Thailand[24]

Setting

- 350-bed university hospital

AMS team

- ID physician
- Clinical microbiologist
- Pharmacists
- Internists
- Hospital epidemiologist
- Infection control specialist
- Computer system analyst

Interventions

- Antibiotic prescription forms
- Restriction of specific antibiotic classes
- Audit and feedback
- Hospital antibiotic guidelines
- Monthly education of medical students and residents
- Regular training sessions for all hospital physicians (every 4 months)

Measures of program effectiveness

- Antibiotic consumption
- Antimicrobial expenditure
- Inappropriate antibiotic use
- Drug-resistant infection rates

Makati Medical Center, the Philippines[29]

Setting

- 600-bed tertiary hospital

AMS team

- ID physician
- Clinical pharmacist
- Infection prevention and control nurse
- Administrative staff member

Interventions

- Formulary restriction
- Educational interventions
- Nurse and pharmacist engagement
- Automatic stop order for therapeutic antimicrobials after 7 days
- Audit and feedback by ID fellows
- Dissemination of guidelines for surgical antibiotic prophylaxis
- Automatic stop order for surgical antibiotic prophylaxis after 24 hours
- IT support for antibiotic prescribing
- Policy on documentation of antibiotic prescribing

Measures of program effectiveness

- Antimicrobial susceptibility (yearly dissemination of antibiogram, along with antibiotic recommendations for clinicians)
- Antimicrobial use (DDD) with feedback to hospital staff
- Point prevalence surveys* informed AMS activities

*For each prescribed antibiotic, the following information was collected: dose, frequency, route of administration, and indication for treatment; prescription quality indicators included documentation of the reason for prescribing, documentation of a stop or review date, and guideline compliance (choice of drug); for therapeutic prescriptions, whether treatment was prescribed empirically or targeted; duration of surgical antibiotic prophylaxis

National Center for Global Health and Medicine Hospital, Japan[23]

Setting

- 781-bed tertiary care hospital

AMS team

- 2 ID physicians
- 2 Pharmacists
- 2 Clinical laboratory technicians
- 1 Infection control nurse

Interventions

- Carbapenem prescriptions prospective audit and feedback

Measures of program effectiveness

- Carbapenem DOT per 100 patient-days per month
- DOT per 100 patient-days per month for 3 antipseudomonal agents (carbapenem, piperacillin/tazobactam, cefepime)*
- DOT per 100 patient-days per month for other antipseudomonal agents (eg, piperacillin, ceftazidime, aztreonam, aminoglycosides, fluoroquinolones)
- Incidence of antibiotic-resistant bacteria (carbapenemase-producing Enterobacteriaceae, carbapenem-resistant *Pseudomonas aeruginosa*) and *C. difficile* infection per 1,000 patient-days
- Yearly cost of purchasing carbapenem antibiotics

*To check whether carbapenem antibiotics were being replaced with other broad-spectrum antipseudomonal agents

Eulji University Hospital, Korea[32]

Setting

- 859-bed secondary hospital

AMS team

- 1 ID physician (2.5-3.5 hours per day)

Interventions

- Antibiotic restriction and approval*
- Follow-up evaluation, usually at 4-7 days

Measures of program effectiveness

- Antibiotic use (DOT per 1,000 patient-days)
- Antimicrobial resistance rate for major pathogens
- In-hospital mortality

*Carbapenems (imipenem, meropenem, ertapenem, and doripenem), tigecycline, glycopeptides (vancomycin and teicoplanin), oxazolidinone (linezolid), and polymyxin (colistin); pending the decision of the ID physician (within 48 hours), antibiotics could be administered to avoid delays in initiating therapy

Kikatsu University Hospital, Japan[35]

Setting

- 1,200-bed tertiary hospital

AMS team

- ID physicians
- ID Pharmacists
- Microbiology technologists

Interventions

- Appropriate Use of Carbapenems Program*

Measures of program effectiveness

- Carbapenem and antipseudomonal antimicrobial DOTs

*Modification of initial treatment strategies in departments with a high rate of carbapenem use after discussions with the AMS team, and communication between physicians and the AMS team if carbapenems used for ≥6 days; implemented after prospective audit and feedback of carbapenems did not yield optimal results in this hospital

Singapore General Hospital, Singapore[40,54]

Setting

- >1,700-bed tertiary hospital

AMS team

- ID physician
- Clinical microbiologist
- ID-trained clinical pharmacists

Interventions:

- One-page antibiotic guidelines for infections of major organs
- IV-to-oral conversion algorithm
- Two-stage prospective audit of selected antibiotics* with immediate concurrent feedback (see Figure 4b for workflow)

Implementation:

- Prospective audit/feedback sequentially piloted in departments that voluntarily asked to participate
- Publicity blitz throughout the hospital to increase awareness of the new guidelines

Measures of program effectiveness

- Proportion of appropriate antibiotic prescriptions
- Intervention acceptance rate
- Antibiotic consumption
- Antibiotic expenditure

*Selection criteria: High procurement costs, broad-spectrum coverage and associated high AMR rates, potential for misuse

Christian Medical College, India[38]

Setting

- Medical and surgical ICU settings of a 2,858-bed tertiary hospital

AMS team

- ID physician

Interventions

- Prospective audit and feedback with regard to the following chosen antibiotics fluoroquinolones, β-lactam/β-lactamase inhibitor combinations, third- and fourth-generation cephalosporins, carbapenems, linezolid, tigecycline, azithromycin, doxycycline, colistin, and vancomycin*

Measures of program effectiveness

- DOT per 1,000 patient-days with the chosen antibiotics
- Proportion of prescriptions with inappropriate antibiotic use (absence of clinical indication, pathogen-antibiotic mismatch, unnecessary double coverage, or antibiotic prescribed at a wrong dose, route and/or frequency)
- Rates of de-escalation according to culture susceptibility and clinical evaluation
- Intervention rate (number of courses of therapy in which a modification is recommended divided by the total number of courses)
- Acceptance rate (number of recommendations accepted divided by the number of recommendations made)
- Compliance with antimicrobial guidelines
- Length of ICU and hospital stay
- All-cause mortality
- ICU readmission rate
- Unintended consequences (eg, adverse drug reactions, *C. difficile* infections and candidemia)
- Prevalence of multidrug-resistant organisms

*Conducted to obtain data to present to hospital administration to advocate for the creation of a formal multidisciplinary AMS team and full-scale AMS program

Taipei Veterans General Hospital, Taiwan[31]

Setting

- 2,941-bed tertiary hospital

AMS team

- ID physicians
- ID clinical pharmacists
- Clinical microbiologists
- Computer data manger

Interventions:

- General ward setting: Pre-approval of restricted antibiotics by ID physician and ID clinical pharmacists (default duration of prescription 3 days for empiric therapy and 7 days for definite therapy), followed by pharmacist review and assistance in the determination of accurate dosing and scheduling
- ICU setting: Use of restricted antibiotics either followed the same protocol as was used in the general ward or was reviewed post-prescription and audited under urgent or empirical conditions (default duration of prescription 3 days)
- Bacterial intervention shifted to Matrix-Assisted Laser Desorption/Ionization Time of Flight Mass Spectometry (MALDI-TOF)
- Appropriate culturing required before hospital inpatients receive empirical antibiotics if prescribed for new-onset fever
- In the ER, restricted antibiotics could be used without ID physician approval, but appropriate culturing required before ER doctors prescribe any antimicrobial agent
- Culture reports from the past 3 days highlighters when providers log into the patient's electronic medical records*
- Reminders regarding culture reports sent by text message to the business cell phones of attending physicians*

Measures of program effectiveness

- Consumption of antibiotics (DDD per 1,000 patient-days)
- Rate of patient mortality
- Incidence of healthcare-associated infections
- Detection rate of healthcare-associated drug-resistant organisms, including vancomycin-resistant enterococci, carbapenem-resistant *A. baumannii,* carbapenem-resistant *P. aeruginosa*, carbapenem-resistant *Escherichia coli*, and carbapenem-resistant *Klebsiella pneumoniae*

*These strategies serve as reminders to providers to re-evaluate antimicrobial use after a culture report becomes available

Chang Gung Memorial Hospital, Taiwan[25,42]

Setting

- 3,700-bed tertiary hospital

AMS team

- ID physicians
- Clinical microbiologists
- Pharmacists
- Infection control nurses

Interventions

- Hospital-wide computerized antimicrobial approval system (HCAAS) (implemented 2004)
- HCAAS extended to include blood culture-guided review (implemented 2010)
- See Figure 4c for workflow

Implementation

- Extended blood culture-guided review piloted in 16 adult ICUs and now implemented in all wards

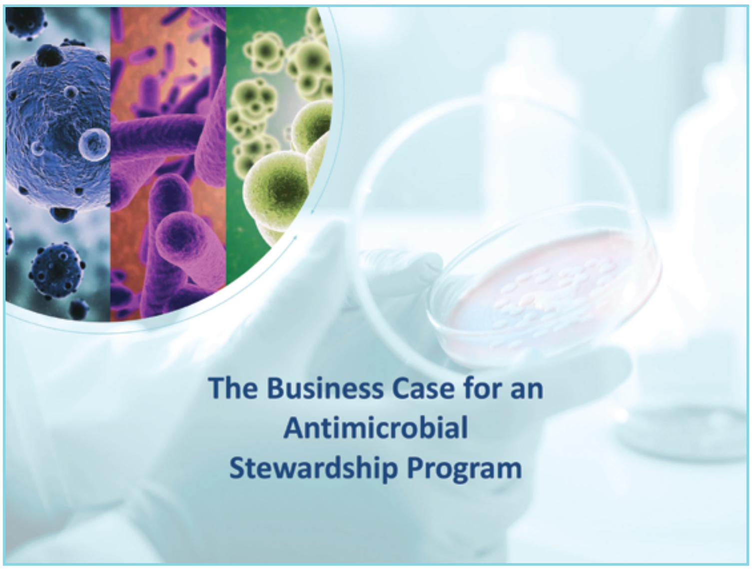
Measures of program effectiveness

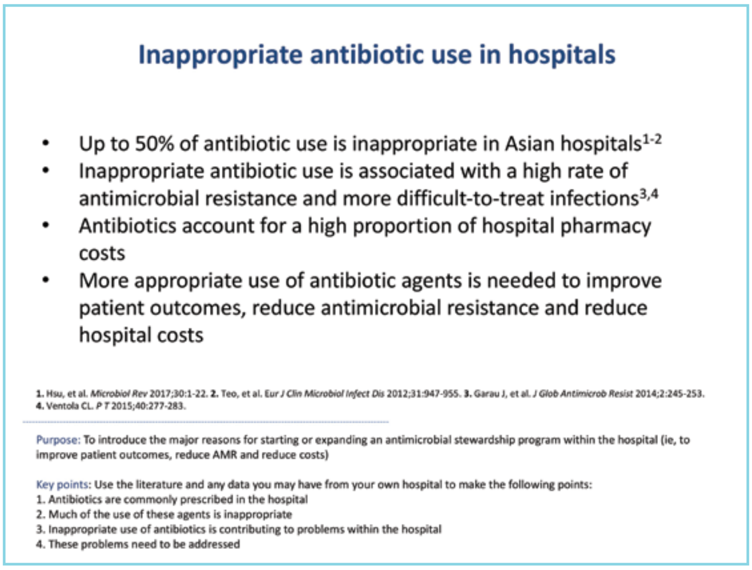
- Approval rate
- Recommendation acceptance rate
- Reasons for disapproval
- Antibiotic consumption
- Antibiotic expenditure
- Healthcare-associated infection density
- AMR profiles

Download AMS program business case sample slides here

Appendix 3: AMS program business case sample slides

These slides are intended to provide headings and key points that AMS leaders can work with and expand on to make a business case for an AMS program to hospital administrators.





Examples of inappropriate antibiotic use

- Treatment of syndromes and symptoms not caused by bacteria[1]
- Treatment for culture results that reflect colonization or contamination rather than infection[1,2]
- Failure to consider likely pathogens and antimicrobial resistance patterns when selecting an antibiotic[3]
- Unnecessary use of an agent with a broad spectrum of activity (failure to narrow spectrum based on culture results)[2,3]
- Prescribing a longer course of therapy than necessary[1]
- Prescribing doses that are too low or too high[3]
- IV administration when oral administration would be adequate[4]

1. Hecker MT, et al. *Arch Intern Med* 2003;163:972-978. **2.** Leekha, et al. *Mayo Clin Proc* 2011;86:156-167. **3.** Healthcare Infection Control Practices Advisory Committee. Antibiotic Stewardship Statement for Antibiotic Guidelines – The recommendations of the Healthcare Infection Control Practices Advisory Committee (HICPAC). 2016. Available at: https://www.cdc.gov/hicpac/pdf/antibiotic-stewardship-statement.pdf. Accessed 25 October 2017. **4.** Barlam TF, et al. *Clin Infect Dis* 2016;62:e51-e77.

Purpose: To give specific examples of the different types of inappropriate antibiotic use that occur in the hospital

Key point: There are many ways that antibiotics are misused in the hospital

Antimicrobial stewardship (AMS)

- AMS is a multidisciplinary approach to optimizing antibiotic use by encouraging selection of the most appropriate[1]:
  - Antibiotic agent
  - Dose
  - Route of administration
  - Duration of therapy

- Goals include[1]:
  - Improved clinical outcomes
  - Reduced antimicrobial resistance
  - Reduced healthcare costs

1. Barlam, et al. *Clin Infect Dis* 2016;62:e51-e77.

Purpose: To define AMS and its goals

Key points: The purpose of AMS is to optimize use of antibiotics to improve outcomes for individual patients and treatment costs, and over the longer term reduce antimicrobial resistance and related healthcare costs

Antimicrobial stewardship (AMS) program

- A hospital AMS program is needed to[1]:
  - Improve antibiotic use
  - Improve patient care
  - Reduce antimicrobial resistance
  - Reduce antibiotic costs
- A hospital AMS program needs[1]:
  - A multidisciplinary team of physicians, pharmacists and other hospital personnel
  - Support from hospital administration

1. Barlam, et al. *Clin Infect Dis* 2016;62:e51-e77.

Purpose: To explain why an AMS program is needed in the hospital and what is required for a successful AMS program

Key points: A multidisciplinary team and support from hospital leadership is critical to an AMS program's success

Antimicrobial stewardship (AMS) strategies

- Core strategies[1]:
  - Prospective audit and feedback
  - Formulary restriction and preauthorization
- Other strategies[1]:
  - Guidelines and clinical pathways
  - Dose optimization
  - IV-to-oral conversion
  - Computerized clinical decision support
  - Education

1. Barlam, et al. *Clin Infect Dis* 2016;62:e51-e77.

Purpose: To list specific strategies that are used by AMS programs to reach their goals

Key points:
1. Core strategies are considered to be the most important, basic components of all AMS programs
2. Other strategies can be incorporated into the program to further improve antibiotic use

Impact of antimicrobial stewardship (AMS) programs

- Hospital AMS programs have been shown to reduce:
  - Antibiotic use by ~10%-30%[1,2]
  - Antibiotic costs by ~10%-80%[1-3]
- Singapore General Hospital (>1,500-bed tertiary-care hospital)
  - 10% reduction in audited antibiotic use led to antibiotic cost savings of S$198,575 over 1 year[4]
- Thammasart University Hospital, Thailand (350-bed tertiary-care hospital)
  - Reduction in antibiotic use led to antibiotic cost savings of US$32,231 over 1 year[5]

1. Honda, et al. *Clin Infect Dis* 2017;64 (Suppl 2):S119-S126. **2.** Karanika, et al. *Antimicrob Agents Chemother* 2016;60:4840-4852. **3.** Lee CF, et al. *J Antimicrob Chemother* 2018;73:844-851. **4.** Teo J, et al. *Eur J Clin Microbiol Infect Dis* 2012;31:947-955. **5.** Apisarnthanarak, et al. *Clin Infect Dis* 2006;15;42:768-775.

Purpose: To present general evidence of the beneficial effects of AMS programs (hospital administration will be most interested in cost outcomes), and to present evidence of cost savings in similar regional hospitals

Key point: Reduced use of antimicrobials can lead to substantial reductions in pharmacy costs

[Enter hospital name]
Antimicrobial stewardship (AMS) program

- How the AMS program will operate
  - Suggested AMS team members
  - Suggested goals
  - Suggested strategies to achieve goals
- Cost summary for the AMS program
  - Ongoing costs (eg, 0.3 FTE physician and 1 FTE pharmacist for every 100 beds)
  - One-off costs (eg, investment in IT and/or microbiology lab infrastructure)
- How much can the AMS program save the hospital?
  - Conservative estimate of anticipated savings (eg, 10%-20% savings in antibiotic costs would translate savings of >$60,000/year for 300 beds)

AMS, antimicrobial stewardship; FTE, full time equivalent, IT, information technology.

Purpose: Outline specific staffing, costs and other details of the proposed AMS program, as well as the anticipated return on investment

Key points: AMS program savings will offset staffing costs (ie, the program will be all or partly self-funding as a result of less antibiotic use)

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