IMPLEMENTING AMS PROGRAM IN ASIA PACIFIC

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February 9, 2021

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Objectives

- AMS Blue Print in Asia Pacific
- Gap Analysis
- Example of Gap Analysis Utilization
- Defining measure outcomes of AMS program

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Antimicrobial stewardship for acute-care hospitals: an Asian perspective

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.

AMR, antimicrobial resistance; AMS, antimicrobial stewardship
Apisarnthanarak A, *et al. Infect Control Hosp Epidemiol.* 2018;39:1237–45.

[a]See Supplementary Material S1 for an AMS programme assessment checklist, for Asian hospitals to assess which aspects of the AMS programmes 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 programmes in Asian hospitals

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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

[a]If no ID specialists are available, another physician or pharmacist with an interest in infectious diseases can assume responsibility for this role.
AMS, antimicrobial stewardship; ID, infectious disease; IV, intravenous; MDR, multidrug-resistant
Apisarnthanarak A, *et al. Infect Control Hosp Epidemiol.* 2018;39:1237–45.

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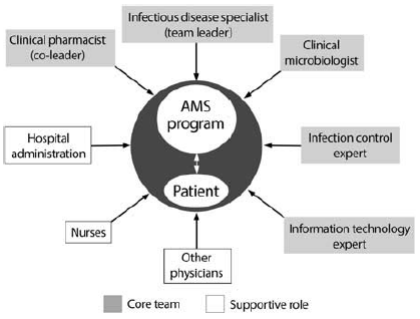

Table 3. Suggested Process-Related Measures and Outcome Measures for AMS Programs

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

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

Intervention	Strength of recommendation	Overall evidence quality[9,17,18]	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,[39,54,45,62] 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
Apisarnthanarak A, *et al. Infect Control Hosp Epidemiol.* 2018;39:1237–45.

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Perform gap analysis

Hospital Antimicrobial Stewardship Program Assessment Checklist

	Hospital leadership support	Yes	No
C1	Does your hospital have a **formal statement of support** from hospital leadership that supports AMS activities to improve antibiotic use?	☐	☐
C2	Does your hospital allocate any **budgeted financial support** for AMS activities (eg, support for salary, training, strengthening microbiology and information technology [IT] services)?	☐	☐

	AMS team and infectious disease training	Yes	No
C3	Does your hospital have a **physician (or other) leader** responsible for AMS activities?	☐	☐
S1	If you answered 'Yes' to C3, does this leader have **specialized infectious disease training**?	☐	☐
C4	Does your hospital have a **pharmacist** working on AMS activities?	☐	☐
S2	If the answer to question C4 is 'Yes', is the pharmacist a **clinical pharmacist** or does this pharmacist have **specialized infectious disease training**?	☐	☐
	Do any of the following staff work with physicians or pharmacists to improve antibiotic use:		
C5	Infection control?	☐	☐
C6	Microbiology?	☐	☐
S3	Nursing?	☐	☐
S4	IT?	☐	☐

	AMS program interventions	Yes	No
C7	Do specified antibiotics need to be approved by a physician or pharmacist prior to dispensing or within 48 hours of dispensing at your hospital (**preauthorization**)? AND/OR Does a physician or pharmacist review courses of therapy and provide suggestions for use of specified antibiotics within 48 hours of prescription at your hospital (**prospective audit and feedback**)?	☐	☐
S5	Does your hospital use **computerized decision support systems** in relation to antibiotic prescribing?	☐	☐
C8	Does your hospital have **facility-specific antibiotic treatment guidelines** for commonly treated infections?	☐	☐
	If you answered 'Yes' to C8, do you have facility-specific antibiotic treatment guidelines for the following infections:		
S6	Community-acquired pneumonia?	☐	☐
S7	Hospital-acquired pneumonia/ventilator-associated pneumonia?	☐	☐
S8	Skin and soft tissue infections?	☐	☐
S9	Sepsis?	☐	☐
S10	Urinary tract infections?	☐	☐
S11	Intra-abdominal infections?	☐	☐
S12	Does your hospital have guidelines for the **de-escalation** of broad-spectrum antibiotics, including carbapenems?	☐	☐
S13	Does your hospital have guidelines for **IV-to-oral conversion** of antibiotics?	☐	☐
S14	If you answered 'Yes' to any of questions S6–S13, are **hospital guidelines readily available** at the point of care?	☐	☐

AMS, antimicrobial stewardship
Apisarnthanarak A, *et al. Infect Control Hosp Epidemiol.* 2018;39:1237–45.

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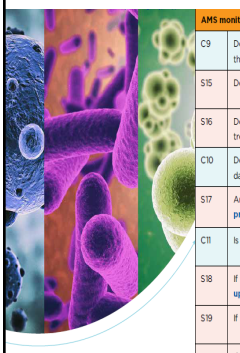
Perform gap analysis



	AMS monitoring and reporting	Yes	No
C9	Does your hospital monitor use of specific antibiotics by days of therapy (**DOT**) or defined daily dose (**DDD**)?	☐	☐
S15	Does your hospital **monitor antibiotic expenditure**?	☐	☐
S16	Does your hospital **monitor compliance** with facility-specific treatment guidelines?	☐	☐
C10	Does your hospital **regularly publish** antimicrobial resistance data and outcomes measures associated with AMS?	☐	☐
S17	Are **results** of antibiotic audits or reviews **shared directly with prescribers**?	☐	☐
C11	Is there a **hospital antibiogram**?	☐	☐
S18	If the answer to C11 is 'Yes', is the antibiogram **regularly updated**?	☐	☐
S19	If the answer to C11 is 'Yes', is the antibiogram **easily accessible**?	☐	☐
S20	If the answer to C11 is 'Yes', are there **unit-specific antibiograms**?	☐	☐

	Hospital infrastructure	Yes	No
S21	Does your hospital have **IT capabilities** to gather and analyze AMS data?	☐	☐
S22	Does your hospital use **electronic health records**?	☐	☐
S23	Does your hospital use **computerized physician order entry**?	☐	☐
C12	Does your hospital have an in-house microbiology laboratory or access to a **timely and reliable microbiology service**?	☐	☐
S24	If the answer to C12 is 'Yes', does your microbiology service make use of **rapid diagnostic reporting**?	☐	☐
S25	If the answer to C12 is 'Yes', does your microbiology service use **selective susceptibility reporting**?	☐	☐

	Education	Yes	No
S26	Does your hospital provide **educational activities** for clinicians and other relevant staff on improving antibiotic prescribing?	☐	☐
S27	If the answer to S26 is 'Yes', is this **mandatory and certified training**?	☐	☐

Scores	
• C-score (number of 'Yes' responses to questions tagged 'C')	/12
• S-score (number of 'Yes' responses to questions tagged 'S')	/27
• Total score	/39

If you answered 'Yes' to all 12 core questions (C-score of 12), your hospital has all of the essential elements of a functioning AMS program in place. However, if you answered 'No' to any of the supplementary questions (S-score <27), you can still improve your AMS program by focusing on the missing supplementary elements.

If you answered 'No' to any of the core questions (C-score <12), you should focus on fulfilling the missing core elements to improve your hospital's AMS program. Although the elements in this checklist all help to improve antibiotic use in hospitals, not all elements may be feasible in all hospitals. Rather than trying to address all missing elements at once, you should initially focus on elements that could be feasibly implemented using available resources and then advance the AMS program from there.

AMS, antimicrobial stewards
Apisarnthanarak A, *et al. Infe*

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Overcome gaps and challenges

Supplementary Material S2. Flowchart of potential next steps to overcome gaps and challenges in antimicrobial stewardship programs in Asian hospitals

Complete the AMS assessment checklist (Supplementary Material S1) and note down the questions you answered 'No' to. Refer to the flowchart below for potential next steps and priorities to overcome the gaps in your hospital AMS program.

If you answered 'No' to any of the question indicated below:

Hospital leadership support

C1
- Prioritize getting formal support and approval from hospital leadership for AMS activities

C2
- Provide hospital administrators with a credible business case to persuade them that funding of an AMS program is beneficial to the hospital

AMS team and infectious disease training

C3
- Prioritize identifying the AMS leader and co-leader, and getting appropriate time commitment and remuneration
- If there is no infectious disease specialist to lead the AMS team, the team leader could be another clinician or a pharmacist with an interest in infectious diseases[1]

S1

C4
- Prioritize getting support for infectious disease and/or AMS training for AMS providers

S2

C5

C6
- Prioritize assembling the AMS team (see Figure 1) and get appropriate time commitment and remuneration for AMS providers
- Define the roles and responsibilities of each team member (see Table 4)

S3

S4

AMS program interventions

C7

Prioritize selecting the AMS interventions (see Table 5) that will help achieve the AMS program goals and can be implemented using available resources

S5

C8
- Prioritize developing and/or implementing hospital-based guidelines for surgical prophylaxis and empiric antibiotic therapy of common infection syndromes

Any of S6–S13

S14
- Prioritize making the hospital-specific antibiotic treatment guidelines easily accessible (e.g., using the intranet, printed pocket guides and electronic summaries at workstations)

If you answered 'No' to any of the question indicated below:

AMS monitoring and reporting

Prioritize selecting a combination of process-related measures and outcome measures (see Table 3) according to local relevance, and accounting for data and resource availability

C9

S15

S16

C10
- Develop a plan to provide regular feedback to prescribers in an easily interpreted format
- Develop a communication plan for reporting AMS program performance to relevant departments and hospital administration (e.g., quarterly report of antibiotic use data; annual report of total antibiotic use and antibiotic susceptibility data)

S17

C11

Prioritize developing a hospital-based antibiogram

Hospital infrastructure

S21

S22

S23

Prioritize getting adequate microbiology and IT services to support AMS activities

C12

S24

S25

Education

S26
- Prioritize making treatment guidelines and hospital antibiograms easily accessible to prescribers (e.g., using the intranet, printed pocket guides)

S27
- Inform and educate prescribers and other stakeholders about AMS activities
- Provide education on the AMS program as part of orientation for new staff, with regular updates to keep staff informed about any changes to the program

AMS, antimicrobial stewardship

Apisarnthanarak A, *et al. Infect Control Hosp Epidemiol.* 2018;39:1237–45.

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Gap analysis on antimicrobial stewardship program in central Thailand

Infection Control & Hospital Epidemiology (2019), **40**, 1077–1086

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Table 1. Hospital Characteristics and Gap Analysis

Variable	No. (%) (n = 45)
Type of ownership	
Private	18 (40)
Government	32 (71.1)
Military	5 (11.1)
Total number of beds	545.9 + 465.5
Total FTE for all infection preventionists	3.2 + 3.6
Affiliated with medical school	24 (53.3)
Participated in collaborative network to prevent HAIs	26 (56.5)
Hospital leadership support	
Formal statement of leadership support	45 (100)
Leadership had budgeted financial support for ASP	15 (33.3)
ASP team and ID training	
Physician lead ASP	45 (100)
Presence of pharmacist working on ASP	32 (71.1)
Presence of microbiologist working on ASP	26 (58)
Presence of IC team working on ASP	45 (100)
ASP program intervention	
Implement preauthorization with or without prospective audit and feedback	45 (100)
Available of computerized support system	14 (33.3)
Available of treatment and surgical prophylaxis guidelines	32 (71.1)
ASP monitoring and reporting	
Available of antibiotic consumption measurement (DDD or DOT)	22 (49)
Regularly published resistant data	24 (53.3)
Regularly published antibiogram	29 (64.4)
Regularly published unit-specific antibiogram	19 (42.2)
Hospital infrastructure	
Available of IT capacity to assist ASP program	14 (31.1)
Available of reliable and timely reporting microbiology data	36 (80)
Hospital with all core elements for ASP in place (C-score, 12)	27 (60)
Hospital with all supplementary elements for ASP in place (S-score, 27)	0 (0)

Observations

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- 27/45 hospitals (60%) fulfill all C scores components; none fulfill all S score components
- 15/45 hospitals (34%) receive financial support from hospital administration for ASP initiation
- For C component, microbiologist, clinical pharmacist, process and outcome measurements, regularly published antimicrobial resistant data were lacking.
- For S component, lack of IT to support ASP, lack of treatment and surgical prophylaxis guidelines, lack of unit specific antibiogram, lack of monitoring for processes and outcomes were commonly reported

Apisarnthanarak A, *et al. Infect Control Hosp Epidemiol.* 2018;39:1237–45;
Apisarnthanarak A, et al. Infect Control Hosp Epidemiol 2019;40:1077-1086.

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Contents lists available at ScienceDirect
International Journal of Infectious Diseases
journal homepage: www.elsevier.com/locate/ijid
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Global Antimicrobial Stewardship with a Focus on Low- and Middle-Income Countries

Jacob Pierce[a,*], Anucha Apisarnthanarak[b], Natalie Schellack[c], Wanda Cornistein[d], Amal Al Maani[e], Syamhanin Adnan[f], Michael P. Stevens[a]

2. Suggested Practice

2.1. Establish ASP as a Priority (National Action plans)

2.2. Medication Management

2.3. Establishing an ASP Committee

2.4. Role of the ASP Committee

2.5. ASP Interventions

2.6. Measure Outcomes

3. Controversial Issues: Challenges in LMICs

3.1. Over-the-counter Antimicrobial Availability and Public Expectations

3.2. Unique Challenges and Knowledge Gaps in Antimicrobial Prescribing Among Providers

3.3. Diagnostic Barriers: Microbiology Laboratory Access

3.4. Access to Antimicrobials

3.5. Insufficient Staffing

3.6. ASPs and Pandemic Preparedness and Response Efforts

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HOW TO SELECT APPROPRIATE MEASUREMENTS OF YOUR AMS PROGRAM

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Defining and Implementing Stewardship Metrics is Complex

- Care of patients with suspected infections is complex
  - Involves nuanced decision making
  - Contains multiple components
- Patient safety outcomes and resistant infection events are infrequent and have multiple confounding factors
- Significant effort is required to extract metrics for antimicrobial stewardship programs (ASPs) from the medial record, complete meaningful analyses, and translate analyses into actionable conclusions

Moehring et al, CID 2017:64, 377-83

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Categories of Outcomes Metrics

- Antimicrobial use (AU) measures
  - Defined daily doses (DDDs), days of therapy (DOTs)
- Quality measures
  - Compliance with guidelines, use of care bundles, appropriate therapy
- Clinical outcome and safety measures
  - Mortality, length of stay (LOS), readmissions, toxicity
- Costs
  - Antibiotic acquisition costs, total costs of care

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ASP Outcomes and Metrics – Divergence Between Practice and Perceived Importance

Table 3. Respondents' Opinion of Most Important Antimicrobial Stewardship Program Outcomes Based on Audience and Those Collected as Metrics (n = 41)

Outcome[a]	Collected by Respondents as ASP Metric	Most Important	Hospital Administrator Perceived Most Important[b]	Pharmacy Director Perceived Most Important[b]	P&T Committee Perceived Most Important[b]	ID Physician Perceived Most Important[b]
Antimicrobial use	30 (73)	6 (15)	1 (2)	9 (22)	13 (32)	1 (2)
Antimicrobial cost	30 (73)	4 (10)	17 (41.5)	23 (56)	6 (15)	0 (0)
Appropriateness of antimicrobial use	21 (51)	23 (56)	2 (4.9)	2 (5)	6 (15)	11 (27)
Infection-related mortality rate	3 (7)	14 (34)	1 (2)	2 (5)	1 (2)	15 (37)
Infection or antibiotic-associated length of stay	5 (12)	9 (22)	2 (4.9)	0 (0)	1 (2)	3 (7)

Abbreviations: ASP, antimicrobial stewardship program; ID, infectious disease; P&T, pharmacy and therapeutics.

[a] Respondents could select >1 outcome.

[b] Respondents selected outcomes that they perceived to be the most important to this audience.

CID 2014:59 (Suppl 3) • Bumpass et al

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STEWARDS Recommended Patient-Level Metrics for Hospitals

Table 2 Stewardship metrics for acute-care hospital ASPs to assess the impact of patient-level interventions as recommended by STEWARDS panel

	Group 1: Ready for immediate use and tracking	Group 2: Identified as useful but questionable feasibility: recommended for future study
Clinical outcomes	• None	• Readmission: related to infectious diagnoses
Unintended consequences	• *C. difficile* infection incidence—healthcare associated • Drug-resistant infections—rate of resistant pathogens isolated from clinical cultures	• Adverse drug events/toxicities
Utilization	• Days of therapy/admission • Days of therapy/patient-days	• Days of therapy/days present • Total duration/admission • Total duration/antimicrobial admission
Process measures	• Redundant therapy events	• Antimicrobial errors • Appropriateness/inappropriateness per institutional guidelines/expert opinion • Adherence to guidelines/formulary/protocol/bundle • Appropriate cultures performed per institutional guidelines/expert opinion • Excess drug use • De-escalation performed (# occurrences) • Culture(s) collected prior to antimicrobial administration • Time to appropriate therapy • Proportion of patients who received initial antibiotic coverage for a targeted nosocomial pathogen who also had positive cultures for that target pathogen

Emberger et al, Curr Infect Dis Rep (2018) 20: 31; Mohering et al, CID, 2017;64(3):377–83

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DDDs and DOTs

- Defined Daily Dose (DDD)
  - Recommended by WHO
  - Average maintenance dose per day for a drug used for its main indication in adults
  - Calculated by determining aggregate grams of antibiotic purchased, dispensed, or administered and dividing by WHO-assigned DDD value
- Days of therapy (DOT)
  - Used by CDC/NHSN for reporting antimicrobial use
  - Calculated by tallying number of calendar days during which a patient received an antibiotic based on administration data
- Denominators
  - Patient days
  - Days present (accounts for partial days)

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DDD vs DOT

Table 2
Antimicrobial consumption metrics

Metric	Definition	Advantages	Disadvantages
Numerator (consumption metric)			
Defined daily dose (DDD)	• Average maintenance dose per day for a drug used for its main indication in adults • Grams of antibiotic administered, purchased, or dispensed divided by WHO-assigned DDD (found on WHO Web site)	• Can be used for international benchmarking as other countries use DDD • Does not require administration data • Facilitates cost analyses	• Discrepancies between WHO-assigned DDD and dose used in practice leads to inaccurate assessment of use • Not appropriate for use in pediatric patients • Not an accurate reflection of use in renal impairment
Days of therapy (DOT)	• Aggregate sum of calendar days during which a patient received any amount of an antibiotic as documented in the eMAR and or BCMA data	• Recommended metric by IDSA/SHEA ASP guidelines • Required for participation in CDCs NHSN AU module (referred to as "antimicrobial days") • Appropriate for use in pediatric patients • Not affected by discrepancies between WHO-assigned DDD and dose used in practice	• Not as useful for international bench-marking as other countries use DDD • Not an accurate reflection of use in renal impairment • Requires administration data, which may not be obtainable in all institutions

Brotherton et al, Med Clin N Am 102 (2018) 965–976

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Limitations of DDD and DOT

- Do not directly measure quality, process or clinical outcomes
- Do not adequately adjust for case-mix/severity of illness/antimicrobial resistance prevalence
- In certain instances, decrease in DDD/DOT might be inappropriate or harmful
- What alternatives are there to measure ASP performance?

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What Will Metrics Be Used For?

- External benchmarking?
- Internal use/benchmarking?
- For a specific intervention?
- Justification for your ASP?
  - What does your leadership see as important?
  - Know metrics impacting payment
- Other purposes?

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Clinical Outcomes Metrics: The Big Four

1. Mortality (infection-related)
2. Length of stay (infection-related) and readmissions
3. *Clostridioides difficile* infection
4. Antimicrobial resistance

- All are important and when possible, should be monitored
- Important limitations with each

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Mortality and Length of Stay

- Advantages
  - Captured routinely on all patients
  - Metrics monitored and valued by clinicians, administration, patients, the public
  - With rapid diagnostics and optimal PK/PD approaches, increased likelihood to impact these outcomes
- Drawbacks and limitations
  - Major issues with confounding, competing risks
  - Very complicated to determine independent impact of antibiotics on outcomes
  - When there is success, various services will want credit
  - Difficult to use to measure impact of day to day interventions
- Good for specific interventions, but ASPs should avoid relying on them routinely

Am J Health-Syst Pharm. 2018; 75:230-8

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Clostridioides difficile Infection (CDI)

- Advantages
  - Widely recognized as important stewardship metric
    - Antimicrobial use is THE critical risk factor
  - Reported to NHSN in the US – SIR reported for hospitals
- Limitations
  - Control requires effective infection prevention
  - Community rates/colonization pressure important in spread
  - Testing differences make interfacility comparisons complex
  - Inappropriate testing impacts rates
  - Relatively low incidence – difficult to demonstrate ASP impact
- Important to measure, important to recognize limitations

Al-Hassan, Antibiotics 2019, 8, 127

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Multi-Drug Resistant Organisms

- Advantages
  - Major focus of healthcare, government, public
  - Antibiotic use important component of multi-drug resistant organism (MDRO) spread in some cases
  - Some MDROs publicly reported
- Limitations
  - Control requires effective infection prevention
  - Community rates/colonization pressure play important role in hospital spread
  - Relatively low incidence for some MDROs – difficult to demonstrate ASP impact
  - Impact of stewardship on some MDROs relatively low

Al-Hassan, Antibiotics 2019, 8, 127

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Types of MDROs Where ASP Matters Most

- Hospital onset *Acinetobacter baumannii*, *Pseudomonas aeruginosa*
  - Resistant strains
- Carbapenem-resistant Enterobacteriaceae (CRE)
- Antibiotics play important role in emergence and dissemination of these MDROs
- Recognized by both WHO and CDC as major threats
- Incidence and rates influenced by factors other than ASP, but as far as MDROs go, ASP has major impact on these and therefore, they might be the most appropriate to use as metrics

Al-Hassan, Antibiotics 2019, 8, 127

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Direct Measurement of Performance: A New Era in Antimicrobial Stewardship

Table 4. Direct antimicrobial stewardship metrics.

ASP Metrics	Description
Antimicrobial use of broad-spectrum agents: Antipseudomonal beta-lactams Carbapenems Anti-MRSA agents Anti-VRE agents	• Most direct measure of ASP performance • Evaluates effectiveness of ASP interventions (e.g., syndrome-specific, prospective audit and feedback, de-escalation of therapy) • Measures both empirical and definitive therapy • Adjustments by quantity (facility size, patient population, or microbiological burden) and quality (appropriateness of therapy) at each healthcare facility are possible
Antimicrobial resistance of predominantly hospital-onset bacteria: *Pseudomonas aeruginosa* *Acinetobacter baumannii*	• Antimicrobial resistance of hospital-onset bacteria is associated with use of broad-spectrum antimicrobials at each institution • Antimicrobial resistance may also be influenced by referrals, especially at tertiary care centers • Patient-to-patient transmission of MDR bacteria may be reduced by effective infection prevention and control methods
Incidence rate of CRE	• Excessive use of carbapenems and other broad-spectrum antimicrobials increases risk of CRE infections or colonization • CRE rates may be influenced by transfers from other hospitals or skilled nursing facilities • Infection prevention and control programs are essential for reducing transmission of CRE in healthcare facilities

Note: ASP: antimicrobial stewardship programs; MRSA: methicillin-resistant *Staphylococcus aureus*; VRE: vancomycin-resistant *Enterococcus* species; MDR: multi-drug resistant; CRE: carbapenem-resistant *Enterobacteriaceae*.

Al-Hassan, Antibiotics 2019, 8, 127

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Toxicity and Adverse Effects

- Often overlooked
- Through optimal dosing, avoiding unnecessary therapy can decrease toxicity
- Example:
  - Change in vancomycin dosing from trough based dosing (targeting levels of 15-20 mg/l) to AUC_{24} targeted dosing (400-600 mg · h/liter)

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Decrease Goal, Decrease Dose, Decrease Exposure

Variable	Values for the following groups: Trough concn-guided dosing (n = 546)	AUC-guided dosing (n = 734)	P value
Vancomycin exposure			
Median (IQR) cumulative vancomycin dose (mg)			
0–24 h	3,250 (2,438–4,250)	3,000 (2,000–3,750)	<0.001
0–48 h	5,250 (4,000–7,500)	5,000 (3,750–6,500)	<0.001
0–72 h	7,500 (5,438–10,250)	7,000 (5,000–9,250)	0.001
Median (IQR) duration of vancomycin therapy (days)	5.6 (4.1–7.3)	5.3 (4.0–7.1)	0.076
Median (IQR) measured trough concn (mg/liter)	15.0 (10.8–19.5)	12.0 (8.4–15.7)	<0.001
Median (IQR) calculated AUC_{24} (mg · h/liter)	Not calculated	471.5 (361.5–576.7)	

Finch et al Antimicrob Agents Chemother. 2017; 61(12)

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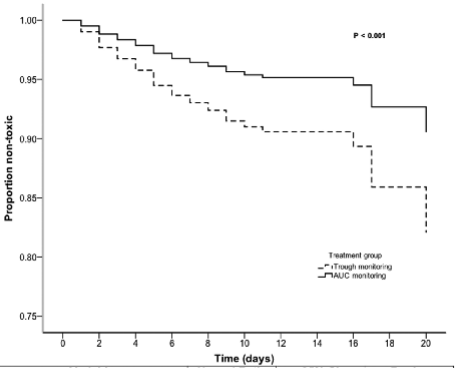
….and Decrease Toxicity



Variable	Hazard Ratio	95% CI	P value
AUC-TD	0.501	0.336 – 0.748	0.001
Concomitant furosemide	1.636	1.072 – 2.496	0.022
Elixhauser Comorbidity Index	1.123	1.044 – 1.208	0.002
APACHE II score	1.066	1.042 – 1.091	<0.001
Concomitant IV contrast	1.508	0.972 – 2.339	0.067
Concomitant tobramycin [a]	-	-	-
Duration of therapy, days [a]	-	-	-

[a] Not retained in final model

Finch et al Antimicrob Agents Chemother. 2017; 61(12)

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Quality Measures

- Appropriateness – difficult and labor intensive to assess "true" appropriateness
  - Concordance with treatment guidelines
  - Number and proportion of ASP recommendations accepted
  - Appropriate empiric/definitive/duration of therapy
- Process – easier (relatively) to measure – a surrogate measure for appropriateness of care
  - Clinical indications
  - Use of order form or set
  - Appropriate use of diagnostics

Brotherton, Med Clin N Am, 2018, 965-976; Morris, Current Treat Options Infect Dis 2014, 101-12

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Appropriateness of Therapy

- Redundancy of therapy
- Initiation of therapy
  - Asymptomatic bacteruria
- Empiric therapy
  - Guideline concordance
  - Targeted review for certain disease types (eg bacteremia)
- Definitive therapy (including time to effective therapy) and de-escalation
  - Bug-drug info often not enough (ie need to consider dosing, route, site of infection)
  - Rapid diagnostics
- Duration of therapy
  - Strong evidence base for some common infections
  - Relatively straightforward metric to obtain

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Conclusions

- Gap analysis can be used to improve quality of AMS program
- Understand what you want to measure and why
- Goal of intervention should help determine metric used
- Utilization and cost metrics are important but don't necessarily reflect quality and appropriateness
- Mortality, LOS, CDI and MDROs are important outcomes but are influenced by factors other than antimicrobial stewardship
  - Don't forget about toxicity and safety!
- Appropriateness of prescribing is important but can be resource-heavy
  - Consider redundancy of therapy, compliance with empiric therapy guidelines and duration of therapy for starters

Implementing AMS Program in Asia Pacific
Prof. Anucha Apisarnthanarak, Thammasat University Hospital, Thailand
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