

Identifying context-specific determinants to inform improvement of antimicrobial stewardship implementation in healthcare facilities in Asia: Results from a scoping review and web-based survey among local experts

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Author contributions

VTLH conceived of the idea, developed the research question and study methods. RLH, RL, DL, AK, TSP, FCL, EDA, DA, and HRvD reviewed and aided in developing the research question and study methods. NHY, EDA, ESE, DHY and VTLH performed searching, identification and finalization of eligible full-text documents. ESE and VTLH performed coding, extracting and summarizing the themes using NVivo. VTLH, EDA and RLH developed the assessment stems which were reviewed by HRvD, RLH, DL, AK and DA. TAQ, NHY, DHY and VTLH coordinated data collection, analysis and visualization of the expert survey data. All authors contributed meaningfully to the drafting and editing, and approved the final manuscript. VLTH is the guarantor for the overall content of the final manuscript.

Competing interests

The authors declared no potential conflicts of interest with respect to the research, authorship, or publication of this article.

Patient and public involvement

It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

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Ethical statement

Ethical approval

The authors declare that all the research meets the ethical guidelines. The study protocol has been approved by the Oxford Tropical Research Ethics Committee (OxTREC Reference: 573-21).

Data availability statement

Review themes, codes, and summary data are available upon request.

Abstract

International guidelines are available for the assessment and improvement of antimicrobial stewardship (AMS) programmes: an important strategy to address the escalating global antimicrobial resistance problem. However, existing AMS assessment tools lack contextual specificity for resource-limited settings, leading to limited applicability in Asia. This project aimed to identify relevant themes from current guidance documents to help develop a context-specific assessment tool that can be applied by healthcare facilities (HCFs) to improve local implementation.

We performed a sequential approach of a scoping review to identify relevant assessment themes for Asia and an expert survey for getting feedback on the relevance of assessment stems developed from the scoping review. We reviewed English-language published documents discussing AMS implementation or assessment at HCFs globally and in Asia. Themes were derived through content analysis and classified following the predefined context dimensions to develop assessment stems, defined as containing one identified determinant that may influence implementation outcomes. The survey consisting of identified assessment stems was reviewed by 20 locally identified experts in Asia who rated the level of relevance of these stems in AMS implementation in the region.

National leadership, training and technical support, and policy and guidance were the most commonly identified themes among 100 themes identified from 73 reviewed documents. From these themes, we developed 131 assessment stems for the expert survey. Of the 131 assessment stems, 117 (89%) were considered relevant for AMS implementation in Asia by at least 80% of respondents. These stems were included in the process of developing a global AMS assessment tool to support healthcare facilities to improve their programmes.

In conclusion, national leadership and support represents a distinct and important aspect affecting AMS implementation in HCFs in Asia. The identified assessment themes have substantial value for the formulation of locally relevant implementation strategies tailored to the Asian context.

Key words: antimicrobial stewardship, implementation, Asia

Key messages

What is already known on this topic

- International assessment tools for antimicrobial stewardship (AMS) implementation are not specifically tailored for resource-limited settings.
- Understanding the factors that influence AMS implementation in Asia is required to develop a context-specific assessment tool that could assist local healthcare facilities to monitor progress and make improvement over time.

What this study adds

- We identified a comprehensive list of assessment themes at four contextual levels (macro, meso, micro and multiple) by reviewing existing guidance documents and obtaining feedback from local experts in Asia.
- Factors at the macro level including national leadership, training and technical support, and policy and guidance were found to play a critical role in improving AMS implementation at the healthcare facility level.

How this study might affect research, practice or policy

- The identified assessment themes comprehensively present the relevant aspects for healthcare facilities in Asia to address in order to improve their AMS implementation over time.

Problem

Despite the recognized importance of antimicrobial stewardship (AMS) globally, AMS programs have been implemented inconsistently across countries and regions. As shown in a recent survey from 10 countries in Asia, a limited proportion of hospitals in Asia implementing all core components following the existing global and regional guidelines and recommendations (47/349 hospitals).¹ Guidance documents for resource-limited settings including the recent World Health Organization (WHO) and the U.S. Centers for Disease Control and Prevention (US CDC)²⁻³ are available, however the application of these are still challenging as they are not sufficiently specific to the context of Asia. In the global collaborative initiative coordinated by US CDC to develop a new tool for assessing AMS in global inpatient healthcare facilities,⁴ there was a need to identify the relevant assessment items resource-limited settings in Asia. Here we report a quality improvement project to develop context-specific assessment themes through a scoping review and survey of local experts that are relevant to the Asian countries, to help improve the local performance and quality of AMS programmes. We aimed to generate relevant assessment stems to be included in the US CDC's initiative to ensure that the contextual determinants of AMS programme in resource-limited settings in Asia are integrated in the global tool and support local hospitals in evaluating and improving implementation.

Background

AMS is one of the strategies contributing to the implementation of global and national action plans to address antimicrobial resistance (AMR) through optimizing antimicrobial use.⁵ AMS encompasses a wide range of strategies from technical aspects of prudent antibiotic use focusing on prescriptions (e.g., drug, dose, duration) to broader concepts of responsible antibiotic use (e.g., careful and responsible decisions to treat).⁶ AMS has been expanded

beyond its core implementation strategies in inpatient settings, with increasing roles of non-physician front-line providers (e.g., nurses and pharmacists), rapidly evolving metrics for impact and success, and wide spectrum of strategies for implementation, engagement, and practices.⁷

Guidance for implementation of AMS programmes is available from various resources such as those from the World Health Organization (WHO) and the U.S. Centers for Disease Control and Prevention (US CDC),^{2-3,8} expert reviews,^{9,10} country and region-specific guidelines. These sources^{8,11,12} have identified a vast list of core elements and components of AMS programmes, such as senior management commitment, including resource allocation; leadership, including accountability; expertise on infection management and antimicrobials; specific actions to improve antimicrobial use; education and training; monitoring use and resistance epidemiology; and reporting and feedback.

However, the existing AMS assessment tools lack contextual specificity, as they are not tailored for resource-limited settings and do not adequately address the barriers to implementation in such contexts. Their applicability is constrained in many countries in Asia given some differences in the healthcare systems, availability of diagnostic testing and antibiotics, public awareness and prescribing practices,^{9,13} and contextual and cultural characteristics^{14,15} from the other regions.

Understanding AMS implementation needs and practices within the Asian context and being able to monitor progress over time are key to assisting local healthcare facilities with improving antimicrobial use. In this project, based on the existing AMS implementation guidance resources, we aimed to develop a comprehensive list of assessment stems, defined as containing one identified determinant that may influence implementation outcomes and can be stated by one or multiple questions that are relevant and responsive to the local conditions. Our report aims to present the results from this activity to support local healthcare

facilities in understanding the factors that can influence AMS implementation in Asia and applying the context-specific assessment tool that could assist in monitoring progress and improving the quality and performance of the programmes over time.

Methods

We performed a sequential approach, starting with a scoping review study, followed by an expert survey, as described in a previously published protocol.¹⁶ The scoping review was conducted and reported in accordance with PRISMA Extension for Scoping Reviews (PRISMA-ScR) (Online Supplement Table S1).¹⁷ The content and format of this paper was also prepared following the recommendations of Revised Standards for Quality Improvement Reporting Excellence (SQUIRE 2.0) (Online Supplement Table S2).

Scoping review

We used the six-steps of scoping review based on Arksey and O'Malley and Levac et al.'s framework: 1) identifying the research question; 2) identifying relevant documents; 3) selection of documents to review; 4) data extraction; 5) data summary and synthesis of results; 6) consultation.^{18,19}

As presented in the protocol,¹⁶ the research question for this scoping review is: “What are the domains and items that can constitute an assessment tool of AMS implementation in Asia at the healthcare facility level?”

To identify relevant studies for the scoping review, we conducted a search of relevant documents that provide guidance on AMS implementation globally and specific to Asia. The selection of the documents for review was based on a set of inclusion and exclusion criteria as below.

Inclusion criteria: English-language documents were included if they provide guidance for and/or input information that can help inform AMS implementation at the healthcare facility level, including those describing frameworks, programme components, and elements, or recommendations for design, implementation, or assessment. Country-specific documents were restricted to countries in three sub-regions: South Asia, East Asia, and Southeast Asia. We chose to limit the search to these sub-regions because of the commonly identified relatedness and similarities in terms of geography, health,²⁰ burden of antimicrobial resistance,²¹ and culture.²²

Exclusion criteria: We used automation tools from the reference management programmes (Endnote, Zotero and Covidence) to screen and exclude the documents with the same title, author(s) and Digital Object Identifier. Then, we excluded any documents that only described methods or results of research studies or reports on AMS programmes implemented at single healthcare facilities with a limited geographical scope. We also excluded documents without identifiable authors, publishers, or year of publication. For guidance documents from the same institutions that were updated over time, we only included the latest version by the review time in the analysis.

We performed the search in August-September 2021 using general electronic databases, such as MEDLINE, Embase, Web of Science and Google Scholar; region-specific databases; national action plans; grey literature sources; and reference lists to identify eligible documents (Online Supplement Figure S1).

We extracted the content of the selected documents using qualitative coding practices following the contextual dimensions described by Nilsen & Bernhardsson²³ in eight contextual domains under different levels, such as micro (patient/prescriber), meso (organizational), macro (broader environment), and multiple level (Online Supplement Table S3). All of the included documents were read in-depth and coded based on the contextual

dimension elements for initial codes and themes, and additional elements were also identified from documents. We summarized and presented the themes under each level of contextual dimensions and the number of documents that contained each theme. From the themes identified, we developed potentially relevant assessment stems on AMS implementation including those that have not been discussed extensively in the literature but suggested to be relevant by the determinant framework.²³ We also extracted and summarized the general information about the reviewed documents including year of publication, authors, title, and geographical scope.

Expert survey

The aim of this survey was to seek feedback from local experts on the level of relevance of each assessment stem to the implementation of AMS programmes at healthcare facilities in the region.

We developed a form for expert survey, incorporating the identified assessment stems. We divided this form into four sub-forms. All identified assessment stems from all eight domains in the scoping review were systematically allocated to the 4 sub-forms so that each stem would appear in at least two sub-forms, and each sub-form contains stems from all categories identified in each domain (Figure 1). Each invited expert was randomly assigned to complete one of these sub-forms, which was configured as a self-administered online survey.

We sent an email invitation for completing the survey to a total of 90 experts with an expected response rate of 30% based on previous experience in similar internet-based surveys.²⁴ To mitigate bias, we invited experts with diverse backgrounds relevant to AMS and originating from different countries in Asia. The identification of potential experts was conducted through both academic literature and professional networks. Subsequently, we randomly assigned one of the four sub-forms to each expert. The invitation email included

information about the survey, inviting the expert to participate in the survey and click the survey link provided if they would like to take part in the survey. The survey link would lead the participants to the sub-form that had been assigned to them. The experts were asked to review and rate the relevance of each stem concerning AMS implementation and to indicate whether the stems were deemed essential for inclusion in the AMS assessment tool applicable to healthcare facilities in Asia. A designated timeline was established for the experts to complete the survey within 3 weeks in January 2022, and a reminder was sent out 2 weeks after the date of the invitation email.

For each stem, the proportion of respondents who rated assessment stems as relevant for AMS implementation in Asia was reported. The results of this survey were instrumental in compiling a list of stems that are specific to the AMS implementation in Asia for the downstream process of developing the assessment tool on a global scale.⁴ This global initiative is led by the US CDC and a technical advisory group, as described in the protocol.¹⁶ The study protocol has been approved by the Oxford Tropical Research Ethics Committee (OxTREC Reference: 573-21).

Results

Assessment themes identified from scoping review

A total of 73 documents met the inclusion and exclusion criteria and were subsequently included in the analysis (Online Supplement Figure S1 and Table S4). Of the 73, 36 (49%) documents were specific to an Asian country: 14 from India, 5 from China, 4 from Korea, 3 from Japan, 2 each from Thailand, Vietnam, and Pakistan, and 1 each from Taiwan, Hong Kong, Indonesia, and Malaysia. Six documents were specific to Asia, and nine were specific to low- and middle-income countries. The remaining 22 were documents that are non-specific to any geographical area.

We identified and extracted 100 themes distributed across four levels of contextual dimensions: 19 at the macro level (identified in 3 to 38 documents), 70 at the meso level (3 to 28 documents), 2 at the micro level (appearing in 5 to 14 documents), 9 encompassing multiple levels (ranging from 3 to 17 documents). Among these, 24 themes were derived from more than 15 documents (exceeding 20%), with 9 themes at the macro level. The theme related to prescriber factors emerged in 14/73 (19%) documents, while the theme associated with patient factors was identified in 5/73 (7%) documents (Online Supplement Table S5). Figure 2 presents the 100 themes at the macro, meso, micro, and multiple levels. Three most common themes at the macro level are national leadership; training and technical support at the national level; and policies, guidelines, and recommendations. At the meso level, specific AMS interventions, such as pre-authorization, guideline implementation, prospective audit and feedback, selective antimicrobial susceptibility test reporting, and education and training on prescribing practices, emerged as the most common themes. Micro level themes centered around prescriber and patient factors. The most prevalent themes that emerged from the multiple level category included localized AMS implementation, integration of feedback mechanisms at all levels, and AMS leadership at all levels. It is noteworthy that among the top 15 themes, only those from the macro (6) and meso (9) levels were represented.

Developing assessment stems of AMS implementation

Based on the scoping review, wherein 100 themes were identified and mapped to the determinant framework, we formulated 131 assessment stems on AMS implementation (11 micro level, 78 meso level, 12 macro level, and 30 multiple level) (Online Supplement Table S6). These stems were categorized into 31 categories belonging to eight domains: 1) patient-prescriber interface (micro level, 11 stems); 2) organizational culture and climate (meso level,

16 stems); 3) organizational readiness to change (meso level, 41 stems); 4) organizational support (meso level, 12 stems); 5) organizational structure (meso level, 9 stems); 6) national systems and policy environment (macro level, 12 stems); 7) social relations and support (multiple level, 7 stems); and 8) financial/technical support and feedback (multiple level, 23 stems) (Figure 1).

Feedback on relevance of assessment stems

From the total of 131 assessment stems in 8 domains identified above, we randomly assigned these stems into 4 sub-forms, each included 66-68 stems.

We received responses from 28 out of 90 invited experts (31% response rate). Of these, 20 experts (10 males and 10 females) completed all parts of the survey, including sub-form stems and demographic information, and therefore their responses were included in the analysis. Based on the demographic information, the areas of expertise of these experts included AMS (10 experts), infectious diseases (10), AMR (6), infection prevention and control (5), and/or clinical pharmacy (4) (15/20 experts had multiple areas of expertise). Of 20 experts, 11 reported working in a healthcare service provider, 8 from government departments, 8 from university/academic institutions, 7 non-government organizations, and 3 from research institutions (10/20 experts had multiple affiliations). Regarding professional roles, 12 had academic/teaching roles, 7 were antibiotic prescribers, 7 were health researchers, and 6 were non-prescriber healthcare professionals (9/20 experts had multiple professional roles). The median reported length of experience in the area related to antimicrobial use, AMR, and/or AMS was 7 years (minimum: 3, maximum: 35). Locations where the experience was obtained were Vietnam (8 experts), Indonesia (6), Thailand (5) and Singapore (1).

Figure 3 illustrates the distribution of expert ratings for assessment stems within eight domains. On average, each assessment stem was reviewed and rated by 11 experts (median: 11, min-max: 10-20). Of the total of 131 assessment stems, 117 (89%) garnered consensus as being relevant for AMS implementation in the context of healthcare facility in Asia by a minimum of 80% of respondents (experts responding to certain stems based on the assigned sub-forms).

In the patient-prescriber interface domain, 6/11 stems were rated as relevant by 80-100% of respondents which cover the following themes: perceptions on the role of the prescribers in antibiotic decision, AMS perceptions of the prescribers, prescriber's knowledge/capability, clinical ward factors in antibiotic decision, antibiotic use history, and promotion materials by pharmaceutical companies. Two stems were considered less relevant in AMS implementation: AMS consultation with patients and community (rated by 7/14 respondents), and patient's preferences and expectations (rated by 8/14 respondents).

The majority (14/16) of stems in organizational culture and climate domain were rated as relevant by 80-100% of respondents. Furthermore, three stems on the leadership at the healthcare facility level were rated relevant by all respondents, such as the role of the leader in communicating the importance of guidelines, encouraging multidisciplinary collaboration, and motivating innovations. Two stems that were rated by less than 80% of respondents were Antibiotic Awareness Week activities (10/13 respondents) and influence of staff hierarchy on AMS implementation (10/14 respondents).

In the organizational readiness to change domain, all 41 stems were rated as relevant by >80% of respondents, indicating agreement on their significance. All respondents affirmed the relevance of monitoring AMS implementation, encompassing monitoring of antimicrobial use, adherence to guidelines, antibiotic susceptibility patterns, AMR rates, and AMS activities. Access to laboratory services and IT systems, coupled with the availability of

regularly updated reports on antibiotic use and antibiogram, were acknowledged as important by all respondents. Moreover, key performance indicators, AMS-related feedback, and prioritization of AMS at the healthcare facility level were rated relevant by all respondents.

In the organizational support domain, 10/12 stems were rated as relevant by 80% or more respondents. Five stems were rated relevant by all respondents: 1) AMS team collective expertise in infection; 2) information/decision support systems in AMS implementation; 3) adequate IT support; 4) drug shortage/stockout; and 5) the role of healthcare facility administration in AMS execution. Two stems, i.e., prescribers' perceptions of substandard drugs affect antimicrobial use and reporting substandard medicine, were rated relevant only by 8/11 and 7/10 of respondents, respectively,

All nine (9) stems of the organizational structure category were rated as relevant by at least 80% of the respondents. All (100%) respondents rated the following three stems as relevant: 1) AMS activities in all relevant clinical wards; 2) effective multidisciplinary teamwork; and 3) integration of AMS in the healthcare facility hierarchy.

Regarding factors associated with national systems and policy environment, a minimum of 80% of the respondents considered 11 out of the 12 stems to be relevant. Universal consensus was reached among all respondents on the relevance of regular feedback on AMS from district health officers or the Ministry of Health, as well as the engagement of clinicians in procurement based on antibiotic needs.

In the domain of social relations and support, 80% or more of the respondents affirmed the relevance of six out of the seven stems assessed. These encompassed aspects such as support from professional networks on AMS, the extension of AMS initiatives to both senior and junior prescribers, and the awareness among healthcare facility staff regarding suboptimal

antibiotic practices. Only 6/10 respondents considered norms and social values across clinical specialties affecting AMS practices.

Under the financial/technical support and feedback domain, 20/23 stems were rated relevant by a minimum of 80% of the respondents. All respondents agreed on the relevance of eight (8) stems in AMS implementation: 1) discussion between microbiologist and clinician; 2) AMS findings are communicated with prescribers; 3) AMS team provides regular feedback to prescribers; 4) AMS activities are integrated in routine clinical practices; 5) dedicated time for AMS activities; 6) management formally identifies the role of AMS leader; 7) AMS champion; and 8) AMS is integrated in the existing funded programmes. On the other hand, three stems were rated as relevant only by 60% or less of respondents, such as financial rewards for compliance (6/10 respondents), financial consequences for non-compliance (5/10), and right timing for implementing AMS (6/10).

Discussion

In this study, we developed assessment stems relevant to AMS implementation at healthcare facilities in Asia from a scoping review and a web-based survey of local experts.

The process was guided by a framework describing the contextual determinants of implementing public health interventions at four context dimensions: micro (patient/prescriber), meso (organizational), macro (broader environment), and multiple level.²³ Our study expanded the previously developed AMS assessment tool for the Asian context, which was published as part of a consensus statement from a panel of regional experts,²⁵ by systematically reviewing and distilling relevant context dimensions and determinants to ensure the applicability of our new assessment tool for implementation at local acute care hospitals.

Both the scoping review and expert survey coherently showed that determinants at macro and meso level were regarded as the crucial factors in driving AMS implementation in healthcare facilities in Asia. At the macro level, the findings highlight the significant influence exerted by national governments in steering the implementation of AMS within healthcare facilities. The leadership of the national government is frequently highlighted as a vital and critical determinant for the success of an AMS programme. This leadership may manifest formal structures such as the establishment of a national AMS team or committee,²⁶ technical working groups as in Taiwan,²⁷ or formulation of a national declaration and an action plan as in India.^{28,29} The establishment of such support structures at the national level is poised to guide regional governments and healthcare facilities in establishing their priorities.²⁹

Besides support structures, fostering network and partnership between the national government and academic institutions are instrumental in laying the groundwork for AMS, as well as the formulation of national AMS guidelines to bridge the knowledge-to-action gap, as evident in Vietnam.³⁰ In addition to assuming a leadership role, the government has to formulate clear and coherent plans and strategies for AMS implementation, complete with binding regulations, policies, financing frameworks, and specified target indicators. This multifaceted approach is crucial for instilling awareness within healthcare facilities about the imperative nature of implementing and adhering to the national AMS guidelines.³¹⁻³³ The absence of robust national implementation policies and financing frameworks poses substantial challenge to ensuring the sustainability of AMS programmes.³⁴⁻³⁶

Within the meso level, we identified overlapping recommendations for AMS interventions from guidance documents developed by the WHO³⁷ and the US CDC,³⁸ which we categorised as readiness to change. Similarly, readiness to change was consistently found to be important in the expert survey. AMS implementation requires access to microbiological culture testing³⁹ and information technology systems.⁴⁰ In addition, monitoring of and feedback on AMS

implementation was deemed important. Yet, the expert survey revealed that social and cultural values and norms, as well as financial implications for compliance or non-compliance, were less relevant in the Asian context. This finding is potentially influenced by the fact that social and cultural factors are yet to be included as the core elements of AMS implementation in the globally accepted AMS guidance.^{37,38}

At the micro level, the scoping review revealed that the roles of prescribers and patients emerged to a lesser extent in the execution of AMS programmes within healthcare facilities. While the influence of prescribers' perspectives on decision-making and patients' expectations concerning specific treatment has been previously acknowledged,⁴¹ it is noteworthy that the role of patients has not yet received significant attention in the existing AMS guidance documents.^{37,38} This observation was further corroborated by the results of the expert survey, wherein the need for AMS consultation with patients and communities, as well as patients' preferences and expectations in AMS implementation, was reported to be comparatively less significant. This finding potentially signifies a gap in the existing AMS implementation guidance documents and underscores a limited awareness concerning the role patients in AMS programmes. This is particularly important since AMR is now recognized as a crisis beyond medical and healthcare boundaries. The WHO's most recent guidance emphasizes the imperative for people-centered interventions in addressing AMR problems and supporting the implementation of national action plans.⁴²

Our findings show that the distinct factor crucial to driving AMS implementation in healthcare facilities in Asia is the leadership of the national government. This finding might relate to the hierarchical culture in Asian countries⁴³ where, in this case, the national government functions as the authoritative figure, presumed to be accorded respect without questioning.⁴⁴ Therefore, the power to initiate and drive the implementation of AMS in healthcare facilities lies in the leadership of the national government.

The strength of this study is a structured review of the existing guidance documents, wherein themes were mapped to a comprehensive framework delineating contextual determinants across different levels of implementation. This method facilitated the identification of an exhaustive list encompassing key salient aspects for assessing AMS implementation in Asia. Moreover, this study highlighted the potential areas that might represent the opportunities to enhance the existing guidance documents. Subsequently, the assessment stems derived from this process underwent a consensus-seeking phase, involving obtaining feedback from the local experts.

This study has three limitations. First, our review was limited to English-language documents, potentially leading to the oversight of crucial elements discernible exclusively in local languages. Second, we did not evaluate contextual factors at the granularity of healthcare facilities, such as distinctions between rural and urban settings or variations between publicly and privately owned facilities. Last, low response rate of experts that responded to the web-based survey which influenced by various factors such as survey topic, respondent characteristics, and contact prior to the survey.⁴⁵ Nevertheless, there were no significant variations in the proportions of respondents' rating relevance across the assessment stems, suggesting the results are likely to represent the perspectives and views of local experts in AMS implementation in Asia.

In conclusion, the distinct driving factor identified for AMS implementation in healthcare facilities in Asia is the leadership of the national government. The identified assessment stems have substantial value for the formulation of locally relevant AMS implementation strategies in the Asian context. The results of this study have been integrated into the development of the US CDC global AMS assessment tool for healthcare facilities with three investigator groups, in collaboration with local partners and stakeholders of global regions: Johns Hopkins University and partners in Latin America, University of Oxford and Duke

University consultants with partners in South and South East Asia (Vietnam, Indonesia, Nepal, and Thailand), and University of Pennsylvania with partners in Southern Africa.⁴⁶ Specifically, the assessment stems that were rated being relevant for AMS implementation in the context of healthcare facilities in Asia by a minimum of 80% of respondents were included in the development of the tool. This tool has been implemented in more than 80 healthcare facilities across 12 countries including 4 countries in Asia (Indonesia, Nepal, Thailand and Vietnam).⁴ In the next steps, the implementation outcomes of the tool will be evaluated, including long-term applicability and continuous improvement of the tool in various contexts of healthcare facilities globally.

References

1. Chang FY, Chuang YC, Veeraraghavan B, Apisarnthanarak A, Tayzon MF, Kwa AL, et al. Gaps in antimicrobial stewardship programmes in Asia: a survey of 10 countries. *JAC Antimicrob Resist.* 2022 Nov 23;4(6):dlac117. doi: 10.1093/jacamr/dlac117.
2. Centers for Disease Control and Prevention [Internet]. Core Elements of Human Antibiotic Stewardship Programmes in Resource-Limited Settings. US Department of Health and Human Services; c2018 [cited 2022 Jun 8]. Available from: <https://www.cdc.gov/antibiotic-use/core-elements/resource-limited.html>.
3. World Health Organization [Internet]. Antimicrobial Stewardship Programmes in Health-Care Facilities in Low- and Middle-Income Countries: A WHO Practical Toolkit; c2019 [cited 2022 Jun 8]. Available from: <https://apps.who.int/iris/handle/10665/329404>.
4. Centers for Disease Control and Prevention [Internet]. Global Antibiotic Stewardship Evaluation Tool (G-ASET) for Inpatient Healthcare Facilities; c2024 [cited 2025 Jan 16]. Available from: <https://www.cdc.gov/international-infection-control/media/pdfs/Global-Stewardship-Tool-508.pdf>.
5. Majumder MAA, Rahman S, Cohall D, Bharatha A, Singh K, Haque M, et al. Antimicrobial stewardship: Fighting antimicrobial resistance and protecting global public health. *Infect Drug Resist.* 2020 Dec 29; 13:4713-38. doi: 10.2147/IDR.S290835
6. Dyar OJ, Huttner B, Schouten J, Pulcini C. What is antimicrobial stewardship? *Clin Microbiol Infect.* 2017 Nov;23(11):793-8. doi: 10.1016/j.cmi.2017.08.026
7. Emberger J, Tassone D, Stevens MP, Markley JD. The current state of antimicrobial stewardship: Challenges, successes, and future directions. *Curr Infect Dis Rep.* 2018 Jun 29;20(9). doi: 10.1007/s11908-018-0637-6

8. Pollack LA, Srinivasan A. Core elements of hospital antibiotic stewardship programmes from the Centers for Disease Control and Prevention. *Clin Infect Dis*. 2014 Oct 15;59 Suppl 3(Suppl 3):S97-S100. doi: 10.1093/cid/ciu542
9. Resman F. Antimicrobial stewardship programmes; a two-part narrative review of step-wise design and issues of controversy Part I: step-wise design of an antimicrobial stewardship programme. *Ther Adv Infect Dis*. 2020 Jun 19;7: 2049936120933187. doi: 10.1177/2049936120933187
10. Mendelson M, Morris AM, Thursky K, Pulcini C. How to start an antimicrobial stewardship programme in a hospital. 2020;26(4):447-453. doi: 10.1016/j.cmi.2019.08.007
11. Transatlantic Taskforce on Antimicrobial Resistance [Internet]. Summary the modified Delphi process for common structure and process indicators for hospital antimicrobial stewardship programmes; c2015 [cited 2024 Jun 6]. Available from: https://strama.se/wp-content/uploads/2022/10/summary_of_tatfar_recommendation0.1.pdf.
12. Pulcini C, Binda F, Lamkang AS, Trett A, Charani E, Goff DA, et al. Developing core elements and checklist stems for global hospital antimicrobial stewardship programmes: a consensus approach. *Clin Microbiol Infect*. 2019 Jan;25(1):20-25. doi: 10.1016/j.cmi.2018.03.033
13. Cox JA, Vlieghe E, Mendelson M, Wertheim H, Ndegwa L, Villegas MV, et al. Antibiotic stewardship in low- and middle-income countries: the same but different? *Clin Microbiol Infect*. 2017 Nov;23(11):812-8. doi: 10.1016/j.cmi.2017.07.010
14. Charani E, Smith I, Skodvin B, Perozziello A, Lucet JC, Lescure FX, et al. Investigating the cultural and contextual determinants of antimicrobial stewardship

- programmes across low-, middle- and high-income countries - A qualitative study. PLoS One. 2019 Jan 16;14(1):e0209847. doi: 10.1371/journal.pone.0209847
15. Gebretekle GB, Mariam DH, Abebe W, Amogne W, Tenna A, Fenta TG, et al. Opportunities and barriers to implementing antibiotic stewardship in low and middle-income countries: Lessons from a mixed-methods study in a tertiary care hospital in Ethiopia. PLoS One. 2018 Dec 20;13(12). doi: 10.1371/journal.pone.0208447
 16. Huong TLV, Raph LH, Ralalicia L, Limmathurotsakul D, Karkey A, Dodds Ashley E, et al. Identifying context-specific domains for assessing antimicrobial stewardship programmes in Asia: protocol for a scoping review. BMJ Open 2022 Sep 15;12(9):e061286. doi: 10.1136/bmjopen-2022-061286
 17. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Intern Med. 2018 Oct 2;169(7):467-473. doi: 10.7326/M18-0850
 18. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. Int J Soc Res Methodol. 2005;8(1):19-32. doi: 10.1080/1364557032000119616
 19. Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. Implement Sci. 2010 Sep 20;5:1-9. doi: 10.1186/1748-5908-5-69
 20. OECD - World Health Organization [Internet]. Health at a Glance: Asia/Pacific 2022; c2022 [cited 2024 Jul 18]. Available from: <https://www.who.int/westernpacific/publications/m/item/health-at-a-glance-asia-pacific-2022>.
 21. Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet. 2022 Feb 12;399(10325):629-55. doi: 10.1016/S0140-6736(21)02724-0

22. Ronen S, Shenkar O. Mapping world cultures: Cluster formation, sources and implications. *J Int Bus Stud.* 2013 Aug 29;44(9):867-97. doi: 10.1057/jibs.2013.42
23. Nilsen P, Bernhardsson S. Context matters in implementation science: a scoping review of determinant frameworks that describe contextual determinants for implementation outcomes. *BMC Health Serv Res.* 2019 Mar 25;19(1):189. doi: 10.1186/s12913-019-4015-3
24. Menon V, Muraleedharan A. Internet-based surveys: relevance, methodological considerations and troubleshooting strategies. *Gen Psychiatr.* 2020 Aug 1;33(5):e100264. doi: 10.1136/gpsych-2020-100264
25. Apisarnthanarak A, Kwa AL, Chiu CH, Kumar S, Thu LTA, Tan BH. Antimicrobial stewardship for acute-care hospitals: An Asian perspective. *Infect Control Hosp Epidemiol.* 2018 Oct;39(10):1237-1245. doi: 10.1017/ice.2018.188
26. Shah RC, Shah P. Antimicrobial stewardship in institutions and office practices. *Indian J Pediatr.* 2008 Aug;75(8):815-20. doi: 10.1007/s12098-008-0153-z
27. Tseng SH, Lee CM, Lin TY, Chang SC, Chuang YC, Yen MY. Combating antimicrobial resistance: antimicrobial stewardship programme in Taiwan. *J Microbiol Immunol Infect.* 2012 Apr 5;45(2):79-89. doi: 10.1016/j.jmii.2012.03.007
28. Voss A, Ghafur A. "The Chennai declaration" - Indian doctors' fight against antimicrobial resistance. *Antimicrob Resist Infect Control.* 2013 Mar 2;2(1):7. doi: 10.1186/2047-2994-2-7
29. Holmes AH, Sharland M. The Chennai Declaration: India's landmark national commitment to antibiotic stewardship demonstrates that 'truth alone triumphs'. *J Antimicrob Chemother.* 2013 Jul;68(7):1453-4. doi: 10.1093/jac/dkt062
30. Wertheim HF, Chandna A, Vu PD, Pham CV, Nguyen PD, Lam YM. Providing impetus, tools, and guidance to strengthen national capacity for antimicrobial

- stewardship in Viet Nam. *PLoS Med.* 2013 May 7;10(5):e1001429. doi: 10.1371/journal.pmed.1001429
31. Charani E, Holmes A. Antibiotic stewardship-Twenty years in the making. *Antibiotics (Basel)*. 2019 Jan 24;8(1):7. doi: 10.3390/antibiotics8010007
 32. Ryu S. The new Korean action plan for containment of antimicrobial resistance. *J Glob Antimicrob Resist.* 2017 Mar;8:70-73. doi: 10.1016/j.jgar.2016.10.013
 33. Tiong JJ, Loo JS, Mai CW. Global antimicrobial stewardship: A closer look at the formidable implementation challenges. *Front Microbiol.* 2016 Nov 16;7:1860. doi: 10.3389/fmicb.2016.01860
 34. Singh S, Charani E, Devi S, Sharma A, Edathadathil F, Kumar A. A road-map for addressing antimicrobial resistance in low- and middle-income countries: lessons learnt from the public private participation and co-designed antimicrobial stewardship programme in the State of Kerala, India. *Antimicrob Resist Infect Control.* 2021 Feb 11;10(1):32. doi: 10.1186/s13756-020-00873-9
 35. Kim BN, Kim HB, Oh MD. Antibiotic control policies in South Korea, 2000-2013. *Infect Chemother.* 2016 Sep 23;48(3):151-59. doi: 10.3947/ic.2016.48.3.151
 36. 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 Nov;10(11):e1001556. doi: 10.1371/journal.pmed.1001556
 37. World Health Organization [Internet]. Antimicrobial stewardship programmes in health-care facilities in low- and middle-income countries: a WHO practical toolkit; c2019 [cited 2024 Jun 6]. Available from: <https://www.who.int/publications/i/item/9789241515481>.

38. Pollack LA, Srinivasan A. Core elements of hospital antibiotic stewardship programmes from the Centers for Disease Control and Prevention. *Clin Infect Dis*; 2014 Oct 15;59 Suppl 3(Suppl 3):S97-100. doi: 10.1093/cid/ciu542
39. Levy Hara G, Kanj SS, Pagani L, Abbo L, Endimiani A, Wertheim HF. 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 Sep;48(3):239-46. doi: 10.1016/j.ijantimicag.2016.06.015
40. Walia K, Ohri VC, Mathai D. Antimicrobial stewardship programme (AMSP) practices in India. *Indian J Med Res*; 2015 Aug;142(2):130-8. doi: 10.4103/0971-5916.164228
41. Charani E. Culture and team dynamics in the implementation of antibiotic stewardship programmes. Imperial College London, 2017
42. World Health Organization [Internet]. People-centred approach to addressing antimicrobial resistance in human health: WHO core package of interventions to support national action plans (Licence: CC BY-NC-SA 3.0 IGO); c2023 [cited 2024 Jun 6]. Available from: <https://www.who.int/publications/i/item/9789240082496>.
43. Kang DC. Hierarchy and legitimacy in international systems: The tribute system in early modern East Asia. *Security Studies*; 2010 Nov;19(4):591-622. doi: 10.1080/09636412.2010.524079
44. Hofstede G, Hofstede GJ, Minkof M. *Cultures and organizations: Software of the mind*. 3rd ed. New York: McGraw Hill; 2010
45. Wu MJ, Zhao K, Fils-Aime F. Response rates of online surveys in published research: A meta-analysis. *Computers in Human Behavior Reports*; 2022 Aug; 7:100206. doi: 10.1016/j.chbr.2022.100206

46. Centers for Disease Control and Prevention [Internet]. Antimicrobial Resistance Investment Map and Funding; c2024 [cited 2024 Jun 6]. Available from: https://www.cdc.gov/antimicrobial-resistance/programmes/ar-investment-map.html?CDC_AAref_Val=https://www.cdc.gov/drugresistance/solutions-initiative/innovations-to-slow-ar/projects.html

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Figure 1. Level, domains and categories of assessment stems reviewed and rated in the expert survey conducted in January 2022 for relevance to AMS implementation in Asia

Figure 2. Main themes identified from the scoping review of 73 documents published from 2005 to 2021, mapped under the macro (broader environment), meso (organizational), micro (patient/prescriber), and multiple levels in relation to antimicrobial stewardship (AMS) implementation in healthcare facilities

Figure 3. Proportions of experts (total 20 experts) rated assessment stems as relevant for AMS implementation in Asia across eight domains (each bar represents the proportion for each stem)