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Utility and Applicability of Rapid Diagnostic Testing in Antimicrobial Stewardship in the Asia-Pacific Region: A Delphi Consensus

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Rapid diagnostic tests (RDTs) facilitate fast and accurate identification of infectious disease microorganisms and are a valuable component of multimodal antimicrobial stewardship (AMS) programs but are currently underutilized in the Asia-Pacific region. An experienced group of infectious diseases clinicians, clinical microbiologists, and a clinical pharmacist used a modified Delphi consensus approach to construct 10 statements, aiming to optimize the utility and applicability of infection-related RDTs for AMS in the Asia-Pacific region. They provide guidance on definition, types, optimal deployment, measuring effectiveness, and overcoming key challenges. The Grading of Recommendations Assessment, Development, and Evaluation system was applied to indicate the strength of the recommendation and the quality of the underlying evidence. Given the diversity of the Asia-Pacific region, the trajectory of RDT development will vary widely; the collection of local data should be prioritized to allow realization and optimization of the full benefits of RDTs in AMS.

Keywords. Asia-Pacific region; antimicrobial stewardship; point-of-care testing; rapid diagnostic testing.

Rapid diagnostic tests (RDTs) offer great potential for fast and accurate identification of infectious organisms and for the evaluation of antimicrobial susceptibility [1]. Thus, they are likely to become an increasingly important component of antimicrobial stewardship (AMS) programs. International guidelines on the implementation of AMS already encourage the adoption of RDTs in selected settings [2, 3]. However, barriers have been identified around the use of RDTs as a component of AMS in the Asia-Pacific region, including a lack of supportive local data and guidelines, inadequate infrastructure, and cost issues [4]. Here, we provide consensus statements on the role and use of RDTs as part of AMS in the Asia-Pacific region. The aim is to help clinicians to evaluate RDT resources, encourage optimal deployment, advise on how to effectively implement AMS in resource-limited settings, and enable policy makers to contextualize the role of RDTs in AMS at the national level.

METHODS

A group of experienced infectious diseases physicians, clinical microbiologists, and a clinical pharmacist from across the Asia-Pacific region was identified using a snowball recruitment method. Purposeful selection was used to ensure a balance of practitioners from resource-replete and low- and middle-income countries (LMICs). One AMS expert was identified from outside the Asia-Pacific region to provide alternate perspectives.

Ten draft statements were developed by the group on the role and use of RDTs in the Asia-Pacific region. A PubMed search was performed to look at literature on different diagnostic methods applied to AMS from 1 January 2015 to 26 February 2020. A second search was undertaken for all

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literature published on different diagnostic methods in AMS in the Asia-Pacific region, up to 14 May 2021 (Supplementary Table 1). Draft statements were then discussed by the group of 12 experts at a meeting on 20 March 2021. Each statement was reviewed, revised, and voted on using a modified Delphi consensus method [5]. In the event that consensus could not be reached, statements were further revised, and iterative voting via e-mail was required to achieve consensus. Interactions were managed using a group e-mail; all members received drafts simultaneously and were followed up for comments and voting. Consensus was set at ≥75% agreement among the group (≥9 of 12 group members). Eight of the 10 statements met with unanimous agreement. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system was applied to each statement (Supplementary Table 1) [6, 7].

DELPHI CONSENSUS STATEMENTS

Statement 1a: RDTs should provide results to the clinician within 4–6 hours; in settings where this is not possible, delivery of results within 24 hours may be acceptable (strong recommendation; moderate quality of evidence)

A preferred RDT is one that can yield results to guide treatment before the second dose of antimicrobial is administered. Ideally, results should be available to the clinician within 4–6 hours. A recent study compared prescription patterns for 484 influenza patients diagnosed using rapid polymerase chain reaction (PCR; available in 1–4 hours) or standard multiplex PCR (requiring 1–4 days for results) [8]. The rapid method was associated with a reduced likelihood of antibiotic commencement (51% vs 67%; $P < .01$) and more frequent commencement of oseltamivir (69% vs 56%; $P = .02$).

Furthermore, the severe acute respiratory syndrome coronavirus 2/coronavirus disease 2019 (SARS-CoV-2/COVID-19) pandemic has heightened focus on the need for rapid differential diagnosis within hours. A recent review found 64 study reports relating to rapid antigen or molecular tests for SARS-CoV-2 suitable for point-of-care testing (POCT) [9], while a scoping review identified 12 validated serological RDTs with apparent testing times of 2–30 minutes [10]. Although sensitivity appears to vary widely [9–11], these methods could be particularly useful in LMICs. Furthermore, rapid deployment of serum procalcitonin (PCT) analysis may help to reduce unnecessary antimicrobial use in patients with COVID-19 [12].

Nonetheless, delivery of results within 4–6 hours will not always be possible. For some RDTs, including those that still rely on a pure growth of an organism, technological limitations make this difficult. Service logistics may not always allow rapid turnaround, particularly in less resource-replete settings where it might only be possible to run services during working hours. In these circumstances, delivery of results within 24 hours (including weekends) may often be acceptable. A meta-analysis in which an "RDT" was defined as a technology that provides results in ≤24 hours demonstrated significantly reduced mortality risk from bloodstream infections (BSIs) with RDTs compared with conventional microbiological methods (odds ratio [OR], 0.66; 95% confidence interval [CI]: .54–.80) [13].

Statement 1b: The definition of an RDT is independent of where the test is conducted, which may be near the patient bedside or further away, depending on the specific technology used (strong recommendation; moderate quality of evidence)

Rapid POCT has great potential in some settings in the Asia-Pacific region. POCT that is based on the detection of key pathogen nucleic acids and proteins, circulating microRNAs, or antibodies can be used in the diagnosis of dengue, malaria, and *Mycobacterium tuberculosis* [14]. POCT also plays a key role in the diagnosis of respiratory tract infections (RTIs) such as influenza and SARS-CoV-2 [15]. The World Health Organization (WHO) has established the following 7 "ASSURED" criteria for optimal POCT: affordable, sensitive, specific, user-friendly, rapid/robust (no refrigeration required), equipment-free, and deliverable to those in need (portable, handheld) [16]. Various assay methods are under investigation (eg, loop-mediated isothermal amplification), lateral flow assays, and serological testing for the presence of antibodies [15]. Such methods are not routinely able to deliver on all ASSURED criteria, but progress is being made.

Statement 2: The role of RDTs must incorporate the identification not only of bacterial pathogens but also of nonbacterial organisms (strong recommendation; moderate quality of evidence)

Fast and accurate identification of pathogens is central to optimal patient management and for minimizing the initiation and continuation of unnecessary antimicrobials. Relevant examples include the identification of nonbacterial tropical diseases (eg, malaria, dengue) and the differential diagnosis of bacterial vs viral RTIs. With regard to tropical disease diagnosis, RDT deployment must consider local epidemiological data in order to avoid unnecessary testing. For RTI diagnosis, several syndromic multiplex PCR panels that can differentiate relevant bacterial and viral pathogens and assess resistance markers are now available, with results typically available within a few hours [17]. Available data suggest that rapid identification of viral infections of the respiratory tract can reduce antibacterial use [8, 18, 19].

Statement 3: RDTs can have a substantial impact on AMS at 3 key decision nodes: the need for initiation, on-treatment (choice of antimicrobial agent), and for deescalation/cessation of treatment (strong recommendation; low to moderate quality of evidence, depending on the stage)

RDTs have the potential to aid AMS at 3 clinical decision nodes (Figure 1). At the initiation stage, the main objective is to determine within the first few hours whether or not an antimicrobial is needed and to deescalate broad-spectrum antibiotics.

Once the patient is on treatment, RDTs can inform the decision on whether to target or broaden therapy. In a randomized, controlled trial of 116 Korean patients with hematologic malignancies and at least 1 positive blood culture, rapid phenotypic antimicrobial susceptibility testing was associated with a significant reduction in the proportion of patients receiving unnecessary broad-spectrum antimicrobials compared with conventional methods (12.5% vs 30.0%, respectively; $P = .031$) [20]. Similarly, a Japanese study found that use of a syndromic PCR panel in patients with bacteremia supported rapid susceptibility testing, and antimicrobial prescription changes were instituted in around one-quarter of cases [21].

When combined with clinical assessment, RDTs can help to facilitate the switch from intravenous to oral antimicrobial treatment and the decision to deescalate/terminate therapy. Akagi and colleagues found that PCT analysis every 3 days in pneumonia patients led to a significant reduction in the overall mean duration of antimicrobial treatment compared with controls (8.0 and 11.0 days, respectively; $P < .001$) without increasing recurrence rates [22]. A Taiwanese study found that combining molecular viral POCT and serum PCT analysis led to a significantly higher rate of antimicrobial discontinuation/deescalation in the emergency department compared with controls (26.0% vs 16.1%; $P = .007$); the duration of intravenous antibacterial use was also reduced (10.0 vs 14.5 days; $P < .001$) [23].

Statement 4: Given significant differences in economic development between countries in the Asia-Pacific region and the wide variety of infective pathogens, implementation of cost-effective RDTs must be tailored to the specific setting (recommendation level as per individual statements below; low quality of evidence)

The implementation of RDTs in the Asia-Pacific region must be customized to the specific needs and resources of individual countries/territories. The 3 stages of the patient care pathway (Figure 1) provide a model for dissecting these needs.

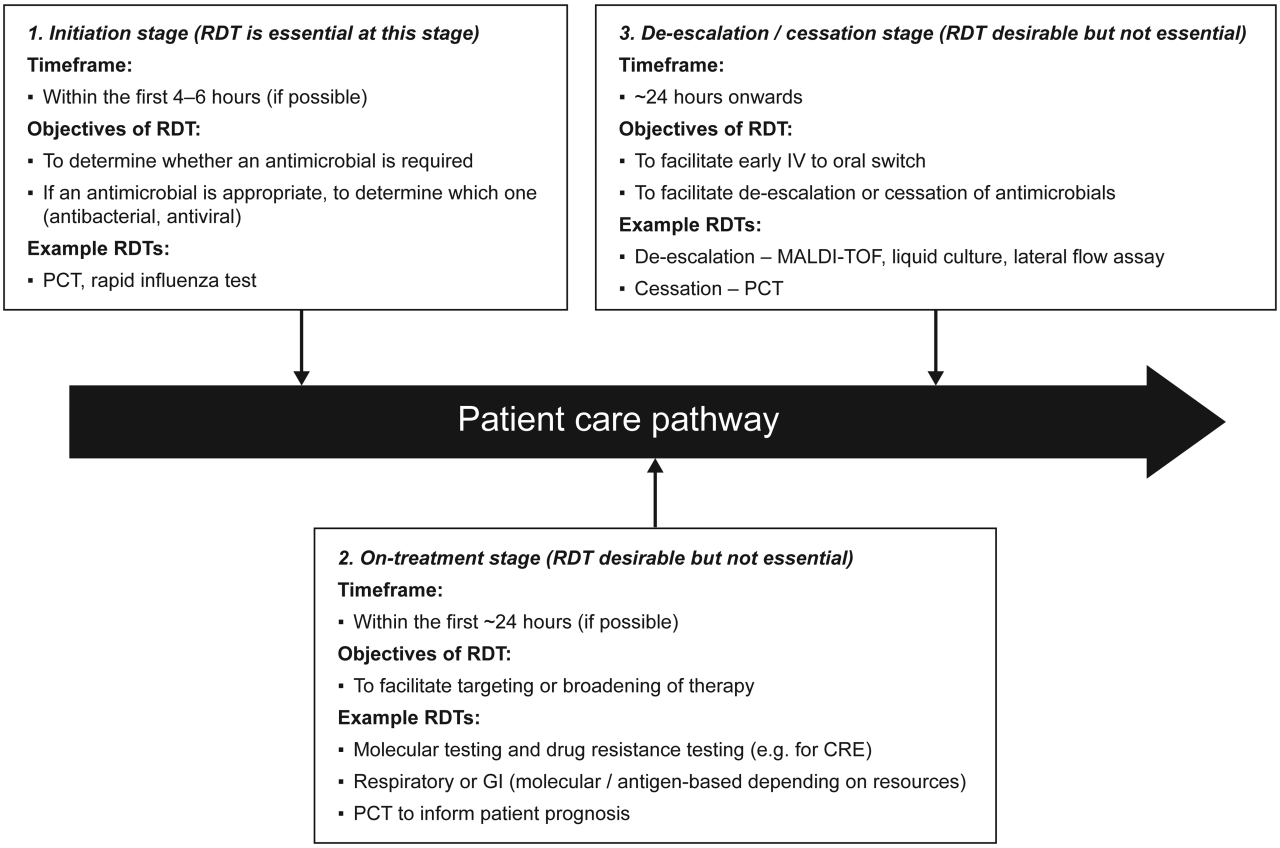

Figure 1. Impact of RDTs on antimicrobial stewardship at different stages of the patient journey. Abbreviations: CRE, carbapenem-resistant Enterobacterales; GI, gastrointestinal; IV, intravenous; MALDI-TOF, matrix-assisted laser desorption/ionization time-of-flight; PCT, procalcitonin; RDT, rapid diagnostic test. Reproduced with permission from Apisarnthanarak et al 2021, an Open Access article, distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives licence (https://creativecommons.org/licenses/by-nc-nd/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is unaltered and is properly cited [4].

Statement 4a: RDTs are particularly essential during antimicrobial initiation, and there is rationale for focusing preferentially on this stage; this may include RDTs that are useful in differentiating bacterial vs viral infection and for identifying locally relevant tropical diseases (strong recommendation)

Among AMS programs looking to build their RDT capacity, we believe there is rationale for focusing resources on the "initiation" stage of the patient care pathway (Figure 1). Example RDTs include PCT, influenza panels, and SARS-CoV-2 testing. There is evidence from pre- and post-intervention comparative studies that RDT-based differentiation of viral RTIs can reduce unnecessary antimicrobial initiation [8, 19]. The use of RDTs at this stage of the care pathway can also be crucial in identifying tropical diseases that are particularly relevant in some parts of the Asia-Pacific region. The evidence base that supports a potential role for RDTs in this area of tropical medicine is growing [14, 24, 25], but more geographically specific studies are required.

Statement 4b: The use of RDTs at the on-treatment and deescalation/cessation stages is also important; in cases of resource limitation, the use of RDTs may be considered as "preferable" rather than "essential," particularly in LMICs (weak recommendation)

There is evidence that RDTs can be effectively used during the other 2 stages of the patient care pathway shown in Figure 1 [20–23]. However, in resource-limited settings, individual centers will have to make decisions about where to target their efforts. In these situations, there is a rationale for focusing on the initiation stage across various AMS performance metrics.

Statement 5: Multiple technologies may fit within the definition of an RDT, dependent on local resources (conditional recommendation; very low quality of evidence)

A range of technologies can potentially meet the definition of an RDT (Supplementary Table 2). The most commonly used in current clinical practice in the Asia-Pacific region are biomarkers, enzyme-linked immunosorbent assay, lateral flow assay, microscopy, and PCR. Some have been studied within the region, but others have not (Table 1), and such analyses will be essential for confirming their local effectiveness. Furthermore, in some settings in the Asia-Pacific region, these technologies may be available but are not "rapid."

Statement 6: An inventory of required RDTs should be identified and prioritized at national and local levels (strong recommendation; very low to moderate quality of evidence)

RDTs should be considered as part of the AMS national action plan for each country. The 2017 Berlin Declaration of the G20 Health Ministers affirmed rapid diagnostics as a key tool for managing global concerns around antimicrobial resistance [26]. The WHO has also stressed the need for rapid diagnostics [3].

A consensus inventory appropriate to the Asia-Pacific region is provided in Table 1. Among these are rapid antigen tests, microscopy, PCT, bacterial culture and susceptibility assessment (eg, matrix-assisted laser desorption/ionization/time-of-flight [MALDI-TOF], VITEK®), immunoassays, and targeted and syndromic PCR. Only 2 were randomized trials comparing the impact of an RDT vs conventional diagnostics [20, 27]. A Korean study showed that rapid susceptibility testing significantly improved targeted antimicrobial optimization within 72 hours compared with conventional methods [20]. A Vietnamese study randomized patient samples with at least 1 pathogenic bacteria or fungus culture to rapid pathogen identification using MALDI-TOF or to conventional methods [27]. Although no difference was found between the methods in the proportion of patients on optimal antimicrobial therapy within 24 hours of positive culture, there was also no AMS program in place, suggesting that embedding AMS infrastructure is essential to the effectiveness of an RDT.

Statement 7: An AMS team should be put in place to interpret rapid diagnostic reports and guide antimicrobial use (strong recommendation; moderate quality of evidence)

A meta-analysis of 31 trials assessed the impact of a molecular RDT compared with conventional microbiology methods in improving clinical outcomes in patients with BSIs [13]. It found a significant mortality benefit with RDTs vs conventional methods when these were coupled with an AMS program (OR, 0.64; 95% CI: .51–.79). However, this advantage was lost in the absence of AMS supporting infrastructure. It should be noted that only 2 of the included studies were conducted in the Asia-Pacific region [28, 29]. However, recent data from this region have suggested that implementing RDTs in the absence of an AMS program results in limited benefits with regard to antimicrobial use or clinical outcomes [27, 30, 31].

Automation of some aspects of AMS is becoming increasingly feasible. A recent pre-/post-intervention comparative study assessed the utility of a simple electronic "best practice alert" sent to practitioners when specific conditions suggestive of viral infection were met (PCT <0.25 ng/mL and a virus identified on respiratory PCR) [32]. Roll-out of this alert led to significant reductions in antibiotic use ($P < .001$). Although automation cannot replace human AMS teams, it offers promise in mitigating logistical and cost issues.

Statement 8: Key performance indicators (KPIs) should be put in place at the institutional level to measure the effectiveness of rapid diagnostic testing; these KPIs must accurately assess the

Table 1. Inventory of Key Infection-related Rapid Diagnostic Tests in the Asia-Pacific Region

Test	Advantages/Disadvantages[a]	Example of Implementation and Impact on AMS in the Asia-Pacific Region
Rapid antigen test (influenza, group A streptococcus, malaria)	*Disadvantages:* Low sensitivity and specificity [23]; technical issues, such as cross-reaction, need for batch testing, long turnaround times [34]	–
Microscopy (eg, malaria, urine, cerebrospinal fluid)	–	–
PCT	*Advantages:* Fast discrimination of bacterial vs nonbacterial infections *Disadvantages:* More expensive than other biomarkers *Use cases:* Antimicrobial initiation or cessation; centralized laboratories *or* point of care	• Liew et al demonstrated that the use of PCT in AMS safely facilitated decision-making on antibiotics deescalation and discontinuation in patients with malignancies [35] • Liew et al suggested from their experience that PCT-guided therapy (recommended by the AMS team) may potentially reduce antibiotic use without compromising safety and clinical outcomes [36] • Drewett et al suggested that measurement of PCT in coronavirus disease 2019 patients, in conjunction with other clinical assessments, could play a key role in prognostication and decision-making, aiding AMS interventions [12] • Akagi et al found that PCT-guided antibiotic discontinuation shortened the duration of antibiotic treatment without increasing pneumonia recurrence or 30-day mortality [22]
Bacterial culture, identification, and susceptibility (eg, MALDI-TOF MS, VITEK®)	*Advantages:* MALDI-TOF MS has low running costs, fast microbial identification, and is not specific to 1 organism *Disadvantages:* Expensive capital purchase cost; no susceptibility data *Use cases:* Antimicrobial deescalation; centralized laboratories, not point of care	• Nadjm et al demonstrated no impact on antimicrobial use at 24 hours after introduction of MALDI-TOF MS in the absence of an established AMS program [27] • Jeon et al demonstrated that MALDI-TOF MS in a setting that lacked an AMS program did not improve clinical outcomes; in the ID intervention subgroup, the time to effective therapy was reduced by almost half, supporting the importance of the role of ID specialist and AMS [30] • Nisa et al suggested that MALDI-TOF MS would be useful in reducing the risk of MRSP, particularly in countries where MRSP is still rare, providing important information around antimicrobial resistance to inform AMS practices [37] • Niwa et al showed that combining MALDI-TOF MS with AMS facilitated early optimization of antimicrobial therapy in patients with bloodstream infections, with concomitant reductions in clinical failure and adverse event rates [38] • Wang et al found that blood culture–guided review of antimicrobial use based on clinical and microbiological evidence improved accuracy in selecting appropriate antimicrobials and encouraged deescalation [39] • Cairns et al suggested that an active review of patients with pathogens in blood cultures by an AMS team improved the time to both active and appropriate antimicrobial therapy for patients with positive blood cultures [40] • Wu et al showed that the implementation of a culture-guided AMS program led to medical expense savings and decreased inappropriate use of antimicrobials, average LOS, mortality, and antimicrobial resistance development [41] • Kim et al demonstrated that AMS based on rapid phenotypic AST allowed fast optimization of antibiotic treatment for bacteremia in individuals with hematologic malignancies by facilitating earlier decisions on deescalation; moreover, rapid phenotypic AST led to less frequent use of unnecessary broad-spectrum antibiotics [20] • Kitano et al proposed a simple AMS intervention that included using blood culture to inform antimicrobial treatment; their AMS protocol was successful in reducing antimicrobial prescriptions in the neonatal intensive care unit of a community hospital without pediatric ID specialists or a microbiology department that was open 24/7; compared with the pre-AMS period, there was a 76.2% reduction in antimicrobial DOT following AMS program implementation [42]
Immunoassays	–	–
Targeted PCRs (eg, respiratory viral)	*Advantages:* High sensitivity and specificity [23] *Disadvantages:* Technically challenging and time-consuming [23]	• Kitano et al demonstrated that use of multiplex PCR contributed to reducing DOT and LOS compared with conventional rapid antigen tests, but noted that the implementation of AMS would be mandatory to facilitate appropriate antimicrobial prescription and maximize cost-effectiveness [43] • Dowson et al showed that the availability of PCR testing results alone did not have an impact on antibiotic prescribing for respiratory tract infections in nursing homes; guidance from clinical algorithms or an AMS team together with PCR testing may be required to change antibiotic prescribing behaviors in nursing homes [44]

Table 1. Continued

Test	Advantages/Disadvantages[a]	Example of Implementation and Impact on AMS in the Asia-Pacific Region
Syndromic PCRs (eg, bioFire, GeneXpert)	*Advantages:* Quick discrimination of a range of causative bacterial, viral, and fungal pathogens; some resistance markers *Disadvantages:* Range of pathogens targeted limited; high capital and running costs *Use cases:* Antimicrobial initiation and deescalation; centralized laboratories or point of care	• Hayakawa et al suggested that the Verigene system may be a key asset for AMS in septic patients; use of this system resulted in high antibiotic prescription changes, of which almost 20% were episodes of deescalation; moreover, the time between the initiation of incubation and reporting of results was more than 3 times lower with Verigene vs conventional testing [21] • Au Yeung et al showed that rapid PCR instead of standard multiplex PCR was associated with benefits in AMS for people at high risk of complications with confirmed influenza; antibiotic prescriptions were significantly decreased from 67% to 51% when rapid PCR was used instead of standard multiplex PCR [8] • Faugno et al found that the implementation of MALDI-TOF MS and GeneXpert alone did not result in improvements in antibiotic prescribing or clinical outcomes among pediatric bacteremia cases; they suggested that rapid diagnostics must be coupled with an active real-time AMS program to guide clinicians in using rapid diagnostic results to streamline antimicrobial prescription [31] • Chavada et al showed that results from Xpert Flu/RSV available within 6–12 hours of patient presentation could help clinicians decide on the cessation of antibiotics in patients with a secondary bacterial infection; they highlighted that rapid influenza test results can facilitate constructive discussions between the AMS team and treating clinicians in decision-making on antibiotic cessation [19] • O'Callaghan and Jones suggested that rapid testing for respiratory viruses on the Xpert Xpress Flu/RSV assay is a potentially useful AMS tool for pediatric patients due to the association between rapid testing and reduced antibiotic use observed in their study [18]

[a]Only the advantages and disadvantages of each technology reported within the cited references are provided here, although there are likely to be others (eg, the turnaround time with mass spectrometry is often longer than 24 hours and therefore does not always qualify as "rapid," while targeted PCR methods may sometimes have suboptimal specificity); the dash (-) indicates that no Asia Pacific publications were found to discuss the advantages or disadvantages of these tests, nor were examples of implementations and impact on AMS found for these tests within Asia Pacific publications. Where no specific reference is given, all of the articles cited in the right-hand column may be considered as relevant references.

Abbreviations: AMS, antimicrobial stewardship; AST, antimicrobial susceptibility testing; DOT, days of therapy; ID, infectious diseases; LOS, length of stay; MALDI-TOF MS, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry; MRSP, methicillin-resistant *Staphylococcus pseudintermedius;* PCR, polymerase chain reaction; PCT, procalcitonin; RDT, rapid diagnostic test; RSV, respiratory syncytial virus.

effectiveness of RDTs against locally defined RDT denominator data and should also be easy to measure (weak to strong recommendation; very low to moderate quality of evidence)

It is essential that the effectiveness of RDTs is assessed at the institutional level. To do this, relevant KPIs must be defined and evaluated. These may be important in demonstrating the potential benefits of RDTs (eg, providing fast and accurate diagnosis, optimizing antimicrobial usage) and in mitigating possible downsides (eg, unnecessary additional costs) [33]. The specific KPIs used should be defined locally (Supplementary Table 3).

There are published reports on the use of some of these KPIs for assessing the effectiveness of RDTs in the Asia-Pacific region. Several studies have compared outcomes before and after implementation of novel RDTs in more resource-replete settings in Japan, Korea, and Taiwan [22, 23, 28, 29, 34, 35]. These studies demonstrated positive effects both on indicators of antimicrobial usage (appropriateness of prescription and duration of therapy, revision/cessation of antibiotics) and on clinical indicators (length of stay, mortality). Nonetheless, there remains little or no data on the use of some other KPIs, such as cost, readmission rates, and effects on multidrug-resistant microorganisms/antibacterial susceptibility.

Statement 9: There is a lack of data on the use of RDTs in the Asia-Pacific region, and high-quality local trials should be a priority and encouraged (strong recommendation; low quality of evidence)

Local data are essential if the potential advantages of RDTs are to be fully realized. Such studies should be performed within the context of AMS programs. However, data are currently limited and come largely from cohort studies (Table 1). Niwa and colleagues compared the impact of MALDI-TOF combined with an AMS program vs prior use of conventional methods in patients with BSIs [34]. The use of RDTs plus AMS decreased the time to organism identification and optimal antimicrobial therapy and reduced rates of clinical failure and adverse events. Another study found that use of rapid PCR instead of standard multiplex PCR in influenza patients was associated with reduced antibacterial commencement (51% vs 67%; $P < .01$) [8]. Furthermore, Japanese researchers demonstrated that replacement of conventional rapid antigen tests with a multiplex PCR respiratory panel for pediatric respiratory infections resulted in significant reductions in mean days of antimicrobial therapy (12.82 vs 8.56 days; $P < .001$) and length of hospital stay (8.18 vs 6.83 days; $P = .032$) [35]. Total costs from admissions were also reduced [35].

Only 2 randomized controlled trials have compared an RDT vs conventional diagnostics in the Asia-Pacific region [20, 27]. One showed that an RDT aided rapid optimization of antimicrobial use [20], whereas the other found it did not [27].

Statement 10: The challenges of implementing RDTs in the Asia-Pacific region are largely specific to individual countries and territories, requiring local solutions (strong recommendation; quality of evidence: not applicable)

We have previously identified 5 key challenges that need to be overcome to implement RDTs in AMS in the Asia-Pacific region [4]. They are based on a lack of funding and access to RDT technologies, the inability of some RDTs to accommodate all locally relevant organisms, a lack of expert microbiology laboratories, and suboptimal patient care pathways and reporting structures. Table 2 provides potential solutions to these challenges.

LIMITATIONS

There are some limitations to this work. First, consensus was reached using a modified Delphi method, which risks biasing the output toward the views of some members. Nonetheless, participants actively participated in all aspects

Table 2. Key Challenges and Solutions in the Deployment of Rapid Diagnostic Tests for Antimicrobial Stewardship in the Asia-Pacific Region

Key Challenges	Potential Solutions[a]	Research Gaps[a]
Insufficient funding of and insufficient access to some or all RDT technologies	• Collect local data on outcomes with RDTs • Develop long-term cost–benefit calculations to confirm the value of RDTs • Develop a rapid, easy, affordable test for low- and middle-income countries • Promote the importance of a national strategy and sustainable funding models for RDT implementation, including through AMS national action plans • Provide more technical support to improve access • Set up a local central laboratory to serve hospitals	• Cost-effectiveness of RDTs and impact analyses on reductions in antimicrobial use • Collaborative research among academia, industry, and healthcare facilities • Implementation science studies
Inability of some RDT platforms to accommodate the full range of relevant organisms, particularly where these differ from North America and Europe (eg, tropical diseases)	• Build peer-to-peer research networks • Build local manufacturing capacity • Develop a tailor-made test panel	• Diagnostic tests for relevant local pathogens • Epidemiologic studies on disease burden in the Asia-Pacific region
Lack of laboratories with sufficient internal expertise and/or external quality assurance	• Promote the development of dedicated local testing facilities and of regional/national reference laboratories • Build the training capacity of laboratory personnel • Develop and apply standardized quality assurance/competency assessments • Apply the WHO GLASS reporting framework [45] to facilitate improved local diagnostic ability and greater data standardization (enabling international comparison) • Promote competency in process and outcome	• Development of point-of-care testing • Cost-effectiveness studies around different models of pathology service provision in the Asia-Pacific region (eg, centralized vs decentralized) • Multisite microbiology studies to assist standardization • Development and evaluation of on-demand (rather than "in batch") services
Suboptimal patient care pathways and reporting structures that hinder the process of obtaining rapid test results and subsequent implementation of findings	• Develop training programs on RDT implementation and reporting • Collect data on implementation of RDTs in routine clinical practice • Expedite communication back to responsible clinician and the AMS team • Bolster support for AMS teams to interpret and implement RDT results, including specific personnel and reimbursement systems; interlink the business cases for these teams with those for RDTs [46, 47] • Standardize electronic medical records	• Integration of information technology on reporting • Implementation science studies • Translation of AMS infrastructure models from elsewhere into the Asia-Pacific region scenarios
Lack of guideline recommendations and general guidance from professional societies, which compounds the lack of awareness and education among physicians regarding RDTs and AMS outside of hospital intensive care and infectious diseases departments	• Develop local evidence-based guidelines that are appropriate to resource levels and requirements • Educate healthcare professionals on the use of RDTs (particularly outside of tertiary centers where acceptance may already be higher), eg, via online learning, continuing medical education, continuing professional development • Incorporate RDTs into medical school curriculums and into postgraduate certification curriculums for infection specialists	• Evidence synthesis of the Asia-Pacific region antimicrobial resistance patterns (eg, from the WHO GLASS system [45]) • xmlGuideline implementation study/conduct studies for the evidence base of local AMS guidelines

[a]"Potential solutions" are those that are currently in existence but may need transferring to each new geographical/healthcare setting. "Research gaps" highlight areas in which more data need to be accrued. Individual countries and institutions must be selective in adapting this menu to their own specific circumstances.

Abbreviations: AMS, antimicrobial stewardship; GLASS, Global Antimicrobial Resistance Surveillance System; RDT, rapid diagnostic test; WHO, World Health Organization.

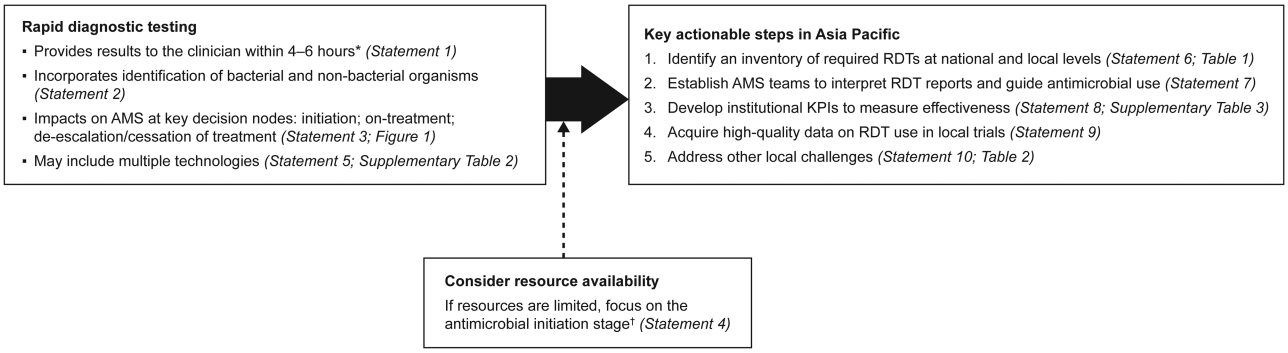

Figure 2. A summary of optimizing the utility and applicability of RDTs in AMS programs in the Asia-Pacific region. *In settings where this is not possible, delivery of results within 24 hours may be acceptable. †For example, for differentiating bacterial vs viral infection and identifying locally relevant tropical diseases. Abbreviations: AMS, antimicrobial stewardship; KPI, key performance indicator; RDT, rapid diagnostic test.

of the consensus. Second, the snowball method for selecting group members risks excluding colleagues with alternative views that may not have been considered. However, iterative development of the consensus statements using a modified Delphi method encouraged point–counterpoint discussions so that all sides of each statement could be examined. Third, the evidence quality was often at the lower end of the GRADE scale, and we have recommended that high-quality local trials be a priority.

CONCLUSIONS

RDTs are currently an underused component of AMS programs in the Asia-Pacific region. In the absence of formal guidelines, we sought to fill a gap in clinical practice and policy development by generating consensus statements on the implementation of RDTs within AMS activities for the Asia-Pacific region (Figure 2). The statements provide guidance on what constitutes an RDT, optimal deployment, measuring effectiveness, and overcoming key challenges. The speed and trajectory of the development of RDT is likely to vary widely across the region. Irrespective of this variation, the consensus statements can provide guiding principles. We strongly advocate the collection of local data across a range of metrics. This remains a key priority if the full benefits of RDTs in AMS are to be realized.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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