



Antimicrobial Resistance Control Strategies: A Coordinated Research Initiative Experience in the Asia Pacific Region

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Abstract

The objective was to gather information on the status of antimicrobial surveillance in the Asia Pacific region and suggest control strategies. Twenty-one economies of the Asia Pacific region participated in this initiative. A survey was conducted on antimicrobial use and surveillance throughout the region. A workshop was carried out to create awareness about the issue and discuss the implementation of control strategies. Based on the survey results and workshop conclusions, it can be established that there is better understanding of the implications of antimicrobial resistance in the human medicine area. Only few economies take actions to control antimicrobial resistance on a veterinary/agricultural level. To confront antimicrobial resistance, it is critical to raise awareness; cooperation between all countries is needed to apply international standards, to be able to have harmonized public policies. Countries must align and improve their systems for surveillance and monitoring of antimicrobial resistance in human, animals, and the environment.

Keywords

antimicrobial control strategies, antimicrobial resistance, antimicrobial surveillance, antimicrobial use, Asia Pacific region

Introduction

Nowadays, antimicrobial resistance (AMR), associated with animal food production is an issue of special concern worldwide.¹ According to the World Health Organization (WHO), AMR has the potential to threaten health security, and damage trade and economies. The growth of animal production, food global trade and travel allows resistant microorganisms to spread rapidly to distant countries and continents. Estimates show that AMR may give rise to losses in gross domestic

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product of 0.4% to 1.6% and that the indirect costs affecting society may be more than 3 times the direct health care expenditures. It affects developing economies proportionally more than developed ones.²

The development and spread of AMR are the result of the selective pressure exerted by the use of antimicrobial agents and the transmission of resistant microorganisms in hospitals, community, and environment.³ Almost as soon as antibacterial drugs were deployed, bacteria responded by manifesting resistance. As antimicrobial usage increases, so does the level and complexity of the resistance mechanisms exhibited by pathogens.⁴ According to the WHO, AMR is a major public health problem because of its severe adverse consequences, causing death of patients who do not respond to standard treatments, threatening infectious disease control, causing pathogen reemergence or increasing virulence. These consequences affect human and animal health, contribute to environmental pollution with waste and resistant microorganisms, impacting negatively in emerging economies' development and thus food security.² Estimation shows that AMR causes 700 000 annual deaths and that this could rise to 20 million by 2050.⁵

The Food and Agriculture Organization of the United Nations (FAO), World Organization for Animal Health (OIE), and WHO Tripartite High-Level Coordinating Forum, have set AMR as 1 of 5 priority issues and a flagship topic for One Health, developing a joint action plan on AMR, built on existing initiatives and with one common voice on AMR. An advisory group on integrated surveillance of AMR has been formed focused on antimicrobial usage monitoring, AMR Surveillance, capacity building, pilot projects, data management, and communication.⁶

Globally, there is consensus on the need for sustainable growth with equity, taking into account the current conditions of the global economy. Likewise, there is consensus on the importance of the economies to engage in capacity building efforts and effective regional and global partnerships across the public and private sectors, with the aim to address emerging infectious diseases and strengthen public health systems.¹ The implementation of interregional control strategies is necessary to assess AMR, like the WHO Global Action Plan on Antimicrobial Resistance⁷ and the Terrestrial Animal Health Code from the OIE.⁸ Currently, there are many differences in management and in the actions taken by the different economies on this issue. These can be evidenced by the different approaches towards the implementation of resistance surveillance systems of each economy. The fact that some countries have developed policies and guidelines and have established surveillance programs to track the antimicrobial resistance in food products and that other economies do not have clear policies about this issue yet, could increase the regulatory burden, affecting especially small and medium food producers, because of the differences in standards and technical regulations. Therefore, the lack of regional integration on this issue has the potential to affect the availability of safe food for the population. In order to continue contributing to regional economic growth and integration of the economies, and support of food safety and food security practices, countries must align and improve their AMR surveillance and monitoring systems in humans, animals and environment.

Considering this, the Asia-Pacific Economic Cooperation is committed to achieve sustainable and equitable growth facing relevant problems to the regional public health.⁹ Among the economies of the Asia Pacific region, 21 are part of the Asia-Pacific Economic Cooperation: Australia, Brunei Darussalam, Canada, Chile, People's Republic of China, Hong Kong, Indonesia, Japan, Republic of Korea, Malaysia, Mexico, New Zealand, Papua New Guinea, Peru, the Philippines, Russia, Singapore, Chinese Taipei, Thailand, the United States, and Vietnam.¹⁰ With the aim to assess AMR in a regional and comprehensive way, the Coordinated Research Initiative for the Implementation of Antimicrobial Resistance Control Strategies project was driven by Chile. This initiative, focused on AMR in strains isolated from humans, animals, environment, and food, in order to lay the foundations that the economies need to establish a resistance surveillance system in the short term. The objective of this article is to show the results of this project, including the

differences that exist within the Asia Pacific region, immediate and short-term evaluations and conclusions reached at the end of it.

Methods

To gather information on the current status of AMR surveillance in the Asia Pacific region, a survey was sent out to the APEC economies. The survey was based on the questionnaire provided by the Pan American Health Organization (PAHO) "Rapid Assessment Tool for the Analysis of the Country's Situation on Antimicrobial Resistance." The survey was adapted for this study and questions focusing on veterinary and agricultural area were added. The survey was sent out to an international panel of experts for validation. It was strongly suggested that the questionnaire was completed in a multidisciplinary way (human, animal health, and food safety experts).

The survey contained 46 questions, divided into 4 topics:

- (a) General information about the use of antimicrobials and the actions taken to control it.
- (b) Existence, permanence and funding of surveillance systems in humans and animals.
- (c) Legal and regulatory aspects concerning antimicrobials and resistance surveillance systems.
- (d) Integration of human health, animal health and food production.

Awareness and Capacity Building Activity

As a second stage, with the aim to extend the capabilities and expertise of the economies and stakeholders of the system (academia, researchers, and policy makers), and awareness among producers and industry, a workshop was held in Santiago, Chile. The activity focused on laying down the foundations needed to establish an AMR resistance surveillance system in the short term. Economies with ongoing surveillance systems contributed with knowhow and shared training materials for the workshop. Also, the experience of FAO, OIE, and WHO, in order to develop a joint action plan on AMR, were shared.

The activity was divided into 3 sessions

Session 1, Awareness: The objective of this session was to enhance awareness, skills, and knowledge in the field of AMR, as a worldwide emerging issue in public health. In this session, the public health impact of AMR and the challenges and importance of developing integrated surveillance systems for AMR were discussed.

Session 2, Where are we? The objective was to strengthen technical competence of the economies' representatives working in the areas related with AMR. It provided delegates with the tools to address this public health problem in order to work toward harmonized and standardized methodologies. It increased understanding of the control strategies of emergence and spread of AMR that have been used by other economies in the region and international organizations in order to improve economies' control measures and regulatory oversights of this hazard.

Session 3, How to implement a program? The objective was to build competency and capacity in AMR surveillance through knowledge transfer between economies with ongoing surveillance programs and other developing economies that did not have ongoing programs.

Economies Working Groups' Procedures

Since the countries have different degrees of development, they were divided into 2 groups as indicated by the International Monetary Fund¹¹ into "Advanced Economies" and "Emerging Markets and Developing Economies."

At the end of the third session, the participants were divided into 3 groups; each group was formed of 3 or 4 representatives from advanced economies or expert speakers from outside the Asia Pacific region and delegates from 3 to 4 developing economies. Group 1 was composed of representatives from the Public Health Agency of Canada, the University of Ireland, Harvard University, People's Republic of China, Mexico, and Papua New Guinea. Group 2 was composed of representatives from the US Food and Drug Administration, Utrecht University, the Colombian Corporation of Agricultural Investigation, Indonesia, Peru, the Philippines, and Vietnam. Group 3 was composed of representatives from PAHO, Food Standards Australia New Zealand, Texas A&M University, Malaysia, Chile, and Thailand. They discussed the difficulties each economy faced and with the help of the experts from advanced economies they considered which actions should be taken, in short and long term, to implement an integrated AMR surveillance program.

Immediate Evaluation Procedures

At the end of the activity the participants were requested to answer a Project Evaluation Survey, in order to have their immediate opinion on the different aspects of the awareness and capacity building activity.

Short-Term Evaluation Procedures

In order to have a follow-up of the activities and measure the impact of the project in the short term, 3 months after the awareness and capacity building activity, a questionnaire was sent out to all the delegates who participated, about the outcomes and what they have been doing on the subject since the activity.

Results

Survey

A total of 17 (81%) responses were received, including Australia, Canada, Chile, People's Republic of China, the United States, Philippines, Hong Kong, Indonesia, Japan, Malaysia, Mexico, New Zealand, Papua New Guinea, Peru, Chinese Taipei, Thailand, and Vietnam. Since the countries are very different from each other and have different degrees of development, they were divided into 2 groups as indicated by the International Monetary Fund.¹¹ The first group called "Advanced Economies" included Australia, Canada, the United States, Hong Kong, Japan, and New Zealand and the second group named "Emerging Markets and Developing Economies" included Chile, China, Indonesia, Malaysia, Mexico, Papua New Guinea, Peru, Taipei, Thailand, and Vietnam. In Figures 1 and 2, the details of the responses to some questions can be observed. The responses to some questions asked in the survey can be seen in Table 1 (also see Supplementary Figure 3).

Awareness and Capacity Building Activity Development

Thirteen economies attended the activity (Australia, Canada, Chile, Peoples Republic of China, Indonesia, Malaysia, Mexico, Papua New Guinea, Peru, the Philippines, Thailand, the United States, and Vietnam), with a total of 31 representatives, including speakers and delegates.

Economies Working groups' Outcomes

The responses obtained from the economies working groups were very similar between them for question 1 "Mention the difficulties you believe exist in your economy, to

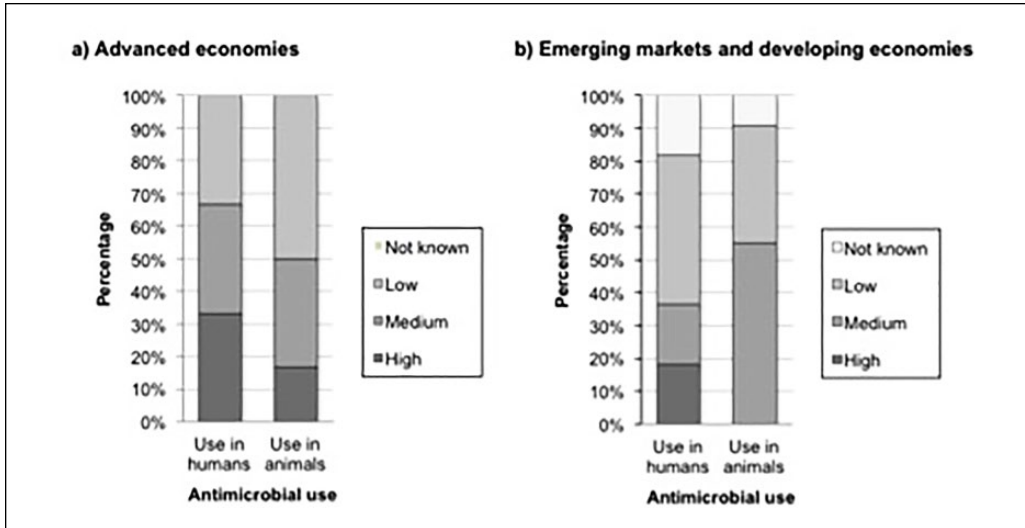


Figure 1. Awareness of human and animal use of antimicrobials and their contribution to antimicrobial resistance (AMR) in human infectious diseases.

implement an integrated AMR surveillance program.” This question allows to identify the immediate challenges that economies should solve before establishing an integrated antimicrobial resistance surveillance program which are; the lack of education and awareness on this issue, a shortage of political commitment and funding, a deficiency in technical expertise and infrastructure, and the need for harmonized international methodologies to address this problem.

For question 2 “Which actions should be taken, in the short and long term, to implement an integrated AMR surveillance program in your economy?,” responses varied between the groups. For group 1, in the short term they proposed to identify the problem, gather important stakeholders and use collaborative data to determine the antimicrobial usage in human and veterinary fields. In the long term, they suggested to carry out more studies on the methods needed for integrated surveillance and reinforce the existing regulations. Group 2 in the short term intended to commit to the One Health vision, and in the long term to train human resources and standardize methodologies. Group 3 in the short term plotted to use the information available to have an integrated baseline of AMR, share standards to create networks and share experiences between economies. In the long term, they proposed integrated surveillance and use the OIE’s tools to strengthen One Health issues.

In general terms, the workshop allowed the participants to enhance their knowledge and the main outcome was to be able to identify which are the main problems that must be addressed in order to start an integrated surveillance program in antimicrobial resistance (see Supplementary Table 2).

Immediate Workshop Evaluation Outcomes

From the 31 representatives from the Asia Pacific region, 21 questionnaires were received. In general terms, all the economies recognize the relevance of this project, 67% replied it was very high, 33% high and 0% medium and low. As well, a 57% of the participants strongly agree and a 43% agree that the project achieved its intended objective. Moreover, we also solicited them to rate their level of knowledge and skills in this topic prior and after participating in this event. Prior to the project a 5% answered it was very high, 10% high, 57%

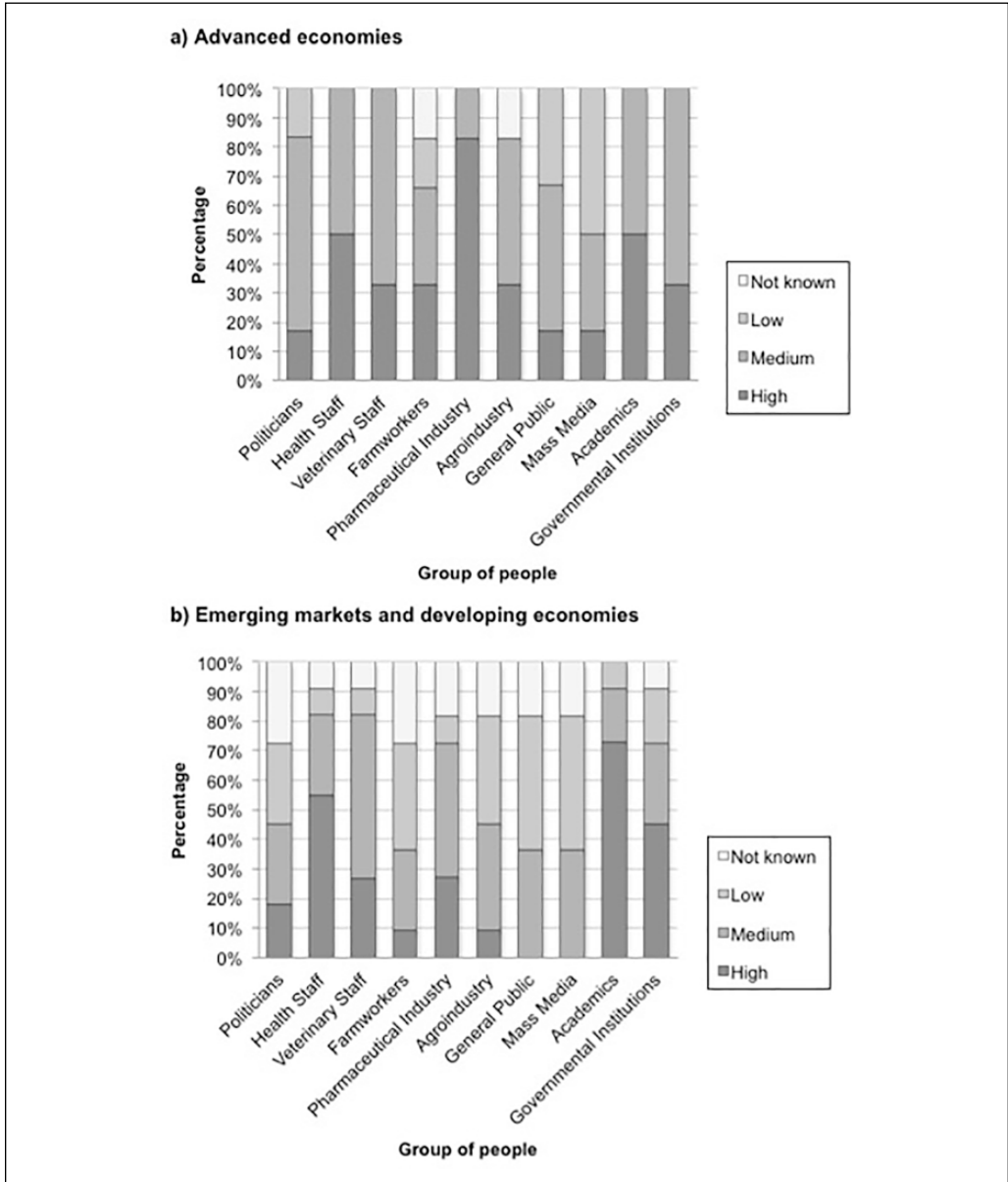


Figure 2. Awareness of antimicrobial resistance (AMR) in different groups of people.

medium and 28% low, after the event these responses changed to 24% very high, 52% high, 24% medium and 0% low (see Supplementary Table 3).

Short-Term Workshop Evaluation Outcomes

Participants were asked if their participation in the workshop enhanced their awareness and knowledge in AMR, to which 62% responded that they strongly agree and 38% said they agree.

However, the most relevant result in this evaluation was that after the project, 85% of the economies state that they had organized or participated in initiatives to address the AMR issue at a local level.

Table 1. Survey Questions.^a

Question	Advanced Economies			Emerging Markets and Developing Economies		
	Yes	No	Not Known	Yes	No	Not Known
(a) General information about the use of antimicrobials and the actions taken to control it						
In your economy, do national standards to approach antimicrobial resistance (AMR) exist?	67	17	17	55	27	18
Is there a mechanism, on a national level, which coordinates AMR activities in your economy?	83	0	17	36	27	36
(b) Existence, permanence, and funding of surveillance systems in humans and animals						
Does the national surveillance system for AMR receive any funding?	83	17	0	0	18	36
(c) Legal and regulatory aspects concerning antimicrobials and surveillance systems						
Is there an official National Reference Laboratory for AB susceptibility testing?	100	0	0	82	0	18
(d) Integration of human health, animal health, and food production						
Does a report of epidemiological surveillance (5 years old or less) in humans exist in your economy?	83	17	0	64	9	27
Are concrete actions taken with the results of surveillance reports on AMR in humans?	67	0	33	45	9	45
Does a report of epidemiological surveillance (5 years old or less) on AMR in animals exist in your economy?	50	50	0	36	45	18
Are concrete actions taken with the results of surveillance reports in animals?	33	33	33	16	36	45

^aAll values are in percentage.

Discussion

From the survey results we can conclude that there is a better understanding of the implications of the emergence of AMR in the area of human medicine than in the field of veterinary, agriculture and food production. Accordingly, most countries take actions to carry out a surveillance system of AMR only in the human health area, and only in advanced economies are these actions also extend to the animal health area. This contradicts the global initiatives recommended by the WHO that surveillance programs should integrate data from bacterial isolates originating from humans, food-producing animals, and retail meats.¹² Greater efforts should be made to establish integrated monitoring programs in order to analyze this topic in a multidisciplinary way.

In general terms, the major outcome of this project in the short term is the setting up of general awareness in the field of AMR among all the participant economies regardless of their level of development. Worldwide experts delivered high levels of knowledge, so the technical competences of the participants were strengthened in order to provide the basis to establish surveillance systems based on harmonized and standardized methodologies. Another important outcome was building capacity in AMR surveillance and encouraging the implementation of monitoring plans in the participant economies. Recommendations to the different countries on how to establish an integrated surveillance system were given, and the steps toward these were clearly exposed. According to these, economies were encouraged to create an action plan for the future in the medium term considering their current surveillance status and where they thought they could be in the medium/long term. This objective was met as can be seen in the short-term evaluation responses where the majority of the economies have participated in initiatives to address AMR since the event.

The main difficulties existing in the economies to implement an integrated AMR surveillance program were determined. Throughout the countries that participated in this study there is a lack of education and awareness on the effect AMR has on food safety, public health, environmental issues,

and on the whole economy; this is in line with the findings from the WHO's Global Report on Surveillance from 2014, where the major gaps in surveillance and data sharing are related to the emergence of AMR in foodborne bacteria and its potential impact on both animal and human health.² Also, there is a deficiency of technical expertise and of laboratory capacity. The inadequate law enforcement on antimicrobial use, insufficient expertise, limited funds and human resources are also considered as main concerns for most of the participants, this reflects what happens in many countries, such as Indonesia and Thailand, where even though antibiotics are prescription only drugs, they can still be purchased freely in informal markets.^{13,14} AMR is not a government priority and there is lack of political will to commit throughout changes of administration, but as presented by the WHO in their Global Action Plan on Antimicrobial Resistance in 2015, political support is needed to combat AMR.⁷ To be able to confront this problem it is very important to raise awareness among all of the stakeholders. Cooperation between the authorities of all economies to apply international standards is needed. It is also mandatory to have harmonized methodologies that assure quality and precision in the laboratories.¹² It is important to note that antimicrobial resistance is a global problem and that all countries should make their maximum effort to control it. The implementation of integrated surveillance programs, that are sustainable over time, may allow them to adopt the most appropriate measures to slow the emergence of AMR. In addition, the data delivered from these monitoring programs will permit them to know whether these measures have worked.

The creation of a network among the Asia Pacific economies regulators and policy makers working in the area of AMR is expected to be a long-term output of this project. This agrees with what was stated by Sachi Gerbin in 2014 that there is a need for a regional or global approach to AMR.¹⁵ However, more activities around this issue are needed in order to reinforce the importance of the harmonization and networking in AMR. This project was the first Asia Pacific initiative about Antimicrobial Resistance, so it can be considered a first step toward managing this worldwide public health and food safety problem.

Conclusions and Recommendations

Throughout the Asia Pacific region, there is a disparity among the economies regarding: education, awareness, technical expertise, laboratory capacity, law enforcement capacities, and the availability of funds, to commit and address AMR in an integrated manner. As was identified through the workshop's group work, this outcome can be used as a starting point to reduce the gap between economies, allowing them to be separated according to their state of progress and carrying out specific actions on each of these groups. Considering AMR as a mayor public health concern, it is important to make this issue a regional priority to be able to confront it, not only at the governmental level but also as part of the education of human and animal health professionals, thus installing the importance of this subject from the base of the training of future professionals who will have to deal with this emerging problem. The implementation of integrated surveillance programs, that are sustainable over time, may allow the different Asia Pacific economies to adopt appropriate measures to slow AMR development, and the information delivered from these monitoring programs will permit them to know whether these measures have worked.

Declaration of Conflicting Interests

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Supplementary Material

Supplementary material is available for this article online.

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