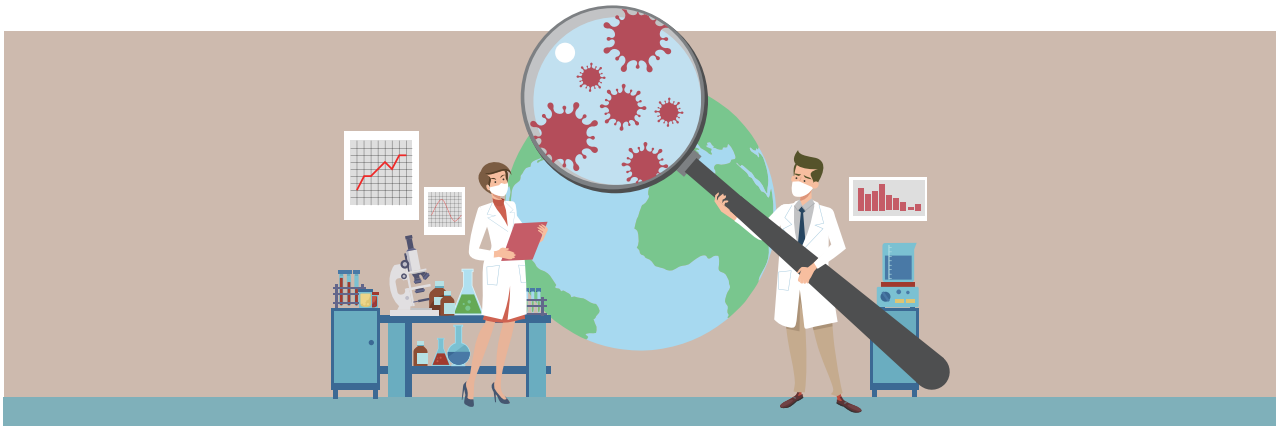
AMR Alliance Japan

POLICY BRIEF



The construction of a domestic AMR surveillance and crisis management system

Executive Summary

- Surveillance of antimicrobial resistance and antimicrobial usage can inform therapy decisions and reduce unnecessary antimicrobial use.
- In Japan, both the Japan Nosocomial Infections Surveillance (JANIS) and National Epidemiological Surveillance of Infectious Disease (NESID) monitor infectious diseases in hospitals, but surveillance has been inadequate outside of hospitals and is not uniform across sectors.
- Crisis management of antimicrobial resistance outbreaks and other infectious diseases depends on the resources of individual medical institutions.
- Greater investment is needed into the AMR surveillance system, especially for facilities not yet implementing surveillance.

Introduction

The surveillance of antimicrobial resistance involves the identification of high-risk patients, the promotion of antimicrobials stewardship, and the detection of outbreaks. Surveillance helps identify antimicrobial resistance patterns and provides information that can limit the unnecessary use of antimicrobials.

The "surveillance loop" for infectious diseases consists of data collection, reporting, analysis, and response.[1] If AMR is suspected in a hospital, laboratories will use diagnostic technology and automatic susceptibility testing to detect AMR organisms. Next, surveillance systems such as Japan Nosocomial Infections Surveillance (JANIS) integrate, analyze, and report the results.[2] These reports can be utilized by healthcare workers to strengthen antimicrobial stewardship programs. In addition, by setting common indicators, such as Drug Resistance Index or Defined Daily Dose (DDD),* comparisons can be made across institutions and countries. [3]

Crisis management is the systematic process by which a government or institution deals with the outbreak of AMR organisms. In Japan, hospital-based outbreaks are largely the responsible of Infectious Control Teams (ICTs) and Antimicrobial Stewardship Teams (ASTs).[4] For large scale outbreaks, hospitals collaborate closely with health centers, with the Government setting up a countermeasure headquarter if needed. Responses to infectious disease outbreaks are prescribed by the Infectious Disease Control Law, which depends on the infectivity and severity of the disease. [5]

Background of the Issue: Japan

Currently, Japan has two major AMR surveillance systems created by the Ministry of Health, Labour, and Welfare (MHLW): the Japan Nosocomial Infections Surveillance (JANIS) and the National Epidemiological Surveillance of Infectious Disease (NESID).

In 2000, the JANIS Clinical Laboratory Division was established to voluntary collect data from hospital-based diagnostic microbiology laboratories for AMR surveillance.[2] Once collected, clinical microbiological data is analyzed, and hospital-specific AMR prevalence is reported. In addition, this data can be examined at the national level, examining geographical trends in AMR prevalence. However, JANIS only monitors in-patients and does not collect data on clinics and nursing care facilities. As of January 2020, 2,358 medical institutions participated in JANIS.[6] For FY2020, MHLW requested ¥82 million (US$750,000) for the

*Defined Daily Doses – assumed average maintenance dose per day for a drug used for its main indication in adults

surveillance of AMR by JANIS. [7]

In accordance with the Infectious Disease Control Law of 1999, NESID requires the reporting of seven antimicrobial-resistant bacteria infections (vancomycin-resistant enterococcus, vancomycin-resistant Staphylococcus aureus, carbapenem-resistant Enterobacteriaceae, multi-drug resistant Acinetobacter, penicillin-resistant Streptococcus pneumonia, methicillin-resistant Staphylococcus aureus, multi-drug resistant Pseudomonas aeruginosa) which are all classified as category V infectious diseases.[8] Of these seven pathogens, four (vancomycin-resistant enterococcus, vancomycin-resistant Staphylococcus aureus, carbapenem-resistant Enterobacteriaceae, multi-drug resistant Acinetobacter) are reported by all physicians and three are reported by the approximately 500 designated sentinel sites across Japan. NESID analyzes these reports and the results are rapidly provided and published to medical practitioners and the general public.

While JANIS and NESID cover specific antimicrobial-resistant organisms (AROs), some antimicrobial-resistant organisms, such as drug-resistant bacilli, tuberculosis, fluoroquinolone-resistant Salmonella, and Shigella are not covered by these systems.[9] As a result, there is limited, if any, information available to manage outbreaks due to these AROs. Moreover, these surveillance systems are not linked and cannot provide case histories of patients who have received antimicrobials. Without the integration of surveillance systems and harmonization of data input, capturing real-time information for the rapid management of AMR outbreaks remains a challenge.

Since 2006, the Three Academic Societies Joint Antimicrobial Susceptibility program has conducted annual nationwide surveys for target diseases and their related infectious disease, including AMR-related diseases such as respiratory infection, urethritis, and simple cystitis.[10] In addition to surveillance, the program measures minimum inhibitory concentration (MIC) of antimicrobial drugs on microorganisms.

Furthermore, under the One Health approach, Japan monitors AMR in food-producing animals. The most notable of these surveillance systems are the Japanese Veterinary Antimicrobial Resistance Monitoring System (JVARM) and the National Veterinary Assay Laboratory (NVAL). [8]

In 2015, to generate reliable antimicrobial consumption data, MHLW created the Japan Antimicrobial Surveillance (JACS), a web-based system that aims to identify the volume of antimicrobial use and infection status in Japan, and to provide information for strengthening infection control. Data collected from pharmacist and wholesalers is used to calculate AUD (Antimicrobial Use Density) and DOT (Days of Therapy).[8] While surveillance of antimicrobial use is largely conducted in in-patient settings, antimicrobial usage in outpatients is largely unknown, which accounts for 90% of prescriptions.

In hospitals, crisis management of AMR outbreaks is under the purview of hospital-based Infection Control Teams (ICTs) and Antimicrobial Stewardship Teams (ASTs). For small- and medium-sized hospitals that lack the resources to set up Antimicrobial Stewardship Teams, the AMR Clinical Reference Center has released guidelines for AMR crisis management in March 2019. [11] The Japanese Government provides appropriate support depending on the specific needs of the hospital, for instance, related to epidemiological expertise needs. For large scale outbreaks, the Government is empowered to set up countermeasure headquarters, headed by the Prime Minister, with the Chief Cabinet Secretary and Minister of Health as vice-chiefs. [5]

Stakeholders and Countermeasure: Japan

Stakeholder	Countermeasure
Ministry of Health, Labour, and Welfare	• Invests in surveillance technology and capacity building in hospitals. • Sets standards and goals for antimicrobial resistance and antimicrobial usage. [9] • Establishes guidelines and standards for crisis management.
AMR Clinical Reference Center	• J-SIPHE: online common infectious disease countermeasure platform.[12] J-SIPHE combines, quantifies, and visualizes data on infectious disease treatment status, infection countermeasures, efforts to promote proper antibacterial usage, occurrence of medical-related AMR infections, occurrence of major bacteria and drug-resistant bacteria, and use of antibacterial agents. • AMR Clinical Reference Center also creates crisis management guidelines for small- and medium-sized hospitals. [11]
Japan Society for Chemotherapy, The Japanese Association for Infectious Disease, and The Japanese Society for Clinical Microbiology	• Three Academic Society Joint Antimicrobial Stewardship Program: collects national data on antimicrobial resistance infections across academic societies.[10] Measures minimum inhibitory concentration (MIC). This program has previously studied infectious disease includes respiratory infections, urinary tract infections, and otorhinolaryngology infections.
Public-private partnerships	• Public institutions, such as the National Institute of Infectious Diseases, has worked with private partners to improve the surveillance of AMR in Japan. Automatic detection of AMR outbreaks (WHONET-SaTScan system). [13]

Background of the Issue: Global

Antimicrobial resistant organisms are not bounded by national borders, and consistent surveillance must be conducted among countries with varying levels of personnel and resources. Global and regional AMR surveillance systems are supported by international collaboration and strengthened by national surveillance systems. The largest and most comprehensive of these is

the Global Antimicrobial Resistance Surveillance System (GLASS), created by the World Health Organization. [14]

Established in October 2015, GLASS provides a standardized approach for collecting, analyzing, and sharing global AMR and antimicrobial consumption data. As of 2020, 87 countries participate in GLASS, including Japan.[15] GLASS harmonizes AMR data across countries and supports national AMR surveillance by developing a National Coordination Centre (NCC), National Reference Laboratory (NRL), and sentential surveillance sites for collecting diagnostic results and epidemiological data . [14]

International surveillance on AMR has made major strides at the regional level. The European Centre for Diseases Prevention and Control created the European Antimicrobial Resistance Surveillance Network (EARS-NET), which, in turn, inspired the Central Asia and Eastern Europe Surveillance of Antimicrobial Resistance (CAESAR).[16] Concomitantly, the Latin American Network for Antimicrobial Resistance Surveillance (ReLAVRA) aggregates AMR surveillance information from 19 Latin American countries.[17] These regional collaborations disseminate know-how and support the development of national antimicrobial surveillance systems.

Although the World Health Association (WHO), Food and Agriculture Organization (FAO), and World Organization for Animal Health (OIE) have produced guidelines on the development of National Action Plans on AMR, the creation of such plans and the implementation of infection prevention and control (IPC) measures has been inconsistent across regions.[18] As of 2019, only 70 countries have created National Action Plans. [19] Also, budgets for AMR surveillance vary by country. For example, for the FY2020, the Center of Disease Control and Prevention (US) allocated US$170 million for AMR activities, including the surveillance of AMR organisms and the strengthening of state, local, and national capacities.[20] In comparison, many countries have AMR surveillance plans but no defined budget (Figure 1). [14]

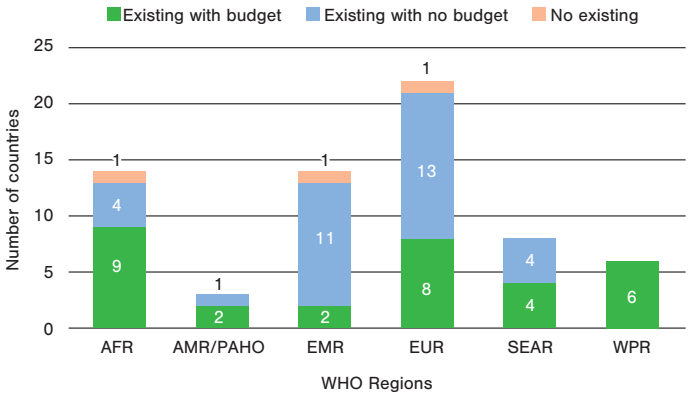


Figure 1. Existence of functioning national AMR surveillance plan per country by region 14

*AFR – WHO African Region; AMR/PAHO – WHO Americas/Pan American Health Organization Region; EMR – WHO Eastern Mediterranean Region; EUR – WHO Europe Region; SEAR – WHO South-East Asia Region; WPRO – WHO Western Pacific Region

Stakeholder and Countermeasures: Global

Stakeholder	Countermeasure
World Health Organization	• Global Antimicrobial Resistance Surveillance System (GLASS) - collects, analyzes, and shares global AMR and antimicrobial consumption data, and supports national surveillance capacities.[21] Currently, GLASS is creating estimates from data provided by 64,000 surveillance sites across 66 countries, covering more than 2 million patients. Furthermore, GLASS has released a protocol toward the establishment of a prospective cohort study. [22] • Global Infection Prevention and Control Network - support low- and middle-income countries and help develop local and national surveillance systems as an issue of human security. [23]
G20	• 2018 G20 Summit Argentina - health ministers from the G20 countries participated in a crisis simulation on cross-border antimicrobial resistant E. coli. Tested leaders' and countries' ability to rapidly respond to a pandemic, and revealed the pressures placed on health systems and economies. [24]
European Centre for Disease Prevention and control	• European Antimicrobial Resistance Surveillance Network (EARS-Net): EU's leading surveillance system for antimicrobial resistance infections that cause serious infections. [25]

Stakeholder	Countermeasure
Private sector initiatives	• AMR Industry Alliance – Davos Declaration to share surveillance data with public health bodies and healthcare professionals. [26] • HealthMap, and the Center for Disease, Dynamics, Economics, and Policy (US) - private-public partnerships to combine skills and resources to monitor national AMR patterns. [27] • Surveillance Partnership to Improve Data for Action on Antimicrobial Resistance (SPIDAAR): Pfizer Japan Inc. and the Wellcome Trust formed a private-public partnership with governments of Ghana, Kenya, Malawi and Uganda to track antimicrobial resistance patterns and investigate the effects of antimicrobial resistant bacteria on patients living in low- and middle-income countries. [28]
Public-academic partnerships	• The National Institute of Infectious Diseases, Teikyo University, Tottori University, Nagoya University, Brigham and Women's Hospital University, and WHO Collaborating Centers in Boston have been working together to automated detection of antimicrobial-resistant infections in Japan using the WHONET-SaTScan system. [13]

AMR Alliance Japan Recommendations

- The Government should recognize AMR as a global-scale threat to humanity and take responsibility for the creation of a sustainable and comprehensive surveillance system operated through public-private cooperation. The Government should invest appropriately in that system based on that recognition.
- In constructing such a system, the Government should take into consideration the following points.
  - The system should be able to capture detailed and real-time info on AMR and antimicrobial usage (including strain data and measurements of antimicrobial usage)
  - The system should make use of a format that makes the effective transfer and collection of data easy, based on the opinions of clinical facilities, and a consideration of the burden the system might place on them.
  - The system should link clinical information, strain data, antimicrobial usage and so on in order to make it possible to follow the case histories of patients that receive antimicrobials
- Data from facilities not currently implementing surveillance measures is of vital importance. A system should also be constructed to provide support to those facilities so that they can hire the personnel needed for surveillance work, which is of particular importance for the surveillance of outpatient facilities.

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