

Antimicrobial Resistance in the Western Pacific Region

A Review of Surveillance and Health Systems Response



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Abbreviations

AGISAR	Advisory Group on Integrated Surveillance of Antimicrobial Resistance
AMR	antimicrobial resistance
APEC	Asia-Pacific Economic Cooperation
ASEAN	Association of Southeast Asian Nations
AST	antibiotic susceptibility testing
ATC	Anatomical, Therapeutic and Chemical (classification system)
AVWG	WHO Expert Working Group on Influenza Viral Susceptibility
CLSI	Clinical and Laboratory Standards Institute
CSA	country situation analysis
DDD	defined daily dose
EaP	Eastern Partnership
EARS-Net	European Antimicrobial Resistance Surveillance Network
ECDC	European Centre for Disease Prevention and Control
EQAS	External quality assurance system
ESAC-Net	European Surveillance of Antimicrobial Consumption Network
EU	European Union
EUCAST	European Committee on Antimicrobial Susceptibility Testing
FAO	Food and Agriculture Organization of the United Nations
GASP	Gonococcal Antimicrobial Surveillance Programme
GFN	Global Foodborne Infections Network
GISRS	Global Influenza Surveillance and Response System
GMP	good manufacturing practices
GPP	good pharmacy practice
GPRIM	Global Plan for Insecticide Resistance Management in Malaria Vectors
GPSC	Global Patient Safety Challenge (of WHO)
HAI	health-care-associated infection
HCF	health-care facility
IPC	infection prevention and control
MDR	multidrug-resistant
MIC	minimum inhibitory concentration
MRSA	methicillin-resistant <i>Staphylococcus aureus</i>
NPS	National Prescribing Service
OECD	Organisation for Economic Co-operation and Development
OIE	World Organisation for Animal Health
OTC	over the counter
POLHN	Pacific Open Learning Health Net
PPTC	Pacific Paramedical Training Centre
REQAP	Regional External Quality Assurance Programme
RCPA	Royal College of Pathologists of Australasia
RCPAQAS	Royal College of Pathologists of Australasia Quality Assurance Programmes
ReLAVR	Latin American Network for Antimicrobial Resistance Surveillance
STGs	standard treatment guidelines
TB	tuberculosis
UK NEQAS	United Kingdom National External Quality Assessment Service
TWG	technical working group
VINARES	Viet Nam Resistance (project)
VRE	vancomycin-resistant enterococci
WePARS	Western Pacific Antimicrobial Resistance Surveillance (network)
WHO	World Health Organization
XDR	extensively drug-resistant

Introduction

Antimicrobial resistance (AMR) is a global public health threat of high concern in the Western Pacific Region. The 2014 World Health Assembly resolution WHA67.25 stresses the need for urgent action to combat AMR. In the Western Pacific Region, priority actions to contain AMR were identified by the World Health Organization (WHO) in consultation with Member States. These actions are outlined in the *Action Agenda for Antimicrobial Resistance in the Western Pacific Region* which was endorsed by the sixty-fifth session of the Regional Committee for the Western Pacific. The action agenda provides a background to AMR in the Region and highlights challenges in addressing this public health threat.

Antimicrobial Resistance in the Western Pacific Region: A review of Surveillance and Health Systems Response provides an in-depth situational review and technical discussion in three main areas for the containment of AMR in the Region:

- (1) Surveillance of AMR in the Western Pacific Region.
- (2) Monitoring of antimicrobial use in the Western Pacific Region.
- (3) Health systems response to support containment of AMR in the Western Pacific Region.

Part 1 describes the progress in the Region on surveillance of AMR and the gaps in laboratory capacity and methodologies. Part two highlights the need to monitor antimicrobial use through common methodologies and indicators, in addition to surveillance of AMR, to inform important policy changes to contain AMR. The health systems response to AMR also varies across the Region. Part three highlights the urgent need to strengthen regulation of pharmaceutical systems, antimicrobial stewardship and infection prevention and control (IPC) to contain AMR in the Region.

Surveillance of Antimicrobial Resistance

1. Surveillance of antimicrobial resistance

Surveillance of Antimicrobial resistance (AMR) is important to contain AMR at local, national, regional and global levels. The Western Pacific Region has a history of discussions, recommendations and actions related to AMR surveillance from 1982 onwards.

The WHO Regional Office for the Western Pacific was the first regional office to implement recommendations on the surveillance of AMR in 1982 at the WHO Consultation Group for Surveillance of Antimicrobial Resistance. (1) In 2011, the Regional Committee resolution WPR/RC62.R3/2011 on antimicrobial resistance again urged Member States to make AMR a priority, along with the WHO six-point policy package on AMR. (2)

The *WHO Global Strategy for Containment of Antimicrobial Resistance* identified two fundamental priorities in efforts to combat AMR: 1) national commitment to the containment of AMR as a public health priority; and 2) surveillance to generate the data required to support the development, implementation and evaluation of resistance-containment efforts, and antimicrobial prescribing guidelines at the local, national and regional levels.

AMR surveillance tracks evolving microbial populations, permits the early detection of resistant strains of public health importance, assists in the development of therapy guidelines, and supports the prompt notification, investigation and containment of new threats. Surveillance findings are needed to inform clinical therapy decisions and to guide policy recommendations and assess the impact of interventions.

A regional technical consultation on AMR surveillance in Manila in August 2013 brought together national and regional experts in AMR surveillance and laboratory quality assurance in both the human and animal sectors. Participants discussed the design and implementation of regional surveillance plans, and proposed objectives, scope, data management, quality assurance, data interpretation, dissemination and use of surveillance data to inform prescribing behaviours. Participants recognized the existence of strong, long-standing national and regional activities in AMR surveillance and external quality assurance (EQA) in many Member States of the Region, and viewed these as a valuable base on which to coordinate, integrate and build on.

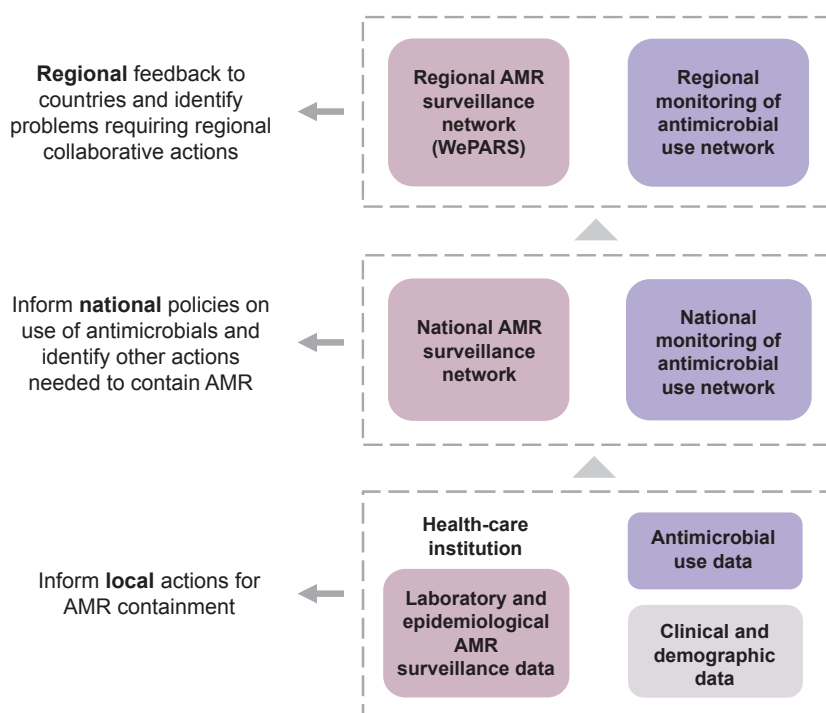
The group recommended the formation of a regional technical working group on AMR (TWG-AMR), which met in December 2013. The TWG-AMR refined the proposals within the context of a broader strategic and operational framework for advancing efforts to combat AMR and to initiate discussions with Member States and other partners for the establishment of a surveillance network for the Region.

The TWG-AMR recognizes the importance of local, national and regional actions, and has identified the following AMR surveillance priorities:

- enhance core laboratory testing capacities at local and national levels;
- strengthen subnational and national AMR surveillance networks;
- establish, in a stepwise and feasible manner, surveillance activities in WHO Member States that lack these;

- promote and support the use of standards and methods for collection of epidemiological and antibiotic susceptibility testing (AST) data and data sharing, in line with the efforts to coordinate and harmonize AMR surveillance at the global level;
- encourage the development of local and national data systems that allow for the linking of microbiology AMR surveillance data with clinical and pharmaceutical data, to support local decision-making for the prevention and control of AMR; and
- ultimately establish and coordinate a regional AMR surveillance initiative based on collaboration with existing programmes with the proposed name Western Pacific Regional Antimicrobial Resistance Surveillance (WePARS). This initiative would be linked to a similar network coordinating the monitoring of antimicrobial use.

Figure 1. The interface between AMR surveillance and antimicrobial use data along with clinical and demographic information to inform local, national and regional levels



Source: WHO

1.1 AMR SURVEILLANCE AND EXTERNAL QUALITY ASSURANCE

Through the long-standing efforts of national and regional bodies, there are a number of active, well-established national and regional initiatives for AMR surveillance in the Western Pacific Region.

Several of these initiatives are pathogen or disease specific, such as those for HIV/AIDS, tuberculosis (TB), malaria, gonorrhoea and foodborne infections. Surveillance is often integrated into vertical disease control programmes, and sample processing and laboratory testing are typically organized by national reference laboratories. The findings are critical for establishing and revising national treatment guidelines and control strategies.

Others programmes focus more broadly on common bacterial pathogens not associated with specific disease control programmes, such as those causing urinary tract infections, health-care-associated infections and sepsis. Laboratory testing is generally performed by community and hospital laboratories in primary, secondary and tertiary care centres.

Core components of any AMR surveillance activity are: 1) coordination across local, national and regional levels with defined allocation of resources for surveillance activities and defined protocols; 2) an epidemiological structure with the necessary expertise for designing surveillance methods; 3) a robust strategy to assure laboratory capacity to test for AMR at local and state levels, including promotion of standardized AMR susceptibility testing; and 4) a platform for timely dissemination of data to interested parties and local and national levels, including public health officials, health workers and researchers.

1.1.1 Examples of disease and pathogen specific surveillance programs

Antibacterial resistance

Tuberculosis – Mycobacterium tuberculosis

Since the launch of the Global Project on Anti-tuberculosis Drug Resistance Surveillance in 1994, data on drug resistance have been collected and analysed with the active engagement of WHO collaborating centres, supranational reference laboratories and other partners. Data collection was later integrated into WHO's annual TB surveillance web-based reporting system since 2010. Data from 136 countries have been analysed and published in the *Global Tuberculosis Report 2013*. (3)

Gonorrhoea – Neisseria gonorrhoeae

The Western Pacific Region has nearly 42 million cases of gonorrhoea per annum, which is roughly 40% of the global gonococcal disease burden. WHO's Gonococcal Antimicrobial Surveillance Programme (GASP) is a global network, based in Australia, with participation of 64 countries. GASP reports from the Western Pacific Region are published annually in the journal *Communicable Diseases Intelligence*. (4)

Leprosy – Mycobacterium leprae

Multidrug therapy has been successfully used to treat leprosy for three decades, and rifampicin remains the key component. Resistance to rifampicin can occur relatively easily if it is used as monotherapy. With the recent development of suitable molecular

methods, surveillance of resistance has been made feasible. A network of sentinel sites was established in 2007 to monitor levels of resistance, and meetings have been held annually to share data, technical developments and trends in new drug developments for leprosy control.

Foodborne infections – Salmonella, Campylobacter and Shigella spp.

Recognizing the morbidity and mortality associated with foodborne pathogens, the global movement of food animals and products, and growing concern about the human public health impact of antimicrobial use in food animals, WHO, the Danish Technical University, and other partners established the Global Foodborne Infections Network (GFN). (5) GFN is a capacity-building programme that promotes integrated, foodborne laboratory-based surveillance and intersectoral collaboration among human health, veterinary and food-related disciplines, in coordination with the WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (WHO AGISAR). (6) GFN is a part of WHO's efforts to strengthen Member State capacities in the surveillance and control of major foodborne diseases and to contribute to the global effort of containing AMR in foodborne pathogens.

Antiviral resistance

HIV

WHO has brought together organizations and experts working in the area of HIV drug resistance to form WHO HIVResNet, a global network advising WHO on the control and surveillance of HIV drug resistance. (7) WHO HIVResNet includes organizations that implement activities to control and monitor the emergence of HIV drug resistance in countries, individual experts working in this area, and a network of designated laboratories that perform quality-assured genotyping to support HIV drug-resistance surveys.

Influenza – influenza virus

Global influenza virological surveillance has been conducted through WHO's Global Influenza Surveillance and Response System (GISRS) for over half a century. It monitors the evolution of influenza viruses and provides recommendations in areas such as laboratory diagnostics, vaccines, antiviral susceptibility and risk assessment. The WHO expert working group on surveillance of influenza antiviral susceptibility (AVWG) was formed in 2011 to support GISRS, and includes representatives from WHO collaborating centres for reference and research on influenza, national influenza centres and public health institutes. The work of the AVWG provided the basis for the development of the WHO guidelines dedicated to antiviral susceptibility monitoring for influenza. (8)

Antiparasitic resistance

Malaria – Plasmodium spp.

Since 2000, WHO has maintained a global database that summarizes the findings from more than 4000 studies, with efficacy data that meet standard criteria and quality. (9) The WHO standard protocol for the assessment of therapeutic efficacy is the global "gold standard" to monitor drug efficacy and update drug policy. This has been adopted by all countries and most research institutes. It is designed for all drugs, including artemisinin-combination therapies. (9)

Helminthiasis – intestinal helminths and schistosomes

Anthelmintics are extremely effective in treating worm infections but do not normally kill 100% of the worms. A considerable increase in the number of individuals treated with preventive chemotherapy is expected in the next few years, with

increasing development of anthelmintic resistance, as recognized in the Report of the WHO Informal Consultation on Monitoring of Drug Efficacy in the Control of Schistosomiasis and Intestinal Helminths. (10) A working group established by WHO has developed a standard protocol for evaluating drug efficacy, updated in the 2013 WHO publication *Assessing the Efficacy of Anthelmintic Drugs Against Schistosomiasis and Soil-transmitted Helminthiasis*. (11)

Insecticide resistance

Insecticide resistance, particularly resistance to pyrethroids, threatens to undermine the progress made in malaria control in the past decade. In response to this threat, WHO's Global Malaria Programme launched its *Global Plan for Insecticide Resistance Management in Malaria Vectors* (GPIRM) in May 2012. (12) WHO has also launched revised testing guidelines for insecticide resistance. (13) Countries have been encouraged to strengthen entomological capacities at the national and subnational levels. The Asia-Pacific Network for Vector Resistance has been established for this purpose.

1.1.2 Regional programs for surveillance of resistance in common bacterial pathogens

There are a number of WHO-coordinated and WHO-affiliated regional and global collaborations for pathogen-/disease-specific surveillance, as described above. However, there is at present no such WHO programme in the Western Pacific Region for monitoring resistance in bacterial pathogens that cause common community- and health-care-associated infections, such as urinary tract infections, respiratory infections and sepsis. Though there is no regional WHO programme at present, many countries in the Region had established national AMR surveillance networks over 25 years ago, with many more initiating activities since then. (14) A short summary of surveillance networks in the Region is provided in Table 1.

Further details about their organization, history and accomplishments will be available in the draft *AMR Surveillance Networks in the Western Pacific Region* (draft document, 2014). In addition to these networks, most Member States are active in collecting resistance data, either through ongoing institution-level surveillance or ad hoc targeted surveys on priority issues, notably in the less populous Member States of the Region.

Core elements of WHO's strategy for the regional AMR surveillance programme must include strengthening national programmes, integrating these activities into a regional collaboration, and linking AMR surveillance findings to action through coordination with policy-makers and national authorities for a local, national and regional response.

Table 1. National and regional networks for AMR surveillance in the Western Pacific Region

Country or areas	Programme name	Contact organization
Asia Region	Asian Network for Surveillance of Resistant Pathogens (ANSORP)	Samsung Medical Center
Australia	Australian Group on Antimicrobial Resistance (AGAR)	Australian Group on Antimicrobial Resistance, Royal Perth Hospital
Cambodia*	NAMRU-2	U.S. Naval Medical Research Unit-2
China	Ministry of Health National Antimicrobial Resistant Investigation Net (MOHNARIN)	Ministry of Health, Zhejiang University
China	CHINET	Hua Shan Hospital, Shanghai Medical University, Institute of Antibiotics
China, Hong Kong (SAR)	Hong Kong Antibiotic Stewardship Program (ASP)	Hong Kong Hospital Authority, Centre for Health Protection
Federated States of Micronesia*	Federated States of Micronesia Surveillance Network	FSM Department of Health and Social Affairs
Japan	Japan Nosocomial Infections Surveillance (JANIS)	National Institute of Infectious Diseases
Malaysia	National Surveillance of Antimicrobial Resistance Programme (NSAR)	Institute for Medical Research
Mongolia	National Laboratory Network	National Center for Communicable Diseases, Health Sciences University of Mongolia
New Zealand	ESR Antibiotic Reference Laboratory	Institute of Environmental Science and Research Ltd (ESR)
Philippines	Antimicrobial Resistance Surveillance Program (ARSP)	Research Institute for Tropical Medicine
Republic of Korea	Korea Antimicrobial Resistance Surveillance Program (KARMS)	Korea National Institute of Health, Center for Infectious Diseases
Republic of Korea	Korean Nationwide Surveillance of Antimicrobial Resistance (KONSAR)	Yonsei University College of Medicine
Republic of Korea	Korean Network for Studies on Infectious Diseases (KONSID)	Samsung Medical Center
Singapore	The Network for Antimicrobial Resistance Surveillance (NARS-Singapore)	Tan Tock Seng Hospital
Viet Nam	Viet Nam Resistance Project (VINARES)	National Hospital for Tropical Diseases

Source: Information adapted from Shaban RZ, Cruickshank M, Christiansen K and the Antimicrobial Resistance Standing Committee. National surveillance and reporting of antimicrobial resistance and antibiotic usage for human health in Australia. Canberra: Antimicrobial Resistance Standing Committee, Australian Health Protection Principal Committee; 2013.

*Additional surveillance networks identified from unpublished WHO Regional Office for the Western Pacific AMR surveillance networks survey conducted in July 2014.

1.1.3 Regional external quality assurance

A survey of regional (non-national) programmes that provide EQA was conducted in 2014. The survey showed that institutions in most Member States participate in one or more programmes. Programmes that had a general bacteriology component included the following (numbers in parentheses indicate the number of Western Pacific countries and areas included in the programme):

- College of American Pathologists, United States of America (not available);
- Hong Kong Institute of Medical Laboratory Sciences, Hong Kong SAR (China); (2);
- Pacific Paramedical Training Centre (PPTC) Regional External Quality Assurance Programme (REQAP), New Zealand (16, notably Pacific islands);
- Royal College of Pathologists of Australasia (RCPA) Quality Assurance Programmes (RCPAQAS), Australia; (11); and
- United Kingdom National External Quality Assurance Scheme (UK NEQAS), United Kingdom of Great Britain and Northern Ireland (6).

The following targeted pathogen- and disease-specific EQA programmes were also identified:

- Gonococcal Antimicrobial Susceptibility Programme (GASP) (15);
- Global Foodborne Infections Network (GFN EQAS) (15);
- HIVResNet (3);
- National Reference Laboratory, Australia (17); and
- Tuberculosis (29).

A number of the above programmes are coordinated by WHO or by designated WHO collaborating centres. Most of the others are commercial ventures, but several have had previous formal collaborations with WHO and most express a strong willingness to collaborate with WHO in promoting EQA in the Region.

A similar survey for national EQA programmes in the Western Pacific Region was conducted in July 2014 to identify the major challenges in quality assurance and laboratory capacity to test for AMR within countries of the Region.

1.2 PROPOSED REGIONAL AMR SURVEILLANCE SYSTEM

National AMR surveillance systems can provide data to be incorporated into a regional database that will generate information to support action to combat AMR, in particular, antibiotic resistance at national and regional levels. The surveillance system will also aim to give AMR its due recognition and attention in Member States as a public health threat that needs to be tackled effectively at the national, regional and global levels.

The proposed name of the regional AMR surveillance system that will eventually coordinate and disseminate national AMR data at a regional level is the Western Pacific Antimicrobial Resistance Surveillance (WePARS).

1.2.1 Goal

The overall goal is to strengthen national network and establish a regional AMR surveillance data-sharing system to provide information for combating AMR in the Region.

1.2.2 Objectives

The objectives are:

- (1) to generate AMR data to permit ongoing tracking of microbial populations at the local, national and regional levels;
- (2) to support the development and evaluation of containment strategies and ultimately to reduce mortality, morbidity and costs of AMR in the Region, in partnership with policy-makers and other stakeholders;
- (3) to enhance early detection mechanisms so that timely alerts are provided for the control of emerging threats, including outbreaks;
- (4) to strengthen laboratory and epidemiological capacity for generating, interpreting and using AMR surveillance to guide and regularly update prescribing guidelines, infection control interventions and public health policy; and
- (5) to contribute national AMR data to a regional and a global AMR surveillance system.

1.2.3 Scope

The focus of this new initiative is the surveillance of AMR in bacteria in the human health sector, not covered by existing pathogen- and disease-specific programmes. AMR surveillance in the food and animal husbandry sector will also be included. AMR surveillance in the Region will generate and collate information to monitor AMR trends, track changes in microbial populations, provide early detection of resistant strains that are of public health importance, promptly notify and control outbreaks due to antimicrobial-resistant microorganisms, and inform local and national containment strategies and prescribing guidelines.

Findings from this surveillance effort, along with those of the disease- and pathogen-specific programmes as well as parallel programmes for monitoring antimicrobial use and health-care-associated infections will be integrated by local, national and regional advisory groups and decision-makers to support integrated resistance-containment strategies.

1.2.4 Critical elements

The following elements, elaborated in subsequent chapters, will be critical to the success of WePARS:

- networked model for regional AMR surveillance
- national AMR surveillance strategies – potential models
- information management and reporting
- quality assurance strategy
- network governance and data ownership
- surveillance to support containment of AMR.

1.2.5 Resource mobilization

The proposed WePARS surveillance system will rely on the mobilization of human and material resources for success and sustainability.

The core of the WePARS data collection strategy and recommendation to national AMR surveillance will be collection of core epidemiological (patient) information and routine microbiological findings from clinical samples collected and processed daily

throughout the Region. With the exception of targeted survey protocols, funds will generally not be needed to support sample collection and testing. However, resources and tools will be critical for:

- assuring the quality of test performance by clinical laboratories through internal and external quality assurance, reagents of sufficient quality, site visits and educational opportunities;
- information management, data analysis and interpretation;
- report preparation, interpretation and dissemination;
- network organization, including meetings with participating institutions; and
- coordinated action with local, national and regional stakeholders.

Participating surveillance sites and network coordinating institutions typically cover these costs. In several initiatives, ministries of health, WHO, nongovernmental organizations, clinical societies, research agencies and industry partners have provided additional support.

Most networks must focus on fundraising to maintain core elements of the surveillance programme (data generation, collection, analysis, report generation and quality assurance). This can be a significant challenge. Unfortunately, the potential impact of surveillance is often limited by insufficient resources to translate information into action, including advocacy, education, and regulation and policy development. To maximize the value of resources and identify priorities, an initial needs assessment should be conducted.

1.2.6 Networked model for regional AMR surveillance

WePARS will be a network of national and subnational networks, building on the activities and accomplishments of Western Pacific Region Member States. The core of these efforts is the collection, processing and testing of patient samples submitted to microbiology laboratories (along with core clinical/epidemiological information) throughout the Region, coupled with their interpretation, sharing and translation into action at the local, national and regional levels.

Critical elements of this networked model include:

- surveillance sites
- surveillance network coordination
- reference laboratories
- integration in the Western Pacific Region
- collaborators and stakeholders.

Surveillance sites

An AMR surveillance system is based on data generated by surveillance sites, including the microbiology laboratory, complemented by core patient demographic, epidemiological and clinical information.

Surveillance network coordinators should strive for wide geographical and demographic representation. To investigate the public health impact of AMR in bacteria from animal origin on human populations, coordinators should also consider the inclusion of food, animal and environmental surveillance sites.

To ensure data quality, participating laboratories must follow standardized protocols and participate in EQA programmes. Additional criteria for selection include laboratory and epidemiology capability and, most importantly, the enthusiasm of personnel to participate in the national programme. There is also a need to strengthen capacity for epidemiological analyses and AMR testing in Member States where it is lacking or irregular.

It is important to identify human resources to conduct surveillance activities and provide education for all participants in the surveillance system, including laboratories, epidemiologists and clinicians who handle and analyse patient data.

Coordination of regional surveillance network

The role of network coordinators is critical in establishing and sustaining the surveillance initiative. In partnership with network members and other stakeholders, coordinators establish the scope, priorities and activities of the programme, set standards and protocols for participation, ensure sufficient human and financial resources to accomplish the work, and work with external partners in tying surveillance findings to policy and action.

Responsibility for the collection, management, analysis and interpretation of data submitted by participating sites resides primarily with the network coordinators; thus, the coordinating team should include people with expertise in microbiology, infectious diseases, epidemiology and information management.

AMR surveillance coordinators should collaborate regularly with national multisectoral groups responsible for establishing and assessing strategies and interventions for containment of resistance. AMR surveillance activities should incorporate experts in antimicrobial use, veterinary sciences and media communications, among others, for a comprehensive approach to containing AMR.

1.2.7 Role of reference laboratories in regional surveillance network

In a surveillance network, the functions of reference laboratories include: confirmation of unlikely or important resistance phenotypes; molecular characterization of resistant strains; and maintenance of an isolate strain bank. Reference laboratories often coordinate EQA schemes, training activities and laboratory site visits. Ideally, the reference laboratory ideally should be in the same country as the surveillance network. If this is not feasible, collaboration with external partners will be needed.

Staff should have a high degree of expertise in microbiological testing, data management and epidemiological methods, and maintain up-to-date knowledge of emerging resistance problems and diagnostic issues.

1.2.8 Regional consolidation of AMR surveillance data

The WHO Regional Office for the Western Pacific can play a key role in consolidating surveillance findings from national surveillance programmes into a regional picture of emerging trends; mentoring and strengthening national programmes; providing EQA for the AMR network; and providing tools, ensuring standardized methods, protocols and guidelines to Member States.

The Regional Office should establish a centralized database for the Region, preferably online, to receive structured data from participating sites, and provide tools and education for the generation of such data. The centralized data-processing location should be resourced to undertake analysis, interpretation and reporting. The system should have the ability to link with data from other systems, such as the WHO global surveillance system being developed and those monitoring antimicrobial use and AMR in animal and food sources.

The Regional Office is the key advocate for advancing resistance-containment initiatives in partnership with ministries of health, nongovernmental organizations and professional societies. Collaboration among partners will ultimately support the development of guidelines and interventions at local, national and regional levels.

Collaborators and stakeholders

The *WHO Global Strategy for Containment of Antimicrobial Resistance* recommends establishment of intersectoral task forces with broad membership for coordinating surveillance activities and overseeing policy interventions and advocacy efforts. These task forces should comprise representatives from authorities responsible for national policy, drug regulation and procurement; health financing groups; clinical professional societies; veterinary and food-production services; pharmaceutical and diagnostic industry; patient advocacy groups and the public media. At the regional level, the World Organisation for Animal Health (OIE), Food and Agriculture Organization of the United Nations (FAO), Association of Southeast Asian Nations (ASEAN) and Asia-Pacific Economic Cooperation (APEC) should be involved.

1.2.9 National AMR surveillance strategies – potential models

Resistant microorganisms present a diverse set of clinical, technical and epidemiological challenges. Consequently, a single surveillance initiative will generally not have the expertise, time and resources to address all the desired therapeutic, disease control, policy and research issues. Thus, in establishing a plan for AMR surveillance, surveillance coordinators should identify critical information needs, understand the richness and limitations of AMR surveillance data resources, and prioritize gaps where additional activities are required.

A rational approach to national AMR surveillance should:

1. maximize the use of information generated in the course of routine diagnostic sampling and testing with an understanding of both the value and limitations of this data source; and
2. integrate complementary additional protocols where routine data are insufficient in quantity, quality or microbiological or epidemiological detail.

The following sections discuss options for national AMR surveillance plans dependent primarily on countries' resource setting (low, middle, high) and laboratory capacity to test for AMR.

Alert organism surveillance

In the course of routine diagnostic work, laboratory staff occasionally come across strains with unlikely, unexpected or important findings of public health significance. Phenotypes may be identified as “unusual” on the basis of their rarity worldwide – vancomycin-resistant *Staphylococcus aureus*, fluoroquinolone-resistant *Salmonella typhi*, or on the basis of the local or national experience – vancomycin-resistant *Enterococcus*, cefotaxime-resistant *Escherichia coli*.

As the noteworthy finding may be due to a laboratory error, laboratories should have mechanisms for the prompt recognition, local confirmation and, if appropriate, national or international confirmation, notification and investigation. The success of an alert organism surveillance system depends on the attention of informed microbiologists performing ongoing review for important or unlikely results, and procedures for confirmation at the national level. Many countries maintain a list of such “reportable”/“alert” organisms for which national confirmation is required.

While the intent of alert organism surveillance is prompt recognition and response to infections of public health importance, an important ancillary benefit is improved laboratory capacity through the recognition, investigation and resolution of deficiencies in laboratory performance and/or test reagent quality.

Routine surveillance

Clinical specimens collected from patients are sent to laboratories and processed by microbiology laboratories worldwide. By capturing, organizing and analysing the clinical information and sample results, investigators can identify new threats, recognize and track strain subpopulations, identify outbreaks, monitor resistance trends and investigate multidrug resistance for the evaluation of therapeutic alternatives.

All of this is possible and paid for through routine practices for clinical sampling and processing. Through investments in information capture, sharing, management, analysis and interpretation, and the accumulated data generated by clinicians and microbiology laboratories, it is possible to observe and respond to changing microbial threats.

This approach has a number of advantages – low cost with excellent long-term sustainability and based on clinical populations. A broad range of patient-, syndrome- and organism-resistance issues can be investigated both prospectively and retrospectively, encompassing wide geographical and demographic coverage. In most countries, this type of monitoring is comprehensive, and includes results from all routinely available microbial species, specimen types and antimicrobials tested, though it is also possible to choose a subset of priority species and sample types.

With advances in information technology, alert notifications are possible in real time as laboratory technologists enter or download results into surveillance information systems: immediate notification of “alert” organisms is possible, with notification of relevant authorities, and recognition of statistical clusters of strain subpopulations suggestive of community or health-care outbreaks.

An ancillary benefit of core routine surveillance is improved laboratory capacity. While internal and external quality assurance strategies focus on a laboratory’s ability to perform good-quality testing, systematic reviews of isolate-based test results provide a much more thorough insight into the laboratory’s routine practices.

On the other hand, routine surveillance usually depends on the clinical samples sent to laboratories for diagnosis and AST. This means that the majority of samples come from patients with severe infections (particularly health-care-associated infections and those for which first-line treatment failed), so that community-acquired infections are underrepresented. This imbalance is likely to result in higher reported resistance rates than would be found for the same bacteria in community or population-based samples, as was shown in some reports with data submitted separately for these patient groups. Non-representativeness and biased sampling are major pitfalls in the interpretation and comparison of results. Treatment guided by limited and biased information may risk driving empirical therapy unnecessarily towards more broad-spectrum antibacterial medicines. This will increase the economic impact of AMR and accelerate the emergence of resistance resulting in the use of last-resort antimicrobials. To address these limitations, investment should be made to improve the design of the surveillance so that microbiological data can be linked to clinical and epidemiological data.

Targeted surveillance and surveys

As mentioned above, routine surveillance may not generate sufficient information on the scope and extent of the AMR problem to guide prevention and containment

policies, advocacy or research needs. Problems may lie in the volume of or epidemiological biases in routine samples, or lack of sufficient patient and clinical details to assess the effectiveness of interventions, risk factors, the clinical and economic impact of resistance, or insufficient microbiological detail to guide vaccine selection, or characterize the clonality of suspected outbreak-related strains.

In targeted surveillance (ongoing) or survey (one-time or periodic) initiatives, programme coordinators have the flexibility to develop protocols that target specific objectives and improve data collection in specimen collection, patient clinical and epidemiological details, and microbiological testing. A well-designed targeted surveillance programme provides an opportunity to elicit specific responses to priority questions of clinical, epidemiological or scientific importance – establish standard treatment guidelines (STGs); evaluate risk factors for resistance, transmission and control strategies, morbidity and mortality; and conduct molecular characterization of clonal populations.

Linkage of AMR surveillance to disease surveillance in targeted surveys is valuable and may permit incidence measurements and evaluation of the impact of control interventions in disease-specific control programmes. Examples of disease surveillance include TB and malaria. Periodic short-term studies for selected populations and diseases can be a viable option if capacity is in place, permitting estimates of disease burden and improving the epidemiological relevance of AMR surveillance activities. Targeted surveillance and survey protocols have some important limitations: 1) they are generally resource and labour intensive; and 2) they typically address priority organisms or issues of clinical or public health importance in relatively small numbers of patients and isolates. The narrow focus of special protocols limits their utility for identifying new threats and tracking strain populations.

1.2.10 Collection, analysis and reporting of AMR surveillance data

AMR surveillance requires a robust practical strategy for timely management of data submitted by participating sites. Steps to be considered are data collection, analysis and interpretation, as well as reporting. Fortunately, due to ongoing advances in information technology as well as improving expertise in informatics within health-care facilities (HCFs), much more is possible today than ever before to support comprehensive real-time approaches to data capture, analysis, alerts and actions at the local, national and regional levels.

Member States have the responsibility to monitor AMR surveillance at the national level and share the data at the regional level for a collective response to containing AMR. For AMR surveillance networks to participate in the WePARS network, participants must also agree on issues of data ownership, confidentiality and use.

Isolate-level data collection

Patient and isolate-level data provide the richest insights into the evolving epidemiology of microbial and resistance threats. Core patient information to guide laboratory testing and interpretation of results should accompany the patient sample to the laboratory and be entered in the same dataset as the AST result. For AST results, ideally quantitative susceptibility test results, such as disk diffusion zone diameters or minimum inhibitory concentration (MIC) values, should be entered.

Laboratories at the local, national and regional levels in over 110 countries used WHONET for this purpose. (15) WHONET is available for free download from the WHO website (<http://www.who.int/drugresistance/whonetsoftware/>). Results may be entered manually or converted from laboratory information systems, instruments

or desktop software with BacLink (part of the WHONET package) for the purposes of data analysis and sharing.

An alternate approach, in settings facing administrative or technical barriers, is to focus on specific clinical entities/syndromes (e.g. sepsis), organisms (e.g. *Staphylococcus aureus* and *Escherichia coli*) and specimen types (e.g. blood).

Regardless of the approach, duplicate findings from the same patient during the same disease episode should be eliminated.

Aggregate data collection

An alternate approach to collecting routine findings is for network coordinators to request specific, predefined aggregate statistics and metrics; for example, the proportion of outpatient blood samples positive for *Escherichia coli* resistant to imipenem or meropenem, or from urinary isolates resistant to co-trimoxazole or fluoroquinolones. One may target specific antimicrobial–microorganism combinations or alternatively collect statistics on all clinically relevant antimicrobials to permit a comparison of therapy alternatives and track their relative trends over time. Data may be aggregated at the level of facilities, provinces, hospital type or nationally. Further guidance is presently being prepared by working groups coordinated by WHO headquarters.

Collection of aggregate statistics is simple from a data-sharing perspective, but there is little ability to evaluate data quality or investigate issues in more depth than that provided by the patient data and resistance proportions collected. This approach is generally not recommended unless barriers prevent the more comprehensive isolate-based approach.

1.2.11 Surveillance network feedback to data contributors

Noteworthy microbiology test-result findings during the first year or two of operation can often be explained by laboratory testing errors, interpretations or epidemiological biases. Surveillance collaborations should thus be viewed in the context of a process of continuous quality improvement. Directed laboratory feedback is an opportunity to address the problems identified and educate microbiology staff, thereby improving the quality of surveillance findings, and the ability of laboratories to provide reliable diagnostic support to health-care providers.

Absent or too limited patient data also compromises adequate analysis, and thus should be fed back to clinicians to improve sampling routines and information.

Network coordinators must provide appropriate, timely feedback and guidance to participating facilities, for example, in the form of individual letters to laboratory and hospital directors detailing some of the questionable or unlikely results in the submitted dataset. In addition to commentary on the quality of susceptibility test results performed, feedback should also address other aspects of laboratory practices, such as the appropriateness of the antimicrobials selected for testing, selective testing practices that may influence resistance estimates, and clinical relevance of reports sent to clinicians. The Western Pacific Region should also provide this type of feedback to network coordinators submitting data to the regional network if unlikely or unusual results are submitted.

1.3 QUALITY ASSURANCE STRATEGIES FOR AMR SURVEILLANCE

An essential requirement of any laboratory providing microbiological services for patient decision support, public health investigation, research and/or regulatory purposes is a robust strategy for ensuring the adequacy of test practices and reagents, and the reliability of test results. In AMR surveillance activities, a comprehensive strategy for ensuring quality should address the clinical quality and epidemiological relevance of samples collected (thus also including patient information provided), the reliability of laboratory findings, and the quality of expertise in result analysis, interpretation and communication.

The reliability of laboratory test practices, strategies and procedures for ensuring quality are generally well defined through standard operating procedures. For antimicrobial susceptibility test results, there are reference bodies such as the Clinical and Laboratory Standards Institute (CLSI) and the European Committee on Antimicrobial Susceptibility Testing (EUCAST). Recommendations for quality control assurance for antimicrobial susceptibility test results are described below.

Biases in sample collection are more difficult to address from a strict laboratory perspective but can be better addressed if patients or populations are defined and this information is included in the dataset. Potential biases in the data must be considered when interpreting and applying findings on resistance. If resources are available for the collection of clinical samples beyond those taken for routine care (and looking beyond the subset of patients that typically presents to medical care), then targeted surveys can ascertain and quantify potential data biases.

A number of tools have been developed for the assessment of laboratories. WHO has produced a tool that has components for assessing individual laboratories and for national laboratory systems (http://www.who.int/ihr/publications/laboratory_tool/en/). These tools are generic and are designed to be adapted to the needs of each user. A questionnaire has also been developed to monitor networks for AMR surveillance (<http://www.who.int/drugresistance/whocdscsrrmd20031.pdf?ua=1>).

1.3.1 Internal quality control

Laboratories require procedures for assuring the quality of test reagents and the adequacy of test performance. The first line of assessment for antimicrobial susceptibility test results is the use of standard quality control strains. The two most commonly used standardized methods for susceptibility testing are published and updated annually by the CLSI and EUCAST. In the Western Pacific Region, CLSI is more commonly used. Results obtained from users of either of these methods are becoming more comparable for most (but not all) of the common pathogens, particularly if the non-susceptible portion is reported. While the CLSI guidelines are available for purchase, EUCAST guidelines are downloadable for free.

Both the CLSI and EUCAST guidelines detail standards for quality control testing and performance. In high-resource settings, many laboratories test over 10 distinct quality control strains daily to ensure compliance with official recommendations. In lower-resource settings, a number of national networks recommend weekly testing of the strains below as a minimal level of testing:

ATCC 25922	<i>Escherichia coli</i>
ATCC 27853	<i>Pseudomonas aeruginosa</i>
ATCC 25923	<i>Staphylococcus aureus</i> (for disk diffusion testing)
ATCC 29213	<i>Staphylococcus aureus</i> (for MIC testing)
ATCC 49619	<i>Streptococcus pneumoniae</i> .

While routine testing of quality control strains is important in assuring a laboratory's capability for quality testing, a complementary strategy that explores the laboratory's routine performance is needed. This includes frequent and systematic reviews of accumulated results for findings suggestive of poor-quality reagents or deficiencies in test performance; for example, the frequent identification of unlikely resistance phenotypes or deformations in zone diameter or MIC distributions, which are suggestive of errors in inoculum or result reading and/or recording.

1.3.2 External quality assurance

Participation in EQA schemes for the identification of organisms, susceptibility testing and test interpretation has proven value in identifying and correcting errors in test performance, evaluating laboratory proficiency to participate in network collaborations, and updating microbiologists on emerging issues of resistance and diagnostic techniques.

National programmes for EQA exist in most of the larger Member States of the Region. They cover a number of clinical laboratory areas, such as microbiology (including organism identification and AST), blood bank and chemistry. A systematic overview of these national programmes does not yet exist, but a survey was conducted in July 2014 and the analysis is currently being undertaken.

There are several well-established, active regional programmes for EQA in general bacteriology. The three most active ones are RCPAQAS, PPTC REQAP, and UK NEQAS, and all have expressed their willingness to discuss possible collaboration with WHO in initiating an EQA programme on AMR for the Region.

Excellent performance in an EQA programme does not necessarily reflect the quality of laboratory testing on a daily basis for typical clinical specimens. To address this discrepancy between capability and reality, careful review by surveillance network coordinators of submitted data files is recommended to identify previously unrecognized issues in susceptibility testing and/or organism identification.

1.3.3 Reference laboratory confirmation and characterization

For strains with important or unusual phenotypes identified by participating laboratories, there should be mechanisms for confirming the results at a central level. This process can conveniently be integrated into an alert organism surveillance programme. If the results of the sending laboratory are incorrect, then directed feedback with appropriate guidance should be returned to the laboratory. Central confirmation of the results permits more definitive statements about the existence of certain resistance phenotypes in the country. Reference laboratories could also provide support for capacity development in terms of training and technical support.

1.3.4 Capacity development for clinical microbiology

While the above recommendations focus on specific technical priorities in laboratory testing relevant for AMR surveillance, a broader view of laboratory and clinical capacity-building is also required. These include strategies to improve “diagnostic stewardship”, i.e. drawing a sample for analysis in patient categories, depending on the needs and the local resistance situation, implementing laboratory quality management systems to address the proper utilization of laboratory services by clinical staff, continuous efforts to strengthen human and material resources, procedures for ensuring the safety of laboratory staff, and proper disposal of biosafety hazards.

1.4 GOVERNANCE AND OWNERSHIP OF AMR SURVEILLANCE DATA

1.4.1 Network structure and coordination

For successful long-term collaboration within WePARS, national network coordinators and participants should establish terms of collaboration and criteria for participation; responsibilities and expectations of network members; policies covering data ownership, security, access and use; and strategies for collaboration with external stakeholders.

Membership in WePARS shall include subnational, national and regional AMR surveillance networks designated by the respective ministries of health of Member States in the Western Pacific Region. The WHO Regional Office will assess the readiness of each such network to join, considering past activities and accomplishments, organizational and technical capacity, surveillance strategy, and willingness and ability to share agreed data with the regional collaboration. Member States have a national responsibility to monitor and share AMR surveillance data with other Member States of the Region and the Regional Office for collective action to contain AMR in the Western Pacific Region.

While each WePARS candidate network will establish its own internal criteria for institutional participation and quality standards, the Regional Office will review these standards and, where appropriate, recommend actions to strengthen these prior to network enrolment in WePARS.

A TWG-AMR was established in December 2013 to provide guidance for the development of AMR containment strategies in the Region that are outlined in this document.

1.4.2 Data ownership

Member States and networks that contribute data are considered to be the owners of the WePARS data, and ultimately must direct the policies and priorities for data management, analysis and use. The Regional Office is a data handler recognized by Member States as the appropriate body to collect, interpret and disseminate surveillance findings to inform policy-makers at the local, national and regional levels in accordance with guidelines and protocols established by WePARS members.

1.5 SURVEILLANCE TO SUPPORT CONTAINMENT OF AMR

The *WHO Global Strategy for Containment of Antimicrobial Resistance* identified as a fundamental priority the establishment of a national multisectoral task force, appropriately funded and empowered, to formulate, implement and evaluate national plans for the containment of AMR. While surveillance is required to recognize emerging threats of AMR, findings must be translated into action within the context of collaborative local, national and regional strategies for containment of resistance.

Information generated through both surveillance of AMR and antimicrobial use should be made widely available to local, national and regional decision-makers. The data will be used for policy development on antimicrobial use at all levels; early recognition of and resistance to new threats, including multidrug-resistant (MDR) microbes; improved diagnostic testing for patient care and outbreak preparedness; benchmarking of institutional and national experiences on AMR; and assessing the impact of disease control and resistance-containment interventions.

This requires effective and sustained collaboration among national authorities; clinicians, pharmacists, epidemiologists, microbiologists, and their professional societies; researchers; pharmaceutical and diagnostic industry leaders; veterinarians and food production experts; patient advocacy groups; and representatives of public media. The format in which the surveillance findings and recommendations are presented must reflect the information needs and scope of responsibility of recipients. These include, for example, network annual reports, newsletters, policy papers, scientific publications and presentations, websites, patient brochures, articles in local newspapers, and interviews with local television and radio representatives.

Given the extensive use of antimicrobials in agriculture and aquiculture, especially as growth promoters in food production, it is important to address the drivers of resistance in the animal health sector as well. Linkage of antimicrobial use and AMR surveillance programmes with ministries of agriculture and aquiculture, food producers, veterinarians, OIE and FAO should thus be viewed as crucial for a comprehensive action plan to address containment of resistance.

Monitoring of antimicrobial use

2. Monitoring of antimicrobial use

Monitoring of antimicrobial use tracks how frequently and in what volumes antimicrobials are used. It also tracks how patients and health-care providers use antimicrobials. The goal of tracking antimicrobial use is to provide information to guide policy and effective decision-making on the appropriate use of antimicrobials in order to contain the increasing burden of resistant microorganisms. Decisions regarding antimicrobial use should support the provision of effective antimicrobial therapy to patients and the preserved usefulness of antimicrobials for future generations.

The overuse, misuse and abuse of antimicrobials have contributed to the alarming spread of AMR worldwide. In the Western Pacific Region, there is a glaring absence of research on the status of antimicrobial use and consumption, and lack of regional monitoring of antimicrobial use as well as the volumes consumed by humans and animals.

Antimicrobial use should be monitored at the local, national, regional and global levels. Data collected regularly on antimicrobial use at the local level can be used to communicate patterns to prescribers who can then accurately prescribe antimicrobials to patients. At national and regional levels, data can be aggregated to show trends in resistance and correlations to antimicrobial consumption. At the global level, monitoring can determine the source and contain the spread of emerging resistant microorganisms.

In the Western Pacific Region, the burden of diseases that are untreatable with antimicrobials will continue to increase if no measures are taken to diminish AMR, resulting in a rising prevalence of resistant pathogens. The ability of antimicrobials to effectively combat infections will be drastically reduced, which would have a detrimental impact on the management of infectious diseases. In addition, the irrational and frequent overconsumption of antimicrobials increases the risk of drug toxicity, antimicrobial-related adverse effects and increased health-care costs.

The combined monitoring of antimicrobial use and the surveillance of resistant microorganisms are essential to provide a better understanding of the relationship between consumption and use, and can support important policy changes to contain AMR. Very few countries in the Region have developed systems to monitor antimicrobial consumption or use. Unlike surveillance of AMR, which is done for at least some pathogens in most countries, very few countries in the Region have comprehensive reports on antimicrobial use.

There are various reasons why the measurement and evaluation of antimicrobial consumption remains a challenge for many countries of the Region. These include:

- lack of national policies that require regular monitoring of antimicrobial use and consumption;
- lack of an integrated national surveillance system for AMR; and
- lack of the necessary capacity and resources to systematically collect data on antimicrobial consumption and use at the national level in both the public and private sectors.

The lack of information on antimicrobial consumption has hindered actions to reduce antimicrobial use and AMR prevalence. Evaluation of antimicrobial use in Member

States is necessary to establish a baseline and monitor progress towards rational antimicrobial use. The information generated can then be used to encourage policy-makers to take action.

2.1 WHO RECOMMENDATIONS FOR MONITORING ANTIMICROBIAL USE

There have been several World Health Assembly resolutions and publications by the WHO urging Member States to take action on AMR. In 1998, AMR was identified as part of the resolution on emerging and other noncommunicable diseases (World Health Assembly resolution WHA51.17/1998). (16) The resolution explicitly identified the need to monitor volumes and patterns of antimicrobial use.

In 2001, the *WHO Global Strategy for Containment of Antibiotic Resistance* identified eight areas of work and made 68 specific recommendations regarding international aspects, and emphasized monitoring antibiotic use to contain antibiotic resistance. Recommendations included (17):

- Consider the information derived from the surveillance of antibiotic use and antibiotic resistance, including the containment thereof, as global public goods for health to which all governments should contribute.
- Encourage governments, nongovernmental organizations, professional societies and international agencies to support the establishment of networks, with trained staff and adequate infrastructures, which can undertake epidemiologically valid surveillance of antibiotic resistance and antibiotic use to provide information for the optimal containment of resistance.

In 2011, AMR was the theme of World Health Day and a six-point policy package was released. (2) The second point emphasizes strengthening monitoring to track the use and misuse of antimicrobial medicines to assess their public health consequences.

Antimicrobial Resistance: Global Report on Surveillance, published in April 2014, summarizes findings from 129 WHO Member States on resistance surveillance and data for bacteria–antibacterial drug combinations. (1) The report reveals the lack of structures for coordination and information sharing that could provide an up-to-date overview of the present situation of AMR. The report focuses on the surveillance of antimicrobial-resistant organisms, and not on the consumption or use of antimicrobials.

In May 2014, the Sixty-seventh World Health Assembly passed resolution WHA67.25 on AMR. In monitoring consumption, Member States are urged to:

- monitor the extent of antimicrobial resistance, including regular monitoring of the use of antibiotics in all relevant sectors, in particular, health and agriculture, including animal husbandry, and to share such information so that national, regional and global trends can be detected and monitored;
- develop antimicrobial resistance surveillance systems in three separate sectors: (i) inpatients in hospitals; (ii) outpatients in all other health-care settings and the community; and (iii) animals and non-human usage of antimicrobials.

Effective strategies are needed to improve the use of antimicrobials in order to contain drug-resistant pathogens. Reliable and comparable data are needed on the incidence, prevalence and prescribing patterns of antimicrobial agents.

Regular monitoring and quantification of antimicrobial use and consumption are essential components of the surveillance strategy at the national, regional and global levels to address AMR. In particular, regular monitoring can help to assess the links between the use of antimicrobial agents and the development of resistant pathogens in humans and animals. The following sections outline the need for monitoring of antimicrobial use in Member States of the Western Pacific Region.

2.2 PROPOSED REGIONAL SYSTEM TO MONITOR ANTIMICROBIAL USE

2.2.1 Goal

The goal is to develop and/or strengthen national systems to monitor antimicrobial use in order to contain AMR in the Region. The data collected will provide evidence to Member States on their progress towards the rational use of antimicrobials and inform policy-makers on the evolving public health threat posed by AMR.

2.2.2 Objectives

The specific objectives are to:

- collect data on the consumption and use of antimicrobials at all levels of health care, applying standardized methodologies and using internationally recognized classification systems to ensure comparable methods;
- develop indicators to regularly monitor prescribing of antimicrobials, using up-to-date, evidence-based guidelines to determine good practices for the management of communicable diseases; and
- report data on antimicrobial consumption and use from all relevant sectors at the national and regional levels on a regular basis, in order to initiate collective action on containing AMR in the Region.

2.2.3 Methodology for monitoring antimicrobial use

Data collection

There are a variety of methods to collect, analyse and present data on antimicrobial consumption and use. A common approach would allow for comparison and monitoring of progress in reducing unnecessary antimicrobial use at local, national, regional and global levels.

The Anatomical, Therapeutic and Chemical (ATC) classification system and the defined daily dose (DDD) are recommended by WHO for measuring drug utilization, including antimicrobial consumption. Other methods to measure antimicrobial consumption include measuring by weight, and using financial data or point-prevalence data. Measuring by ATC/DDD facilitates the comparison of consumption information between countries, regions and health-care settings, and examination of trends in drug use over time and in different settings. The DDD corresponds to the average daily maintenance dose for a drug's major indication and is commonly represented per 1000 inhabitants per day to average usage on a population level. The ATC/DDD method is commonly used in the European Union (EU), Eastern Partnership (EaP) and member countries of the Organisation for Economic Co-operation and Development (OECD). A limitation of this method is that it does not provide any indication as to why the antimicrobials are used and whether their use is appropriate.

Measuring the total quantity used by weight can be useful for measuring antimicrobial use in the animal sector. With varying outlets for the purchase of antimicrobial agents in bulk for animal husbandry and little regulation to control sales, it may be difficult to obtain these data.

To provide insights into the rational use of antimicrobials, point-prevalence data can be collected. Each HCF conducts a “snapshot” survey on the diagnosis and reasoning for antimicrobial use for each patient. A particular benefit of the point-prevalence method is its universal applicability to any type of health-care institution, thereby allowing for broad comparisons.

The quality use of antimicrobials can also be monitored by collecting data on simple indicators. For example, measuring the percentage of patients prescribed antibiotics, especially in areas where systematic monitoring is not in place. Quality use and prescribing patterns can be monitored by recording the percentage of specific disease cases prescribed antibiotics, for example, patients prescribed antibiotics for upper respiratory tract infections or diarrhoea.

Other quality use indicators, such as duration of surgical prophylaxis, oral versus parenteral use and compliance with STG, can be helpful for monitoring antimicrobial use. Local and national surveys applying these indicators can provide valuable data on changes over time, and can show patterns of use and responses to interventions.

2.2.4 Data sources

Data on antimicrobial use can be collected from multiple data sources and, with the application of appropriate analytical methodologies, used at the national and subregional levels. Data sources include:

- **Sales data.** Wholesale data can be obtained on pharmaceutical sales at a national, subnational or local level.
- **Dispensing data (either comprehensive or sampled).** Computerized pharmacies can easily collect data on the drugs dispensed. Alternatively, sample data can be collected manually.
- **Reimbursement systems.** National-level reimbursement systems that provide comprehensive dispensing data down to the individual prescription can be used. Similar data are often available through health insurance databases. When linked, these databases allow the collection of demographic information on patients and information on dose, duration of treatment and co-prescribing. Less commonly, linkage to hospital and medical databases can provide information on indications and outcomes, such as hospitalization, use of specific medical services and adverse drug reactions. Many high-income countries in the Region have sophisticated, linked health insurance or dispensing databases that allow detailed analysis of antibiotic use patterns.
- **Patient encounter-based data.** Data are collected by specially designed sampling studies, such as those carried out by market research organizations (for example, IMS Health data). The increasing use of information technology at the medical practice level will make such data available more widely in the near future. These methods have the advantage of potentially providing accurate information on prescribed daily doses, patient demographics, duration of therapy, co-prescribing, indications, morbidity and co-morbidity, and sometimes therapy outcomes.
- **Patient survey data.** Collection of patient data can provide information on drug consumption and can take into account compliance with filling prescriptions and taking medications as prescribed. Patient survey data can also provide qualitative information on perceptions, beliefs and attitudes towards the use of medicines.

- **Health-care facility data.** Data on medication use at all the above levels is often available in health-care settings, such as hospitals and health centres at the national, regional, district or community level.

Need for a common methodology

Monitoring at the regional level is needed to collect data and present results from all Member States on antimicrobial consumption to inform regional efforts to contain AMR. The methodological approaches to collect data and the sources for obtaining data will depend on the country setting. Standardized indicators are needed to assess progress in monitoring antimicrobial use and consumption across the Region. Methods and indicators should be defined through expert consultations and among Member States.

When attempting to define ideal levels of consumption, several factors should be considered including local disease prevalence, resistance susceptibility patterns and antibiotic prescribing practices. Optimal levels of antimicrobial use to serve as target levels will also need to be researched and determined through future regional consultations.

2.3 GLOBAL SYSTEMS FOR MONITORING ANTIMICROBIAL USE

Other WHO regions and international associations have systems in place for monitoring the consumption and use of antimicrobials worldwide. The data collected by these systems vary, depending on the country infrastructure and type of health-care system, but include data sources from pharmaceutical sales, insurance reimbursements, exports and hospitals.

2.3.1 Other WHO regions

There is still a need to gather comprehensive antimicrobial consumption data in many WHO regions. Most regions have an AMR surveillance network; however, systems for collecting inclusive data on antimicrobial consumption with comparable indicators have not been established. Individual studies show trends in antimicrobial consumption rates in various regions, but this information is usually taken from sales data of select countries and may not be available for all countries.

The Regional Office for Europe obtains AMR data from the most well-established antimicrobial use monitoring system: the European Surveillance of Antimicrobial Consumption Network (ESAC-Net). ESAC-Net is an EU-funded project managed by the European Centre for Disease Prevention and Control (ECDC). The network provides data to the European Region by collecting national statistics on antimicrobial consumption in hospital and community settings. The data are collected from national sales and reimbursement data, including information from national drug registers in addition to point-prevalence surveys. The network has developed protocols for assessing quantitative and qualitative patterns of use. ESAC-Net data can be accessed online via an interactive database and are used in conjunction with the European Antimicrobial Resistance Surveillance Network (EARS-Net). The data are collected for three major groups of antimicrobials: antibacterials for systemic use (ATC group J01); antimycotics and antifungals for systemic use (ATC groups J02 and D01BA); and antivirals for systemic use (ATC group J05). The data collected from ESAC-Net allows countries to audit their antimicrobial use and compare national use with

other countries reporting to the database. The data show the relationship between antimicrobial use and resistance, and the summary report generated each year is an important tool for advocacy and assessing policy guidelines.

The Latin American Network for Antimicrobial Resistance Surveillance (ReLAVRA) is a network within the Pan American Health Organization, which coordinates both AMR surveillance and monitoring of antimicrobial consumption for the Latin American region.

To better understand usage patterns of antibiotics in developing and transitional countries, WHO created a database with studies published from 1990 to 2006, and published these data in *Medicines Use in Primary Care in Developing and Transitional Countries: Fact Book*. (18) This database provided insights into inappropriate use of antibiotics, especially for upper respiratory infections and diarrhoeal diseases; however, these data were collected from published studies and no attempt was made to establish a system to continuously monitor antibiotic use.

2.3.2 Other organizations

Surveillance data on antimicrobial consumption are also collected by other organizations. The OECD collects the overall volume of antibiotics prescribed in member countries. These data are obtained only for member countries and are collected from a variety of organizations, including ESAC-Net for European countries, IMS Health for the United States, and self-reported data from ministries of health and pharmaceutical sales. For Member States of the Western Pacific Region who are OECD members (Australia, Japan and the Republic of Korea), aggregate data on the overall volume of antibiotics prescribed (DDDs per 1000) are included in the OECD database but there is no differentiation between the types of antibiotics prescribed. There are also variations in the methodology used to collect these data. For example, Australia does not report antibiotics dispensed in hospitals, non-reimbursed drugs or over the counter (OTC) medications, whereas the Republic of Korea includes these data. Discrepancies in methodology make it difficult to compare data across Member States. ASEAN, which includes seven Western Pacific Member States, does not collect data on antibiotic consumption or prescription rates for humans, or the use of antimicrobials in animal husbandry.

2.4 PRESENTATION AND DISSEMINATION OF SURVEILLANCE DATA

To improve the use of antimicrobials and contain AMR, antimicrobial use and consumption must be measured to set a benchmark and track progress towards quality use of antimicrobials. The data collected through monitoring the consumption and use of antimicrobials can then be presented in a way that will stimulate a sense of urgency and provide impetus for increased awareness and policy actions.

2.4.1 Combined surveillance of antimicrobial resistance and use

There is a known correlation between rates of antimicrobial consumption and the prevalence of AMR. Data monitoring antimicrobial consumption should be used together with AMR surveillance data to track trends in resistance and predict future susceptibility patterns of resistant pathogens. The data can then be used to improve STGs and influence prescribing behaviour when new resistant

strains emerge. Monitoring antimicrobial use will also measure compliance with new treatment recommendations by tracking the volume of first- and second-line antimicrobials that are prescribed. Complementary data on monitoring of antimicrobial use and surveillance of AMR will also allow for long-term temporal and geographical associations that can be easily visualized to support insights and policy recommendations. The ECDC system, which can combine data from EARS-Net and ESAC-Net, allows antimicrobial consumption data to be linked with resistance data. Analysis requires the system to be harmonized, including entry codes and denominator data.

Cost of AMR and irrational use of antimicrobials

There is evidence that AMR has significant adverse impacts on clinical outcomes, leading to higher health-care costs. The increased economic burden associated with AMR is attributed to the higher price of antimicrobial drugs beyond the first line of defence and to consuming more health-care resources. Irrational antimicrobial use also unnecessarily increases the risk of adverse side-effects of antimicrobials. Studies carried out in other regions highlight the economic burden of AMR. However, to assess the economic burden, the current levels of antimicrobial consumption must be measured. Data generated from an antimicrobial consumption database can also help to quantify the burden of AMR on society and health-care systems.

Encouraging effective policies

Antimicrobial monitoring data can be used to improve rational antimicrobial use locally, inform policies and identify priorities for action at the national level. As improving the use of antimicrobials is a key element in containing AMR, strategies to reduce antimicrobial use have been prioritized. However, without documenting the baseline for monitoring the effects of interventions, it is impossible to track progress towards rational use. Appropriate data on antimicrobial use will inform policy-makers to make appropriate decisions. For example, in the Republic of Korea, it was common practice for antibiotic prescribers to also dispense antimicrobials. Growing concerns of high antimicrobial consumption rates and high rates of resistance led to a national policy in 2000, which prohibited doctors from dispensing drugs. Subsequently, inappropriate antibiotic prescribing was shown to decrease. (19) Without a system to monitor the use of antimicrobials, there would be no evidence to support new policies and no way to measure the effectiveness of these policies after implementation. Lack of surveillance can lead to misdirected and ineffective policies that waste already limited resources and provide inappropriate therapy that can increase patient suffering and increase health-care costs.

In 2011, China initiated an antibiotic restraining policy and launched a strategy to reduce irrational prescribing of antibiotics. The initiatives limited the variety of antibiotics granted to hospitals, set targets for the percentage of antibiotic prescriptions and penalized doctors who prescribed antibiotics inappropriately. Regional systems were developed to monitor implementation of the national policy in hospitals using audits and inspections. Hospitals were publicly recognized for achieving specific antibiotic targets and some hospitals that failed were publicly criticized. Following these initiatives, an IMS Health hospital audit showed that antibiotic use in hospitals decreased by 15% after six months of initiating the new antibiotic strategy. (22) Additionally, data released by the Chinese Ministry of Health indicated that the percentage of prescriptions for antimicrobials decreased from 68% to 58% for hospitalized patients and from 25% to 15% for outpatients. (21) The data collected by the Ministry of Health and outside research organizations such as IMS Health are powerful tools to show the effectiveness of China's antibiotic reforms and enable otherwise impossible tracking. Continual monitoring of antibiotic use will be needed to track the sustainability of policies.

Resource mobilization and advocacy

Data collected via the monitoring network for antimicrobial use are essential to quantify the burden of AMR on society and health systems. Data are needed to promote effective policies and campaigns to improve rational use of antimicrobials and dedicate the resources to sustain these initiatives. Comparisons between countries have also proved to be an important stimulus for quality improvements. Measuring antimicrobial consumption will allow individual countries to assess their position in relation to other countries and trigger actions to improve antimicrobial prescribing.

2.5 CHALLENGES FOR MONITORING ANTIMICROBIAL USE IN THE REGION

There are major challenges to monitoring antimicrobial use in the Western Pacific Region. Some of these are the lack of commitment to support the monitoring of antimicrobial use, lack of agreement on the methodology for collecting valid, reliable data, and lack of systems infrastructure, including human resources and technical inputs to support data collection.

2.5.1 Commitment to support monitoring of antimicrobial use

There is a need to commit to developing systems to monitor antimicrobial consumption. Currently, the majority of surveillance is at the microbiological level – testing resistant microorganisms. As there is a clear relationship between the consumption of antimicrobials and the prevalence of resistant strains, consumption data must be measured. Health-care facilities, pharmacies, industry and interdisciplinary government entities need to collaborate to develop integrated systems to share information. The commitment of all stakeholders is essential.

2.5.2 Methodology and consistency of available data

At the methodological level, each Member State must ensure the validity of population exposure to antibiotics. Inadequate or insufficient population coverage may cause significant bias in data analysis. Under detection bias is also possible in countries where drug coverage is not verified, and where there are substantial OTC sales.

Compliance with the ATC/DDD classification is important. Some countries do not aggregate data according to the WHO classification. Moreover, there is a lack of reporting on new antimicrobials such as telithromycin and linezolid. There are also antibiotics and antibiotic combinations that have no official DDD. If no DDD is assigned, the consumption of a particular substance is not recorded and leads to underestimation of consumption in that class. Other differences to consider include the variations in antibiotic consumption in hospitals and in ambulatory health-care settings.

Apart from agreeing on a common methodology to measure consumption and use, there are other challenges to collecting antimicrobial consumption data in the Western Pacific Region. For example, the majority of the data collected are via prescription logs, pharmacy databases, drug purchases or sales, or medicines inventories. In many countries of the Region, these data are not available either because they are not recorded or are owned by manufacturers or pharmacies, which have no legal obligation to share the information. Consumption data is particularly difficult to collect in countries where antimicrobial agents are available OTC without a prescription. Obtaining this information also does not necessarily reflect the total amount consumed

if the patient does not have access to the medication, does not complete the full treatment course, or shares the course with another patient.

2.5.3 Lack of systems infrastructure

Developing a monitoring system and network will require appropriate human resources and technical support. Many Member States in the Region do not have systems for tracking antimicrobial use data. Systems will thus need to be developed and implemented in conjunction with efforts to strengthen health systems. When possible, new monitoring systems should be linked to existing systems, and mechanisms to incorporate data into each country's health information system should be explored. Finally, when developing a network for monitoring antimicrobial use, Member States must also agree on issues of data ownership, confidentiality and use. Member States have the responsibility to monitor antimicrobial consumption at the national level and share data at a regional level for a collective response to contain AMR.

2.5.4 Linkage of antimicrobial use in animal husbandry

WHO has a role in establishing formal mechanisms for data sharing between health authorities, the veterinary sector and food authorities to reduce antimicrobial use and contain the spread of resistant bacterial strains through food, animals and agriculture. The OIE and FAO are important stakeholders for further collaboration on antibiotic consumption and monitoring.

There is a need to extend the collaboration and agreement between FAO, OIE and WHO at the global level to the regional level, in particular, regarding data collection for antimicrobial use in the animal husbandry sector. The Regional Office for the Western Pacific will collaborate with FAO and OIE on how consumption data from the agricultural sector may be collected and disseminated.

2.6 THE WAY FORWARD

There is a need to develop an integrated system to regularly monitor the consumption and use of antimicrobials in the Western Pacific Region. Information on antimicrobial use and consumption should be shared across sectors to inform national and regional policies and strategies to reduce unnecessary antimicrobial use. The next steps for monitoring antimicrobial use are:

- (1) to conduct a country situation and capacity analysis to determine the availability of reliable data on antimicrobial consumption and use in the Region;
- (2) for countries with little data, to develop a strategy to provide advice on policies and capacity-building to set up systems to collect data for monitoring antimicrobial consumption;
- (3) to develop a common methodology for Member States in the Western Pacific Region and train local stakeholders in its use; and
- (4) to encourage resource mobilization to build a regional database and develop country capacity to monitor antimicrobial consumption and use.

**Health systems
response
to support
containment of
antimicrobial
resistance**

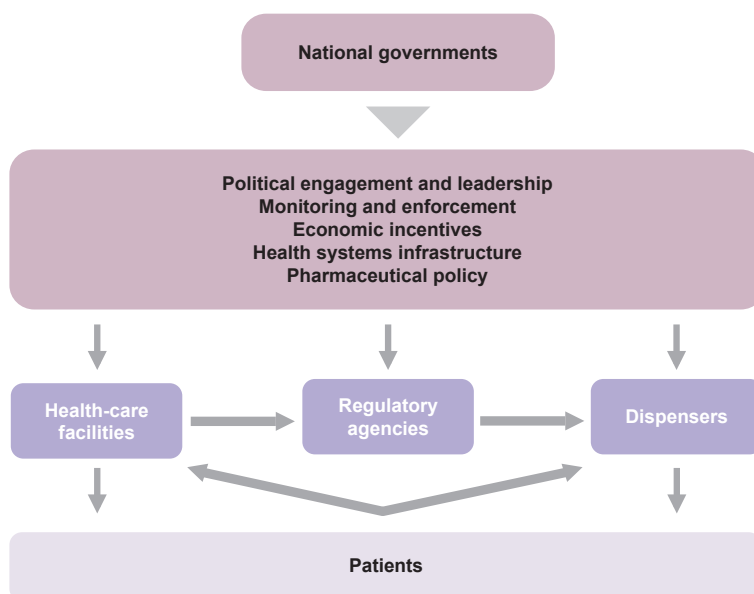
3. Health systems response to support containment of antimicrobial resistance

It is essential to strengthen health systems in order to contain AMR. National plans to contain AMR need to consider strategies that strengthen health systems overall, such as IPC programmes in hospitals and health facilities, education and training of health-care providers using pre-service and in-service curricula that address AMR and rational antimicrobial use, and establishment of effective antimicrobial stewardship programmes. Health system responses also need to cover public awareness and education campaigns, the formulation and enforcement of AMR-related policies and regulations, strengthening the regulatory framework to reduce abuse of antimicrobials, and institution of surveillance of antimicrobial use and resistance, in addition to strengthening laboratory capacity. In most countries, there is a lack of a comprehensive, multisectoral policy and regulatory framework to contain AMR, in particular, antibiotic resistance. Better regulatory systems with effective enforcement mechanisms are needed to improve the appropriate use of antimicrobial agents in all sectors.

Pharmaceutical system

The emergence of AMR is a complex problem driven by many interconnected factors, in particular, the use and misuse of antimicrobials. In turn, antimicrobial use is influenced by the interplay of knowledge, expectations and interactions of prescribers and patients, financial incentives, the characteristics of health systems and the regulatory environment. Given this complexity, coordinated interventions are needed to simultaneously target the behaviours of individual stakeholders and the environments in which they interact (Fig. 2). Strategies to address different components of health systems and drug supply chains can reduce antibiotic consumption, thereby limiting the development and spread of AMR.

Figure 2. Health systems perspective and structures influencing the use of antibiotics



Source: Compiled from: Nordberg P, Stålsby Lundborg C, Tomson G. Consumers and providers – could they make better use of antibiotics? *Int J Risk Saf Med.* 2005;17:117–25.

Responsible use of antimicrobials

Consumption of antimicrobials correlates with the prevalence of AMR. Both overuse and underuse of antibiotics can lead to resistance. Therefore, promoting the appropriate and responsible use of antimicrobials is one of the most urgent interventions needed to reduce AMR.

Rational use of medicines minimizes the morbidity and mortality due to antimicrobial-resistant infections by preserving the effectiveness of antimicrobial agents as a therapeutic option. The choice of antimicrobials should be guided by local or national resistance surveillance data and STGs. In the Western Pacific Region, 69% of Member States responding to the country situation analysis (CSA) have at least one disease-specific AMR surveillance programme; however, only 22% have a coordinated AMR surveillance programme at the national level. Sixty-two per cent of Member States have a defined process for the development of STGs for antimicrobial use. Rational use of antimicrobials should be promoted through strategies that strengthen health systems, and by implementing and enforcing national regulations involving antimicrobial use.

There is a lack of current data on antimicrobial consumption from all Member States in the Western Pacific Region. However, studies from China and Viet Nam indicate that antimicrobial consumption is high. (22,23) Compared to other OECD countries, Australia and the Republic of Korea have higher antibiotic consumption than the OECD average, i.e. 24.1 and 27.0 DDD/1000 population/day, respectively, versus 20.9 DDD/1000 population/day. (24)

Less than half the Member States in the Western Pacific Region (48%) report that antibiotic use has been monitored in the past five years. Financial or prescription data can provide evidence to show consumption levels of antimicrobials, but it is as important to know whether or not the antimicrobial agent has been appropriately prescribed and consumed. In conjunction with monitoring trends regarding the prevalence of drug-resistant infections and pathogens, monitoring of antimicrobial consumption is also necessary to understand the trends in AMR.

3.1 REGION-SPECIFIC CHALLENGES

In the Western Pacific Region, health system characteristics, expectations and interactions of prescribers and patients, economic incentives and the regulatory environment all contribute to AMR. There is wide variation between countries with respect to health-care financing mechanisms, availability of health facilities, services and a competent health workforce, and access to quality essential medicines and health technologies. All of these impact how patients and professionals use antimicrobials with consequences for AMR.

2.1 Lack of strategies at the health systems level

Containing AMR requires strengthening of health systems. Developing national antibiotic policies, STGs and establishing essential drugs lists or formularies can encourage the rational use of antimicrobials and promote proper access to them. Key informant interviews in the Western Pacific Region acknowledge that although STGs exist in many countries, there is little connection between adherence to these guidelines and accreditation or licensing. (25) Health-care workers often lack sufficient training and supervision to prescribe rationally and contribute to improper antimicrobial-prescribing practices. A report from Singapore of vancomycin and carbapenem audits showed that 23.5% and 44% of these, respectively, were inappropriately prescribed. (26)

Only 31% of Member States report that health-care workers have a high awareness of AMR. Prescribers must adopt and abide by clinical practice guidelines and monitor prescribing habits. Only 10 Member States in the Region report having a mechanism to do so. In China, the percentage of prescriptions containing antibiotics in rural clinics was around 50% – this is higher than in other middle- and high-income countries. (27)

Weak infrastructure, including poor access to rapid diagnostic tests, makes it difficult for laboratory results to support treatment decisions, further contributing to improper antimicrobial use. With high diagnostic costs and poor availability of good diagnostic services, it is sometimes less expensive to prescribe an antibiotic for treatment than to order laboratory results to validate the correct treatment. A study in a western province of China found that bacteriology samples were rarely taken before antibiotics were prescribed. (28) While empirical treatment is often necessary because low-cost point-of-care diagnostics suited for resource-limited settings are currently not available, strengthening laboratory diagnostic capacity is an important requirement for more accurate and appropriate use of antimicrobials.

Strengthening health systems will require political commitment and financial investments, but the health and economic burden associated with AMR can be higher, especially in low-income countries, and therefore such investments may bring substantial returns. Surveillance and monitoring of antimicrobial use is integral to provide information on microbiological susceptibility.

3.1.2 Expectations and interactions of prescribers and patients

Patient behaviour, including misperceptions, expectations, self-medication and poor adherence to dosage regimens, contributes to AMR. Often, patients are unaware of the pharmacological actions of antimicrobial agents and therefore do not understand when or how they should be used (Box 1).

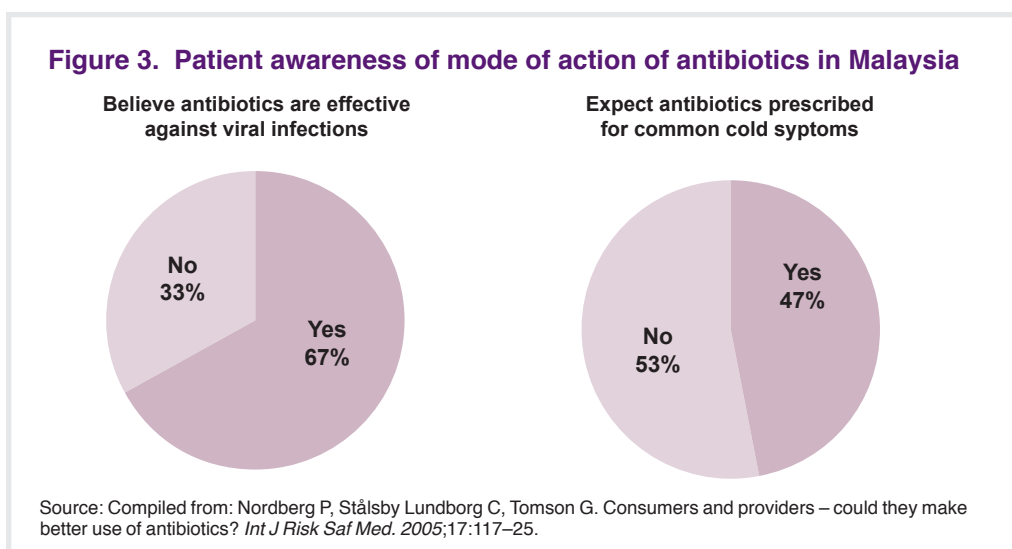
Box 1. An innovative approach to antimicrobial stewardship in Australia (29)

The National Prescribing Service of Australia (NPS MedicineWise) designs behaviour change interventions to improve the use of medicines and health technologies. The goal is to provide health professionals, consumers, government officials and industry with evidence-based information to support informed decision-making on medicine use.

In February 2012, NPS MedicineWise launched a five-year campaign against antibiotic resistance with a strong emphasis on community education and with the goal of reducing inappropriate prescribing of antibiotics in Australia by 25% in five years. Using an innovative, multimedia approach, including outreach activities through social media, television spotlights, local celebrities and traditional advertising, the campaign aims to educate the public on AMR and empower them to be part of the solution.

A preliminary evaluation of the campaign shows an increase in AMR awareness in Australia; however, more time is needed to evaluate the long-term impacts of the campaigns on changing consumer behaviours towards antimicrobial consumption. Patient behaviour, including misperceptions, expectations, self-medication and poor adherence to dosage regimens, contributes to AMR. Often, patients are unaware of the pharmacological actions of antimicrobial agents and therefore do not understand when or how they should be used.

Interactions between prescribers and patients also influence antimicrobial usage. Often patients spend little or no time with a health-care provider before receiving antimicrobial therapy. Providers feel pressure to treat patients with antimicrobials and therefore unnecessarily prescribe antibiotics to satisfy them. Providers have an interest in quick treatment options as it helps to attract and retain patients. Providers may thus choose the shortest course of treatment or opt for the newer, more expensive antimicrobials. (30)



Patients who purchase antimicrobials without a prescription may not receive the necessary therapeutic instructions from a licensed prescriber. A study in Malaysia showed that 67% of patients incorrectly believed that antibiotics are effective against viral infections (Fig. 3). Better communication and patient education can improve the rational use of antibiotics and discourage patients from abusing antimicrobials.

3.1.3 Financial incentives that encourage overuse and overprescribing

Financial incentives can encourage overprescribing of antimicrobials, leading to the development of AMR. In China for example, where pharmaceutical sales are a direct source of income for hospitals and health-care providers, there may be an incentive to overprescribe. (30) Evidence shows that when such perverse financial incentives are removed, along with implementation of other interventions as part of the nationwide special antibiotic stewardship programme in China, significant reductions can be achieved in the overuse of antibiotics. (32)

Pharmaceutical companies can influence prescribing habits by offering profit-sharing to prescribers. Physicians who dispense medications may also have an incentive to overprescribe. In the Republic of Korea, a national policy that prohibited doctors from dispensing drugs in 2000 was shown to selectively reduce inappropriate antibiotic prescribing. (33) This example provides evidence that prohibiting medication dispensing by physicians can contribute significantly to promoting the quality of drug use. Local incentive structures should be examined to identify incentives that may influence antimicrobial prescribing practices.

Financial incentives that encourage the overuse of antibiotics also exist in veterinary medical practice and in animal husbandry. STGs should be used to establish methods of payment and reimbursement, and financial incentives that promote overprescribing should be eliminated.

3.1.4 Poor awareness and civil society engagement

Education and awareness among those involved in antimicrobial use is vital. These include policy-makers, regulators, the pharmaceutical industry, prescribers, dispensers and consumers. In the Western Pacific Region, awareness of AMR is lacking. Public awareness is reported to be absent or very low among 93% of Member States. At the national level, information can be incorporated into awareness campaigns and antibiotic stewardship programmes to promote prudent use of antibiotics. Eleven Member States in the Western Pacific Region report that a public awareness campaign for antimicrobial use has been implemented within the past two years.

In a study of children in an urban community in Mongolia, 42% of the children were given non-prescribed antibiotics by their caretakers. (34) This percentage is higher than similar reports from Viet Nam (35) and China. (36) The study highlighted that mothers with a better knowledge of antibiotics were less likely to give their children antibiotics without a prescription, emphasizing the need for public education on antibiotics.

Information that is unbiased and independent from promotional activities or pharmaceutical companies should be provided to consumers and prescribers on antimicrobial use. Together with regulations on antimicrobial use, awareness campaigns and continuing education can enhance the knowledge and attitudes of consumers and prescribers, and improve antimicrobial use. To contain AMR, policy-makers and regulators must also be educated to implement the necessary legal and regulatory frameworks for pharmaceutical promotion and its potential adverse impact.

3.2 IMPROVING REGULATIONS

Health and pharmaceutical regulations shape the way in which antimicrobials are used. In the Western Pacific Region, many countries do not have a solid legal and regulatory framework to mandate, support and enforce the rational use of medicines. Countries with weak regulatory systems have limited capacity for ensuring drug quality, improving dispensing of medicines, restricting the use of antibiotics in animals, and controlling the movement of drugs in the supply system.

3.2.1 Ensuring quality

Controlling the quality of all antimicrobials is essential for safe and effective delivery to patients. Through regulations, Member States can control the quality, safety and efficacy of drugs. Counterfeit, substandard or degraded antimicrobials are likely to drive drug resistance. Antimicrobials containing less than the stated dose may result in therapeutic failures and selection of drug-resistant strains. Counterfeit products commonly contain little or none of the active substance stated on the label or may contain an entirely different active ingredient. A counterfeit drug with no active ingredient will not directly facilitate selection of antibiotic-resistant bacteria; however, resistant bacteria may still emerge if the active ingredients include other antibiotics. Through regular inspections, governments can ensure that drug manufacturers adhere to good manufacturing practices (GMP), product specifications and licensing requirements. Countries without systems for controlling the quality and assessing the safety and efficacy of drugs face an increased risk of exposure to substandard, inferior and counterfeit drugs that penetrate the market.

Substandard medicines that may contain lower amounts of active ingredients or fail to deliver (due to poor dissolution, dispersion of tablets, injections) the

required amount of active ingredient are a particular threat for increasing the emergence of resistant bacteria. In countries where regulatory capacity is limited to ensure adherence to GMP, many manufacturers with deficient and inconsistent manufacturing practices may sell poor-quality, substandard products legally in national, regional and international markets.

In the Western Pacific Region, 68% of Member States report having national quality standards for antimicrobials; however, only 40% of Member States report that there are special mechanisms for detecting and combating counterfeit medicines. Ensuring the quality of available antimicrobials can reduce the risk of AMR.

3.2.2 Improving dispensing

In many countries of the Western Pacific Region, antimicrobials are commonly dispensed by unauthorized people who lack the appropriate training. Over half of the Member States in the Region report that antimicrobials are sold OTC without a prescription. Key informant interviews in the Region revealed that many countries have laws for the accessibility of antimicrobials only by prescription, but these laws are not enforced adequately. (25) For example, in Mongolia, a ministerial decree announced measures to stop OTC sales of non-prescribed drugs in 2011, but in practice it continues. (37) As poor enforcement of prescription-only regulations is almost universally associated with inappropriate antimicrobial usage, regulation to limit non-prescription dispensing of antimicrobials is crucial to controlling the emergence of AMR (Box 2).

Box 2: Developing a road map for antimicrobial stewardship in Viet Nam

In 1986, Viet Nam implemented several market-based reforms, including privatization of the pharmaceutical industry and deregulation of the retail drug trade. Following the reforms, the number of private pharmacies increased from zero to 6000 between 1986 and 1992. During the same period, there was a six-fold increase in the annual per capita consumption of pharmaceuticals, with antibiotics representing the highest proportion of the increase. (38)

Good Pharmacy Practice (GPP) standards were issued in 1997 to improve standards. These required pharmacies to monitor drug quality, record consumption and comply with prescription-only regulations. GPP pharmacies continued to dispense antibiotics to patients without a prescription. A study of antimicrobial use was conducted in Hanoi from 1997 to 2000, following the implementation of a series of interventions in 68 private pharmacies. (39) The study indicated that improvements in private pharmacy practice are possible with a combination of enhanced regulatory enforcement, education and personal involvement through peer networks.

In 2012, the Viet Nam Resistance (VINARES) project was launched to build the capacity of health workers and strengthen AMR stewardship in health-care settings. The VINARES programme aimed to control hospital-acquired infections, prevent irrational antibiotic consumption and strengthen laboratory surveillance. The stewardship programme is currently being implemented through training workshops with support from VINARES. However, in the long term, through capacity-building, the programme aims to equip hospitals with the tools to conduct self-sufficient antimicrobial stewardship programmes. (40) The VINARES project could serve as a model framework for other settings.

While regulations should be enforced to limit OTC sales, patient access to high-quality antimicrobials must be ensured through prescription of appropriate treatment regimens by trained health-care workers. Often, patients seek treatment from pharmacists and drug sellers who are not trained to diagnose or prescribe. Going directly to the pharmacist often costs less and is less time consuming than first seeing a licensed health-care worker. Enforcing regulations that prohibit OTC sales is critical for promoting the rational use of antibiotics.

The way antimicrobials are packaged and dispensed may also contribute to AMR. Antimicrobial tablets that are sold individually, rather than in the full treatment course, may promote the underuse of antimicrobials, leading to the development of resistant strains. Limited financial means is also a factor, as patients often purchase only as much medication as they can afford, and may stop the treatment course once they begin to feel better. Studies have shown that an estimated 90% of consumers buy three days' supply, or less, of antibiotics, making compliance with the recommended dosage impossible. (41) Packaging regulations that require full treatment courses to be dispensed, in addition to easy-to-read package labels with symbols, can improve patient adherence and limit AMR.

3.2.3 Regulations to restrict the use of antibiotics in animals

Antimicrobial use in food-producing animals affects human health due to the presence of active antimicrobial residues in foods, and particularly by the selection of resistant bacteria in animals. The consequences of such selection include an increased risk of development of resistant pathogens, the vertical spread of microbes harbouring resistance genes between animals, as well as their transfer to humans

The underlying principles of appropriate antimicrobial use and containment of resistance are similar to those applicable to humans. A "One Health" approach is required to coordinate the food, veterinary and health sectors at the national level. The national regulatory authority in 66% of Member States in the Region does not have mechanisms in place to enforce requirements for rational use of antimicrobials in animals. Likewise, there is a legal provision to reduce the use of antibiotics as growth promoters for food animals in only 32% of Member States. Enhanced collaboration between veterinary and human medicine would accelerate interdisciplinary and international action to contain AMR through a One Health approach.

3.2.4 Securing the supply of effective, quality antimicrobials through regulation

The ability of prescribers and dispensers to provide appropriate, high-quality antimicrobial agents is determined by the consistent supply of the necessary antimicrobials. The role of government regulators is to ensure access to good-quality medicines and secure the supply chain from the manufacturer to the patient. Often, the drug supply chain is inadequately secured due to limited or inappropriate regulation related to the procurement, storage and sales of quality antimicrobials. Additionally, in the Western Pacific Region, with only 32% of Member States reported to manufacture antimicrobial medicines in their country, it is necessary to strictly enforce importation requirements and inspect the quality of medications. The individual steps in the supply chain can contribute to AMR if not properly regulated and enforced across both the public and private sectors.

3.3 STRENGTHENING INFECTION PREVENTION AND CONTROL

IPC programmes are important in preventing the spread of infectious AMR pathogens within and between HCFs. Resistant microorganisms also easily spread from HCFs to the community and to other countries through international and medical tourism. IPC has an integral role in containing AMR, as it can prevent the acquisition and transmission of, and infection by, resistant strains of microorganisms, and inadvertently reduce antimicrobial use. The 2001 *WHO Global Strategy for Containment of Antimicrobial Resistance* recommended that all hospitals establish IPCs with responsibility for effective management of AMR. (17) IPC was further highlighted by the 2011 World Health Day policy package, which identified enhanced IPC as important for the containment of AMR. (42) In 2012, the need for IPC in HCFs was further emphasized in the WHO publication entitled *Evolving Threat of Antimicrobial Resistance: Options for Action*. (43)

Successful IPC programmes in HCFs and the community require infrastructure, human resources, financial commitment, protocols and practices, monitoring and evaluation, and linkages with public health services. Screening patients with AMR and using isolation methods for infected patients can further assist to contain AMR. IPC programmes go hand in hand with laboratory testing to inform the need for patient isolation and antimicrobial susceptibility testing, surveillance of AMR and antimicrobial use, as well as good antibiotic stewardship.

The spread of resistant pathogens in hospitals and other facilities contributes significantly to the increasing global burden of AMR. Interventions to bring about system change in HCFs involve improving infrastructure, ensuring adequate human resources, and collecting appropriate data for monitoring and evaluation to inform IPC practices.

3.3.1 Region-specific examples

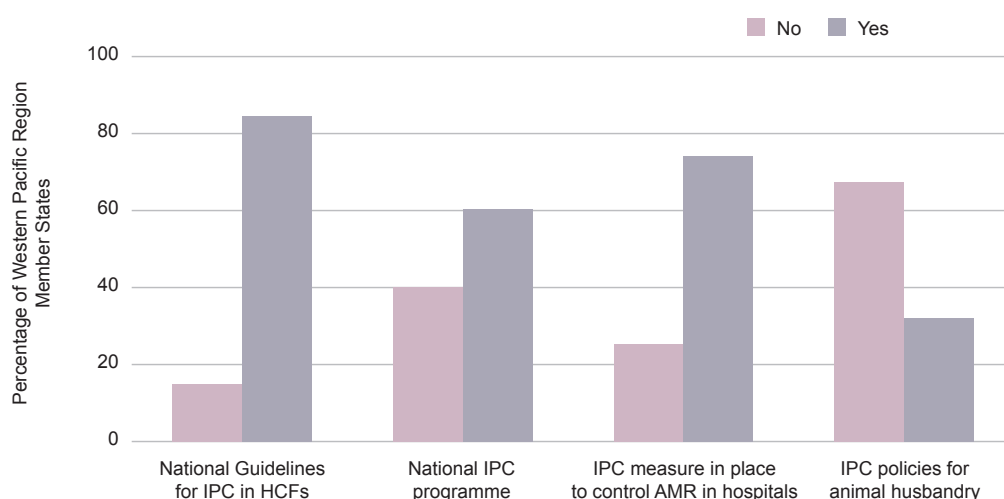
Many facilities in the Western Pacific Region have made good progress in implementing recommendations on IPC, but there are still marked differences in the level of implementation within and between countries, in particular, in low- and middle-income countries. This contributes significantly to the inequalities in health-care delivery, and spread and containment of AMR pathogens. (44) Strengthening current IPC programmes and developing new ones in areas where these are lacking are important to contain AMR at the global, regional, national and local levels.

In the Western Pacific Region, 85% of Member States report that there are national guidelines for IPC in HCFs, with 60% of Member States reporting that they have a national IPC programme. With regard to AMR containment, 74% of Member States have specific IPC measures in place to control AMR in hospitals. Although there have been improvements in the development of IPC programmes in the health-care setting, IPC policies are lacking in the animal husbandry sector, with only 32% of Member States in the Region reporting that they have these in place.

Inadequate infrastructure and human resources

Applying the core elements of IPC in HCFs is the essential first step in IPC strategies and in limiting the spread of resistant microorganisms. Deficiencies in HCF infrastructure, along with insufficiently trained health-care workers to manage IPC, are major barriers to implementing IPC programmes.

Figure 4. Results of a country situation analysis on IPC guidelines and programmes to address AMR in the Western Pacific Region



Source: World Health Organization. Rapid assessment tool for country situation analysis on antimicrobial resistance in Western Pacific Region. Unpublished data. 2013.

HCF infrastructure, equipment, supplies and resources are needed to enable effective IPC practices, including AMR-containment measures. Seventy-four per cent of Western Pacific Member States reported having incorporated the control of AMR into their IPC policies in hospitals (Fig. 4). Effective and feasible implementation strategies are needed to translate these IPC policies and recommendations into best practices. Implementation requires situation analyses at the national and HCF levels to set realistic goals and strategies for progressive improvements in IPC within the local context. There is also a need for a clear structure or committee in the hospital setting under whose authority the IPC programmes exist. Designated AMR focal points should be a part of the committee. Antimicrobial stewardship committees have successfully set up AMR subcommittees, and a similar approach is required for IPC committees.

Inadequate awareness among health-care workers of AMR transmission dynamics and prevention methods are additional challenges in implementing IPC practices. With only 31% of Member States reporting high awareness of AMR among health-care workers in the Western Pacific Region, ongoing education and feedback to staff is necessary to maintain standards and compliance with IPC practices. AMR must also be incorporated into the basic medical, nursing and pharmacy curricula to educate future medical practitioners and ensure that they are aware of the importance of IPC to contain AMR.

Inadequate data on AMR infections

The lack of surveillance data on resistant microorganisms in the Western Pacific Region limits the implementation of effective IPC practices to contain AMR. The majority of the available data is restricted to high-income countries. Infectious disease incidence and prevalence rates at the national and individual HCF levels are essential to identify and prioritize IPC practices to contain AMR; however, microbiology capacity quality controls are often limited. Poorly established AMR surveillance systems may lack the data to assess the magnitude of harm to patients, or the additional resources required to manage hospital-acquired infections (HAIs), especially resistant pathogens. Data from community-acquired infections due to resistant microorganisms is even more rare.

The lack of standardized methods and universally applicable standards for measuring HAIs makes it difficult to assess the current situation, especially when comparing between and within HCFs, or attempting to measure the effectiveness of different interventions. Accepted methods largely require laboratory support and quality assurance programmes to effectively collect clinical data. In addition to surveillance, rapid diagnostic testing is essential to identify asymptomatic carriers and/or patients infected with drug-resistant pathogens to allow timely implementation of IPC measures.

Lack of information on costs and cost-effectiveness of infection prevention and control

Information that addresses the cost-effectiveness of infection control interventions in containing AMR is limited. The health and economic consequences of AMR are high, though they are difficult to quantify, as the data available are incomplete in many countries. Most of the data on the economic burden of antimicrobial-resistant infections in hospital settings have been limited to high-income countries. In the Western Pacific Region, comprehensive studies assessing the cost-effectiveness of interventions have not been published.

The costs for specific interventions may vary considerably, depending on multiple local factors. To quantify the savings resulting from the interventions, a variety of local issues need to be taken into account, including the pre-intervention burden, the effectiveness of interventions and potential direct savings for health-care systems, as well as savings for social security systems and/or increased productivity. The potential direct savings for health-care systems include shorter hospital stays, fewer readmissions, reduced diagnostic tests and need for antimicrobial treatment. Research is needed to develop tools to evaluate the impact and cost-effectiveness of IPC measures in containing AMR in individual Member States of the Western Pacific Region.

3.3.2 Implementing core elements of IPC in health-care facilities

Hospital patients are a main reservoir of resistant microorganisms and it is thus important to implement core IPC elements in HCFs.

There are multiple elements to the implementation of successful IPC programmes to reduce HAIs and prevent the emergence of AMR, and/or dissemination of resistant strains of microorganisms. The development of IPC guidelines to contain AMR is site, area and pathogen specific. IPC programmes should be locally tailored with goals announced to health-care workers through awareness campaigns, and IPC elements prioritized according to feasibility at the local level. These should also demonstrate the cost-effectiveness of IPC interventions, for example, in reducing the cost associated with the burden of disease and the length of hospital stay.

A formal organizational structure to facilitate the development and maintenance of IPC policies and strategies is essential. A multidisciplinary IPC committee should be established to develop and support IPC programmes. Following the implementation of IPC practices, a monitoring and evaluation framework should be in place to enable timely adaptation of IPC strategies to current needs. There is also a need for an appropriate infrastructure to apply IPC practices, including the availability of quality products and equipment (gloves, masks, gowns, etc.). Quality microbiology laboratory services are also needed to inform the prescription of cost-effective antimicrobials as well as rapid and accurate detection of resistant microorganisms for timely implementation of IPC. Collaboration between IPC programmes and microbiology laboratories, including information on AMR surveillance, will enable rapid detection and containment of current and emerging drug-resistant microorganisms. Active linkages between IPC

programmes/committees and public health services or other societal bodies can facilitate communication about AMR at the local, national and regional levels. Collaboration can encourage multifaceted solutions to contain AMR and improve patient safety through standard IPC practices, both in hospital and community settings. (44) Basic IPC practices should also be promoted among the general population. (25)

Standard precautions for infection prevention and control

Standard precautions include basic hand hygiene, sterilization and disinfection of medical materials, prevention and management of injuries from sharp instruments, and a safe and effective waste management system. The promotion of good hand hygiene practices will limit the transmission of microorganisms, including AMR isolates, carried on the hands of hospital staff, visitors and patients. Examples of resistant bacteria primarily transmitted between staff and patients are methicillin resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE).

More complex interventions are needed for some microorganisms, such as MDR Gram-negative bacteria. (44) Currently, eight Member States in the Western Pacific Region have signed the WHO First Global Patient Safety Challenge (GPSC) pledge document to commit to reducing HAIs. The GPSC programme also issued the WHO Guidelines on Hand Hygiene in Health Care as part of the WHO global annual campaign SAVE LIVES: Clean Your Hands (Box 3). (45)

Box 3. WHO SAVE LIVES: Clean your hands – the Malaysia Story (45)

As part of a global effort by WHO to support health-care workers in improving hand-hygiene practices and reduce HAIs, SAVE LIVES: Clean Your Hands is part of the WHO First Global Patient Safety Challenge “Clean Care is Safer Care” launched in 2005. Currently, 132 Member States have signed the pledge, eight of which are Member States in the Western Pacific Region.

The Ministry of Health of Malaysia joined the Clean Care is Safer Care challenge and has experienced a gradual increase in the hand hygiene compliance rate over time, from 56.6% in June 2008 to 82.2% in the fourth quarter of 2012. This was accompanied by a reduction in HAIs from 3.57% per 100 patients in March 2007 to 1.15 per 100 patients in September 2012. An obligatory hygiene awareness day is held in most tertiary hospitals every year around 5 May.

Together with hand hygiene, barrier practices are also a large component of IPC. Barrier practices, including patient isolation and the use of gloves, gowns or masks, are widely recommended for the control of endemic AMR. Barrier practices cannot by themselves fully prevent or contain the progression of resistance. (46) In addition, good practices need to be observed for the prevention and management of injuries from sharp instruments as well as safe and effective waste management.

Screening of patients for AMR bacteria

Another important element of IPC practices for the containment of AMR is the accurate and timely identification of patients infected with drug-resistant pathogens, in particular, AMR bacterial infections. As culture can take up to three days to provide a diagnosis, there is a need for rapid detection. For example, the use of rapid molecular testing methods to test for MRSA and MDR-TB is required for timely diagnosis, ensuring correct treatment and isolation measures if needed.

Isolation of patients infected with AMR bacteria

The rapid spread of resistant microorganisms is facilitated by the transfer of patients between wards and between different HCFs. (44) Depending on the microorganism, isolation of patients, such as those with MDR- or extensively drug-resistant (XDR)-TB may be required. The spatial separation/isolation of patients goes hand in hand with physical barriers to reduce the chance of transmitting infectious diseases between patients and/or health-care workers.

Implementing these practices can reduce the transmission of drug-resistant pathogens. However, no single practice alone can prevent or contain the emergence and progression of resistant microorganisms. Thus, a multicomponent approach that encompasses all levels of IPC in the hospital and community setting is needed.

3.3.3 WHO guidance on infection prevention and control

The primary purpose of IPC in HCFs is to reduce the burden of HAIs in patients, health workers, visitors and other people associated with HCFs. HAIs can be endemic, epidemic (within the population of the HCF) or can occur as a consequence of transmission of a community-acquired infection to patients in HCFs, leading to amplification or an epidemic of community-acquired infections.

In 2014, the WHO Strategic and Technical Advisory Group for addressing AMR established a set of four basic IPC guidelines specific to the containment of AMR (47):

1. **Standard precautions**
 - a. Hand hygiene
 - b. Sterilization and disinfection of medical materials
 - c. Prevention and management of injuries from sharp instruments
2. **Early detection of disease and isolation precautions**
 - a. Patient displacement
 - b. Use of personal protective equipment
3. **Aseptic technique and device management for clinical procedures, according to the scope of care**
4. **Waste management.**

These guidelines are basic and indispensable. Their inclusion in IPC programmes can contain HAIs and the spread of antimicrobial-resistant pathogens. To comply with the WHO-recommended IPC guidelines, surveillance systems need to be in place for HAIs and for the assessment of compliance with IPC guidelines and practices. This

information also directly contributes to assessing the impact of IPC interventions in reducing and containing the spread of HAIs, in particular, AMR. (25)

In addition to the WHO IPC guidelines, the Regional Office for the Western Pacific has been supporting IPC capacity-building through the online learning via the Pacific Open Learning Health Net (POLHN) in partnership with Pacific ministries of health. (48) To date, there are 38 POLHN learning centres located in 12 countries: Cook Islands, the Federated States of Micronesia, Fiji, Kiribati, the Marshall Islands, Nauru, Palau, Samoa, Solomon Islands, Tonga, Tuvalu and Vanuatu. As of January 2015, more than 180 Pacific health workers had enrolled in POLHN's online IPC course which was launched in early 2014.

3.3.4 National coordinated IPC programmes and networks

There is urgent need for a system-wide approach to integrate AMR control into national IPC policies and practices in HCFs. AMR components must be incorporated into all areas of HCF operations. To coordinate national IPC programmes and networks, a national advisory committee should be set up to design and monitor the implementation of effective IPC policies. (49) The IPC advisory committee should consist of experienced and knowledgeable members who can provide evidence-based advice and support. However, hospital directors should ultimately take full responsibility for IPC. Adequate financial support is also needed to maintain national IPC activities and support IPC implementation in HCFs. The committee should develop and regularly update national IPC guidelines for a streamlined effort to contain HAIs and AMR in HCFs throughout the country. The inclusion of IPC indicators and practices in the national hospital accreditation system would further enhance IPC activities.

The progress of IPC programmes should also be measured. Indicators of progress can include regular monitoring of compliance rates of hand hygiene and consumption of alcohol-based hand rubs. Other indicators include the continued monitoring of important pathogens that cause HAIs through surveillance. These include MRSA, extended-spectrum beta-lactamase-producing Enterobacteriaceae and carbapenem-resistant Enterobacteriaceae, all of which pose serious health threats in hospital and community settings.

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