Progress towards antimicrobial resistance containment and control in Indonesia

A pilot programme to evaluate Indonesia's antimicrobial resistance containment plan shows that progress is on the right track, but substantial strengthening is needed, say **Harry Parathon and colleagues**

In May 2015 member states at the World Health Assembly endorsed the World Health Organization's global action plan on antimicrobial resistance (GAP-AMR).¹ Through adoption of the GAP-AMR, member states committed to having a national action plan on antimicrobial resistance in place by May 2017.^{1,2} The South East Asia region has moved from having one (10%) country with a national action plan in December 2015 to 10 countries (90%) by May 2017. WHO supported the Indonesian Ministry of Health to develop a national action plan, first by conducting a review of current activities.³ The review focused on a situation analysis of challenges to tackling AMR. The South East Asia Regional Office (SEARO) of WHO has proposed a stepwise, incremental approach to implementing GAP-AMR, consisting of five phases. Phase 5 is defined as a fully operational AMR containment programme with evidence of a sustained funding mechanism and incorporating a functional monitoring and evaluation system. Here we evaluate Indonesia's progress towards this goal.

KEY MESSAGES

- A national action plan to combat antimicrobial resistance (AMR) in line with the Global Action Plan was finalised and shared with WHO before the WHO General Assembly in May 2017
- Indonesia's programme to contain AMR is in the early phase of implementation based on the situation analysis tool produced by the South East Asia Regional Office of WHO
- A substantial achievement of the programme in the past year was the provision of considerable national funds to support national activities to combat AMR
- Indonesia's health authorities recognised many major challenges including setting up a strong governance that incorporates a multisectoral collaboration and coordination, national surveillance of AMR and enforcement of policies for rational use of antibiotics and AMR stewardship

Antimicrobial resistance in Indonesia

With an estimated population of 258 million people, Indonesia is the fourth most populous country in the world and is categorised as a lower middle income country.⁴ Despite no formal estimation of its burden, AMR is thought to be high and on the rise. Data on AMR in Indonesia have been patchy, sporadic, and selective, commonly generated by a few laboratories from large universities, which are not connected in a national network.⁵

Epidemiological data on *Streptococcus pneumoniae* carriage and invasive disease are currently limited in Indonesia.⁶ In the mid 1990s studies reported 21% and 36% of penicillin non-susceptible and erythromycin resistant *S pneumoniae*, respectively, in Jakarta.⁷ In Lombok Island, the prevalence of *S pneumoniae* carriage was 48% in healthy children, of which all isolates were susceptible to penicillin and cefotaxime and 12% were non-susceptible to sulfamethoxazole or chloramphenicol.⁸ In 2000-01, the prevalence of tetracycline resistant *S pneumoniae* tested at the University of Jakarta's microbiology laboratory was 46%, compared with 1-5% in studies from northern Europe.^{7,9} In Semarang, Indonesia, prevalence of *S pneumoniae* in 2010 was 43% in children aged 6-60 months and 11% in adults aged 45-75 years, of which isolates 24% were penicillin non-susceptible and 45% were resistant to cotrimoxazole.¹⁰

In 2001, *E coli* from rectal samples showed remarkably high resistance to ampicillin (73%), trimethoprim-sulfamethoxazole (56%) and ciprofloxacin (22%), especially at the time of hospital discharge.¹¹ Until the late 1990s, extended spectrum β lactamase producing bacteria were mainly isolated in hospitals worldwide; later, resistance increased along with the emergence of genes related to CTX-M in hospitals and the community.^{12,13} In 2005 a survey in a hospital in Surabaya, Indonesia, found prevalences of extended spectrum β lactamases (including CTX-M) of 20% and 28% among clinical *E coli* and *Klebsiella pneumoniae*, respectively.¹⁴

Over the past decade the emergence of extended spectrum β lactamase producing bacteria and carbapenem

resistant Enterobacteriaceae has become a worldwide threat to public health. From 2001 to 2012, resistance to imipenem rates reached 30% in some epidemic areas of the Middle East, while the top two Asian countries with the highest resistance rates to imipenem were Indonesia (6%) and the Philippines (4%).^{15,16,17} In 2009 the gene for New Delhi metallo- β -lactamase (bla_{NDM-1}) was found in a sample of *K pneumoniae* in Indonesia.¹⁸

In 2001-02 the nasal carriage of *Staphylococcus aureus* was surveyed in two cities on Java island (Semarang and Surabaya); low prevalence of methicillin resistant *S aureus* (MRSA) (<1%) was found among 263 isolates from healthy people in the community.¹⁹ In 2007-08, 24% of surgical patients were screened for MRSA carriage at discharge in three teaching hospitals in Indonesia. Of these, 24% patients carried *S aureus*, 4.3% of whom had MRSA. This was surprising low, as the prevalence of MRSA in some Asian countries, such as Taiwan and mainland China, is among the highest in the world, ranging from 28% to over 70%.^{20,21} Prevention of spread of MRSA is crucial in Indonesia because of the surprisingly high prevalence of the Panton-Valentine leukocidin genes (11%) among MRSA in the country, a virulence factor that is associated with skin infections and severe necrotising pneumonia.²²

The challenges of AMR that Indonesia faces are similar as those of many other low and middle income countries in the region and beyond. Misuse and overuse of antibiotics in humans and in livestock and aquaculture are the key drivers of resistance in the country. With the economy prospering for the past decade and a growing demand for poultry products and the development of aquaculture exports, agricultural use probably exceeds medical use in Indonesia.²³ Despite current policies related to antimicrobial use, common and unnecessary prescription of antibiotics by physicians, high rates of self medication, and over-the-counter purchase of antibiotics are common.²⁴ Many contextual factors influencing antibiotic use are known, including weak policy enforcement and poor governance, lack of education, and easy access to cheap antibiotics.²⁵

Situational analysis methods

The Indonesian ministry of health agreed to pilot the situation analysis tool developed by SEARO, the objectives of which are to report on the baseline, development, implementation, monitoring, and evaluating progress made by the national AMR prevention and containment programme.³ The tool has seven focus areas consistent with the strategic objectives of the GAP-AMR: national AMR action plan in line with GAP-AMR; AMR awareness raising; national AMR surveillance; antimicrobial stewardship and surveillance of antimicrobial use and consumption in the community; infection prevention control in healthcare settings; research and innovation to combat AMR; and One Health engagement. Each focus area is composed of a list of indicators that are graded on five levels to show the incremental extent of AMR programme implementation.

The situation analysis process consists of guided discussions between members of the ministry of health's AMR control committee, senior technical leaders of the national health authorities, the veterinary, agriculture and food sector, and a WHO team. The situation analysis focuses on the level of development of the national AMR containment programme in terms of governance structure, policy, and systems. It is a broad system analysis rather than assessing quality of official documents such as guidelines, regulations, and policies. Details of the definitions and methodology of the situation analysis tool are described elsewhere.³

Monitoring Indonesia's progress

The results of situation analysis are summarised in table 1. The review confirmed that the AMR containment programme is in

the early phase of implementation, ranging from programme installation to full operation phases for most of the core activities of the GAP-AMR. Since 2016 the ministry of health has boosted the programme, with substantial funding for the national AMR control committee. The AMR prevention and control programme is on the right track but needs further strengthening.

The Indonesian authorities are committed to supporting AMR containment activities and understand the complexity of AMR and its challenges in Indonesia, particularly multisectoral coordination and policy enforcement issues. This review of the situation was useful in several ways. Firstly, it emphasised among multidisciplinary participants that a comprehensive One Health approach—that is, coordination and collaboration between the human, animal, and the environmental

Table 1 | Situation analysis and monitoring of antimicrobial resistance in Indonesia: results summary June 2016

Indicators	Phases					Phase achieved in Indonesia
	1—Exploration and adoption	2—Programme installation	3—Initial implementation	4—Full operation	5—Sustainable operation	
1. National AMR action plan						
NAP in line with GAP-AMRGAP	No action plan or no national multisectoral committee or AMR committee established but involving one ministry	AMR working group established and national action plan under way	Action plan aligned with GAP including operational plan with defined activities and respective budget available	Action plan includes operational plan being rolled out and scaled up with defined activities and respective budget	Action plan includes operational plan being rolled out and scaled up with defined activities and respective budget	2+
2. Awareness raising						
Awareness campaigns to the public	Government not involved in awareness raising activities on antibiotic resistance	Some government led activities in parts of the country to raise awareness about AMR and actions to tackle it	Nationwide, government led antibiotic awareness campaign targeting the general public or professionals	Nationwide, government led antibiotic awareness campaign targeting public and professionals	Assessing effects of government led awareness campaigns on behaviour changes in public and professionals	3+
Education and training strategies for professionals	No policy or strategy	Relevant policies developed but ad hoc training courses in some disciplines	AMR included in some preservice training or special courses or both OR Continuous professional development and regular audit of learning	AMR included in some preservice training or some special courses or both AND Continuous professional development and regular audit of learning	AMR included in preservice training for all relevant cadres Regular continuing professional development	3+
3. National AMR surveillance system						
National human AMR surveillance	No capacity for AMR laboratory or limited reporting or both, or no surveillance guidelines	Guidelines developed but not fully implemented. Limited quality data and analysis and not fully representative of country	Standardised national AMR surveillance in place and representative of country but limited number of operational sites	Surveillance in place and functional to monitor AMR trends accurately and timely but no contributing data to GLASS	National AMR surveillance regularly assessed and adjusted; and contributing to GLASS	2–
National laboratory network strengthening	No national network developed	A national network with testing according to the international standards is planned	A national reference laboratory is identified, and quality assured laboratory networks have been developed only at few surveillance sites	A national network of EQA health laboratories has been developed in most or all surveillance sites	A laboratory network is established, EQA measures are in place, and the reference laboratory has demonstrated capacity for research	1
4. Rational use of antimicrobials and surveillance of use and sale (community based)						
A national AMR containment policy for control of human use of antimicrobials; AMR stewardship (AMS)	No or weak national policy and plan, regulations for antimicrobial use, and availability	National AMS programme (AMSP) planned and under development	AMSP is developed, including tools to implement and monitor AMS progress and impact	AMSP implemented by relevant institutions. Regulations for antimicrobial use and availability are implemented in limited capacity	A national AMSP for control of human use of antimicrobials has been implemented and enforced for more than 2 years	4

Table 1 | Continued

Indicators	Phases					Phase achieved in Indonesia
	1—Exploration and adoption	2—Programme installation	3—Initial implementation	4—Full operation	5—Sustainable operation	
National Regulatory Authorities (NRA) or Drug Regulatory Authorities (DRA)	No official NRA or DRA or those existing have limited capacity	NRA or DRA with limited capacity but strategic planning in place for capacity building and appropriate budgeting	NRA or DRA system set up for oversight but not fully functional	Tools for quality assurance and registration of antibiotics in place and inspection implemented but limited capacity for enforcement of policies and regulation	Competent and functional NRA or DRA with capacity to ensuring or enforcing antibiotic quality standards, to take measures against substandard products and to inspect pharmacies	4
Surveillance of antimicrobial use and sales in humans	No guidelines for surveillance of use or sales of antimicrobials or both	National policy and plan on surveillance of use of antimicrobials under development or developed and approved but not implemented (surveillance in individual facilities and national level sales)	Monitoring sales of antimicrobials at national level not implemented. Monitoring of use is irregular and limited to few facilities that are not representative	National sales data are collected on a regular basis (every 1-2 years). Data are collected from a small and not representative sample individual healthcare facilities. No established analysis with national AMR laboratory based surveillance	National sales data are collected on a regular basis (every 1-2 years). AMU surveys are conducted in a representative sample of facilities and translated into actions. Links with national AMR surveillance data are analysed and reported	3
5. Infection prevention control and AMR stewardship programme						
AMR stewardship programme in healthcare setting	No national AMR stewardship policy or operational plan is available or approved	A national IPC or AMR policy or operational plan is available but weak. SOPs, guidelines, and protocols not available to all hospitals (limited updates)	National IPC, AMR aligned IPC, or AMR plans implemented in limited number of healthcare settings	National IPC, AMR aligned IPC, or AMR plans are implemented in about all healthcare settings	IPC or AMR measures are widely implemented and regularly evaluated and shared	3
National HAI and related AMR surveillance	No policies, limited national plan and guidelines to mandate hospitals for HAI surveillance	Few public and private facilities have HAI surveillance but data not centralised at national level	Few public and private facilities have HAI surveillance and share data at national level	Centralised data on HAI from several hospitals but with limited capacity for data analysis and detection	Monitoring and response frameworks established to identify critical HAI events, especially related to emergence of AMR indicator bacteria against critical drugs	2–
6. Research and innovation						
Research and development and innovation on AMR prevention and containment (plus research funding)	No policies fostering research environment although capacity exists for research	Policies planned and existing structure has a plan to foster research and innovation on AMR	Presence of policies and investments to foster research and innovation on AMR	Research consortium and dynamic research programme are ongoing led by government agenda	Government led research outputs related to AMR global research agenda	2
7. One Health engagement						
A national AMR containment policy and regulatory framework for control of animal use and their registration for use	No national policy or plan to reduce use of antibiotics	National policy and plan on use of antimicrobials developed and approved or regulatory framework for control of animal use and their registration for use is developed but not implemented	Implementation of policy and plan but limited capacity for monitoring use and quality of drugs	Policy and plan implemented with some capacity for monitoring but limited capacity for enforcement	Policy and plan implemented with proper capacity for monitoring and increased capacity for enforcement	2
National surveillance of AMR and use and sales of antimicrobials at national level in the veterinary sector	No or weak national policy and guidelines	Limited capacity for surveillance of sales, AMR, or AMU	Some capacity and data generated from sales, AMR or AMU	Some comparative analysis of surveillance data between AMR and AMU	Comprehensive approach of surveillance with coordinated analysis between humans and animals	2
Infection prevention and control in the animal sector	No policy and national guidelines developed for biosecurity to reduce infection rates in food and both large producers and small holders	Policies and national guidelines in line with international standards planned including vaccination policy and Codex Alimentarius standards	Limited implementation, particularly in large producers	Full implementation	Fully implemented in multiple areas with a monitoring framework in place	3
AMR awareness generation and education in the animal sector	No policies or strategies exist or are only planned	Policies or strategies developed	AMR in some pre-service training or special courses or both OR Continuous professional development and regular audit of learning	AMR in some pre-service training or special courses or both AND Continuous professional development and regular audit of learning	Effect of education programme on behaviour changes is assessed	1
NAP=national action plan; GAP-AMR=global action plan on antimicrobial resistance; AMR=antimicrobial resistance; GLASS=global AMR surveillance system; EQA=external quality assurance; API=active pharmaceutical ingredient; IPC=infection, prevention, and control; SOP=standard operating procedures; HAI=health associated infection; AMU=antimicrobial use.						

health sectors—is non-negotiable to contain AMR in the country.² Secondly, by highlighting common challenges it provides a sense of direction when building systems among all people and groups. Finally, we support the definition of what constitutes “sustainable operation” as provided by the tool, which includes funded programme operation bundled with a monitoring and evaluation mechanism for detecting, measuring, and interpreting changes over time.

Much has happened in the country on combating AMR since 2005. As shown, some concrete measures have been taken by the government. The ministry of health has recently developed the 2015-19 strategic plans for implementing existing regulations and guidelines and rolling out AMR related activities nationwide. These initiatives include piloting hospital and community based strategies to promote rational use of antibiotics. Local public awareness initiatives have also been taken up by non-governmental organisations and medical associations. Nevertheless, we acknowledge the urgent need to develop a comprehensive multisector national action plan, while simultaneously implementing existing evidence based AMR prevention and containment interventions. The immediate way forward is to establish an overarching governance system for AMR that will provide proper oversight of the problem and will implement sustainable strategies and interventions to policy makers. Also the AMR containment programme needs to urgently tackle three priority areas: surveillance of AMR and antimicrobial use in human health and livestock, a comprehensive strategy for raising awareness, and transforming national level policies to community outreach implementation across the country. Operational plans are being developed as part of the national action plan to tackle these priorities.

Our review has some limitations. Firstly, our findings are just a snapshot of the programme's situation, which is dynamic and can change for better or worse. These findings are as accurate and complete as the quality and diversity of the participants. This baseline analysis should be seen as the first step in a long process of a monitoring the national action plan led by WHO. We support this tool and its approach, which gives people working on the programmes the opportunity to share their perceptions of the challenges and needs and to discuss grading with external partners. This review provides a sense of direction for our national programme.

Secondly, the findings are based on broad review of systems, structures, and organisations rather than a quality analysis

of documents or direct observations of performance. A good level of implementation or functionality indicates that the country is taking steps to ensure that the programme is moving towards sustainable operation, in alignment with the GAP-AMR. Moreover, a fully operational programme is not necessarily effective—a step that needs further evaluations as part of the WHO roadmap. Thirdly, some areas were not well covered by the review, such as the sanitation and hygiene programme in the community and further assessment of activities in the livestock sector. Further collaboration between the Food and Agriculture Organisation of the United Nations and WHO is warranted, as is further work on harmonising the present tool with that of WHO's Joint External Evaluation (JEE) under the International Health Regulations (2005). Lastly, we hope that other countries are encouraged by this transparent and constructive process, where WHO and national participants worked together in interactive sessions to reach a consensus.

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