

Operational Actions of the Thailand Antimicrobial Resistance (AMR) Containment and Prevention Program in Response to the World Health Organization (WHO) Global Action Plan on AMR

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Abstract

The Thailand Antimicrobial Resistance (AMR) Containment and Prevention Program, utilizing a One Health approach, has been implementing the following 10 operational actions in accordance with the World Health Organization (WHO) global action plan on AMR since 2013. They are: 1) estimate the national AMR burden; 2) determine the AMR prevalence and AMR chain in Thailand; 3) develop a national AMR containment and prevention governance structure; 4) develop laboratory and information technology systems for surveillance of AMR, antibiotic use and hospital-acquired infections; 5) regulate the use and distribution of antibiotics in humans and food animals; 6) design AMR containment and prevention campaigns; 7) generate local evidence to promote responsible antibiotic use and infection prevention and control practices; 8) create the AMR campaign packages; 9) implement the AMR campaign packages in selected communities; and 10) conduct research and development of AMR surveillance, diagnostics, and therapy and prevention of AMR infections. The major outputs, outcomes and impacts of the Thailand AMR program are: the magnitude of the AMR burden in Thailand was established; AMR campaign packages for health professionals and laypeople were developed according to the established AMR chain and AMR prevalence in Thailand; and locally-generated evidence on the responsible use of antibiotics and infection prevention and control (IPC) is available. Implementation of AMR campaign packages in 4 pilot communities revealed their effectiveness in terms of improved awareness and understanding of AMR, responsible use of antibiotics, and compliance with IPC practices. Many containment and prevention measures from the Thailand AMR program have been adopted as national policy and implemented nationally.

Keywords: Thailand AMR program, World Health Organization, WHO, Global Action Plan on AMR

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บทคัดย่อ การดำเนินงานชุดโครงการควบคุมและป้องกันการดื้อยาต้านจุลชีพในประเทศไทยตามแผนปฏิบัติการการดื้อยาต้านจุลชีพขององค์การอนามัยโลก

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ผู้รับผิดชอบบทความ: วิชญ์ ธรรมลิขิตกุล

โครงการควบคุมและป้องกันการดื้อยาต้านจุลชีพในประเทศไทยได้ดำเนินการ 10 กิจกรรม ในการควบคุมและป้องกันการดื้อยาต้านจุลชีพตามแผนปฏิบัติการการดื้อยาต้านจุลชีพขององค์การอนามัยโลก ได้แก่ 1) ประเมินการระบาดของดื้อยาต้านจุลชีพในประเทศไทย 2) ระบุวงจรการดื้อยาต้านจุลชีพและพลวัตของการเกิดและการแพร่กระจายของเชื้อดื้อยาต้านจุลชีพในประเทศไทย รวมถึงความชุกของเชื้อที่สำคัญ 3) พัฒนาโครงสร้างระดับชาติในการควบคุมและป้องกันการดื้อยาต้านจุลชีพของประเทศไทย 4) พัฒนาห้องปฏิบัติการและระบบการเฝ้าระวังการดื้อยาต้านจุลชีพ เฝ้าระวังการใช้ยาต้านจุลชีพและเฝ้าระวังการติดเชื้อในโรงพยาบาล 5) ควบคุมการกระจายยาต้านจุลชีพในมนุษย์และสัตว์ที่มนุษย์เลี้ยงไว้ใช้เป็นอาหาร 6) ออกแบบการรณรงค์เพื่อป้องกันและควบคุมการดื้อยาต้านจุลชีพ 7) สร้างหลักฐานเชิงประจักษ์เพื่อสนับสนุนการส่งเสริมการใช้ยาต้านจุลชีพอย่างรับผิดชอบและการควบคุมและป้องกันการดื้อยาต้านจุลชีพในบริบทของประเทศไทย 8) พัฒนาชุดรณรงค์ต่อต้านการดื้อยาต้านจุลชีพ 9) นำชุดรณรงค์ต่อต้านการดื้อยาต้านจุลชีพไปใช้ควบคุมและป้องกันการดื้อยาต้านจุลชีพในกลุ่มเป้าหมายนำร่อง และ 10) วิจัยและพัฒนาการเฝ้าระวังการดื้อยาต้านจุลชีพ การวินิจฉัย การรักษา และการป้องกันการติดเชื้อดื้อยาต้านจุลชีพ โครงการควบคุมและป้องกันการดื้อยาต้านจุลชีพในประเทศไทยมีผลงานที่สำคัญ เช่น ทราบขนาดของปัญหาการดื้อยาต้านจุลชีพในประเทศไทย มีชุดรณรงค์ต่อต้านการดื้อยาต้านจุลชีพสำหรับประชาชนและบุคลากรสาธารณสุขที่พัฒนาอย่างสอดคล้องกับความชุกและวงจรการเกิดการดื้อยาต้านจุลชีพในประเทศไทยและได้หลักฐานของการใช้ยาปฏิชีวนะอย่างรับผิดชอบและการควบคุมป้องกันการติดเชื้อ การนำชุดรณรงค์ต่อต้านการดื้อยาต้านจุลชีพไปใช้ในกลุ่มเป้าหมายนำร่องพบว่ามีประสิทธิผลในการเพิ่มความตระหนักและความเข้าใจเกี่ยวกับการดื้อยาต้านจุลชีพ เกิดการใช้ยาต้านจุลชีพอย่างรับผิดชอบมากขึ้น และเกิดการปฏิบัติตามแนวทางการควบคุมและป้องกันการติดเชื้อมากขึ้น ผลงานของโครงการควบคุมและป้องกันการดื้อยาต้านจุลชีพในประเทศไทยถูกนำไปใช้ขับเคลื่อนแผนปฏิบัติการควบคุมและป้องกันการดื้อยาต้านจุลชีพระดับชาติแล้ว

คำสำคัญ: ชุดโครงการควบคุมและป้องกันการดื้อยาต้านจุลชีพในประเทศไทย, แผนปฏิบัติการด้านการดื้อยาต้านจุลชีพขององค์การอนามัยโลก, องค์การอนามัยโลก

Antimicrobial resistance (AMR) is a continually evolving public health crisis around the world, and it has become one of the biggest threats to global health, endangering other major priorities such as human development. It is projected that there will be 10 million AMR-related deaths each year with a 3% annual reduction in world GDP by 2050 if effective AMR containment is not implemented globally.⁽¹⁾ The most recent

attempt of the World Health Organization (WHO) to combat AMR was the launch of a global action plan on AMR at the 68th World Health Assembly in 2015.⁽²⁾ That plan is a tripartite collaborative effort among WHO, the World Organisation for Animal Health (OIE), and the Food and Agriculture Organization of the United Nations (FAO). All WHO Member States subsequently endorsed the global action plan on AMR, and they agreed to

develop their own national AMR action plans, in accordance with the global action plan, in May 2017. The political declaration of the high-level meeting of the United Nations General Assembly on AMR was issued on 21 September 2016, wherein 193 Member States committed to developing their national action plans on AMR in line with the global action plan, and they agreed to mobilize adequate resources to implement those national plans. As at June 2017, 128 Member States, including Thailand, have completed, or are completing their national action plans on AMR. In addition to the WHO global action plan on AMR, the OIE strategy on AMR and the Prudent Use of Antimicrobials,⁽³⁾ as well as the FAO Action Plan on AMR 2016–2020, were launched by OIE and FAO,⁽⁴⁾ respectively.

The Thailand Antimicrobial Resistance Containment and Prevention Program, or the Thailand AMR Program, was founded by individuals with academic and social credentials and with a history of leadership in AMR at the Faculty of Medicine, Siriraj Hospital, Mahidol University, in 2011. The program's vision is to contain and prevent the emergence and spread of important antimicrobial-resistant bacterial infections in Thailand as a 'One Health' approach by performing studies to understand the key drivers of AMR, developing effective AMR prevention and containment measures in the local context, and implementing those measures among the relevant stakeholders and pilot communities. The stepwise development of the program began in 2013 with three phases as part of a One Health approach which

covered all key drivers and stakeholders related to AMR. Phase I of the program (2013–2016) focused on humans, whereas phases II (2016–2018) and III (2017–2019) are focused on animals and plants, and the environment, respectively. Since 2013, the Thailand AMR Program has been supported by the Thai Health Promotion Foundation; Health Systems Research Institute (Thailand); Faculty of Medicine, Siriraj Hospital; Government Pharmaceutical Organization (Thailand); Agricultural Research Development Agency (Thailand); International Development Research Center (Canada); National Institute of Allergy and Infectious Diseases (NIAID); National Institutes of Health (NIH), USA; WHO; and the private sector. Since its establishment, the Thailand AMR Program has been implementing, or has executed, the following 10 operational actions: 1) estimate the national AMR burden; 2) determine the AMR prevalence and AMR chain in Thailand; 3) develop a national AMR containment and prevention governance structure; 4) develop laboratory and information technology systems for surveillance of AMR, antibiotic use and hospital-acquired infections; 5) regulate the use and distribution of antibiotics in humans and food animals; 6) design AMR containment and prevention campaigns; 7) generate local evidence to promote responsible antibiotic use and infection prevention and control practices; 8) create the AMR campaign packages; 9) implement the AMR campaign packages in selected communities; and 10) conduct research and development of AMR surveillance, diagnostics, and therapy and prevention of AMR infections. Some of the pro-

cesses, outputs, outcomes and impacts of the Thailand AMR Program have been published elsewhere.^(5,6)

This article describes some of the key operational actions of the Thailand AMR Program that have been conducted or implemented in response to the global agenda on AMR, especially the global action plan on AMR launched by WHO in 2015, which has 5 strategic objectives: 1) improve awareness and understanding of AMR through effective communication, education and training; 2) strengthen the knowledge and evidence base through surveillance and research; 3) reduce the incidence of infections through effective sanitation, hygiene and infection prevention measures; 4) optimize the use of antimicrobial medicines in human and animal health; 5) develop an economic case for sustainable investment that considers the needs of all countries, and increases the investments in new medicines, diagnostic tools, vaccines and other interventions.

The key operational actions of the Thailand

AMR Program that have been conducted or implemented in response to the global agenda on AMR, and the rationales for those actions, are presented below.

1. The global action plan on AMR proposed that an analysis of the health and economic burden of AMR on low- and middle-income countries is one of the challenges that needs to be established.

The Thailand AMR Program estimated the AMR burden in Thailand and found that there were 87,000 new AMR infections, an additional 3 million days of hospital stay, and 38,000 deaths of patients with AMR infections per year.⁽⁷⁾ The annual cost of AMR infections in Thailand was estimated at US\$200 million for the cost of antibiotics for the therapy of AMR infections, and US\$13,000 million, or 0.6% of GDP, for the total economic loss.⁽⁷⁾ The aforementioned AMR burden on Thailand does not include community-acquired AMR infections. A comparison of the health and economic burden due to AMR in the European Union

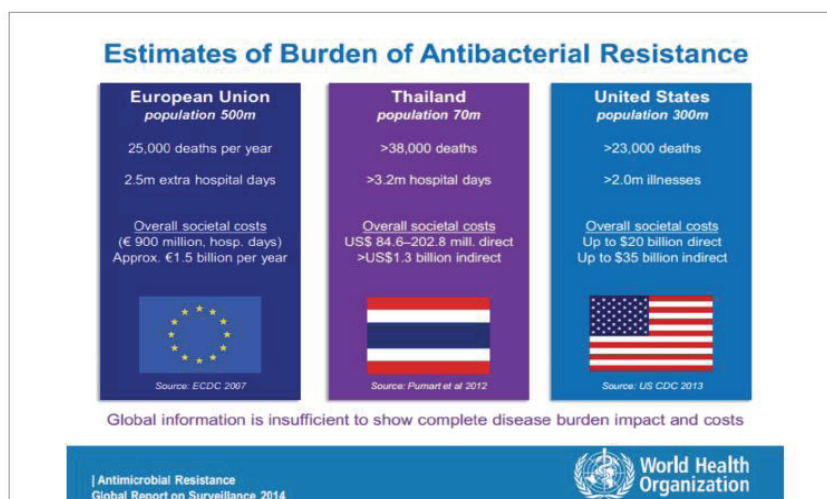


Figure 1. Comparison of health and economic burden due to AMR on the EU, Thailand and the USA

(EU), Thailand and the United States of America (USA) is at Figure 1. Although the number and proportion of deaths due to AMR infections in Thailand is higher than in the EU and USA, the economic loss is lower.

The Thailand AMR program has been communicating with the stakeholders responsible for developing the 11th revision of the International Classification of Diseases (ICD-11) to strengthen the coding system for AMR in ICD-11. This will allow the AMR burden to be estimated by collecting and analyzing information on AMR infections of patients receiving healthcare services from hospitals by using the ICD-11 codes.

2. The global action plan on AMR emphasized the concept of ‘whole-of-society engagement’, including a ‘One Health’ approach, because AMR affects everybody, regardless of where they live, or their health, economic circumstances, lifestyle or behavior. AMR also affects sectors beyond human health, such as animal health, agriculture, food security and economic development.

The scope of the Thailand AMR program includes basic and clinical medicine, veterinary science, agriculture, the environment, and the social science and economics disciplines. The spectrum of the program ranges from the molecular aspects of AMR to the containment and prevention of AMR in the community. The operational actions of the program were developed and implemented according to the One Health concept. The national AMR containment and prevention governance included all stakeholders

related to, or potential drivers of, an emergence of AMR, and they were the target groups for implementing AMR containment and prevention measures.⁽⁶⁾ The generic governance of national AMR containment and prevention as a national alliance for developing and implementing the national action plan on AMR were proposed by the Thailand AMR program to the WHO Regional Director for South-East Asia, in accordance with an agreement to perform work between the WHO South-East Asia Regional Office and the leader of the Thailand AMR program in 2015. The proposed national alliance for developing and implementing the national action plan on AMR was composed of a) a national multi-sectoral steering committee to combat AMR; b) subcommittees on the surveillance of AMR, the surveillance of antibiotic consumption and use, the promotion of responsible antibiotic use, infection prevention and control, and the research and development of AMR; and c) technical working groups under each subcommittee, as needed. The compositions, qualifications, and appointment procedures of the multi-sectoral steering committee, each subcommittee and the technical working groups were also described. Moreover, the interactions among the multi-sectoral steering committee, subcommittees and technical working groups under each subcommittee, and the national focal point-of-contact, were also proposed.

3. Strategic objective 1 of the global action plan on AMR is concerned with a) making AMR a core component of professional education, training, certification, and continuing education and



development, and b) improving awareness and understanding of AMR, and promoting behavioral change through effective communication, education and training that target the different audiences in human health, animal health, agricultural practice, consumers and laypeople.

The Thailand AMR program reviewed the contents of the educational curricula and training courses in general education (both elementary and secondary levels), Medicine, Dentistry, Veterinary Science, Nursing Education, and Pharmaceutical Sciences regarding antibiotics, antibiotic use and AMR. Analyses of health professional certifications based on the knowledge and awareness of antibiotic use and AMR were also performed. We found that the contents of the educational curricula and training courses, and of the health professional certifications related to antibiotics, antibiotic use and AMR of the aforementioned disciplines, were insufficient and needed strengthening to raise awareness and understanding of antibiotics, antibiotic use and AMR.⁽⁶⁾ The results of the curricula and health professional certification analyses, as well as specific suggestions to promote better understanding and awareness of antibiotics, antibiotic use and AMR, were submitted to the Ministry of Education and relevant health professional institutes, councils and authorities for their consideration.

The Thailand AMR program conducted a survey among 2,700 first-year university students in Thailand and found that most lacked awareness and knowledge of the responsible use of antibiotics.⁽⁸⁾ Another survey among 20,000 laypeople

in 4 pilot communities of the program in 2 provinces revealed that most lacked awareness and knowledge of the good practices for the responsible use of antibiotics and AMR prevention and containment. A further survey of antibiotics sold by 215 grocery stores and retail shops located in the pilot communities of the program was done by local people, who were instructed to either purchase specified antibiotics or present to such stores and shops with symptoms of common ailments (namely, sore throat, backache, common cold, acute diarrhea, inflamed uterus, and dysuria).⁽⁹⁾ Up to 75% of the grocery stores and retail shops in the pilot communities sold antibiotics to those local people. However, in almost all cases, antibiotics were inappropriately given. The Thailand AMR program also conducted a survey among health professionals at healthcare facilities in the pilot communities. We observed that there were many gaps that needed to be closed in the awareness, knowledge, and behavior needed for the responsible use of antibiotics and AMR prevention and containment.⁽⁶⁾

The Thailand AMR program developed AMR campaign packages for laypeople and health professionals, based on the information derived from several surveys, global evidence, and evidence in the local context generated by the program. The key messages of the campaigns were stop producing AMR through the more responsible use of antibiotics, stop transmitting and acquiring AMR through good sanitation and hygiene, and comply with infection prevention and control practices (see Figure 2). Each AMR campaign pack-



Figure 2. Core AMR campaign of Thailand Antimicrobial Resistance Containment and Prevention Program

age contained manuals, handbooks, tools (forms, devices and instruments), media (brochures, posters, videos, social media, and a hotline telephone service) and activities (education, training, social marketing, and social mobilization). All media in the AMR campaign packages developed by the Thailand AMR program are available via <http://www.hsri.or.th/amr>.

4. Strategic objective 2 of the global action plan on AMR is concerned with a) strengthening the AMR surveillance system; b) having information on the incidence, prevalence, and range across pathogens and the geographical patterns related to AMR; c) understanding how resistance develops and spreads, including how resistance circulates within and between humans and animals, and through food, water and the environment; d) developing the ability to rapidly characterizing newly emerged resistance in microorganisms; e) understanding social science and behavior and other research needed to support the achievement of other relevant objectives, including stud-

ies to support effective antimicrobial stewardship programs in human and animal health, and in agriculture; f) conducting research on the treatment and prevention measures for common bacterial infections in the local context, and translating relevant effective interventions to contain and prevent AMR; and g) developing models to assess the cost of AMR and the costs and benefits of this action plan.

The Thailand AMR program conducted a systematic review of 110 original study reports related to the electronic surveillance of infectious diseases, with an emphasis on AMR in resource-limited health-care settings.⁽¹⁰⁾ It revealed that most surveillance systems were developed and implemented in high-income countries; less than a quarter of the studies were conducted in low- or middle-income countries. Such observations highlight a lack of resources in areas where an effective, rapid surveillance system is most needed. Information technologies can be used to facilitate the process of obtaining laboratory, clinical, and



pharmacological data for the surveillance of infectious diseases, including AMR infections. These novel systems require greater resources; however, using electronic surveillance systems could result in shorter time to detect targeted infectious diseases and improved data collection. The availability of information technology for the electronic surveillance of infectious diseases, including AMR infections, will facilitate the prevention and containment of emerging infectious diseases.

The Thailand AMR program has been implementing the Global Antimicrobial Resistance Surveillance System (GLASS), according to the manual for early implementation of GLASS in human infections recommended by WHO in 2015.⁽¹¹⁾ GLASS is a case finding strategy that evaluates priority specimens routinely sent to laboratories for clinical purposes. The benefit of GLASS is that clinical data is combined with microbiological data, and deduplication of the microbiological results is performed to eliminate duplicate copies of repeating data. Another potential benefit is that supplementary clinical information (e.g., morbidity, mortality, and cost), intervention outcomes, and potential drivers of AMR can be collected upon availability of resources. GLASS facilitates the monitoring of AMR trends, and the development of antibiotic guidelines for specific types of infection based on GLASS data should be more beneficial than if based on data from laboratory-based AMR surveillance. The stepwise implementation of GLASS began at Siriraj Hospital, a 2,300-bed, tertiary care university hospital in Bangkok, in June 2016. Surveillance of blood cul-

ture specimens was implemented first, followed by feces, sputum, and urine specimens. GLASS was implemented by having infection control nurses and physicians at hospital wards use a locally developed web application program (app) installed on their smart phones to transfer blood culture specimen data and enter the clinical data of patients with a positive culture. The results of the AMR surveillance of blood culture specimens using the GLASS methodology at Siriraj Hospital are available.⁽¹²⁾ It is clear that the blood culture results from the microbiology laboratory combined with the patient clinical data obtained by GLASS had more clinical benefits and were more helpful in the development of local antibiotic treatment guidelines for patients suspected of having bacteremia than the conventional, laboratory-based, AMR surveillance system. However, GLASS consumed more time and resources than the conventional laboratory-based AMR surveillance system.

The Thailand AMR program analyzed the trends in the emergence of AMR bacteria causing common or serious infections in Thais over the past 15 years, and it proposed the following bacteria as having been AMR threats to humans in Thailand since 2014. The AMR bacteria posing an urgent threat in Thailand included extended spectrum β -lactamase (ESBL) producing Gram-negative bacteria, carbapenem-resistant *Acinetobacter baumannii*, carbapenem-resistant *Pseudomonas aeruginosa*, and carbapenem-resistant Enterobacteriaceae. The AMR bacteria presenting a serious threat included drug-resistant *Neisseria gonorrhoe-*

ae, drug-resistant *Salmonella* & *Shigella* & *Campylobacter* spp., methicillin-resistant *Staphylococcus aureus* (MRSA), drug-resistant *Streptococcus pneumoniae*, vancomycin-resistant Enterococci (VRE), and colistin-resistant Gram-negative bacteria. In February 2017, the WHO announced a priority list of 12 AMR bacteria posing the greatest threat to human health. They were classified into 3 categories: Category 1 (AMR bacteria with critical priority), comprising carbapenem-resistant *A. baumannii*, carbapenem-resistant *P. aeruginosa*, ESBL-producing Enterobacteriaceae, and carbapenem-resistant Enterobacteriaceae; Category 2 (AMR bacteria with high priority), made up of vancomycin-resistant *Enterococcus faecium*, methicillin-resistant and vancomycin-intermediate *S. aureus*, clarithromycin-resistant *Helicobacter pylori*, fluoroquinolone-resistant *Campylobacter* spp., fluoroquinolone-resistant Salmonellae, and cephalosporin- and fluoroquinolone-resistant *N. gonorrhoeae*; and Category 3 (AMR bacteria with medium priority), consisting of penicillin-non-susceptible *S. pneumoniae*, ampicillin-resistant *Haemophilus influenzae*, and fluoroquinolone-resistant *Shigella* spp.⁽¹³⁾ All AMR bacteria presenting an urgent threat to humans in Thailand belong to Category 1 (AMR bacteria with critical priority) in the WHO priority list of AMR bacteria.

The Thailand AMR program also proposed that the bacteria to be targeted for monitoring in food animals to track the emergence of AMR should include fluoroquinolone- and extended-spectrum cephalosporin-resistant *Salmonella* spp., and ESBL-producing *E. coli*. The optional list

of bacteria in food animals that could be monitored for the emergence of AMR includes fluoroquinolone- and macrolide-resistant *Campylobacter* spp., fluoroquinolone-, tetracycline- and extended-spectrum cephalosporin-resistant *Vibrio* spp., and vancomycin-resistant *Enterococcus* spp.

The Thailand AMR program developed a manual for the detection and identification of common or important bacteria in humans, and for the antibiotic susceptibility testing of the isolated pathogenic bacteria. The program also strengthened the capacity of personnel in microbiology laboratories in healthcare centers in the program's pilot communities to perform appropriate microbiological tests of clinical specimens collected from patients.

The Thailand AMR program coordinated with the Department of Livestock Development, Ministry of Agriculture and Cooperatives, to perform active surveillance of AMR bacteria in food animals from farm to market.

In addition, the program established AMR chains both in the community and in hospitals, as depicted at Figures 3 and 4, by reviewing information in literature and conducting additional studies on integrated surveillance of AMR in humans, animals, foods and the environment.^(6,9,14) Therefore, information on how AMR in Thailand develops and spreads, including how resistance circulates within and between humans and animals and through food, water, and the environment, were made available. Expanded studies on AMR bacteria contamination and antibiotic residues in the food chain and the environment are

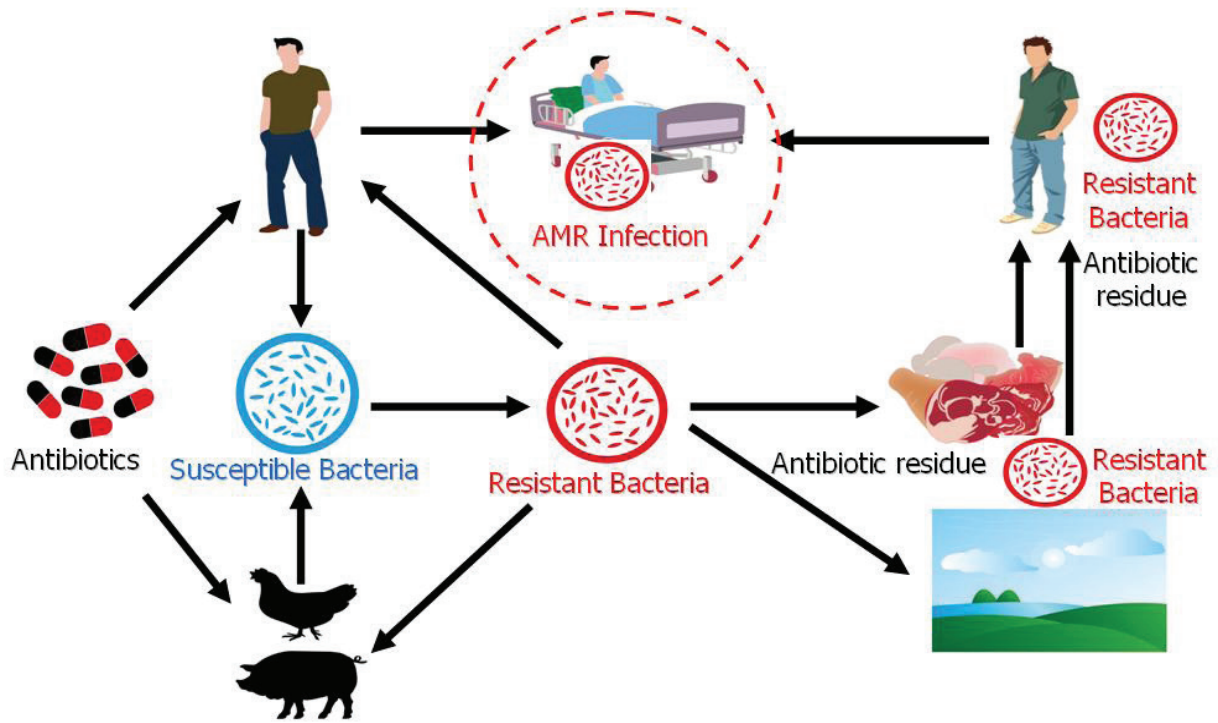


Figure 3. AMR chain in the community in Thailand

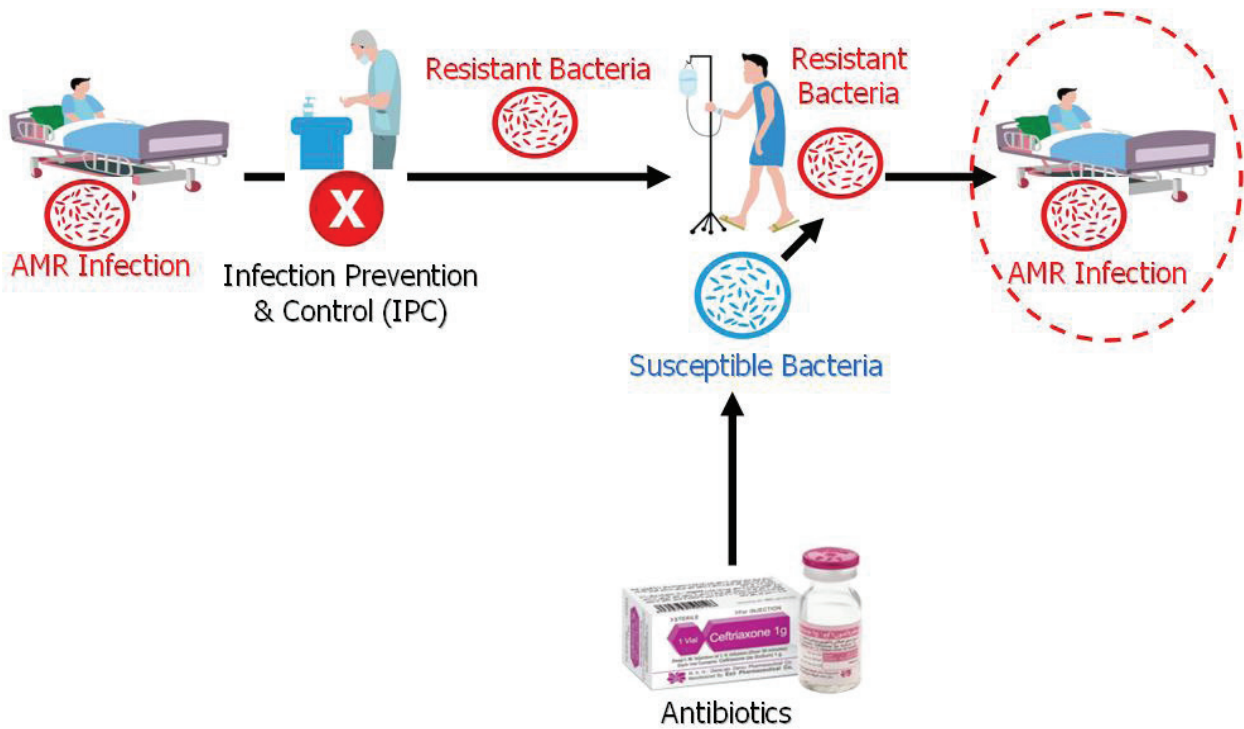


Figure 4. AMR chain in hospitals in Thailand

being conducted. The Thailand AMR program also joined the global sewage project to study the AMR genes of bacteria in sewage samples collected from many countries around the World. As well, the program joined the Tricycle project initiated by the WHO in 2017 to study the presence of ESBL-producing *E. coli* in humans, the food chain and the environment. The established AMR chains in the community and in hospitals, and the prevalence of AMR bacteria representing urgent and serious threats to Thais, were used to design the core AMR campaign to stop producing AMR through the responsible use of antibiotics, to stop transmitting and acquiring AMR through good sanitation and hygiene, and to comply with infection prevention and control practices, as mentioned earlier.

Moreover, the Thailand AMR program has been studying the mechanisms of resistance among bacteria collected from healthy people, patients, food animals, food, companion animals, and the environment over the last 4 years. The program has been collaborating with Toho University in Japan, NIH in the USA, Pathosystems Resource Integration Center (PATRIC) in the USA, and the private sector to determine the genomics of AMR bacteria in order to understand the resistance mechanisms.

The Thailand AMR program has been studying rapid tests for the detection of emerging AMR bacteria, including carbapenem- and colistin-resistant Gram negative bacteria. The program has been collaborating with the private sector to develop a simple, innovative device to detect

AMR bacteria within several hours.

In addition, the program has been generating local evidence to assist with the promotion of the responsible use of antibiotics; with effective interventions to contain and prevent healthcare-associated infections; with the diagnosis, treatment and prevention of common or important infections, including AMR bacterial infections; and with the review of effective interventions to contain AMR in the local context.^(9,15-59) This evidence was used to develop and implement the AMR campaign packages described earlier.

Finally, the program performed a cost-effectiveness analysis of the infection prevention and control (IPC) program in a hospital, finding that the IPC program was cost-effective.⁽⁶⁰⁾ This evidence should convince the relevant policy makers to promote the IPC program and to allocate sufficient resources to IPC programs in individual hospitals.

5. Strategic objective 3 of the global action plan on AMR is concerned with the reduction in the incidence of infections through effective sanitation, hygiene, and infection prevention measures.

The Thailand AMR program implemented an AMR campaign package for the health personnel of the public hospitals in the pilot communities of the program. The package comprised a handbook for infection prevention and control in a hospital setting; tools for the surveillance of hospital-acquired infections; devices for isolation precautions; the installation of alcohol hand-rubs at each patient's bed, common areas in patients'



wards, and emergency rooms; the use of more efficient antiseptics (namely, 2% chlorhexidine in 70% alcohol for use for skin antiseptics before performing invasive procedures, and 2% chlorhexidine in water as a mouth-care solution for the prevention of ventilator-associated pneumonia); and training courses for relevant health personnel to increase compliance with the infection prevention and control measures. Implementation of this campaign package in the pilot communities of the program led to an improvement in many indicators of infection prevention and control, such as a higher hand-hygiene compliance and a decline in some hospital-acquired infection rates.⁽⁶⁾

Moreover, the program has been coordinating with the Department of Livestock Development, Ministry of Agriculture and Cooperatives, to facilitate the use by key stakeholders of biosecurity practices for food animals, to encourage the development of autogenous vaccines for the prevention of infections in food animals, and to conduct studies on the use of alternatives to antibiotics in food animal production.⁽⁶¹⁾ These measures should result in a reduction in antibiotic use in the near future, and they may delay the emergence of AMR bacteria in food animals.

6. Strategic objective 4 of the global action plan on AMR is concerned with optimizing the use of antimicrobial medicines in humans and animals.

The Thailand AMR program has been coordinating with the Food and Drug Administration (FDA), Department of Livestock Development and other relevant stakeholders in Thailand to regulate antibiotic distribution and use in food animals and

humans since 2015.

As for antibiotic distribution and use in food animals, the following actions have been employed: a) existing registered antibiotics have not been allowed to be used as a growth promoter in food animals, in accordance with a regulation of the Ministry of Agriculture and Cooperatives, since August 2015; b) the registration of antibiotic to be used as a growth promoter in food animals is no longer permitted by the FDA; c) the FDA deleted all indications of growth promotion properties from the labels of existing antibiotics registered for use in food animals; e) the importation, production or sale of certain pharmaceutical chemicals (e.g., fluoroquinolones, cephalosporins, and polymyxins) for use in food animals has to be reported to the FDA more often, and they will be closely monitored; f) certain classes of antibiotics are no longer permitted for use in the prevention and control of infections in food animals; g) all finished products belonging to selected antibiotic classes (e.g., fluoroquinolones, cephalosporins, polymyxins) to be used in food animals have been reclassified as restricted drugs and must be prescribed by veterinarians; h) a medicated premix with an inclusion rate of ≤ 2 kg/ton can only be sold to animal feed factories that have received Good Manufacturing Practice (GMP) certification; i) medicated feeds will be exempted from being classified as drugs, and they will be controlled under the Animal Feed Quality Control Act of the Ministry of Agriculture and Cooperatives; j) the FDA will reject applications for the use in food animals of any new antibiotics that have

been designed for human care (e.g., carbapenems); k) colistin is not permitted to be used for the prevention of infections in food animals, and it can only be used for the treatment of food animal infections on a short-term basis under the supervision of a veterinarian. The aforementioned actions are in accordance with WHO Guidelines on Use of Medically Important Antimicrobials in Food-Producing Animals.⁽⁶²⁾

As for the reclassification of antibiotic distribution and use in humans, an appropriate balance between ‘access to antibiotics’ and ‘excessive use of antibiotics’ as well as the list of critically-important antibiotics have been taken into account. Several antibiotics (such as the oral formulation of colistin sulphate) have been deregistered by the FDA. Many antibiotics have been reclassified from ‘dangerous drugs’ to ‘restricted drugs’ that require prescriptions from physician. The restricted antibiotics can be distributed via quality pharmacies, medical clinics, general hospitals, special hospitals, and central distributors. Reclassification of the antibiotics for human use is now finalized by a subcommittee and is subject to a public hearing.

The Thailand AMR program implemented the AMR campaign package for laypeople to 6,000 village health volunteers and 300,000 people in the pilot communities of the program. Evaluation of the campaign’s implementation by the 6,000 village health volunteers and 20,000 people revealed that the awareness, knowledge and behavior needed for the responsible use of antibiotics and AMR prevention and containment among

these individuals were much improved.⁽⁶⁾ Assessment for behavioral change on responsible use of antibiotics and AMR prevention and containment of the people after implementing AMR campaign package using a proxy composite indicator is being conducted in the pilot communities.

Moreover, the Thailand AMR program implemented an AMR campaign package promoting the responsible use of antibiotics by healthcare personnel in 65 public health facilities in the pilot communities. An improvement in many indicators of the responsible use of antibiotics was subsequently observed.⁽⁶⁾

Since 2015, the Thailand AMR program has also been collaborating with the Rational Drug Use Hospital (RDU Hospital) project to promote the responsible use of antibiotics for 4 targeted conditions, namely, acute respiratory infections, acute diarrhea, fresh traumatic wounds in ambulatory patients, and the vaginal delivery of a normal term labor. The targeted percentages of antibiotic use for these conditions were derived from the local evidence generated by the program, and they are $\leq 20\%$ for acute respiratory infections and acute diarrhea, $\leq 40\%$ for fresh traumatic wounds, and $\leq 10\%$ for the vaginal delivery of a normal term labor. Decreasing trends for the use of antibiotics for these 4 conditions have been observed at many healthcare facilities nationwide.⁽⁶⁾ In addition, the Thailand AMR program has been collaborating with the Ministry of Public Health in the implementation of the 15th service plan to promote the responsible use of antibiotics for the aforementioned 4 conditions, as well as to en-



courage the adoption of infection prevention and control measures to contain AMR at all levels of public healthcare facility since 2016. A steady decline in the rates of antibiotic use for the 4 conditions has been observed.

Furthermore, the Thailand AMR program is implementing an antimicrobial stewardship program for hospitalized patients on a pilot scale to determine the feasibility, utility and effectiveness of the stewardship program before disseminating it to other healthcare facilities nationally. Similarly, the Thailand AMR program is collaborating with the Center for Disease Dynamics, Economics and Policy (CDDEP) on conducting Hospital Antibiotic Stewardship Programs.

The Thailand AMR program is working jointly with the WHO and its international network on conducting a national point prevalence survey on antibiotic use, antibiotic consumption, and AMR at hospitals. The data obtained at the national level will be invaluable in estimating the magnitude of antibiotic consumption, inappropriate antibiotic use, the AMR burden and the areas needing to be improved. Moreover, such data can be used as a baseline to monitor and evaluate the effectiveness of the implementation of the national action plan for AMR.

7. Strategic objective 5 of the global action plan on AMR is concerned with developing an economic case for sustainable investment that takes cognizance of the needs of all countries, and increases the investments in new medicines, diagnostic tools, vaccines, and other interventions.

The Thailand AMR program has been collect-

ing AMR bacteria isolated from healthy people, patients (colonization and infection), food animals, foods, companion animals, and the environment. Our repository of bacteria contains more than 5,000 isolates of ESBL-producing Gram-negative bacteria, carbapenem-resistant *Acinetobacter baumannii*, carbapenem-resistant *Pseudomonas aeruginosa*, carbapenem-resistant Enterobacteriaceae, drug-resistant *Neisseria gonorrhoeae*, drug-resistant *Salmonella* spp., MRSA, drug-resistant *Streptococcus pneumoniae*, VRE, and colistin-resistant Gram-negative bacteria. This repository of bacteria from known sources of collection is invaluable for the in vitro testing of the compounds that are candidates for becoming antibacterial agents. The Thailand AMR program tested some old antibiotics, novel chemical compounds, and the compounds extracted from herbs and seaweeds for antibacterial activities using the bacteria in the repository. The program has also provided some isolates of AMR bacteria from its repository to academic institutes and the private sector to study the mechanisms of AMR in order to develop new agents.

The Thailand AMR program has been cooperating with academic institutes and the private sector on multicenter and multinational studies on the efficacy and safety of new antibacterial agents (e.g., cefiderocol) and combinations of antibiotics (e.g., colistin plus carbapenems) for the therapy of extremely-drug resistant Gram-negative bacterial infections.

As well, the program has been collaborating with the Drugs for Neglected Diseases initiative

(DNDi) in facilitating the research and development of the unmet-need antibiotics for the therapy of antibiotic-resistant infections.

In summary, many of the key actions for Member States recommended in the WHO global action plan on AMR have been performed, are being conducted, or will be completed in the near future by the Thailand AMR program. The implications of the actions that have been done by the program including some processes and outputs of the program have been adopted as national policy on the responsible use of antibiotics and infection prevention and control to contain AMR in healthcare settings since October 2016. The lessons and experiences learned from the Thailand AMR program should be able to be used in the implementation of the action plan on AMR as a One Health approach at the national level of Thailand and other Member States.

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