

STOP Antimicrobial Resistance: Everybody's Business

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Antimicrobial resistance has been recognized as an important, serious and urgent global health threat over the past few decades.^{1,2} The main contributors to antimicrobial resistance are overuse of antimicrobials in humans and non-humans, poor hygiene and sanitation, and inefficient prevention and control of infections in healthcare settings. Major and important antimicrobial resistant bacteria causing serious infections in Thailand are extended-spectrum β -lactamase (ESBL)-producing Enterobacteriaceae, carbapenem-resistant non-fermenters (*Pseudomonas aeruginosa* and *Acinetobacter baumannii*) and methicillin-resistant *Staphylococcus aureus* (MRSA).³⁻⁸ Antimicrobial resistance has enormous health and economic impacts. Analysis of the health burden of antimicrobial resistance in Thailand based on the national data of 2010 revealed that at least 90,000 hospitalized patients per year had infections caused by antimicrobial resistant bacteria and approximately 30,000 of these patients died.⁹ Furthermore, antimicrobial resistant bacterial infections resulted in at least 3 million excess days of hospitalization.⁹ The cost of antimicrobials for treatment of these antimicrobial resistant infections was US\$ 200 million, and the total annual cost of antimicrobial resistance was at least US\$ 1 billion when the morbidity and mortality of the patients with antimicrobial resistant bacterial infections were taken into account.⁹ Therefore, antimicrobial resistance burden in Thailand has consumed 0.6% of gross domestic product (GDP) of the country.

Antimicrobial resistance chains or dynamics of emergence of antimicrobial resistance in

community and in hospital in Thailand are well defined and documented.

Antimicrobial resistance chain in community in Thailand is illustrated in Fig 1. Antimicrobial resistance in community begins with the use of antimicrobials in humans and in non-humans, especially in food animals. Antimicrobial use for people in community seeking care from drug stores and hospitals in Thailand is very prevalent and is often inappropriate.¹⁰⁻¹³ Antimicrobials are usually given for minor self-limiting ailments that do not need antimicrobials, such as upper respiratory tract infection, acute bronchitis, acute diarrhea, and simple fresh traumatic wound.¹⁰⁻¹³ The evidence from meta-analysis revealed that individuals who received short courses of antimicrobials in primary care for common community-acquired illnesses, such as respiratory or urinary tract infection, could induce antimicrobial resistance within the month immediately after treatment and might persist for up to 12 months.¹⁴ The association between antimicrobial resistance and the amount and duration of antimicrobial use was also observed.¹⁴ The prevalence of ESBL-producing Enterobacteriaceae in feces of asymptomatic individuals in Thailand has been quite high, from 29% to 93%.¹⁵⁻¹⁹ Risk factors associated with fecal carriage of these resistant bacteria include being animal farm workers, prior hospitalization, use of antimicrobials without prescription, and use of antimicrobials within the last 3 months. Antimicrobial resistant bacteria from these individuals can be transmitted to foods, water, our environment and other people. Antimicrobial use for enhancing growth and preventing infection in food animals is also very common

in Thailand. There are more than 1,700 antimicrobial formulations registered with Thai Food and Drug Administration to be used in animals. Antimicrobial use in food animals, especially its use as herd consumption, is associated with antimicrobial resistance in enteric flora of those animals. The prevalence of ESBL-producing Enterobacteriaceae in feces of asymptomatic pigs and chickens in the farms in selected areas in Thailand is high.¹⁹ Antimicrobial resistant bacteria from these food animals can be transmitted to foods, water, our environment and people. ESBL-producing Enterobacteriaceae are isolated from fresh meat at slaughterhouses, fresh foods, cooked foods, canal water and water sources in animal farms.^{19,20} Moreover, antimicrobial resistance in bacteria living in the environment could be induced by their exposure to low concentrations of antimicrobials in feces and urine of humans and animals receiving antimicrobials that are contaminating the environment. Antimicrobial resistant plasmids in a particular species of bacteria can be transferred to other species of bacteria in humans, animals and environment leading to a widespread antimicrobial resistance. Therefore, the foods along the production chain from farm to consumer and the environment in Thailand are contaminated with antimicrobial resistant bacteria transmitted from humans and animals. Consumption of foods and water contaminated with antimicrobial resistant bacteria results in colonization of or infection due to antimicrobial resistant bacteria. The prevalence of colonization with ESBL-producing Enterobacteriaceae in the gastrointestinal tract of travelers from Sweden, the Netherlands, and Australia was from 2.4% to 8.6% prior to travel, but increased to 30% to 49% following travel to Asia including Thailand.²¹⁻²³ Risk factors of acquiring antimicrobial resistant bacteria in these travelers include traveling to the Indian subcontinent and Asia, and taking antimicrobials while traveling. Traveler's diarrhea associated with ESBL-producing pathogens has also been observed among patients returning from Thailand.²⁴ Ingestion of foods contaminated with leftover antimicrobials can also induce developing antimicrobial resistance in the bacteria colonizing the gastrointestinal tract of the consumers. Antimi-

crobial resistant bacteria can initially cause a silent carrier state and may later cause infections, such as urinary tract or abdominal infections caused by ESBL-producing *E.coli*. Thai individuals with colonization with antibiotic resistant bacteria, such as ESBL-producing Enterobacteriaceae in their gastrointestinal tract, are at risk of developing antimicrobial resistant infection.²⁵ The prevalence of community-acquired infections caused by ESBL-producing Enterobacteriaceae in Thailand, including urinary tract infection and sepsis, has been increasing.^{26,27} Patients with infections due to ESBL-producing Enterobacteriaceae were more likely to die, had prolonged hospitalization, and had higher hospitalization costs than those infected with ESBL-non-producing Enterobacteriaceae.²⁵

Antimicrobial resistance chain in hospital in Thailand is illustrated in Fig 2. Some hospitalized patients have community-acquired antimicrobial resistant infections and some have hospital-acquired infections. Hospital-acquired infection, infection that occurred after hospitalization for at least 48 hours, is common in Thailand and most of these infections are caused by antimicrobial resistant bacteria, including ESBL-producing Enterobacteriaceae, carbapenem-resistant *P.aeruginosa* and *A.baumannii*, and MRSA.^{3-8,28-31} Antimicrobial resistance in hospital is usually related to inappropriate use of antimicrobials and inefficient infection prevention and control. Inappropriate use of antimicrobials for surgical prophylaxis and therapy of suspected or documented infections in hospitalized patients in Thailand is very prevalent, from 25% to 92%.³²⁻³⁴ Many hospital-acquired infections caused by antimicrobial resistant bacteria in Thailand can be prevented with infection prevention and control measures, especially hand hygiene, barrier precautions and environmental decontamination.³⁵⁻³⁷ However, the compliance with a single most effective and basic infection prevention and control measure, hand hygiene, of many healthcare personnel in many Thai hospitals is still inadequate.³⁸⁻⁴¹

The aforementioned antimicrobial resistance burdens and antimicrobial resistance chains indicate that antimicrobial resistance in Thailand is also an important, serious and urgent health threat, and containment and prevention of antimicrobial

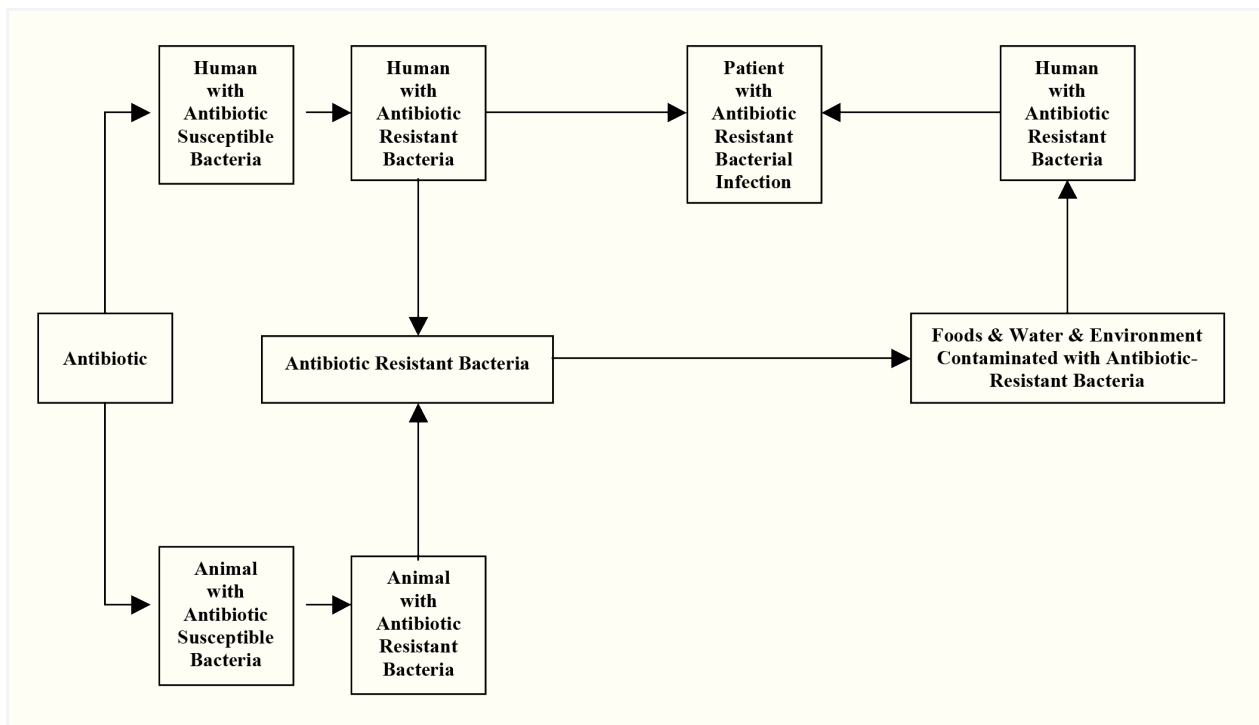


Fig 1. Antimicrobial Resistance Chain in Community in Thailand.

resistance in Thailand is urgently needed. The Antimicrobial Resistance Containment and Prevention Program in Thailand under generous support from the Thai Health Promotion Foundation, Health Systems Research Institute (Thailand), Faculty of Medicine Siriraj Hospital, Mahidol University, and International Development Research Center (Canada), has been implemented in Thailand since 2013. The goals of the program are to develop national infrastructure of antimicrobial resistance containment, to develop antimicrobial resistance containment measures and campaigns in terms of antimicrobial resistance surveillance, antimicrobial use surveillance, responsible use of antimicrobials as well as infection prevention and control, and to implement such antimicrobial resistance containment measures and campaigns to all responsible stakeholders in order to delay, reduce or eliminate antimicrobial resistance, and to ultimately minimize the health and economic burdens of antimicrobial resistance in Thailand. The key components of the antimicrobial resistance containment and prevention package in Thailand include 1) fundamental systems development for antimicrobial resistance containment and prevention, 2) research and development of antimicrobial resistance containment and prevention

measures, and 3) implementation of antimicrobial resistance containment and prevention bundles in selected areas of Thailand.

The fundamental systems development for antimicrobial resistance containment and prevention includes facilitating establishment of national infrastructure of antimicrobial resistance containment and prevention; facilitating legislation of banning over-the-counter sale of selected antimicrobials and non-therapeutic use of antimicrobials in animals; facilitating development of laboratory facility and information technology for surveillance of antimicrobial resistance and antimicrobial use; developing manuals, tools and media for responsible use of antimicrobials and infection control for responsible human and animal health personnel, patients and publics; raising awareness on antimicrobial resistance of all relevant stakeholders; campaigning containment and prevention of antimicrobial resistance of all relevant stakeholders; coordinating with the responsible institutes to incorporate antimicrobial resistance and responsible use of antimicrobials in health and non-health educational curricula and professional trainings; proposing antimicrobial resistance and responsible use of antimicrobials as being the criteria for hospital accreditation,

pay-for-performance and quality of care audit; and organizing new business model for selling and distributing the reserved antimicrobials and orphan antimicrobials.

The research and development of antimicrobial resistance containment and prevention measures includes generating local evidence for promoting responsible use of antimicrobials and efficient practices for infection control in local context of limited-resource setting; testing the activity of oral antimicrobials that could be used for therapy of antimicrobial resistant bacterial infections in out-patient setting; and conducting research on innovative therapy and prevention of antimicrobial resistant infections.

The implementation of antimicrobial resistance containment bundles in selected areas is to develop prototype antimicrobial resistance containment community with culture norm of responsible use of antimicrobials, safety culture to prevent infection, and minimum antimicrobial resistance burden; and to determine the resources and benefits of such implementation. Several target districts, including healthcare facilities, farms and people, in several provinces in Thailand are selected. The information on knowledge, attitude and practice on antimicrobial resistance, infection control, and responsible use of antimicrobials of the relevant stakeholders in the target districts will be collected, analyzed, and used for developing antimicrobial resistance containment bundles which will be later implemented in the target districts. The antimicrobial resistance containment bundles are practical guides, manuals, tools, media, trainings and social marketing activities related to antimicrobial resistance, responsible use of antimicrobials, and infection

prevention and control practices. The indicators related to antimicrobial resistance, responsible use of antimicrobials, and infection prevention and control practices before and after implementing the antimicrobial resistance containment bundles in the target districts will be collected, analyzed and compared. The effectiveness and efficiency of the implementation of antimicrobial resistance containment bundles in the prototype communities will be considered prior to developing stepwise to a nationwide scale.

The logo and motto of the campaign for Antimicrobial Resistance Containment and Prevention Program in Thailand is “STOP AntiMicrobial Resistance” or “STOP AMR” as illustrated in Fig 3. The word “STOP” in the campaign refers to “action” to discontinue or avoid inappropriate behaviors and practices along the antimicrobial resistance chains in community and in hospital which have been illustrated in Fig 1 and Fig 2.



Fig 3. Logo and motto of the campaign for antimicrobial resistance containment and prevention in Thailand.

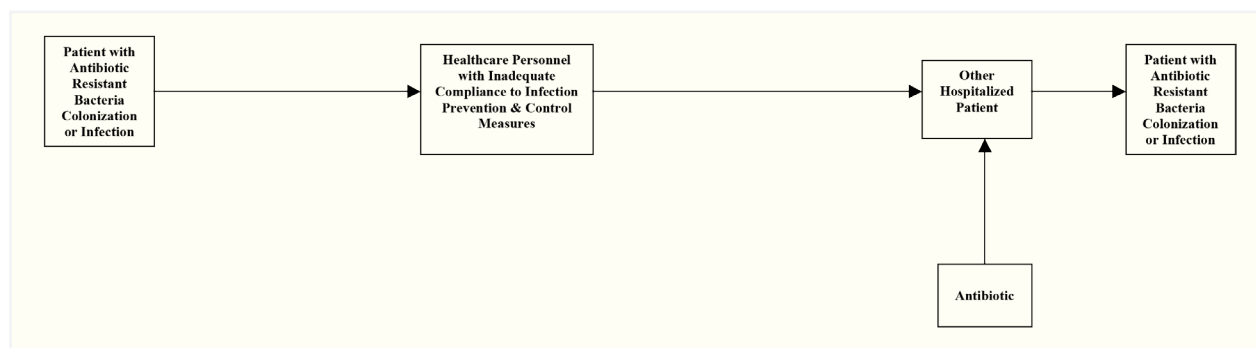


Fig 2. Antimicrobial Resistance Chain in Hospital in Thailand.

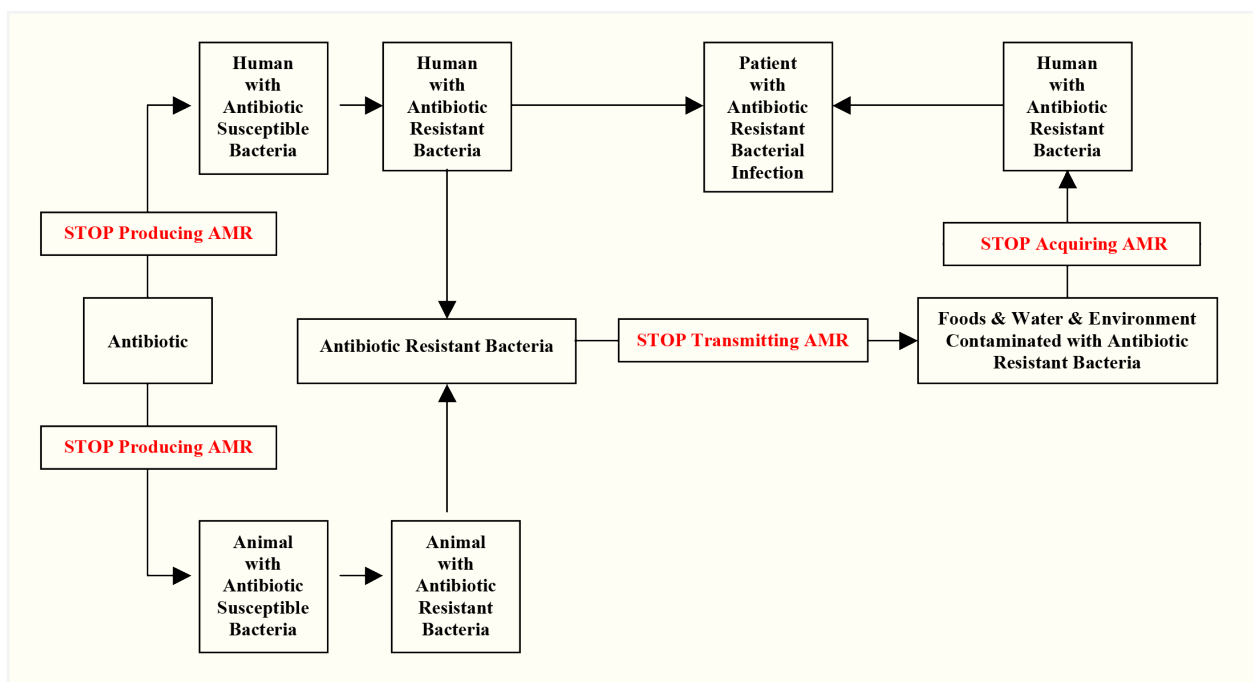


Fig 4. Key behaviors to contain and prevent antimicrobial resistance in community.

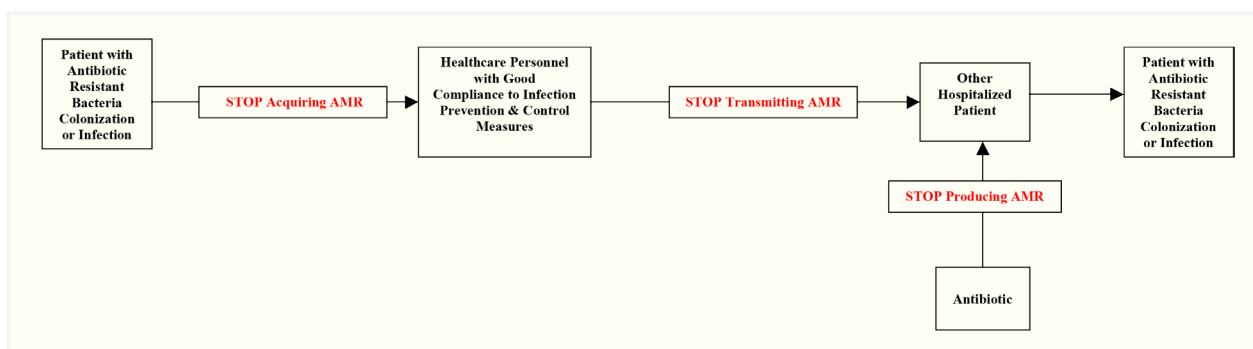


Fig 5. Key behaviors to contain and prevent antimicrobial resistance in hospital.

Key behaviors and practices for containing and preventing antimicrobial resistance in community are illustrated in Fig 4. “STOP Producing AMR” can be performed by responsible use of antimicrobials whereas “STOP Acquiring AMR” and “STOP Transmitting AMR” should be done via good personal and interpersonal sanitation and hygiene.

Key behaviors and practices for containing and preventing antimicrobial resistance in hospital are illustrated in Fig 5. “STOP Producing AMR” can be performed by responsible use of antimicrobials whereas “STOP Acquiring AMR” and “STOP Transmitting AMR” should be done via good compliance with infection control practices of healthcare personnel and relevant sectors.

Antimicrobial resistance is similar to global warming in terms of the causes, effects and impacts. Both phenomena are caused by human and they affect other people in addition to those who create the problems, and they involve non-renewable global resources. Antimicrobial resistance is much worse than global warming since the antimicrobial resistant pathogens can be directly or indirectly transmitted from one person to other people and environment. Therefore, containment and prevention of antimicrobial resistance is everybody’s business. It is hoped that the antimicrobial resistance burden in Thailand should be delayed, reduced or eliminated in the near future if everybody adopts the aforementioned 3 key behaviors and practices, namely, “STOP

Producing AMR”, “STOP Acquiring AMR” and “STOP Transmitting AMR” which are applicable to everyone.

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