Thailand's One Health Report

on Antimicrobial Consumption and Antimicrobial Resistance in 2018

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This Report was developed on behalf of
the National Steering Committee
on Antimicrobial Resistance.

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Editor:
Thai working group on Health Policy and Systems Research on Antimicrobial Resistance (HPSR-AMR)
International Health Policy Program, Ministry of Public Health, Thailand

Published by:
International Health Policy Program, Ministry of Public Health, Thailand

Address:
Ministry of Public Health,
Tiwanon Rd. Nonthaburi 11000, Thailand
Phone: +66 (0) 2590-2366-7
Fax: +66 (0) 2590-2385

Suggested citation:
National Steering Committee on Antimicrobial Resistance of Thailand, 2020.
Thailand's One Health Report on Antimicrobial Consumption and Antimicrobial Resistance in 2018.

This report is available at www.ihppthaigov.net

ISBN:
978-616-11-4154-7

Layout:
International Health Policy Program, Ministry of Public Health, Thailand

First published:
January 2020

Correspondence:
Any correspondence relating to this report should be sent by e-mail to: hpsr_amr@ihpp.thaigov.net

Acknowledgments

All of the people working in the human and animal sectors
in Thailand who have contributed to the data used in this report are acknowledged.

The funding of this report is made possible by
the World Health Organization Country Cooperation Strategy (WHO-CCS),
which is a multi-funding platform contributed by
the World Health Organization and the Royal Thai Government, and their partners including
Ministry of Public Health, Thai Health Promotion Foundation, National Health Security Office,
Health Systems Research Institute and National Health Commission Office,
and is greatly appreciated.

Foreword

On behalf of the National Steering Committee on Antimicrobial Resistance, I welcome the publication of Thailand's One Health Report on Antimicrobial Consumption and Antimicrobial Resistance.

The Committee monitors and oversees the implementation of Thailand's first National Strategic Plan on Antimicrobial Resistance 2017-2021 (NSP-AMR), which was endorsed by the Cabinet in August 2016. The development of this report was one of the responses to the strategic objectives of the NSP-AMR. This report was produced through a collaborative process involving professionals working in the human and animal health sectors in Thailand.

The development of this report is guided by two principles: the 'One Health' approach which recognizes the interconnectivity across human, animal and environmental health; and the 'Triangle that Moves the Mountain' concept which emphasizes the importance of resolving complex intersectoral issues through policy engagement and social movement guided by evidence.

This report provides data in 2018, and compares it with 2017 baseline data for the monitoring of NSP-AMR (2017-2021) strategic goals. The plan makes the commitment by 2021 to reduce morbidity attributable to antimicrobial resistance by 50.0%; reduce antimicrobial consumption by 20.0% in the human sector and 30.0% in the animal sector; and increase the proportion of the population shown to have a predefined basic level of knowledge and awareness of antimicrobial resistance by 20.0%.

We also expect that in future reports, data on consumption in humans and animals will allow for assessment of the relationship between antibiotic consumption and resistance in both sectors.

We thank the members of the Thai working group on Health Policy and Systems Research on Antimicrobial Resistance (HPSR-AMR) and the International Health Policy Program, Ministry of Public Health, Thailand for their contribution to the development of this report, in particular the authors of each chapter.

We fully believe that cross-sectoral cooperation based on the One Health approach can effectively address antimicrobial resistance.

Dr. Paisarn Dunkum
Secretary-General of Food and Drug Administration
On behalf of the National Steering Committee on Antimicrobial Resistance

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Abbreviations and Acronyms

AI	Active ingredient
ACFS	Agricultural Commodity and Food Standards
AMC	Antimicrobial consumption
AMR	Antimicrobial resistance
AMU	Antimicrobial use
API	Active pharmaceutical ingredient
ASP	Antimicrobial Stewardship Programs
AST	Antimicrobial susceptibility testing
ATC	Anatomical Therapeutic Chemical
Aw	Average weight at the time of treatment
BIDI	Bamrasnaradura Infectious Disease Institute, Ministry of Public Health, Thailand
BSI	Bloodstream infection
CAUTI	Catheter-associated urinary tract infection
CIA	Critically Important Antimicrobials
CLABSI	Central Line-associated Bloodstream Infection
CLSI	Clinical and Laboratory Standards Institute
CRE	Carbapenem-resistant *Enterobacteriaceae*
DDD	Defined Daily Dose
DID	Defined Daily Dose per 1,000 inhabitants per day
DLD	Department of Livestock Development, Ministry of Agriculture and Cooperatives, Thailand
DOF	Department of Fishery, Ministry of Agriculture and Cooperatives, Thailand
ECV	Epidemiological cutoff value
EFSA	European Food Safety Authority
ESAC-Net	European Surveillance of Antimicrobial Consumption Network
ESBLs	Extended-spectrum beta-lactamases
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption
EUCAST	European Committee on Antimicrobial Susceptibility Testing
FAO	Food and Agriculture Organization
FDA	Food and Drug Administration, Ministry of Public Health, Thailand
GI	Gastrointestinal
GLASS	Global Antimicrobial Resistance Surveillance System
HAI	Hospital-associated infection
HPSR-AMR	Health Policy and Systems Research on Antimicrobial Resistance
I	Intermediate
ICNs	Infection Control Nurses
ICU	Intensive care unit
ICWNs	Infection Control Ward Nurses
IHPP	International Health Policy Program, Ministry of Public Health, Thailand
IPC	Infection prevention and control
ISO	International Organization for Standardization
JEE	Joint External Evaluation of International Health Regulations (IHR) 2005
Kg	Kilogram
MDR	Multidrug resistance
MIC	Minimum inhibitory concentration
MOPH	Ministry of Public Health, Thailand

MRCNS	Methicillin-resistant coagulase-negative *Staphylococcus* spp.
MRSA	Methicillin-resistant *Staphylococcus aureus*
NARST	National Antimicrobial Resistance Surveillance Center, Thailand
NWT	Non wild-type
NSP-AMR	National Strategic Plan on Antimicrobial Resistance
OIE	World Organization for Animal Health, or Office International des Epizooties
PCU	Population Correction Unit
PLO	Provincial Livestock office, Department of Livestock Development
PLWH	People living with HIV
PNSP	Penicillin non-susceptible *S. pneumoniae*
PRSP	Penicillin-resistant *S. pneumoniae*
R	Resistant
RIT	Repeat infection timeframe
S	Susceptible
SAC	Surveillance of Antimicrobial Consumption
SDD	Susceptible-dose dependent
SSI	Surgical site infection
STIs	Sexually Transmitted Infections
UTI	Urinary tract infection
VAP	Ventilator-associated pneumonia
VRE	Vancomycin resistant *Enterococcus*
WHO	World Health Organization
WT	Wild type

Types and Abbreviations of Antimicrobials

Antibiotic name	Code*
Penicillins	
Ampicillin	AMP
Ampicillin/sulbactam	SAM
Amoxicillin/clavulanic acid	AMC
Cloxacillin	OB
Methicillin	Meth/MRSA
Oxacillin	OX
Penicillin	P
Piperacillin/tazobactam	TZP
Cephalosporins	
Cefazolin	CZ**
Cefepime	FEP
Cefixime	CFM
Cefoperazone/sulbactam	SCF
Cefotaxime	CTX
Cefoxitin	FOX
Cefpodoxime	CPD
Ceftazidime	CAZ
Ceftriaxone	CRO
Cefuroxime sodium	CXM
Carbapenems	
Ertapenem	ETP
Imipenem	IPM
Meropenem	MEM
Fluoroquinolones	
Ciprofloxacin	CIP
Levofloxacin	LEV
Nalidixic acid	NA
Norfloxacin	NOR
Ofloxacin	OFX

Antibiotic name	Code*
Macrolides	
Azithromycin	AZM
Erythromycin	E
Tetracyclines	
Tetracycline	TE
Amphenicols	
Chloramphenicol	C
Lincosamides	
Clindamycin	CC**
Sulfonamides	
Sulfamethoxazole	SUL
Trimethoprim	TMP**
Trimethoprim/sulfamethoxazole	SXT
Aminoglycosides	
Amikacin	AK
Gentamicin	GM**
Netilmicin	NET
Streptomycin	S
Spectinomycin	SPT**
Glycopeptides	
Teicoplanin	TEC
Vancomycin	VA
Miscellaneous	
Colistin	CL**
Fosfomycin	FOS
Nitrofurantoin	F

*Thermo Scientific™ Oxoid™ Antimicrobial Susceptibility Disks

**BBL™ Sensi-Disc™ Antimicrobial Susceptibility

Glossary

Antimicrobial consumption (AMC)

Antimicrobial consumption is the quantity of consumption of antimicrobial drugs, which can be measured at the national level as the quantity of its production plus imports minus the quantity of its exports. AMC can be expressed as the number of Defined Daily Doses (DDDs) per 1,000 inhabitants per day for human antimicrobials, and milligram per Population Correction Unit, modified by Thailand ($mg/PCU_{Thailand}$) for food-producing animals.

Antimicrobial resistance (AMR)

AMR is the ability of microbes (e.g. bacteria, viruses and fungi) to grow or survive even after exposure to antimicrobial agents at concentrations that are normally sufficient to inhibit or kill that particular strain of organism. In this report, AMR predominantly means AMR in bacteria.

Antituberculous drug

Antituberculous drugs in Thailand Surveillance of Antimicrobial Consumption (Thailand SAC) are drugs used solely for treatment of tuberculosis; however, this may or may not include certain groups of drugs such as macrolides, fluoroquinolones and ansamycins due to their other indications for non-mycobacterial infections.

Antimicrobial agent

Antimicrobial agents have antimicrobial properties or the ability to inhibit growth or metabolic processes in microbes (e.g. bacteria, viruses and fungi). They are obtained from living organisms or through synthesis. In this report, antimicrobial medicines predominantly mean antimicrobial medicines with bactericidal properties, including those with the ability to stop bacterial growth; except in the human antimicrobial consumption chapter in which antimicrobial agent means antibiotics, antituberculous, antimalarial, antivirus and antifungal medicines.

Antibiotics

Antibiotics are antimicrobial medicines with bactericidal properties, (including those with the ability to stop bacterial growth), obtained from living organisms or through synthesis. Examples include penicillin, amoxicillin, tetracycline, norfloxacin and azithromycin. The terms microbicide (microbe killer), antibacterial medicines and antibiotics are used interchangeably.

Bacteria

Bacteria are one of the major groups of microorganisms or microbes, some of which can infect and cause disease in humans and animals. A range of descriptive terms are used. Bacteria cultivated in a laboratory are referred to as isolates, those capable of causing disease are referred to as pathogens (pathogens that are transmissible between animals and humans are zoonotic), and those that are normally resident on or in humans or animals without causing disease are referred to as commensals or colonizers.

Critically Important Antimicrobials (CIA)

In this report, Critically Important Antimicrobials refer to the list of CIA for human medicine defined by the World Health Organization [1]. It ranks medically important antimicrobials for risk management of antimicrobial resistance due to non-human use. It was developed for cautious use in mitigating the human health risks associated with antimicrobial use (AMU) in both humans and food-producing animals.

One Health

A concept promoting a 'whole of society' approach to attain optimal health for people and animals, and a healthy environment.

Surveillance

Surveillance means a continuing process of collecting, collating and analyzing data and communicating information to all relevant actors. It involves the generation and timely provision of information that can inform appropriate decision-making and action.

Susceptible

A category defined by a breakpoint that implies that isolates with an minimum inhibitory concentration (MIC) at or below or zone diameters at or above the susceptible breakpoint are inhibited by the usually achievable concentrations of antimicrobial agent when the dosage recommended to treat the site of infection is used, resulting in likely clinical efficacy.

Susceptible-dose dependent (SDD)

A category defined by a breakpoint that implies that susceptibility of an isolate is dependent on the dosing regimen that is used in the patient. In order to achieve levels that are likely to be clinically effective against isolates for which the susceptibility testing results are in the SDD category, it is necessary to use a dosing regimen (i.e., higher doses, more frequent doses, or both) that results in higher drug exposure than the dose that was used to establish the susceptible breakpoint.

Intermediate

A category defined by a breakpoint that includes isolates with minimum inhibitory concentrations (MICs) or zone diameters within the intermediate range that approach usually attainable blood and tissue levels and for which response rates may be lower than for susceptible isolates. The intermediate category implies clinical efficacy in body sites where the drugs are physiologically concentrated or when a higher than normal dosage of a drug can be used.

Resistant

A category defined by a breakpoint that implies that isolates with an minimum inhibitory concentration at or above or zone diameters at or below the resistant breakpoint are not inhibited by the usually achievable concentrations of the agent with normal dosage schedules and/or that demonstrate MICs or zone diameters that fall in the range in which specific microbial resistance mechanisms are likely, and clinical efficacy of the agent against the isolate has not been reliably shown in treatment studies.

Non-susceptible

A category used for isolates for which only a susceptible breakpoint is designated because of the absence or rare occurrence of resistant strains. Isolates for which the antimicrobial agent minimum inhibitory concentrations are above or zone diameters below the value indicated for the susceptible breakpoint should be reported as non-susceptible.

Summary

This One Health report is Thailand's second cross-sectoral report on antimicrobial consumption (AMC) and antimicrobial resistance (AMR) in humans and food-producing animals that compares data between 2017 and 2018.

This second report indicates and provides better explanation to increase understanding about the current situation of AMC and AMR rates in Thailand between 2017 and 2018. It contributes to monitoring and further development of national policies in order to encourage prudent antimicrobial use (AMU) and therefore reduce AMR. The report's main findings are presented below.

Antimicrobial consumption

Antimicrobial consumption in humans

(Source: Food and Drug Administration, Ministry of Public Health)

Overall human antimicrobial consumption

Year	Consumption (DDD)	Human population (inhabitant)	Consumption (DDD/1,000 inhabitants/day; DID)
2017	1,807,944,442.6	72,438,300	68.4
2018	1,992,132,889.2 [↑10.2%]	73,341,782 [↑1.2%]	74.4 [↑8.8%]

Consumption of core and optional antimicrobial classes

For core antimicrobial class, other beta-lactams ranked first, followed by beta-lactams and penicillins and tetracyclines. The top-three core antimicrobials (at Anatomical Therapeutic Chemical (ATC) level 5) were ceftriaxone, amoxicillin and tetracycline.

Among antimicrobials in the optional class, antivirals intended for systemic infections were consumed most (there were a total of 360,000 people living with HIV (PLWH) who are on antiviral treatment, which is 75.0% of a total 480,000 PLWH) [2]. Antimycotics used for systemic infections and antituberculous drugs, ranked second and third respectively. The three most-consumed antimicrobials in the group were lamivudine, followed by ketoconazole and a combination of emtricitabine, tenofovir disoproxil and efavirenz.

Consumption of Critically Important Antimicrobials

More than half of antibacterials consumed at 48.2 Defined Daily Dose per 1,000 inhabitants per day (DID), or 64.8% of the total antimicrobial consumption, belonged to the Critically Important Antimicrobials (CIA) as classified by the World Health Organization (WHO) [1], of which 65.9% and 34.1% were in the sub-category of highest and high priority CIA, respectively. Of the three most-consumed antimicrobial groups in the highest priority CIA, ceftriaxone was consumed most, followed by roxithromycin and norfloxacin. The top three antibiotics in the high priority CIA group were amoxicillin, amoxicillin and beta-lactamase inhibitor, and ampicillin.

Antimicrobial consumption in food-producing animals

(Source: Food and Drug Administration, Ministry of Public Health)

Overall food-producing animal antimicrobial consumption

Year	Consumption (tonne of API)	Animal population (kg of $PCU_{Thailand}$)	Consumption (mg/$PCU_{Thailand}$)
2017	3,690.3	6,618,137,577.6	557.6
2018	3,816.3 [↑ 3.4%]	7,309,777,857.1 [↑10.5%]	522.1 [↓ 6.4%]

Similar to trends in 2017, antimicrobials for systemic use (QJ01) ranked highest, followed by those indicated for intestinal use. The third- and fourth-ranked antimicrobials were those for intramammary and intrauterine use, respectively.

Consumption of each antimicrobial class

Penicillins were the most common antimicrobial consumed and mainly comprised of amoxicillin. The other two major antimicrobials used in animals were tetracyclines and other antibacterials, the latter of which were primarily from halquinol and bacitracin.

Consumption by dosage form and route of administration

Over half of veterinary antimicrobial consumption (59.1%) was used through premix, mainly from halquinol, amoxicillin and tiamulin. Unlike in 2017, the subsequent ranked dose forms were oral powder and injectable products.

A quarter of consumption from injectable antimicrobials was amoxicillin. For intramammary products, the majority of drugs consumed were dihydrostreptomycin and cloxacillin.

Consumption of Critically Important Antimicrobials

In comparison with 2017, overall consumption of CIA has increased but with different drug profiles. For the highest priority group of CIA, macrolides were consumed the most, mainly from tilmicosin and tylosin, but to a slightly lesser extent than in 2017. The second-ranked CIA used in animals was polymyxins (colistin), followed by quinolones with enrofloxacin as a main drug. The consumption of both polymyxin and quinolones has decreased in 2018. The top-three antimicrobials in the highest priority group were colistin, followed by tilmicosin and tylosin.

For the high priority group of CIA, penicillins, as a whole, were consumed at a higher rate compared with 2017. This was followed by aminoglycosides and phosphonic acid derivatives, consumption of which had decreased since 2017. The top-three antimicrobials in the high priority group were amoxicillin, neomycin and dihydrostreptomycin.

Antimicrobial resistance

Antimicrobial resistance in humans

Surveillance of AMR in humans

(Source: Department of Medical Sciences, and Department of Disease Control, Ministry of Public Health)

Gram-negative bacteria

Overall, there has been an increasing antimicrobial resistance trend over the period of this study, especially in Gram-negative bacteria.

The highest rise was observed for colistin resistance in *Acinetobacter calcoaceticus-baumannii* complex, *Pseudomonas aeruginosa* and *Enterobacteriaceae*. Although the resistant isolates comprised a small portion of each species due to limited feasibility for MIC determination, colistin resistance signified the worrisome situation as it is the last resort.

The proportion of carbapenem resistance among *Acinetobacter baumannii* and *Pseudomonas aeruginosa* were stable, but proportion was remarkably increased in *Escherichia coli* and *Klebsiella pneumoniae.*

Gram-positive bacteria

An increasing trend of methicillin-resistant coagulase-negative *Staphylococcus* (MRCNS) prevalence was seen. On the other hand, the methicillin-resistant *Staphylococcus aureus* (MRSA) rate has gradually declined over the period.

Growing numbers of vancomycin-resistant *Enterococcus* (VRE) tested by the MIC method have been reported in 2018, although only a small number of isolates were performed with the MIC test. However, the VRE rate remained unchanged at less than 10.0% when disk diffusion data were considered.

A similar rate of penicillin-nonsusceptibility and cefotaxime-nonsusceptibility was observed among *Streptococcus pneumoniae* isolates from both sterile and non-sterile sites in 2017 and 2018.

Other antimicrobial resistant bacteria

Of non-typhoidal *Salmonella* spp. isolated in 2017-2018, the proportion of third-generation cephalosporin-resistant was constant, while increasing proportion of fluoroquinolone resistance was observed.

All gonococcal isolates in 2017-2018 remained susceptible to ceftriaxone and cefixime, but high azithromycin MIC was occasionally observed.

Morbidity of AMR in patients with Hospital-Associated Infections

(Source: Bamrasnaradura Infectious Disease Institute, Ministry of Public Health)

Overall, in 2018, the incidence rate and incidence proportion of hospital-associated infections (HAI) were 2.5 per 1,000 patient-days and 0.8% of total discharged patients respectively. Additionally, the incidence rate and incidence proportion of AMR in patients with HAI were 1.4 per 1,000 patient-days and 0.5% of total discharged patients respectively. More than half (60.2%) of HAI patients had AMR infections. *Acinetobacter baumannii* (47.2%), *K. pneumoniae* (21.8%) and *E. coli* (19.1%) were the top three AMR pathogens among inpatients with HAI.

Antimicrobial resistance in food-producing animals

(Source: Department of Livestock Development, Ministry of Agriculture and Cooperatives)

Escherichia coli

E. coli isolates from samples collected from cecums in both chickens and pigs and from chicken meat samples collected at slaughterhouses, the highest resistance rate of *E. coli* was found in ampicillin, followed by tetracycline and chloramphenicol. Resistance rates in pork samples from slaughterhouses were similar to those of meats from retail markets in both species with the highest resistance to ampicillin, followed by tetracycline and trimethoprim/sulfamethoxazole.

Salmonella spp.

Salmonella spp. isolates from samples collected from cecums of chickens and pigs and from chicken meat samples collected at slaughterhouses, the highest resistance rate of *Salmonella* spp. was found in ampicillin, followed by tetracycline and ciprofloxacin. Resistance rates in pork samples from slaughterhouses were similar to those of meats from retail markets in both species with the highest resistance to ampicillin, followed by tetracycline and trimethoprim/sulfamethoxazole.

Enterococcus faecium and *Enterococcus faecalis*

In chickens and pigs, *E. faecium* and *E. faecalis* were found with highest resistance rates to tetracycline, followed by erythromycin and streptomycin.

Campylobacter coli and *Campylobacter jejuni*

For *C. coli* and *C. jejuni* isolated from cecums of chickens and pigs, the resistance profile in 2018 was between 50.0% to 80.0% including ciprofloxacin, erythromycin, gentamicin, streptomycin and tetracycline.

Antimicrobial resistance in the food chain

(Source: Food and Drug Administration, Ministry of Public Health)

A first step of antimicrobial-risk management is to generate food safety data of resistant bacteria with the potential to contaminate meat. Findings from the isolation of *Salmonella* spp. and *E. coli* in pork and chicken showed that the overall contamination rate of *Salmonella* spp. was higher than that of *E. coli* ($P < 0.0001$). *Salmonella* contamination was higher in pork than in chicken ($P < 0.0001$). In contrast, *E. coli* contamination was higher in chicken than in pork ($P < 0.0001$). All isolates were tested for their antimicrobial susceptibility and extended spectrum beta-lactamases (ESBLs) production. Antimicrobial resistance (AMR) rates varied according to the type of antibiotics. Most *Salmonella* spp. and *E. coli* exhibited multidrug resistance phenotype. The ampicillin resistance rate was highest in *Salmonella* spp. (53.7%) and *E. coli* (60.6%). Colistin resistance rates were found to be approximately 3.0% and none of the isolates was resistant to meropenem. ESBL producing *Salmonella* spp. (8.9%) and *E. coli* (7.1%) were detected. All the ESBL-positive isolates were multidrug-resistant. The results highlighted that pork and chicken play a role as reservoirs of resistant *Salmonella* spp. and *E. coli.* Therefore, appropriate risk control measures as well as in-depth research study regarding the relatedness of these resistance genes/ organisms to human health are required.

INTRODUCTION

1. Introduction

Authors
Sunicha Chanvatik
Supapat Kirivan
Anond Kulthanmanusorn
Sang Usayaporn
Julaporn Srinha
Wanwisa Kaewkhankhaeng

Editors
Viroj Tangcharoensathien
Kumthorn Malathum
Angkana Lekagul

1.1 Problems

Antimicrobial resistance (AMR), one of the greatest health threats of the 21st century, causes approximately 700,000 annual deaths globally [3]. It has been estimated that failure to address AMR today will result in up to 10 million annual deaths and US$ 100 trillion economic losses by 2050. The highest impact will affect Asian and African regions, accounting for 4.7 and 4.2 million annual deaths, respectively [4].

Lack of effective infection prevention and control (IPC) measures and failure to curb and optimize antimicrobial use (AMU), in particular the reserved group of Critically Important Antimicrobials (CIA) as defined by the World Health Organization (WHO) [1] in both human and animal sectors are key drivers for the emergence and spread of AMR. Unfortunately, evidence indicates that antimicrobial consumption (AMC) is on the rise worldwide, with a 36.0% increase between 2000 and 2010 [5].

Cephalosporins and broad-spectrum penicillins are the most frequently used antibiotics, representing 55.0% of worldwide consumption. There is also alarming evidence of increased global use of carbapenems and polymyxins, by 45.0% and by 13.0% respectively; these are two last-resort classes of antibiotics to combat highly resistant bacteria [5].

An equally important area is antibiotic use in companion animals, agriculture and aquaculture as well as poor hygienic practices in meat production-supply chains, which could induce the emergence and spread of resistant bacteria among animals, to farm workers, and through contamination in meat products, in the environment and negative impacts on consumers of animal products. A recent study estimates that global use of antimicrobials in livestock will increase by 67.0% (from 63,000 to 106,000 tonnes) over the next 10 years [6].

While AMU is on the rise and AMR is increasing, the pipeline of antimicrobials is running dry. This situation will eventually lead to a post-antibiotic era and potential catastrophe of modern medicine; a situation where modern medical techniques that rely on the effectiveness of antibiotics, such as organ transplantation and chemotherapy become impossible and surgical operations cannot be performed because of the risk of untreatable infections [7].

In addressing AMR issues, Thailand has various policies, mechanisms and initiatives in place. Although all AMR data in both human and animal sectors exist, they are not systematically combined and fully used to guide clinical management in human sector, and decisions to prescribe antibiotics by veterinarians for both livestock and companion animal sectors.

Therefore, in this report, we respond to the need for comprehensive information and made them widely and publicly available. This is the second Thailand report which combines data on AMC and AMR under the One Health approach; including morbidity on HAI and AMR among inpatients. The data in the report will contribute to monitoring impact of policies and further fine-tuning the implementation of national antimicrobial policies in order to support and encourage prudent AMU, ultimately resulting in the mitigation of AMR problems.

1.2 National Strategic Plan on Antimicrobial Resistance 2017-2021

The National Strategic Plan on Antimicrobial Resistance (2017-2021) (NSP-AMR) is the first Thai strategy which addresses AMR specifically. It was developed by the AMR Coordination and Integration Committee, which is a multi-sectoral committee under the Public Health Ministerial Order. The Committee is chaired by the Deputy Permanent Secretary and its secretariat team consists of representatives from the Ministry of Public Health, the Ministry of Agriculture and Cooperatives, and universities.

The process to develop the NSP-AMR took 16 months (May 2015-August 2016) and was based on full participation and engagement by multiple stakeholders, through a series of public hearings and a National Health Assembly resolution [8]. The Cabinet endorsed the NSP on 17 August 2016, entrusting the legality of cross-sectoral actions.

The NSP-AMR aims to reduce morbidity, mortality and economic impacts due to AMR. The strategy sets five goals to be achieved by 2021. These are: 50.0% reduction in AMR morbidity; 20.0% reduction in antimicrobial consumption in humans; 30.0% reduction in antimicrobial consumption in animals; 20.0% increase of public knowledge on AMR and awareness of appropriate use of antimicrobials; and improvement of the capacity of the national AMR management system to level 4 as defined by the WHO Joint External Evaluation Tool (JEE) of International Health Regulations 2005 [9]. The details of NSP-AMR are summarized in Box 1.

To achieve the five goals, the NSP-AMR consists of six strategic actions (see Box 1). The strategic actions 1-5 cover key areas to resolve AMR whereas strategic action 6 aims to develop governance mechanisms to implement and sustain AMR actions in accordance with the NSP-AMR.

Box 1. Summary of NSP-AMR (2017-2021)

Vision: Reduction of mortality, morbidity and economic impacts from AMR

Mission: Establish policies and national multi-sectoral mechanisms which support an effective and sustained AMR management system

Goals:
1. 50.0% reduction in AMR morbidity
2. 20.0% reduction in antimicrobial consumption in humans
3. 30.0% reduction in antimicrobials consumption in animals
4. 20.0% increase in public knowledge on AMR and awareness of appropriate use of antimicrobials
5. Capacity of the national AMR management system is increased to level 4 as measured by the WHO's Joint External Evaluation Tool (JEE) for International Health Regulations (2005)

Strategies:
1. AMR surveillance system using 'One Health' approach
2. Regulation of antimicrobial distribution
3. Infection prevention and control and antimicrobial stewardship in humans
4. AMR prevention and control and antimicrobial stewardship in agriculture and companion animals
5. Public knowledge on AMR and awareness of appropriate use of antimicrobials
6. Governance mechanisms to implement and sustain AMR actions

1.3 Scope of a report

The report covers:

a) AMC in human and food-producing animals;
b) AMR in humans (lab-based and case-based morbidity of AMR in patients with HAI), food-producing animals and the food chain.

The scope of antimicrobials for human consumption also includes: antivirals, antifungals, antiprotozoals, antimalarials and drugs for treatment of tuberculosis according to the WHO recommendation. We also apply the World Organisation for Animal Health (OIE) recommendation on the scope of AMC in food-producing animals for monitoring purposes.

1.4 One Health Surveillance Information

In Thailand, data on AMC and AMR from the human and animal sectors are jointly collated by HPSR-AMR working group aggregated at the national level. It is assembled from various channels and there is currently no central depository for this inter-sectoral data set; where further development is needed.

AMC data in humans and animals

As shown in Figure 1, pharmaceutical operators, who are mandated by the Drug Act 1967, to report the volume of import and local production, need to login to PROLOG SYSTEM and prepare an annual report to submit to the Thai Food Drug Administration (Thai FDA) by March 31 of the following year. Then, a responsible and authorized pharmacist of the pharmaceutical company submits the report to the Thai FDA via a web portal. After Thai FDA officers have reviewed the report based on its completeness and identification of any irregularities, the result is fed back to the pharmaceutical company to notify it of further actions needed before final acceptance by the FDA. If there are no comments for corrections or amendments, the report will be accepted by the Thai FDA without amendments. If some errors need to be rectified, the report will be cancelled and the pharmaceutical operator has to re-submit the revised annual report within a specified period. Failure to do so will result in legal sanction by the Thai FDA.

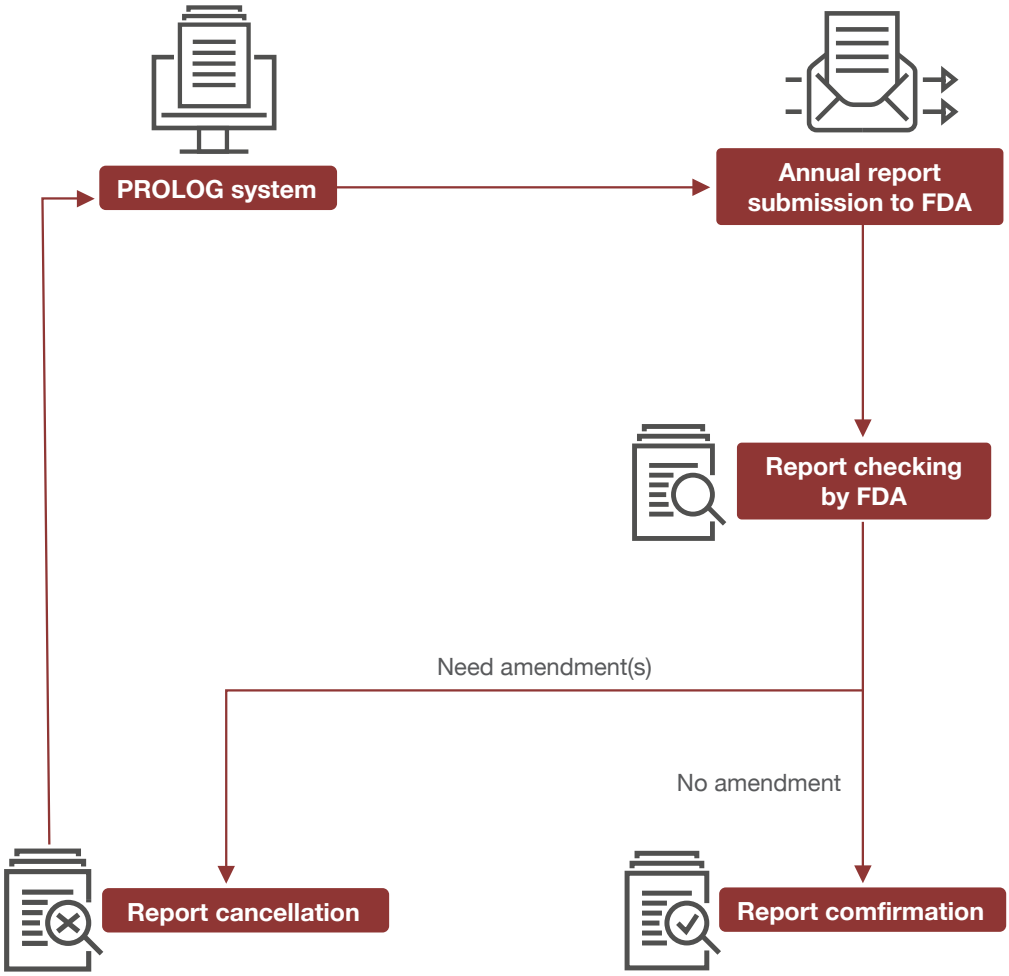


Figure 1. Source and flow of information on consumption

AMR data in humans

Laboratory-based AMR data

Laboratory-based AMR data in humans were submitted by participating public and private hospitals nationwide to the National Antimicrobial Resistance Surveillance Center, Thailand (NARST), National Institute of Health, Department of Medical Sciences, The Ministry of Public Health, Thailand. The NARST, a mature and well-established system, was founded in 1998 and was designated as a WHO Collaborating Center in 2005.

Hospitals in the NARST system have limited numbers of patients with gonococcal infection as they either sought care from specialized Sexually Transmitted Infections (STIs) centers or healthcare facilities in private sector. The data on gonococcal AMR in this report were collected from Bangrak STIs center, Silom Community Clinic @TropMed, and three and six centers of The Office of Disease Prevention and Control under the Department of Disease Control, Ministry of Public Health, Thailand in 2017 and 2018, respectively.

Case-based AMR data

A prospective data collections on patients identified as Hospital-associated infection (HAI) from hospital-wide surveillance (where all HAI inpatients were identified during the whole year of 2018, not only patients with sites specific HAI such as CAUTI, VAP, CLABSI) was conducted during January and December 2018 by Bamrasnaradura Infectious Disease Institute (BIDI), Ministry of Public Health.

All HAI occurring in these hospitals were detected by well trained Infection Control Ward Nurses (ICWNs) and confirmed by Infection Control Nurses (ICNs) in each hospital using the definition in the Thai Manual of HAI Diagnosis 2018. The data of patients with HAI were manually submitted to the surveillance web portal on a monthly basis by ICNs. To simplify the data entering process, only the susceptibility data (Susceptible, Intermediate or Resistant) of each drug group reported in laboratory results were collected; as a result, there was no zone size or minimum inhibitory concentration (MIC) data. In addition to HAI patient surveillance data, hospital service profiles such as the number of patient-days, the number of discharged patients, the number of device-days, and number of surgical procedure performed were used as a denominator.

In 2018, 302 hospitals participated in the surveillance system but only 103 hospitals submitted complete data. Hospitals also submitted incomplete drug susceptibility data and as a result, data verification was needed. Finally, only 23 hospitals from 103 hospitals were included in the study and ICN in these hospitals were requested to review, verify and complete some missing data through the use of relevant hospital database.

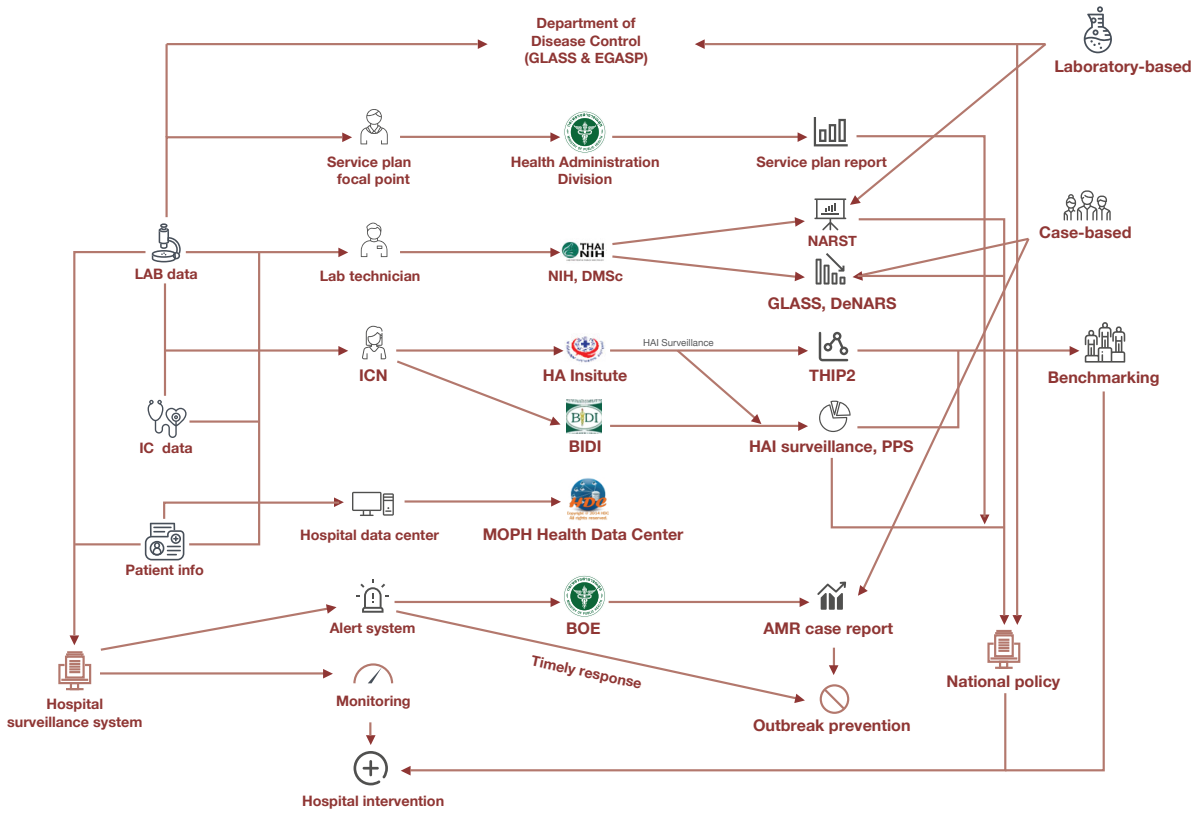


Figure 2. Sources and flow of information on AMR in humans

AMR data in food-producing animals

The national surveillance of AMR in food-producing animals has been focused on broilers and pigs, since both are major food-producing animals in Thailand. This surveillance covered cecums from slaughterhouse, and meats from slaughterhouse and retail markets. All of the samples were tested for bacterial identification and antimicrobial susceptibility testing (AST) by the National Institute of Animal Health (NIAH), Bureau of Quality Control of Livestock Product (BQCLP), and Regional Veterinary Research and Development Center. In compliance with OIE guidelines, the target bacteria of AMR surveillance included zoonotic bacteria (*Salmonella* spp., *Campylobacter jejuni* and *Campylobacter coli*) and indicator bacteria (*Enterococcus faecium, Enterococcus faecalis,* and *Escherichia coli*). The AST was performed in accordance with the guidelines developed by a) Clinical and Laboratory Standards Institute (CLSI), ISO 20776-1, and b) the European Committee on Antimicrobial Susceptibility Testing (EUCAST). The antimicrobials for AST included polymyxins (colistin), fluoroquinolones (ciprofloxacin), 3rd generation cephalosporins (cefotaxime and ceftazidime), carbapenems (meropenem), and other antimicrobials commonly used in livestock.

AMR data in food chain

All cuts of uncooked pork and chicken samples were randomly collected by the Thai FDA from selected retail supermarkets from four provinces in central region of Thailand including Bangkok, Nonthaburi, Pathumtani and Samutprakan. Whenever available, the whole package or 50 grams of unpackaged meat was taken and kept in an icebox. Then, the samples were delivered within three hours to a laboratory of the Department of Veterinary Public Health, Faculty of Veterinary Sciences, Chulalongkorn University for analysis. In the surveillance programme, *Salmonella* spp. (pathogenic bacteria) and *E. coli* (commensal bacteria) were investigated. AST was performed in accordance with internationally accepted procedures in order to characterise the antimicrobial resistance isolates. The MIC was applied in each test. The isolates were further tested for extended spectrum beta-lactamases (ESBLs) production using the method of Clinical and Laboratory Standards Institute (2013).

1.5 Populations

Human and Animal Populations

The numbers of human and animal population in Thailand, 2018, have been collected and verified by various relevant stakeholders to ensure their accuracy. On the basis of populations potentially exposed to antimicrobials, the figure of each particular population was used as a denominator to calculate the amount of national AMC.

1.5.1 Human population

In 2018, the mid-year population in Thailand including both Thai citizens and migrants was estimated to be 73,341,782 (Table 1).

Table 1. Human population 2018

	Male	Female	Total
Citizen	33,833,163	35,595,361	69,428,524
Migrant	3,913,258		3,913,258
Total			**73,341,782**

World Bank, World Development Indicator 2017 [10]

1.5.2 Animal population

1.5.2.1 Food-producing animal population

The number of food-producing animals was collected and verified through the cooperation among Department of Livestock Development (DLD), Department of Fisheries (DOF), private sector and relevant stakeholders.

For terrestrial food-producing animals, the data were collected and verified from three sources: livestock surveys by regional DLD offices, data records from the E-movement system of DLD, and large-scale producers. As can be seen in Table 2, some of the average weights at the time of treatment (Aw) for certain species were not available from the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC), but those were produced in Thailand [11]. Consequently, these missing Aw were estimated based on standing weight of these animals (Table 2). Population Correction Unit (PCU) is used as a denominator for AMC in food-producing animals and calculated by applying ESVAC methodology. According to the ESVAC, PCU is assumed to be a surrogate for the animal population at risk of being exposed to antimicrobials [12]. However, the PCU in this report was modified from ESVAC, so it is called $PCU_{Thailand}$.

Regarding the aquatic animal population, data were collected from surveys and estimated by the Fisheries Development Policy and Strategy Division of the DOF, but the actual figure will be officially published next year in 2019. In this report, the actual figures of biomass from 2014 to 2017 were used to project biomass for 2018. Note that the figures can be inconsistent with those of the official report [11]. The species included were major fishes and shrimps produced from coastal and fresh waters (Table 2). The figures of aquatic animals are shown in kilogram (kg) of biomass.

Table 2. Food-producing animal population 2018

Animal category	Aw (kg)	Number of animals	Biomass (tonnes)	$PCU_{Thailand}$ (kg)
Terrestrial animals				
Pigs				
Breeding pigs	240**	1,198,529		287,646,960.0
Fattening pigs	65**	22,816,918		1,483,099,670.0
Poultry				
Broiler breeders	4*	12,601,103		50,404,412.0
Broilers	1**	1,672,905,728		1,672,905,728.0
Layer breeders	2*	546,303		1,092,606.0
Laying hens	2*	57,322,295		114,644,590.0
Pullets	1.5*	54,959,880		82,439,820.0
Broiler duck breeders	3.5*	318,318		1,114,113.0
Integrated broiler ducks	3.3*	31,831,808		105,044,966.4
Free-market broiler ducks	3.3*	15,040,424		49,633,399.2

Animal category	Aw (kg)	Number of animals	Biomass (tonnes)	$PCU_{Thailand}$ (kg)
Integrated layer ducks	2.5*	5,797,734		14,494,335.0
Free-market layer ducks	2.5*	8,691,473		21,728,682.5
Cattle				
Dairy cows	425**	275,358		117,027,150.0
Dry cows	425*	298,770		126,977,250.0
Beef cows	425**	5,445,351		2,314,274,175.0
Aquatic animals				
Coastal aquatic animals			426,575	426,575,000.0
Fresh aquatic animals			440,675	440,675,000.0
Grand total PCU (kg)				**7,309,777,857.1**

*Thailand Surveillance of antimicrobial consumption (SAC) 2017 [11]
**ESVAC 2017 [13]

1.5.2.2 Companion animal population

The number of companion animals could not be accurately estimated. Although companion animals, due to its small size of population, are estimated to have much lower AMC than terrestrial food-producing and aquatic animals, the HPSR-AMR Working Group plans to collect data on the companion animal population to fill gaps under the One Health approach. Studies have shown the off-label use of antibiotics registered as human antibiotics as the major share of antibiotics used by companion animals. Assessment of animal hospital electronic prescription/dispensing database by HPSR AMR team found feasible to establish AMU in this group in the near future.

1.6 Critically Important Antimicrobials (CIA)

WHO has produced a list of Critically Important Antimicrobials for Human Medicine since 2005 and the latest updated WHO CIA list was announced in 2018. The CIA list is prioritized to address AMR and promote the prudent use of antimicrobials in both human and veterinary medicine [1].

WHO criteria for inclusion of antimicrobial substances in the CIA list require that two parameters are fulfilled:

1. The antimicrobial class is the sole, or one of limited available therapies, to treat serious bacterial infections in humans.
2. The antimicrobial class is used to treat infections in people caused by either: 1) bacteria that may be transmitted to humans from non-human sources; or 2) bacteria that may acquire resistant genes from non-human sources.

Three prioritization criteria are used to further categorize antimicrobial substances in the CIA list into two sub-groups of Highest Priority CIA and High Priority CIA:

1. High absolute number of people, or high proportion of use in patients with serious infections in healthcare settings affected by bacterial diseases for which the antimicrobial class is the sole or one of few alternatives to treat serious infections in humans.
2. High frequency of use of the antimicrobial class for any indication in human medicine, or high proportion of use in patients with serious infections in healthcare settings, since use may favour selection of resistance in both settings.
3. The antimicrobial class is used to treat infections in people for whom there is evidence of transmission of resistant bacteria (e.g. non-typhoidal *Salmonella* and *Campylobacter* spp.) or resistance genes (high for *E. coli* and *Enterococcus* spp.) from non-human sources.

The Highest and High Priority CIA defined by WHO are fully applied in this report (Table 3).

Table 3. Antimicrobial classes in WHO Critically Important Antimicrobials

Categorization	Antimicrobial class
Highest Priority CIA	Cephalosporins (3rd, 4th and 5th generation)
	Glycopeptides and lipoglycopeptides
	Macrolides and ketolides
	Polymyxins
	Quinolones
High Priority CIA	Aminoglycosides
	Ansamycins
	Carbapenems and other penems
	Glycylcyclines
	Lipopeptides
	Monobactams
	Oxazolidinones
	Penicillins (antipseudomonal)
	Penicillins (aminopenicillins)
	Penicillins (aminopenicillins with beta-lactamase inhibitors)
	Phosphonic acid derivatives
	Drug used solely to treat tuberculosis or other mycobacterial diseases

2

ANTIMICROBIAL CONSUMPTION

2.1 Antimicrobial consumption in humans

Data source

Food and Drug Administration, Ministry of Public Health

Authors

Supapat Kirivan
Charunee Krisanaphan
Varavoot Sermsinsiri
Kritsada Limpananont
Chutamas Luangaroonchai
Sitanan Poonpolsub
Pongsathid Virungrojint
Khunjira Udomaksorn
Inthira Kanchanaphibool
Nussaraporn Kessomboon
Rungpetch Sakulbumrungsil

Editors

Viroj Tangcharoensathien
Kumthorn Malathum
Angkana Lekagul
Sunicha Chanvatik
Wanwisa Kaewkhankhaeng

Key summary

Overall human antimicrobial consumption

Year	Consumption (DDD)	Human population (inhabitant)	Consumption (DDD/1,000 inhabitants/day; DID)
2017	1,807,944,442.6	72,438,300	68.4
2018	1,992,132,889.2 [↑10.2%]	73,341,782 [↑1.2%]	74.4 [↑8.8%]

Consumption of core and optional antimicrobial classes

For the core class, other beta-lactams (including cephalosporins and carbapenems) ranked first, followed by beta-lactams and penicillins and tetracyclines. The top-three core antimicrobials were ceftriaxone, amoxicillin, and tetracycline.

Among antimicrobials in the optional class, antivirals intended for systemic infections were consumed most (there were a total of 360,000 people living with HIV (PLWH) who are on antiviral treatment, which were 75.0% of total 480,000 PLWH) [2]. Antimycotics used for systemic infections and antituberculous drugs, ranked second and third respectively. The three most-consumed antimicrobials in the group were lamivudine, followed by ketoconazole and a combination of emtricitabine, tenofovir disoproxil and efavirenz.

Consumption of Critically Important Antimicrobials

More than half of antibacterials consumed at 48.2 DID, or 64.8% of total, belonged to the CIA group of which 65.9% and 34.1% were in the sub-category of highest and high priority CIA respectively. Of the three most-consumed antimicrobial groups in the highest priority CIA, ceftriaxone was consumed most, followed by roxithromycin and norfloxacin. The top three in the high priority CIA group were amoxicillin, amoxicillin and beta-lactamase inhibitor, and ampicillin.

2.1.1 General

In Thailand, most human antimicrobials are classified by the Thai Food and Drug Administration (Thai FDA) as dangerous drugs, which means they must be dispensed only by a licensed pharmacist without prescription. Only a few important antibiotics are classified as special controlled drugs which require a prescription from a licensed physician to be dispensed.

According to the National Strategic Plan on Antimicrobial Resistance 2017-2021 (NSP-AMR), Goal 2 is to reduce human antimicrobial consumption by 20.0% by 2021. In order to make the goal measurable, the method of monitoring human antimicrobial consumption is of critical importance, and it is one of the reasons that the Thailand Surveillance on Antimicrobial Consumption (Thailand SAC) has been developed and sustained on an annual basis. Aside from the national goal, the data from Thailand SAC are useful for both health professionals and policymakers. This is due to the fact that consumption data can help assess the effects of policy implementation, particularly improving the Antimicrobial Stewardship Program (ASP) and law enforcement such as the re-classification of antibiotics as a specially controlled medicine, which limits the use of antimicrobials only through a licensed physician or an infectious disease specialist. With some improvements in methodology and data granularity, such useful information can be utilized not only at national, but also at local and regional levels to tackle AMR problems in an efficient and practical way.

2.1.2 Data source

According to the Drug Act B.E. 2510 (1967) Section 85, all pharmaceutical manufacturers and importers are required by the Thai FDA to submit an annual report, which consists of their total production and/or importation volumes of registered products by 31 March of the following year [14]. The data for 2018 were then electronically retrieved after 31 March 2019 for analysis. In an effort to reach the actual domestic consumption as shown in the scheme of Thailand's drug distribution, the manufacturers and importers, though not mandated by law, were requested to submit their total export volume for subtraction from the total consumption [15].

For target human antimicrobials, Thailand SAC covered the core and optional classes of antimicrobials as recommended by the World Health Organization (Table 4) [16]. The data were analysed using the amount of active pharmaceutical ingredients (API) in Defined Daily Dose (DDD) as a nominator and the mid-year human population as a denominator, ultimately resulting in DDD/1,000 inhabitants/day (DID) [17]. DDD in this report applies the updated version of Anatomical Therapeutic Chemical (ATC)/DDD alterations 2019 which is produced by the WHO Collaborating Centre for Drug Statistics Methodology [1].

Table 4. The core and optional classes of target human antimicrobials by WHO

Target human antimicrobials	ATC code
1. Core class	
• Antibacterials for systemic use	J01
• Antibiotics for alimentary tract	A07AA
• Nitroimidazole derivatives	P01AB
2. Optional class	
• Antimycotics for systemic use	J02
• Antifungals for systemic use	D01BA
• Antivirals for systemic use	J05
• Drugs for treatment of tuberculosis	J04A
• Antimalarials	P01B

2.1.3 Results

1. Overall consumption of human antimicrobials

Overall, the national consumption of human antimicrobials in 2018 was 74.4 DID, which had increased by 8.8% from 2017. Of the total human consumption, antibacterials indicated for systemic use (J01) still ranked highest with 57.1 DID, which had increased by 23.1% from 2017. The most-consumed antimicrobials were antivirals intended for systemic use (J05) at 10.7 DID, which had reduced by 17.7%. The third-ranked antimicrobials still belonged to antimycotics for systemic use at 2.8 DID, which had reduced by 33.6%. For antimicrobials with the biggest change in proportion, antimalarials were consumed at 0.5 DID which was a reduction of 67.1% from 2017 (Figure 3).

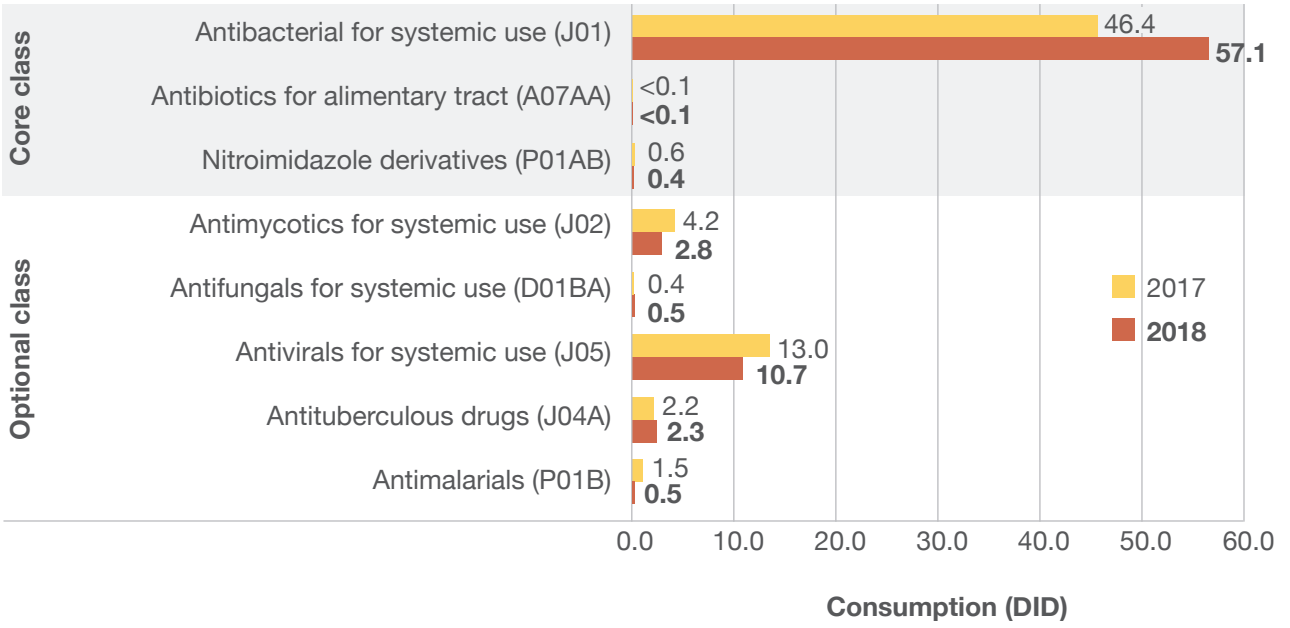


Figure 3. Consumption of human antimicrobials classified by scope of WHO, 2018 compared with 2017 (DDD/1,000 inhabitants/day, DID)

2. Core class breakdown

In the core class, the majority of consumption was from antibacterials intended for systemic use (J01) (57.1 DID), followed by nitroimidazoles (P01AB) and antibiotics used for alimentary infections (A07AA). Of the antimicrobials for systemic use, other beta-lactams (J01D) ranked first at 26.0 DID (34.9%), which had increased by 63.9% from 2017. Of the other beta-lactams, the majority of increases in other beta-lactam consumption came from ceftriaxone (23.0 DID) (increased by 9.5 DID or 70.1%), cefotaxime (0.5 DID) (increased by 0.5 DID or 3,699.9%) and ceftazidime (1.2 DID) (increased by 0.3 DID or 30.8%). The second-ranked antibacterials were beta-lactams and penicillins (J01C) with 16.4 DID, which had increased by 6.9%. The majority of increased consumption in this group was from amoxicillin with beta-lactamase inhibitor (2.4 DID) (increased by 0.7 DID or 38.7%), ampicillin (2.2 DID) (increased by 0.7 DID or 52.6%) and phenoxymethylpenicillin (increased by 0.3 DID or 402.0%). However, the amount of consumption in this group had not increased much due to a slight reduction of the major drug (56.5% of beta-lactam and penicillin consumption) amoxicillin (decreased by 0.7 DID or 7.1%). Ranked third in antibacterials used for systemic infections, tetracyclines (J01A) were consumed at 6.0 DID, which had increased by 2.0%. This increase came from tetracycline (3.7 DID) (increased by 0.3 DID or 8.1%) as the most-consumed drug in the group (61.7% of tetracycline consumption); nevertheless, the consumption of doxycycline, the second-ranked tetracycline, was reduced from 2.4 to 2.2 DID or by 6.5% (Figure 4 and Table A1).

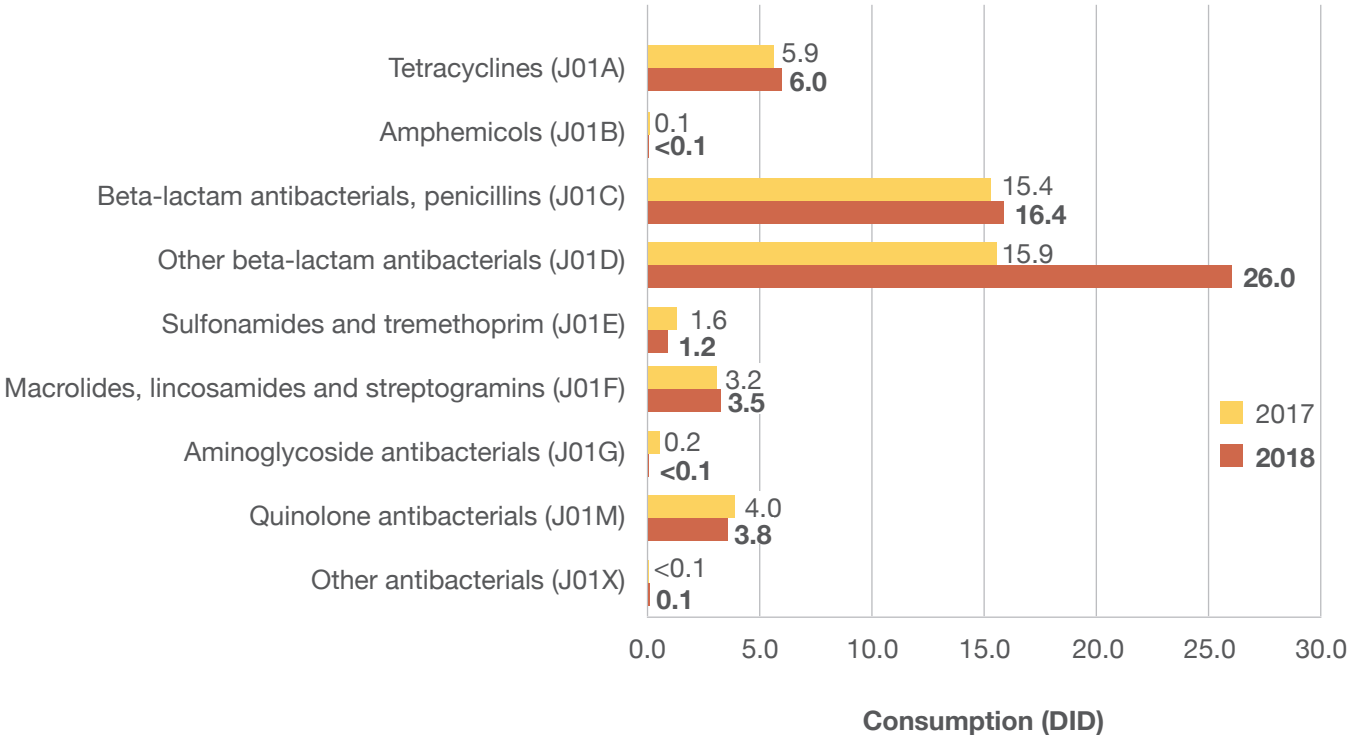


Figure 4. Comparison of consumption from human antimicrobials indicated for systemic use between 2017 and 2018, classified by ATC level 3, (DDD/1,000 inhabitants/day, DID)

As the second-ranked core class, nitroimidazoles were consumed at 0.4 DID, which had reduced by 27.9% from 2017. The reduced consumption of nitroimidazoles came from metronidazole (0.4 DID) (decreased by 0.2 DID or 28.7%). For the last core class, antibiotics used for alimentary tract was consumed 39.9% more than in 2017, mainly from nystatin (<0.1 DID) (increase by <0.1 DID or 42.8%) (Table A2).

3. Optional class breakdown

Among the consumption of optional antimicrobial classes (16.8 DID), antivirals intended for systemic infections (J05) were consumed most at 10.7 DID, followed by antimycotics used for systemic infections (J02) (2.8 DID), antituberculous drugs (J04A) (2.3 DID), antimalarials (P01BA) (0.5 DID) and antifungals for systemic use (D01BA) (0.5 DID) (Figure 3). The three antimicrobials consumed most in the optional classes were lamivudine (2.5 DID), followed by ketoconazole (2.1 DID) and a combination of emtricitabine, tenofovir disoproxil and efavirenz (1.8 DID) (Tables A3 and A4).

Ranking most-consumed antimicrobials in the optional class, the consumption of antivirals reduced by 2.3 DID or 17.7%. Countering the increased use of abacavir (0.5 DID) (increased by 0.4 DID or 362.1%), nevirapine (1.4 DID) (increased by 0.3 DID or 21.7%), and oseltamivir (0.2 DID) (increased by 0.2 DID or 446.1%), the main reduction came from efavirenz (0.8 DID) (decreased by 2.2 DID or 72.8%), tenofovir disoproxil (0.2 DID) (decreased by 1.9 DID or 89.7%) and lamivudine (2.5 DID) (decreased by 0.2 DID or 9.1%). The top-three most consumed antivirals were lamivudine (2.5 DID), a combination of emtricitabine, tenofovir disoproxil and efavirenz (1.8 DID) and nevirapine (1.4 DID) (Figure 5). For the top-five antivirals for systemic used between 2017 and 2018, lamivudine stepped up to the first-ranked antivirals, despite a slight decrease in consumption, but efavirenz moved down from the first to the fifth rank.

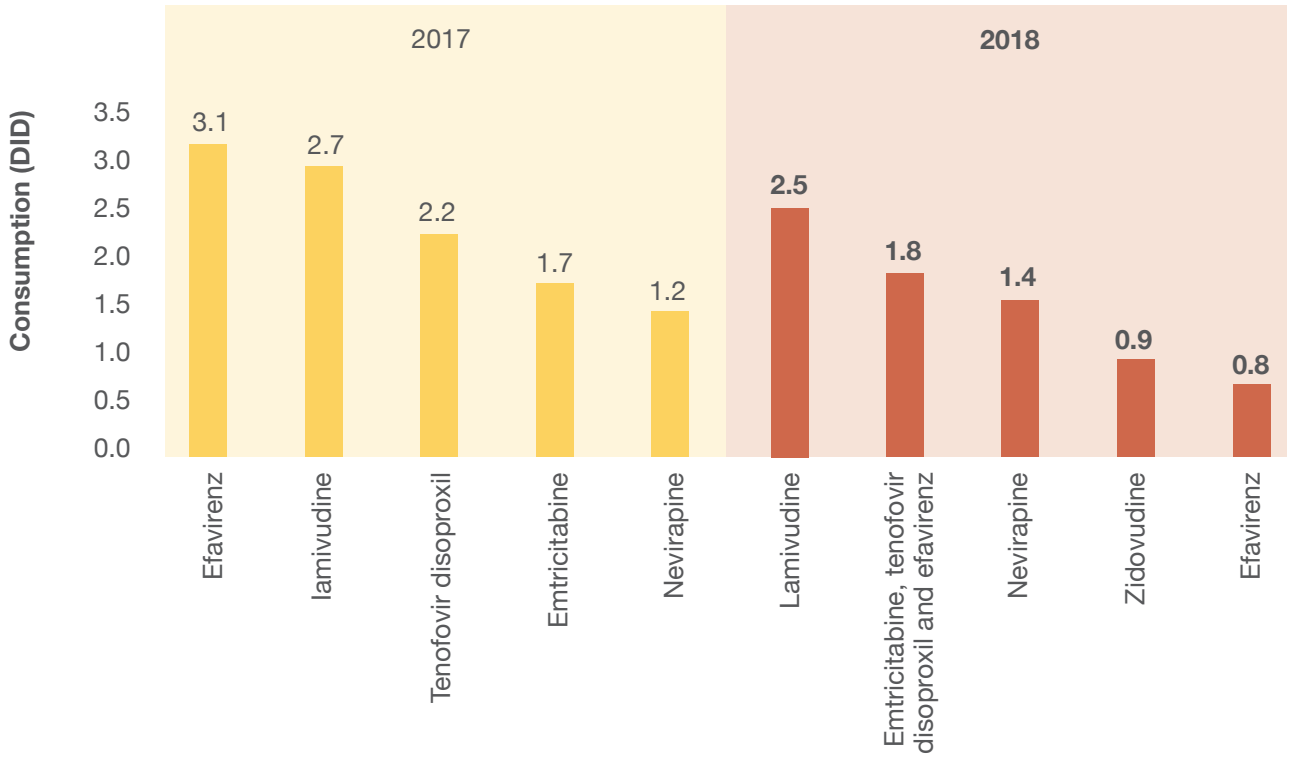


Figure 5. Comparison of consumption of the top-five antivirals indicated for systemic use between 2017 and 2018 classified by ATC level 5 (DDD/1,000 inhabitants/day, DID)

As the second rank in the optional class, the consumption of antimycotics used for systemic infections was reduced by 1.4 DID or 33.6%. The decrease in consumption mainly came from the first-ranked antimycotics, ketoconazole (2.1 DID) (decrease by 1.6 DID or 44.1%). However, in the second and third ranks, fluconazole (0.4 DID) and itraconazole (0.3 DID) were consumed at 0.1 DID more than in 2017, or by 35.3% and 38.3% respectively (Table A4). The first top-five antimycotics for systemic use remained the same as that of 2017, despite differences in the degree of increase and decrease (Figure 6).

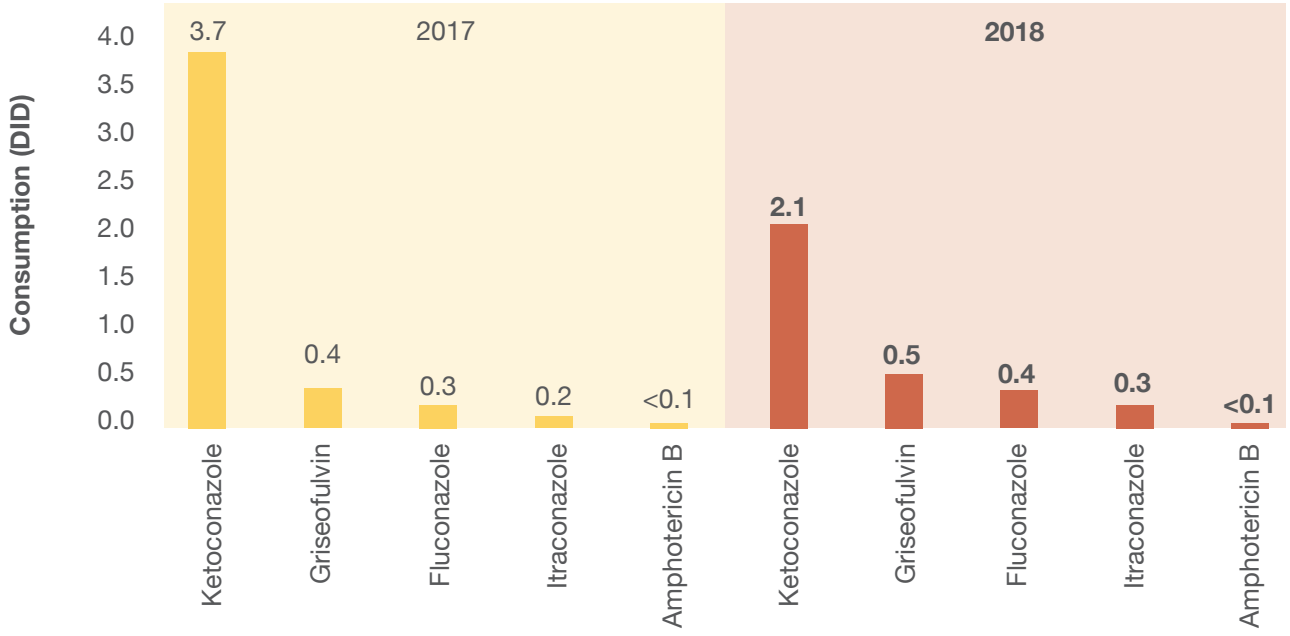


Figure 6. Comparison of consumption of the top-five antimycotics and antifungals for systemic use between 2017 and 2018 classified by ATC level 5 (DDD/1,000 inhabitants/day, DID)

For the third rank in the optional class, the consumption of antituberculous drugs was increased by 0.1 DID or 4.8%. As a whole, the majority of increased consumption was derived from three of the top-five antituberculous drugs: rifampicin (0.9 DID) (increased by <0.1 DID or 4.6%), pyrazinamide (0.3 DID) (increased by <0.1 DID or 29.4%), and ethambutol (0.3 DID) (increase by <0.1 DID or 12.3%) (Figure 6). For the first two ranks of antituberculous drugs, rifampicin and isoniazid were switched in order of ranking compared with 2017. For the other three top-five antituberculous drugs in 2018, pyrazinamide and ethambutol stayed in the same rank; nevertheless, the fifth rank was replaced by a combination of rifampicin, pyrazinamide, ethambutol and isoniazid (Figure 7).

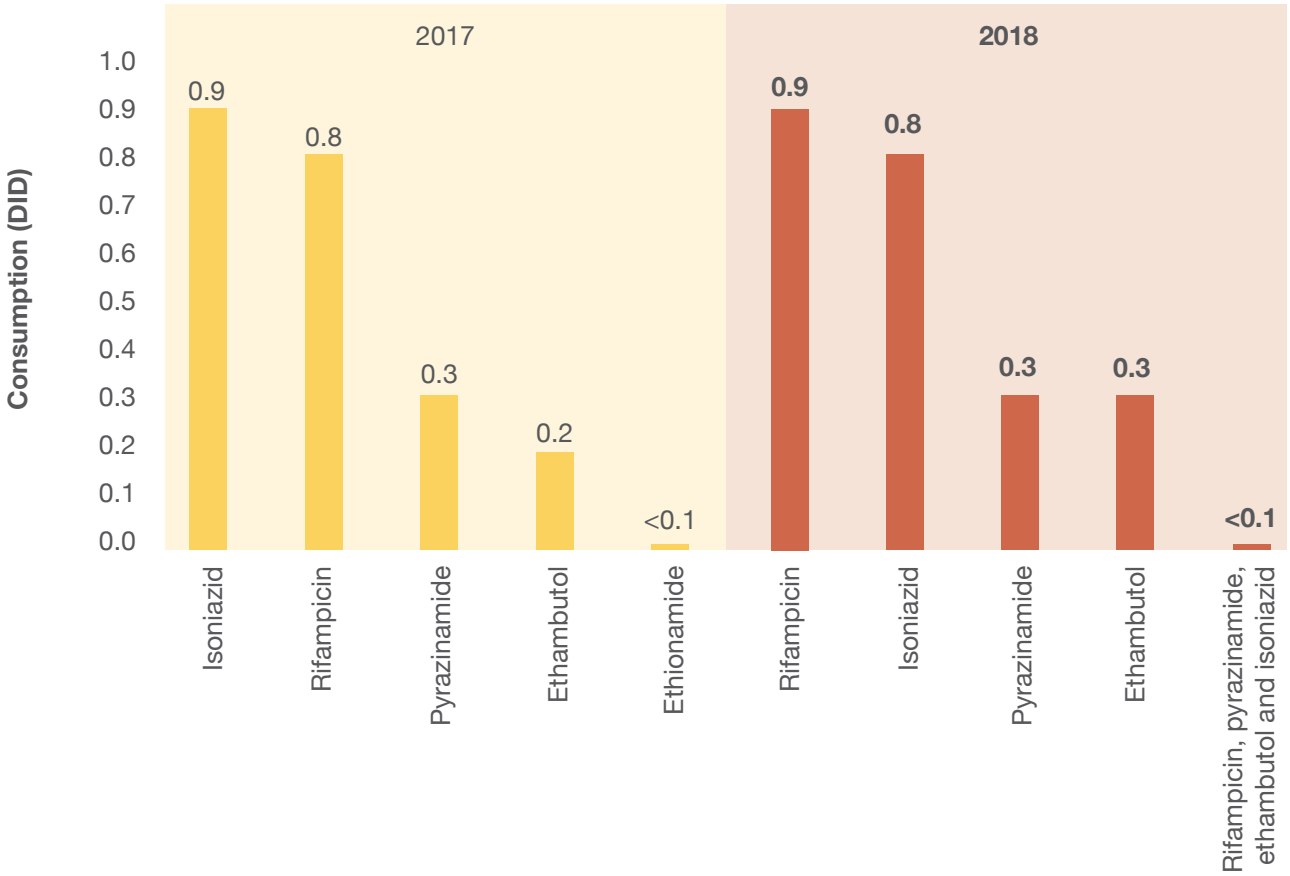


Figure 7. Comparison of consumption of the top-five antituberculous drugs for systemic use between 2017 and 2018 classified by ATC level 5 (DDD/1,000 inhabitants/day, DID)

For antimalarial drugs, consumption decreased by 1.0 DID or 67.1%. The reduced consumption mainly came from three of the five most-consumed antimalarials: chloroquine (0.3 DID) (decreased by 0.5 DID or 62.8%), hydroxychloroquine (0.2 DID) (decreased by <0.1 DID or 20.3%) and quinine (<0.1 DID) (decreased by <0.1 DID or 69.8%) (Figure 8). Of the top-five antimalarials, only primaquine (<0.1 DID) (increased by <0.1 DID or 119.8%). The top-five antimalarials remained the same as in 2017, except in a different order and the fifth rank was replaced by a combination of artenimol and piperaquine (<0.1 DID) (Figure 8).

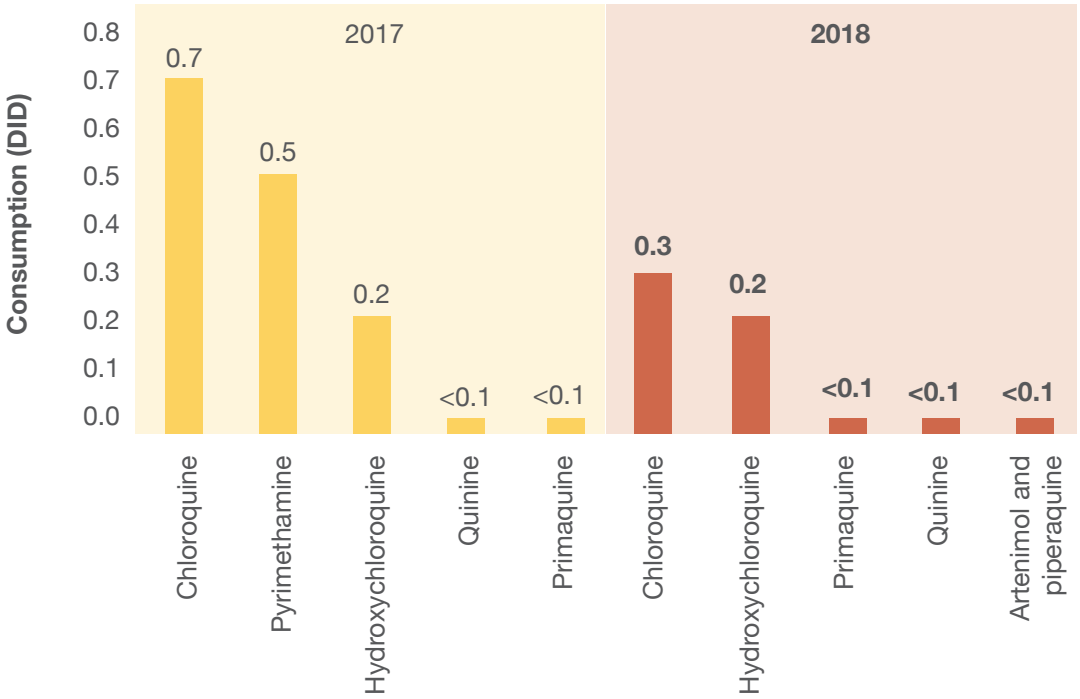


Figure 8. Comparison of consumption of the top-five antimalarials between 2017 and 2018 classified by ATC level 5 (DDD/1,000 inhabitants/day, DID)

4. Consumption of Critically Important Antimicrobials

Among all antimicrobials, more than half of the consumption was of CIA accounting for 48.2 DID (64.8% of total consumption), which had increased by 29.5% from 2017 (Figure 9). Moreover, over half of CIA consumption (65.9%) are antimicrobials in the highest priority group at 31.8 DID, in comparison with the high priority group at 16.4 DID or 34.1% (Table A7). The top-three most-consumed groups of antimicrobials in CIA were cephalosporins (3rd and 4th generation) at 25.0 DID (51.9% of CIA consumption), aminopenicillins at 11.5 DID (23.8% of CIA consumption) and quinolones at 3.8 DID (8.0% of CIA consumption) (Figure 10) As a whole, the top-three antimicrobials in the highest priority group of CIA were ceftriaxone (23.0 DID or 47.8% of CIA consumption), roxithromycin (1.7 DID or 3.5% of CIA consumption) and norfloxacin (1.4 DID or 3.0% of CIA consumption. For the high priority group of CIA, the top-three most consumed antimicrobials were amoxicillin (9.3 DID or 19.3% of CIA consumption), amoxicillin with beta-lactamase inhibitor (2.4 DID or 4.9% of CIA consumption) and ampicillin (2.2 DID or 4.5% of CIA consumption) (Table A7).

For the highest priority group of CIA, consumption increased by 10.3 DID or 47.7% compared to 2017, contributing to 93.4% of increased CIA consumption (Figure 10). As the most-consumed antimicrobials in the highest priority, cephalosporins (3rd and 4th generation) were consumed at an increase of 10.2 DID or 68.5% compared with 2017. Most of the increased consumption came from ceftriaxone (23.0 DID) (increased by 9.5 DID or 70.1%), cefotaxime (0.5 DID) (increased by 0.5 DID or 3,699.9%), and ceftazidime (increased by 0.3 DID or 30.8%). Following the first-rank group of CIA in highest priority, the consumption of quinolones decreased by 0.2 DID or 5.0%. The decreased consumption of quinolones included the most-used fluoroquinolone, which was norfloxacin (1.4 DID) (decreased by 0.6 DID or 28.8%); however, such reduction in quinolone consumption was countered by an increase in second and third ranks of quinolones: ciprofloxacin (1.4 DID) (increased by 0.2 DID or 12.6%) and levofloxacin (0.5 DID) (increased by 0.2 DID or 54.0%) respectively. For macrolides and ketolides, its consumption increased by 0.3 DID or 10.9%, which came from increased consumption of the two most-used macrolides, roxithromycin (1.7 DID) (increased by 0.2 DID or 12.9%) and azithromycin (0.6 DID) (increased by <0.1 DID or 14.8%). Ranked fourth in the highest

priority group of CIA, glycopeptides and lipoglycopeptides were consumed at <0.1 DID (increased by <0.1 DID or 15.7%), solely from vancomycin (<0.1 DID) (increased by <0.1 DID or 18.2%) and teicoplanin (<0.1 DID) (decreased by <0.1 DID or 65.2%). As the least-consumed antimicrobials in the highest priority group, polymyxins were consumed at <0.1 DID, solely from colistin (<0.1 DID) (increased by <0.1 DID or 474.1%) (Table A7).

Regarding high priority CIA, consumption also increased only by 0.7 DID or 4.6%, accounting for 6.6% of increased CIA consumption (Figure 10). As most-consumed in the high priority group of CIA, aminopenicillins was consumed with a constant DID of 11.5 (increased by <0.1 DID or 0.4%). Aminopenicillins consumption was mainly from amoxicillin (9.3 DID) (decreased by 0.7 DID or 7.1%) and ampicillin (2.2 DID) (increased by 0.7 DID or 52.6%). Ranked second in the high priority group of CIA, aminopenicillins with beta-lactamase inhibitors were consumed at 2.4 DID (increased by 0.7 DID or 38.4%), almost solely from amoxicillin in combination with beta-lactamase inhibitor (2.4 DID) (increased by 0.7 DID or 38.7%). For drugs solely used to treat mycobacterial infections, consumption was at 1.5 DID (increased by <0.1 DID or 4.9%). The consumption of antituberculous drugs mainly came from isoniazid (0.8 DID) (decreased by <0.1 DID or 5.6%), pyrazinamide (0.3 DID) (increased by <0.1 DID or 29.4%), and ethambutol (0.3 DID) (increased by <0.1 DID or 12.3%). As a group of drugs used to treat both mycobacterial and other infections, ansamycins were consumed at 0.9 DID (increase by <0.1 DID or 4.6%), solely from rifampicin (Table A7).

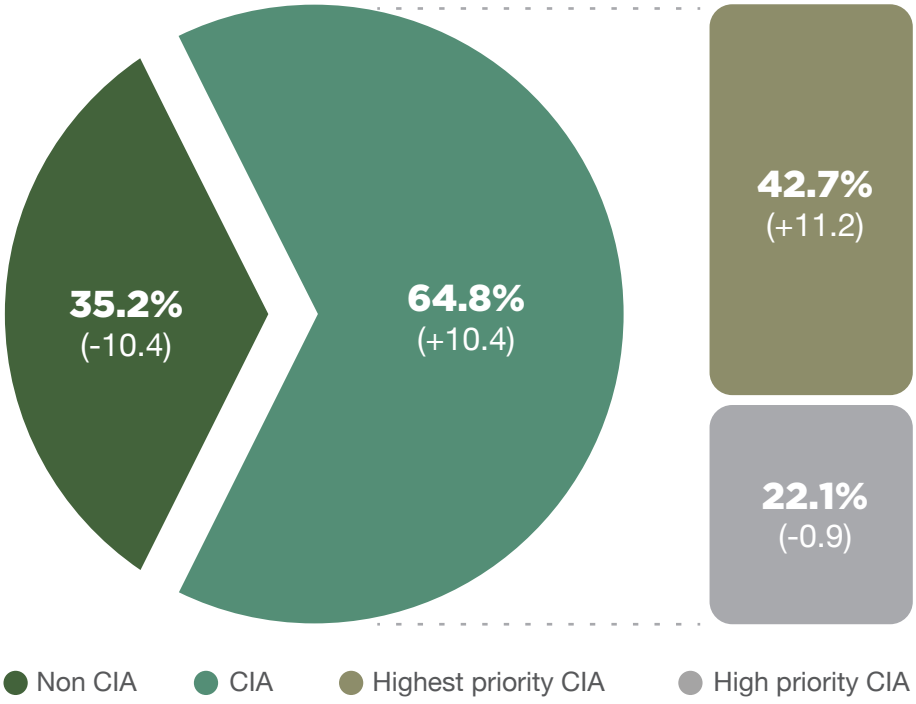


Figure 9. Proportion of consumption of Critically Important Antimicrobials to non CIA, and percent point change from 2017

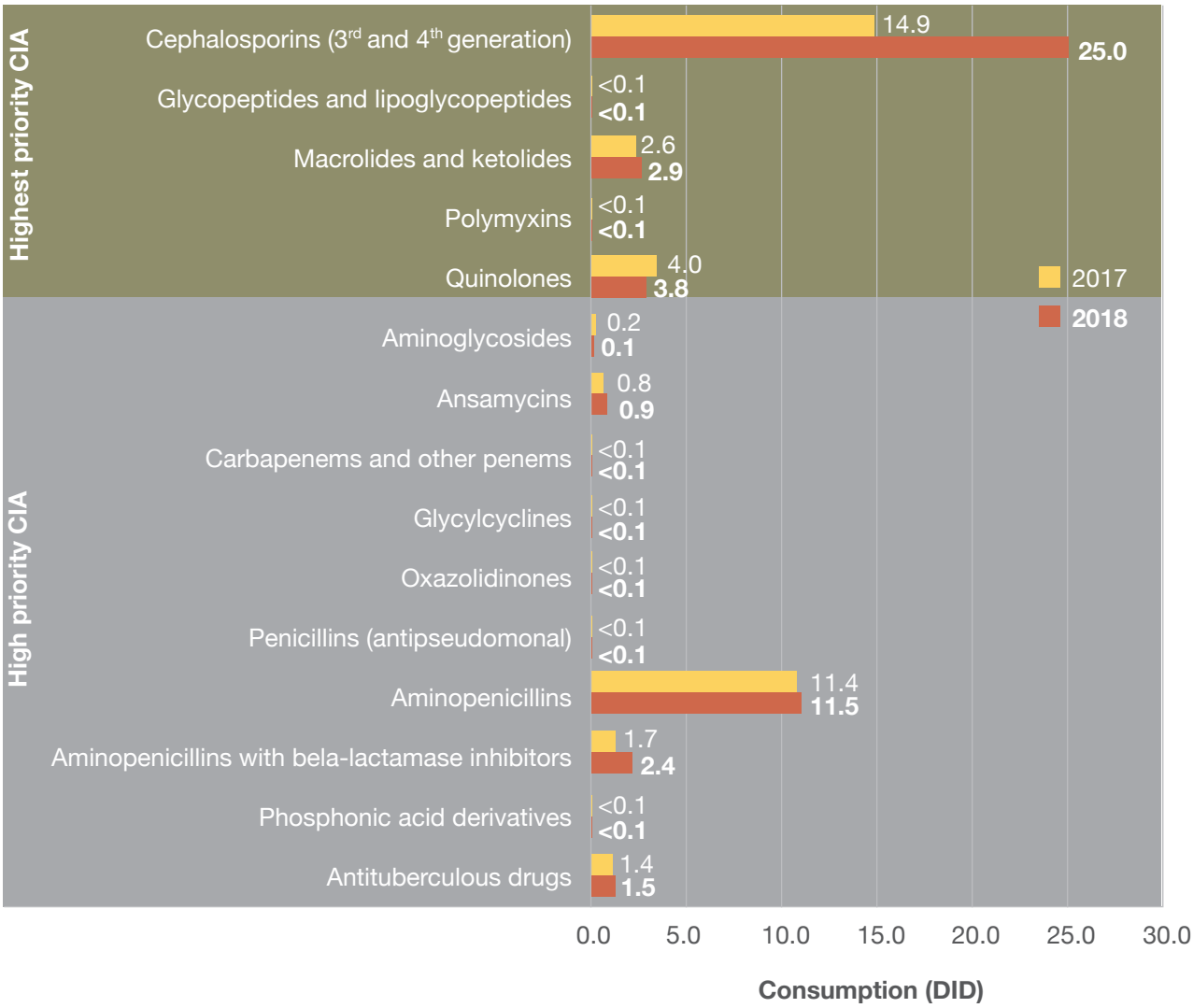


Figure 10. Comparison of Critically Important Antimicrobials between 2017 and 2018 classified by class of antimicrobials (DDD/1,000 inhabitants/day, DID)

2.1.4 Limitations

A few limitations are addressed. The law did not require pharmaceutical operators to submit export volumes, so not all pharmaceutical manufacturers and importers voluntarily submitted data to the Thai FDA. Consequently, the amount of human antimicrobial consumption might be overestimated. Moreover, unlike European Surveillance of Antimicrobial Consumption Network (ESAC-Net) which relies on sales data or the national electronic prescription database, Thailand SAC relies on manufacture and importation data minus the export volume; this has an inevitable disadvantage because the accuracy of the data could be disturbed by the amount of unconsumed stock products. However, in an efficient private pharmaceutical market, it is assumed that the stock level should be constant over the year in order to minimize the cost of large stock. We therefore assume that the total amount of importation and manufacture minus exports reflect the total consumption in Thailand. Such approach is the only feasible solution; while awaiting for sales data which requires legislative process of amendment of the Drug Act. Meanwhile, Thai FDA will request for voluntary reporting by pharmaceutical operators of sales volume for calendar year 2019.

In its effort to achieve the actual national consumption figures, Thai FDA received cooperation from pharmaceutical operators in reporting and improved methodology to capture all antimicrobials, resulting in not only number of reported registered products but also improved quality of the reports. Along with

verification of registration database from 2017 especially relating to drug strengths and ATC codes, the differences in consumption data may be derived not only from policies in relation to antimicrobial distribution but from these methodological improvements as well.

Aside from the limitations above, annual reports to the Thai FDA do not capture illegal imports and products, and need on-site regular verification for data integrity and quality. Lastly, but most importantly, the consumption identified by Thailand SAC cannot be compared with that of other countries due to differences in human epidemiology and disease burdens.

2.1.5 Prospect

In order to fully capture antimicrobial consumption, all export values need to be reported and verified with other sources such as port of entry for air, land and sea borders. In doing so, it not only increases the accuracy of the data, but also prevents illegal importation and smuggling along borders. As an unavoidable disadvantage of using total manufacture and import data, the consumption data cannot provide information on how many drugs have been used annually at primary healthcare, retail sector and inpatient hospital care, which results in a lack of granularity of data about use by patients according to age, gender and clinical department. Therefore, sales data would be more accurate than import, local production and export data. The HPSR AMR working group decided that the Thai FDA will request voluntary reporting on sales for 2019. Mandatory reporting requires legislative amendments. The new amendments of Ministerial regulation are expected to endorse a new submission form for mandatory annual reporting of distribution channels and export volumes of all medicines including antimicrobials, electronic submission for pharmaceutical operators and four monthly reporting of high-risk drugs. Despite the fact that the draft of the amendments passed through a public hearing in November 2018, the legislation needs many steps of endorsement and is now in process of review by the Secretariat of the Cabinet, which will be followed by the endorsement of the Council of State before coming into effect.

For the ultimate goal, antimicrobial consumption at user level such as by clinical departments, age and gender for inpatient services and primary health and retail sector for outpatient care, should be considered; in this way the data can actually reflect the amount of antimicrobials used and support identification of policy consequences. However, such implementation requires a good drug-dispensing system aligned with reliable information systems such as host-to-host services or other timely systems with internal validation.

2.1.6 Acknowledgments

Thailand SAC is locally initiated and established. It receives financial supports from various partners, in particular the World Health Organization South-East Asia, the United States Agency for International Development, the Food and Agriculture Organization of the United Nations (FAO), WHO-CCS.

We acknowledge support from a number of colleagues — Suwit Wibulpolprasert, Suriya Wongkongkathep, Walaiporn Patcharanaruemol, Chutima Akaleephan, Pansak Pramokchon, Nithima Sumpradit, Sukanya Numsawat, Raththar Benchapalanont, Sudarat Damrongwatanapokin, Wantanee Kalpravidh, Kachen Wongsathapornchai, Pennapa Matayompong, Orratai Waleewong, Klara Tisocki, Richard Brown, Dennis Carroll, Daniel Schar, Katinka de Balogh, Ronello Abila, Animal Health Products Association and Thai Feed Mill Association.

Arno Muller, Hege Salvesen Blix, Birgitte Borck Høg, Laura Mie Jensen, Fraser Broadfoot, Gunilla Skoog Ståhlgren, Kari Grave and Christina Greko are acknowledged for their independent external peer review of the methodology applied by Thailand SAC and their invaluable advice to this report.

Supon Limwattananon and Anond Kulthanmanusorn are acknowledged for their internal peer review, data verification and invaluable comments to the report.

2.2 Antimicrobial consumption in food-producing animals

Data source
Food and Drug Administration, Ministry of Public Health

Authors
Supapat Kirivan, Charunee Krisanaphan, Varavoot Sermsinsiri, Pischa Lusanandana, Chaiporn Pumkam, Kritsada Limpananont, Chutamas Luangaroonchai, Sitanan Poonpolsub, Pongsathid Virungrojint, Thanida Harintharanon, Sasi Jareonpoj, Warangkana Toros, Julaporn Srinha, Suchana Sukklad, Natthapong Supimon, Somsajee Sivilaikul, Thanawan Na Thalang, Janejit Kongkumnerd, Thitiporn Laoprasert, Chanotit Nakmanoc, Narintha Boonkuang, Jutamas Auewongaree, Suppaluck Chambang
In collaboration with Thai Feed Mill Association, and Animal Health Products Association

Editors
Viroj Tangcharoensathien
Kumthorn Malathum
Angkana Lekagul
Sunicha Chanvatik
Wanwisa Kaewkhankhaeng

Key summary

Overall food-producing animal antimicrobial consumption

Year	Consumption (tonne of API)	Animal population (kg of $PCU_{Thailand}$)	Consumption (mg/$PCU_{Thailand}$)
2017	3,690.3	6,618,137,577.6	557.6
2018	3,816.3 [↑ 3.4%]	7,309,777,857.1 [↑10.5%]	522.1 [↓ 6.4%]

Similar to trends in 2017, antimicrobials for systemic use (QJ01) ranked highest, followed by those indicated for intestinal use. The third- and fourth-ranked antimicrobials were those for intramammary and intrauterine use, respectively.

Consumption of each antimicrobial class

Penicillins were the most common antimicrobial consumed and mainly comprised of amoxicillin. The other two major antimicrobials used in animals were tetracyclines and other antibacterials, the latter of which were primarily from halquinol and bacitracin.

Consumption by dosage form and route of administration

Over half of veterinary antimicrobial consumption (59.1%) was used through premix, mainly from halquinol, amoxicillin and tiamulin. Unlike in 2017, the subsequent ranked dose forms were oral powder and injectable products.

A quarter of consumption from injectable antimicrobials was amoxicillin. For intramammary products, the majority of consumption came from dihydrostreptomycin and cloxacillin.

Consumption of Critically Important Antimicrobials

In comparison with 2017, overall consumption of CIA has increased but with different drug profiles. For the highest priority group of CIA, macrolides were consumed the most, mainly from tilmicosin and tylosin, but to a slightly lesser extent than in 2017. The second-ranked CIA used in animals was polymyxins (colistin), followed by quinolones with enrofloxacin as a main drug. The consumption of both polymyxin and quinolones has decreased in 2018. The top-three antimicrobials in the highest priority group were colistin, followed by tilmicosin and tylosin.

For the high priority group of CIA, penicillins, as a whole, were consumed at a higher rate compared with 2017. This was followed by aminoglycosides and phosphonic acid derivatives, of which consumptions were decreased. The top-three antimicrobials in high priority were amoxicillin, neomycin and dihydrostreptomycin.

2.2.1 General

Unlike human medicines, almost all veterinary medicines including antimicrobials are classified by the Thai FDA as dangerous drugs, which mean they must be dispensed only by a licensed pharmacist or veterinarian without prescription. But, only a few of them are classified as specially-controlled drugs which require a prescription from a veterinarian, for example, antibacterials (medicated premix), quinolones and derivatives, cephalosporins (all dosage forms), macrolides (all dosage forms), and polymyxins (all dosage forms).

According to the NSP-AMR 2017-2021, Goal 3 is to reduce antimicrobial consumption in animals by 30.0% by 2021. In order to make the goal measurable, developing and sustaining Thailand SAC is of substantial importance as the only monitoring and evaluation platform. Aside from reaching the national goal, data from Thailand SAC are useful for both health professionals and policymakers. This stems from the fact that the consumption data can help monitor and assess the effects of policy implementation, law enforcement, ASP and other relevant interventions. With some improvements in methodology and data granularity such as specific antibiotics consumption by animal species, this useful information can be utilized at national, regional and local levels to tackle antimicrobial resistance problems in an efficient and practical way.

2.2.2 Data source

Similar to human antimicrobials, all pharmaceutical manufacturers and importers are required by the Thai FDA to submit an annual report, which consists of their total production and/or importation volumes of registered veterinary medicinal products, by 31 March of the following year. The data were then electronically retrieved after 31 March 2018 for analysis. In an effort to reach actual domestic consumption, the manufacturers and importers, although voluntarily, were requested to submit their total export volume for subtraction from the total consumption. The validation process was conducted at the same time with human medicines because some human pharmaceutical companies also produce animal drugs.

For the scope of veterinary target antimicrobials, Thailand SAC covered the list of antimicrobials in line with the World Organisation for Animal Health (OIE) and ESVAC [18] (Table 6).

Table 6. The scope of target antimicrobials intended for use in animals (mainly food-producing animals)

Target veterinary antimicrobials	ATC vet codes
1. Antimicrobial agents for intestinal use	
• Antibiotics	QA07AA
• Sulfonamides	QA07AB
• Other intestinal antiinfectives	QA07AX
2. Antimicrobial agents for intrauterine use	
• Antibiotics	QG01AA, QG01BA
• Sulfonamides	QG01AE, QG01BE
• Antibacterials	QG51AA
• Antiinfectives for intrauterine use	QG51AG
3. Antimicrobial agents for systemic use	QJ01
4. Antimicrobial agents for intramammary use	QJ51

2.2.3 Results

1. Overall veterinary antimicrobial consumption

Total national antimicrobial consumption includes the amounts of manufactured and imported antimicrobials for use in food-producing animals, which covers all pharmaceutical dose forms except oral tablets and capsules due to their main use in companion animals. Compared with that of 2017, the total consumption of antimicrobials in food-producing animals in 2018 (522.1 mg/$PCU_{Thailand}$) was reduced by 6.4%; however, both nominator and denominator were increased especially with an increase in the animal population by 10.5%. Of the total national consumption, antimicrobials indicated for systemic use (QJ01) ranked highest with an mg/$PCU_{Thailand}$ of 395.3 (a reduction of 10.5% from 2017). Following the antimicrobial agents for systemic use, the second most consumed antimicrobials were those for intestinal use with an increase of 9.3% from 2017, the majority of which came from other intestinal anti-infectives (QA07AX) (80.5 mg/$PCU_{Thailand}$). The third-ranked antimicrobials in veterinary consumption were antimicrobials used for intramammary infections with an enormous increase of 176.2% from 2017 (Figure 11).

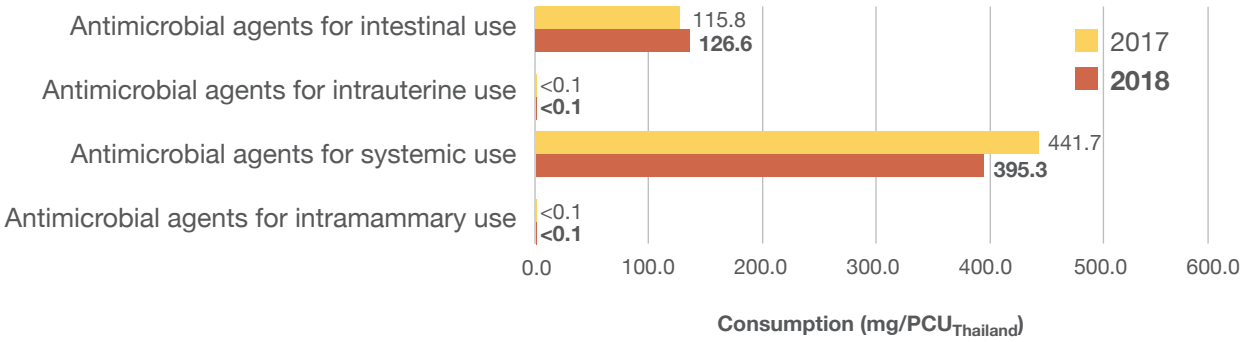


Figure 11. Comparison of consumption from target veterinary antimicrobials between 2017 and 2018 (mg/$PCU_{Thailand}$)

As shown in Figure 12 of the antimicrobials used for systemic infections (J01), beta lactams (QJ01C and QJ01D) were consumed most, accounting for 213.0 mg/$PCU_{Thailand}$ and increased in use by 41.1% from 2017. The most-consumed beta lactam was amoxicillin with an mg/$PCU_{Thailand}$ of 210.4 followed by procaine benzylpenicillin (1.1 mg/$PCU_{Thailand}$) and benzathine benzylpenicillin (0.5 mg/$PCU_{Thailand}$) (Table A8). Contributing to 12.1% of total consumption, the second-ranked antimicrobials consumed in this group were tetracyclines (QJ01A), of which consumption decreased by 41.2% from 2017. The main tetracyclines were chlortetracycline (42.8 mg/$PCU_{Thailand}$), doxycycline (14.6 mg/$PCU_{Thailand}$) and oxytetracycline (5.8 mg/$PCU_{Thailand}$). Unlike the results of 2017, the third rank belonged to other antibacterials (QJ01X), accounting for 12.1% of total national consumption, which increased by 28.5% compared with 2017. Most consumption in this group came from tiamulin (60.2 mg/$PCU_{Thailand}$), spectinomycin (2.0 mg/$PCU_{Thailand}$) and fosfomycin (0.9 mg/ $PCU_{Thailand}$).

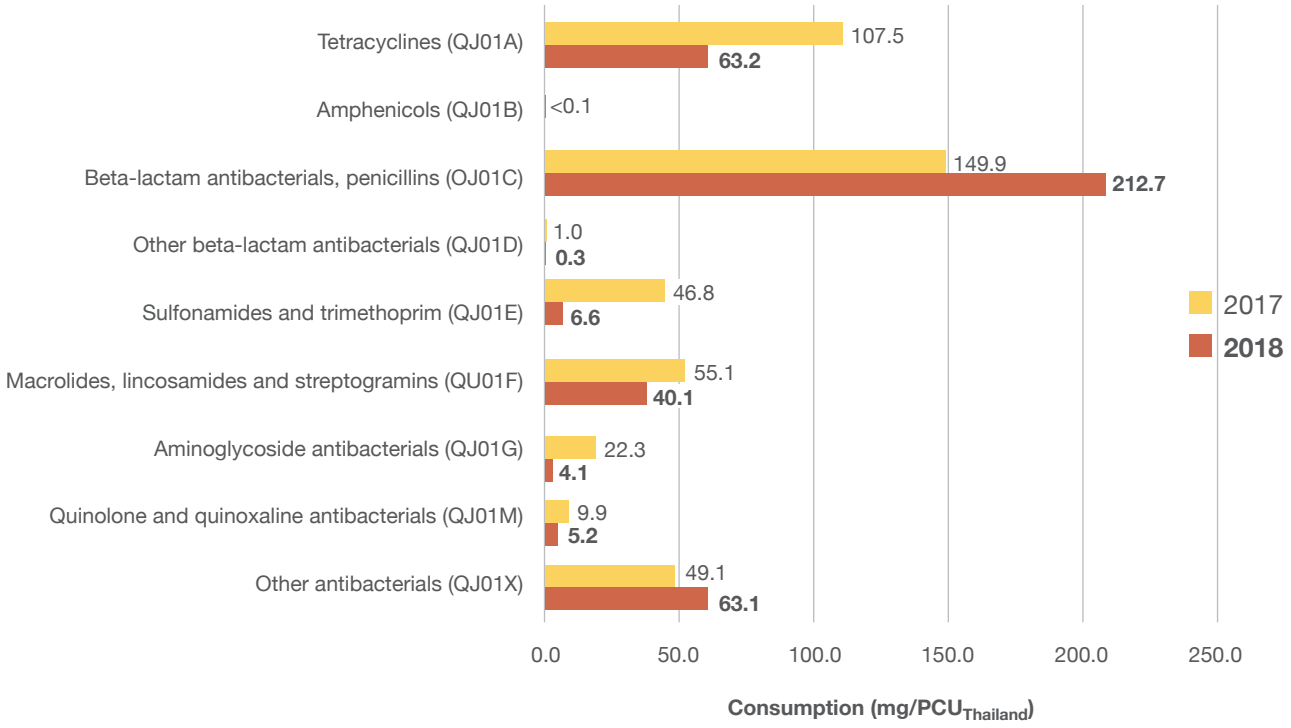


Figure 12. Comparison of consumption from veterinary antimicrobials indicated for systemic use (J01) between 2017 and 2018 (mg/$PCU_{Thailand}$)

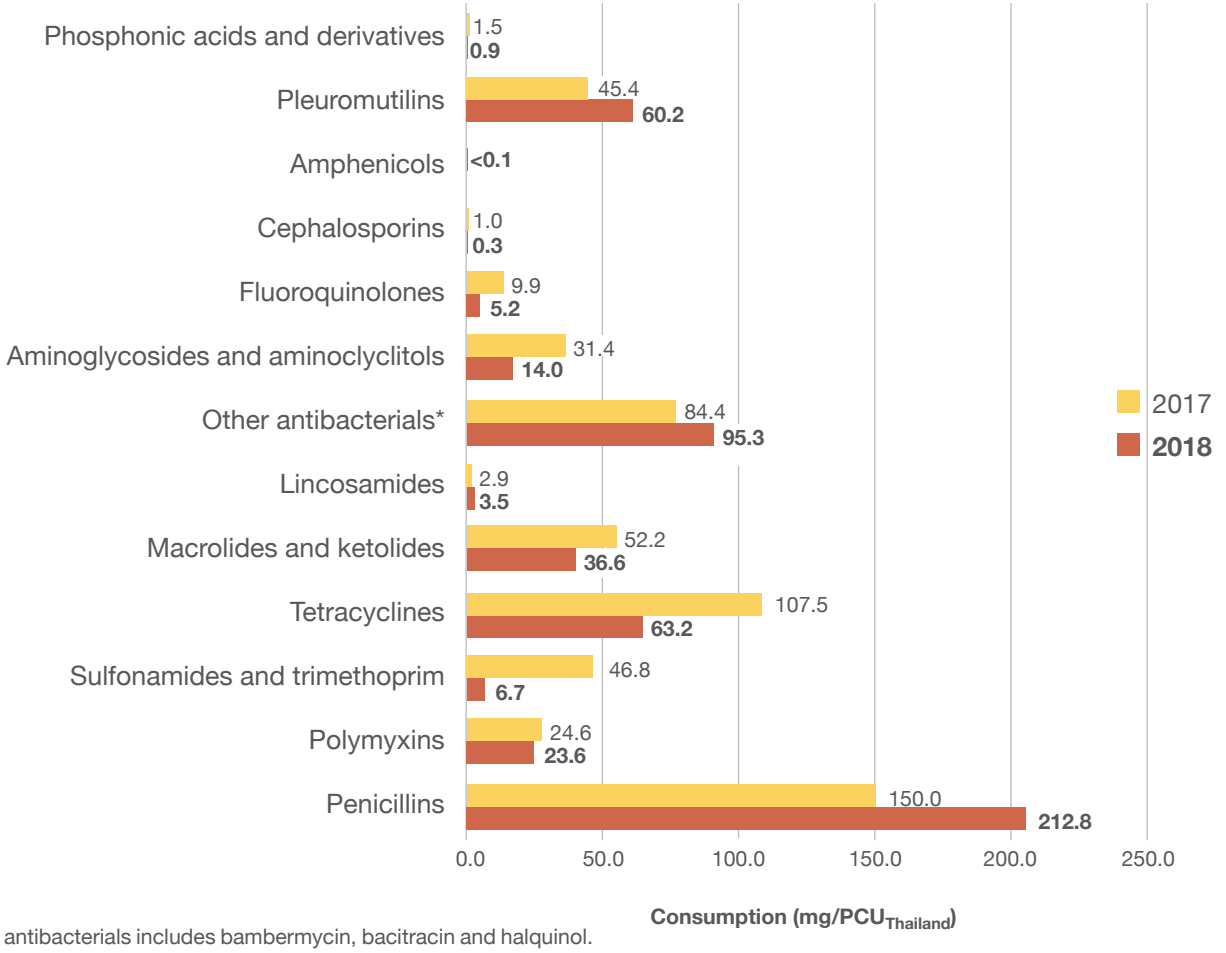
For antimicrobials used for gastrointestinal infections (QA07AX), halquinol was used most at an mg/$PCU_{Thailand}$ of 80.5 (Table A9). This was followed by colistin and bacitracin, with an mg/$PCU_{Thailand}$ of 23.5 and 14.6 respectively. The third-ranked antimicrobials in the scope belonged to antimicrobials intended for intramammary use, mainly from cloxacillin (<0.1 mg/$PCU_{Thailand}$) and an aminoglycosidic agent - dihydrostreptomycin (<0.1 mg/$PCU_{Thailand}$) (Table A10).

2. Veterinary antimicrobial consumption breakdown

a) Antimicrobial class

Consideration by class of antimicrobials in Figure 13, penicillins were consumed most (40.8%), mainly from amoxicillin with 210.4 mg/$PCU_{Thailand}$. However, the consumption of penicillins increased with the highest change of all antimicrobials of 56.7% compared with 2017. The second-ranked consumed antimicrobials belonged to other antibacterials, accounting for 18.3%. Over 80.0% of other antibacterial consumption was from halquinol in the form of premix. The third-ranked antimicrobials consumed were tetracyclines (12.1%). The majority of tetracycline consumption was from chlortetracycline and doxycycline, both of which were intended for systemic use (Table A11).

Unlike in 2017, sulfonamides, dihydrofolate reductase inhibitors and combinations were consumed in humans more than in animals; the animal consumption of sulfonamides and trimethoprim was reduced by the highest change of 84.3% compared with 2017. The top-three sulfonamides consumed were sulfadiazine (3.3 mg/$PCU_{Thailand}$), sulfadimidine (1.7 mg/$PCU_{Thailand}$) and trimethoprim (1 mg/$PCU_{Thailand}$). The other group of antimicrobials consumed in 2017 but not in 2018 was amphenicols (Table A11). Regarding the antimicrobial class with a constant consumption for two consecutive years, polymyxins, solely from colistin, were consumed at a proportion of 4.5% to total veterinary consumption.



*Other antibacterials includes bambermycin, bacitracin and halquinol.

Figure 13. Comparison of consumption from veterinary antimicrobials classified by drug class between 2017 and 2018 (mg/$PCU_{Thailand}$)

b) Dosage form and route of administration breakdown

When grouped by pharmaceutical dose form, more than half of veterinary antimicrobials were in the form of premix, similar to that of 2017 (Figure 14). Compared with the total premix consumption, the three major antimicrobials used as premix were halquinol (26.1%), amoxicillin (19.2%) and tiamulin (18.9%) (Table A11). In addition to a slight increase in premix consumption (increased by 5.3 mg/ $PCU_{Thailand}$ or 1.8%), the top-five antimicrobials used as premix remained the same as in 2017, but in a different sequence (Figure 15). As the second-ranked most-used dosage form, oral powder was consumed at 192 mg/$PCU_{Thailand}$, the majority of which came from powder for drinking water (88.1%) and powder for drinking water/milk (10.0%). Amoxicillin accounted for 66.2% of consumption through drinking water. The third-ranked most-consumed dose form was injection, approximately a quarter of which came from amoxicillin used as suspension for injection (3.8 mg/$PCU_{Thailand}$).

The pharmaceutical dosage form with the highest change from 2017 was oral solution (-8.2 percent point change of total consumption), consumed more than 70.0% in drinking water, over 75.0% of which was from enrofloxacin. Regarding one of two dosage forms with a constant proportion of consumption, consumption of antimicrobials for intramammary use mainly came from intramammary suspension 89.0% the majority of which was from dihydrostreptomycin (27.6%) and cloxacillin (26.4%). Accounting only for 0.1 mg/$PCU_{Thailand}$, other dose forms were consumed mostly from oral paste, followed by vaginal tablet and intrauterine suspension (Figure 14).

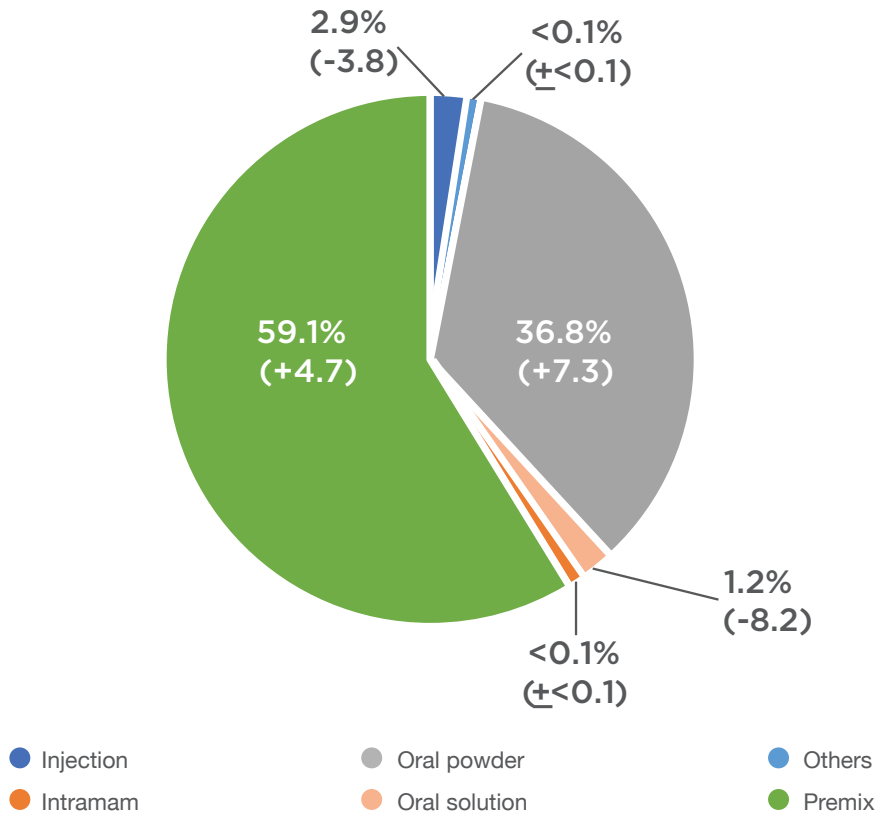


Figure 14. Proportion of consumption of veterinary antimicrobials in 2018 and percent point change from 2017 classified by pharmaceutical dosage form

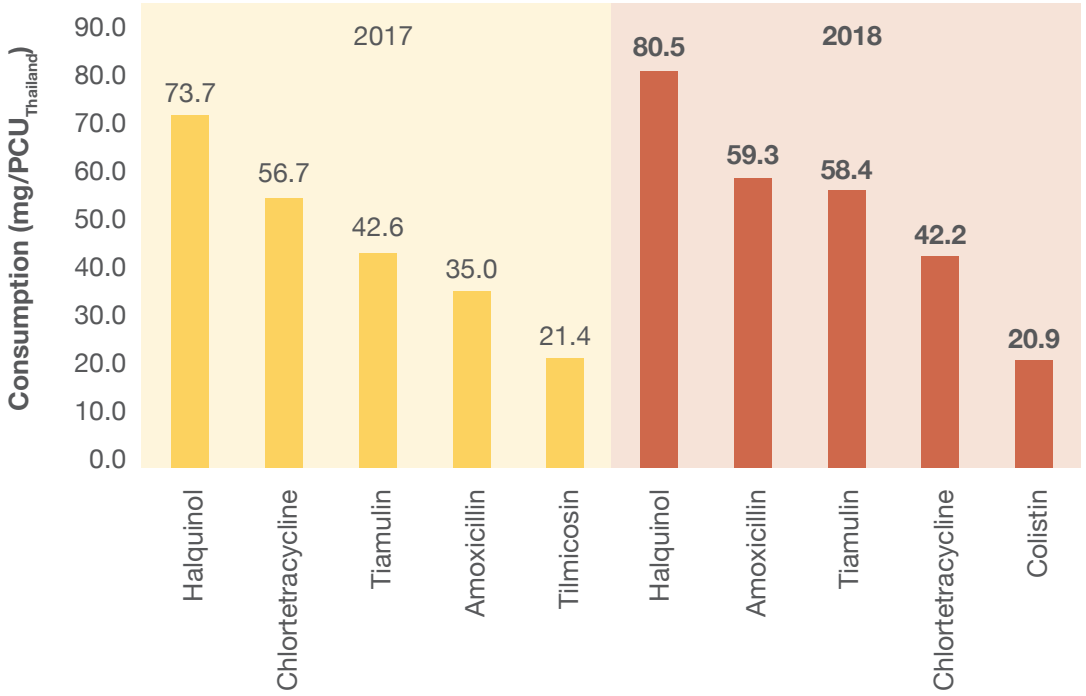


Figure 15. Comparison of consumption of top-five veterinary antimicrobials used as premix between 2017 and 2018 (mg/PCU$_{Thailand}$)

3. Consumption of Critically Important Antimicrobials

In 2018 the consumption of human CIA in animals increased by 8.6% compared with 2017, with a shift in proportion to more than half of total consumption. However, the profile of CIA in detail was shifted to antimicrobials belonging to the high priority group of CIA, and this followed the trend of 2017 (Figure 16).

Regarding the highest priority group of CIA, the three major CIA consumed in animals were the same as in 2017: macrolides, polymyxins and quinolones (Figure 17). The top-three antimicrobials consumed were colistin, tilmicosin and tylosin. As the first-ranked group of most-consumed antimicrobials in highest priority CIA in 2018, the consumption of macrolides decreased by 29.8%. The main consumption of macrolides came from tilmicosin (45.7% of macrolide consumption), tylosin 39.0% of macrolide consumption) and kitasamycin (7.4% of macrolide consumption) (Table A12). Ranked second in consumption among the highest priority group of CIA, polymyxins were solely from colistin; however, the consumption of colistin remained almost constant with a slight reduction of 4.2% compared with 2017. As the third-ranked highest priority group of CIA, quinolones were consumed mainly from enrofloxacin (98.9% of total quinolone consumption); however, the overall quinolone consumption decreased by 47.8% because of a massive decrease in consumption of danofloxacin and enrofloxacin. Despite being ranked last in the highest priority group of CIA, the consumption of cephalosporins (3rd and 4th generation) was further reduced by 71.2% mainly due to reductions of cefquinome and cefovecin by 99.4% and 14.4%, respectively (Table A12).

With respect to the high priority group of CIA, the top-three were amoxicillin, neomycin and dihydrostreptomycin. Similar to 2017, penicillins were consumed most in the animal sector. Interestingly, the consumption of aminopenicillins alone was three times more than that consumed in the highest priority group of CIA, and the most-consumed drug in the high priority group. Unlike other CIA, which decreased in consumption, the consumption of aminopenicillins increased by a massive amount of 42.5% compared with 2017. Almost all aminopenicillins consumption came from amoxicillin. However, the consumption of aminopenicillins in combination with beta-lactamase inhibitors was reduced by 24.6% from 2017. As the

second-ranked CIA in this priority, the consumption of aminoglycosides decreased by 59.1% due to the reduction in consumption of gentamicin and streptomycin. The majority of aminoglycoside consumption in 2018 was derived from neomycin (65.3%) and dihydrostreptomycin (16.5%) (Table A12). Another group of high priority CIA, phosphoric acids and their derivatives, were consumed solely from fosfomycin and more in animal sectors as premix for medicated feeding stuff. Like most other CIA, the consumption of this group decreased by 43.5%.

As shown in Figure 18, the profile of CIA consumption in animals is different to that of humans. Regarding the highest priority group of CIA, humans consumed cephalosporins (3rd and 4th generation) and quinolones more than animals did. On the other hand, animals consumed macrolides and ketolides and polymyxins more than humans did. For the high priority group of CIA, aminopenicillins was consumed most in the animal sector (977.9 tonnes), twice as much as that of humans (474.9 tonnes). Aminoglycosides and phosphonic acids were the other two groups of high priority CIA, and consumed much more in animals than in humans. Aminopenicillins with beta-lactamase inhibitors was the only group in this priority consumed by humans more than by animals.

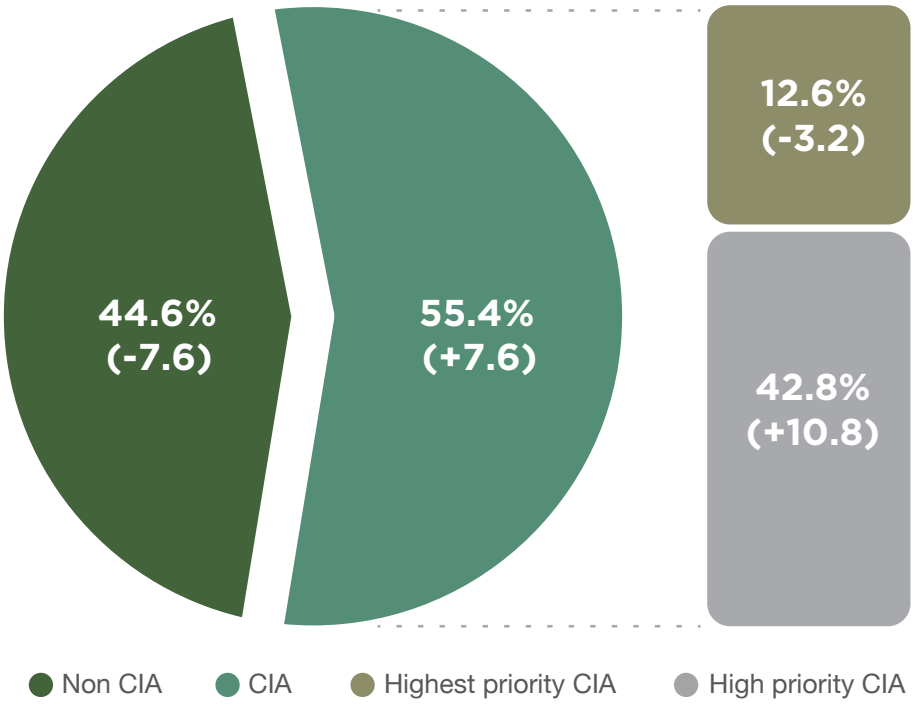


Figure 16. Proportion of consumption of Critically Important Antimicrobials to non CIA in animals and percent point change from 2017

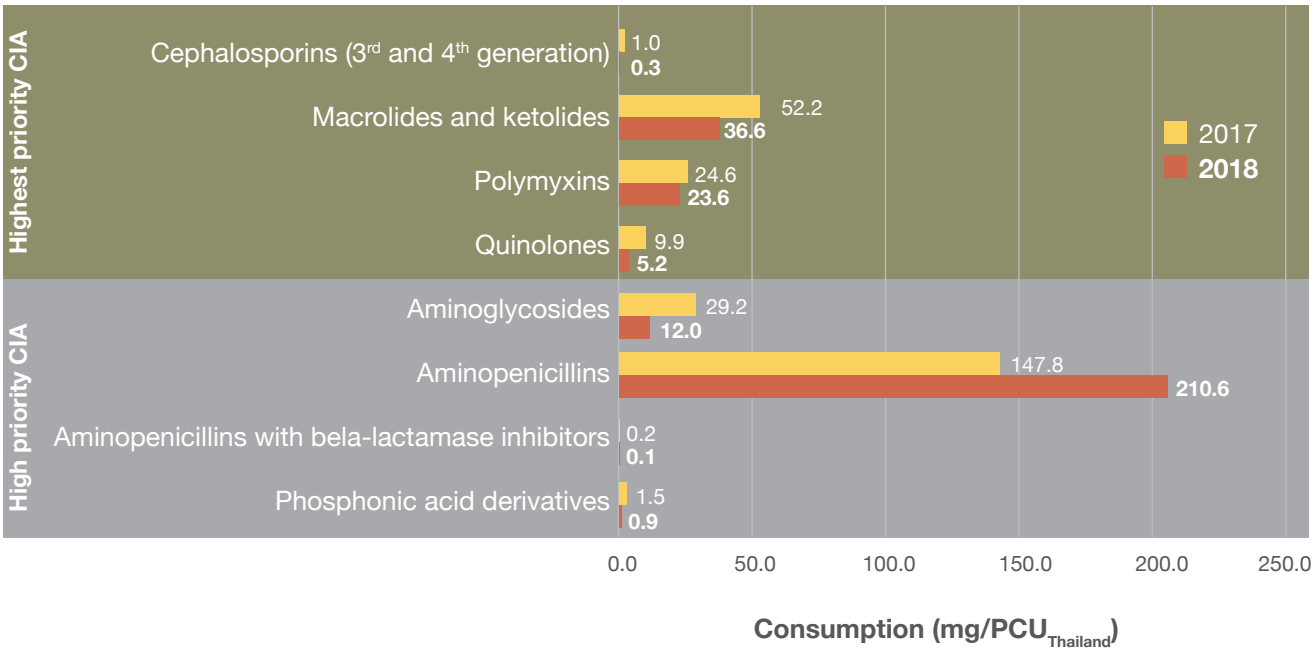


Figure 17. Consumption of Critically Important Antimicrobials (mg/PCU$_{Thailand}$)

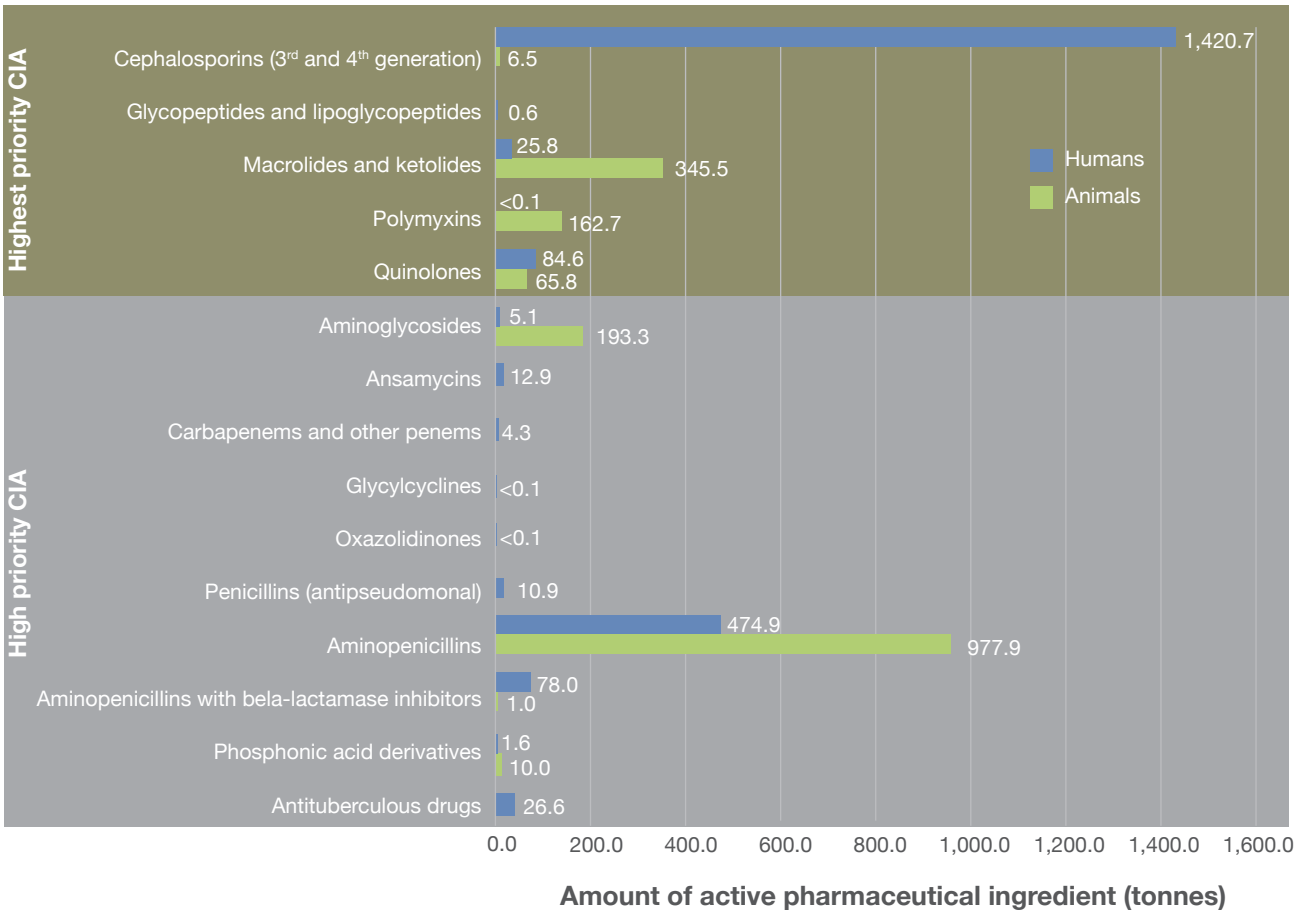


Figure 18. Comparison of consumption of Critically Important Antimicrobials between human and animal sectors in 2018 (tonnes of active pharmaceutical ingredient)

2.2.4 Limitations

Despite efforts made so far, the law does not require pharmaceutical operators to submit export volume. Therefore, it cannot be assured that all pharmaceutical manufacturers and importers submitted the data to the FDA and that the data quality is acceptable in term of accuracy and completeness. The same limitations apply to human antimicrobials.

With an effort to achieve the actual national consumption, the Thai FDA received cooperation from pharmaceutical operators in reporting and improved methodologies to capture all antimicrobials, resulting in not only an increased number of reported registered products but also better quality of the reports. Along with verification of the registration database from 2017 especially relating to drug strengths and ATC codes, the differences in consumption data may be derived not only from policies in relation to antimicrobial distribution but from these methodological improvements as well.

Moreover, the consumption of veterinary antimicrobials cannot be compared with data from other countries due to differences in animal epidemiology, farm management and burdens of disease in tropical climates. Additionally, the consumption data cannot be broken down by animal species, so it was not possible to identify which sector has extensively used antimicrobials and in which sector policy changes need to be implemented.

2.2.5 Prospect

Similar to human consumption data, veterinary consumption data - assuming that total import and production minus total export is the total national consumption - cannot provide accurate information on how drugs are used annually; therefore, acquiring sales data would be more accurate. The Thai FDA will request that sales data be provided on a voluntary basis in the 2019 annual report. Mandatory reporting requires legislative amendment. The new amendments of Ministerial regulation are expected to endorse a new submission form for mandatory annual reporting of distribution channel and export volumes of all medicines including antimicrobials, electronic submission for pharmaceutical operators and four-monthly reporting of high-risk drugs. Despite the fact that the draft of the amendments passed through public hearing in November 2018, the legislation needs many steps of endorsement and is now in process of review by the Secretariat of the Cabinet, which will be followed by the endorsement of the Council of State before coming into effect.

In the future development of Thailand SAC, consumption of antimicrobials in the animal sector needs to be classified by species in order to provide more accurate policy recommendations on optimizing antimicrobial use. In doing so, it requires collaboration among other competent authorities such as the Department of Livestock Development, Department of Fisheries and other relevant sectors.

2.2.6 Acknowledgments

Thailand SAC is locally initiated and established. It receives financial supports from various partners, in particular the World Health Organization South-East Asia, the United States Agency for International Development, the Food and Agriculture Organization of the United Nations (FAO), WHO-CCS.

We acknowledge support from a number of colleagues — Suwit Wibulpolprasert, Suriya Wongkongkathep, Walaiporn Patcharanaruemol, Chutima Akaleephan, Pansak Pramokchon, Nithima Sumpradit, Sukanya Numsawat, Raththar Benchapalanont, Sudarat Damrongwatanapokin, Wantanee Kalpravidh, Kachen Wongsathapornchai, Pennapa Matayompong, Orratai Waleewong, Klara Tisocki, Richard Brown, Dennis Carroll, Daniel Schar, Katinka de Balogh, Ronello Abila, Animal Health Products Association and Thai Feed Mill Association.

Arno Muller, Hege Salvesen Blix, Birgitte Borck Høg, Laura Mie Jensen, Fraser Broadfoot, Gunilla Skoog Ståhlgren, Kari Grave and Christina Greko are acknowledged for their independent external peer review of the methodology applied by Thailand SAC and their invaluable advice to this report.

Supon Limwattananon and Anond Kulthanmanusorn are acknowledged for their internal peer review, data verification and invaluable comments to the report.

2.3 Antimicrobial consumption in companion animals

In the Fiscal Year (FY) 2021, the Thai working group on Health Policy and Systems Research on AMR planned to conduct research on system analysis of AMU in companion animals and to conduct a pilot surveillance of antimicrobial consumption in Thailand. Based on these pilots and systems development, the routine monitoring of AMU in companion animals will be launched in FY2022. Assessment by HPSR-AMR team of electronic databases which capture prescription/dispensing in a number of animal hospitals which applied commercial software by two major vendors found it feasible to develop a system of antimicrobial use from these dispensing database.

ANTIMICROBIAL RESISTANCE

3.1 Surveillance of antimicrobial resistance in humans

Data source
National Antimicrobial Resistance Surveillance Center Thailand (NARST),
National Institute of Health, Department of Medical Sciences, Ministry of Public Health,
Department of Disease Control, Ministry of Public Health, Thailand

Authors
Sang Usayaporn
Ratchanu Charoenpak
Abhisit Prawang
Noppavan Janejai
Wantana Paveenkittiporn
Aekkawat Unahalekhaka
Pimrata Leethongdee

Editors
Kumthorn Malathum
Viroj Tangcharoensathien
Angkana Lekagul
Sunicha Chanvatik
Wanwisa Kaewkhankhaeng

Key summary

Gram-negative bacteria

Overall, there has been an increasing antimicrobial resistance trend over the period of this study, especially in Gram-negative bacteria.

The highest rise was observed for colistin resistance in *Acinetobacter calcoaceticus-baumannii* complex, *Pseudomonas aeruginosa* and *Enterobacteriaceae*. Although the resistant isolates comprised a small portion of each species due to limited feasibility for MIC determination, colistin resistance signified the worrisome situation as it is the last resort.

The proportion of carbapenem resistance among *Acinetobacter baumannii* and *Pseudomonas aeruginosa* were stable, but proportion has remarkably increased in *Escherichia coli* and *Klebsiella pneumoniae.*

Gram-positive bacteria

An increasing trend of methicillin-resistant coagulase-negative *Staphylococcus* (MRCNS) prevalence was seen. On the other hand, the methicillin-resistant *Staphylococcus aureus* (MRSA) rate has gradually declined over the period.

Growing numbers of vancomycin-resistant *Enterococcus* (VRE) tested by the MIC method have been reported in 2018, although only a small number of isolates were performed with the MIC test. However, the VRE rate remained unchanged at less than 10.0% when disk diffusion data were considered.

A similar rate of penicillin-nonsusceptibility and cefotaxime-nonsusceptibility was observed among *Streptococcus pneumoniae* isolates from both sterile and non-sterile sites in 2017 and 2018.

Other antimicrobial resistant bacteria

Of the non-typhoidal *Salmonella* spp. isolated in 2017-2018, the proportion of third-generation cephalosporin resistance was constant, while increasing proportion of fluoroquinolone resistance was observed.

All gonococcal isolates in 2017-2018 remained susceptible to ceftriaxone and cefixime, but high azithromycin MIC was occasionally seen.

3.1.1 General

In Thailand, AMR in bacterial isolates from humans has been increasing continuously. The burden and consequences of AMR present most serious public health problems. Accordingly, the NSP-AMR 2017-2021 focusing on AMR surveillance and monitoring of key pathogens causing morbidity and mortality is established to better understand the situation and direct policy. The surveillance has been designed to cover human, agriculture, and environment. However, at the initial stages only antimicrobial resistance in humans was within the scope of this surveillance report.

To date, trends in antimicrobial resistance have been routinely reported by NARST, however systematically combined report on AMC and AMR. The objective of this One Health report for 2018 was to identify national trends on AMR in humans for 2017-2018, in particular, major resistant bacteria and CIAs as recommended by Thailand's National Strategic Plan, and to produce clinically relevant data that can be utilized for clinical applications.

3.1.2 Data Sources

Antimicrobial resistance data were collected from 74 and 85 hospitals in Thailand during 2017 and 2018, with support from NARST, National Institute of Health, Department of Medical Sciences, The Ministry of Public Health, Thailand.

The 2017 and 2018 gonococcal antimicrobial resistance data were provided by the Department of Disease Control, The Ministry of Public Health, Thailand through Bangrak STIs center, Silom Community Clinic @TropMed and three and six centers of The Office of Disease Prevention and Control, respectively.

Data on antimicrobial resistance and MIC values in 2017 and 2018 were interpreted according to CLSI susceptibility breakpoints 2017 and 2018, respectively.

Note: Unless otherwise specified, all antimicrobial resistance data in intermediate category was classified as resistance.

3.1.3 Results

Gram-negative bacteria

1. *Acinetobacter calcoaceticus-baumannii* complex

Due to the limited capability of many microbiology laboratories, identification of *Acinetobacter baumannii (A. baumannii)* cannot be ascertained. Thus, some non-baumannii *Acinetobacter* might be included in this susceptibility data set. Given its higher prevalence in clinical specimens tested in laboratories where accurate species can be performed and virulence properties, the majority of *Acinetobacter calcoaceticus-baumannii* complex is considered as *A. baumannii* in this report. The trends in carbapenem-resistant *A. calcoaceticus-baumannii* complex were steady at around 70.0% (Table 7). Meanwhile, an increasing trend in resistance was observed for ampicillin/sulbactam from 60.3% in 2017 to 65.3% in 2018, when intermediate category were not included in resistance data.

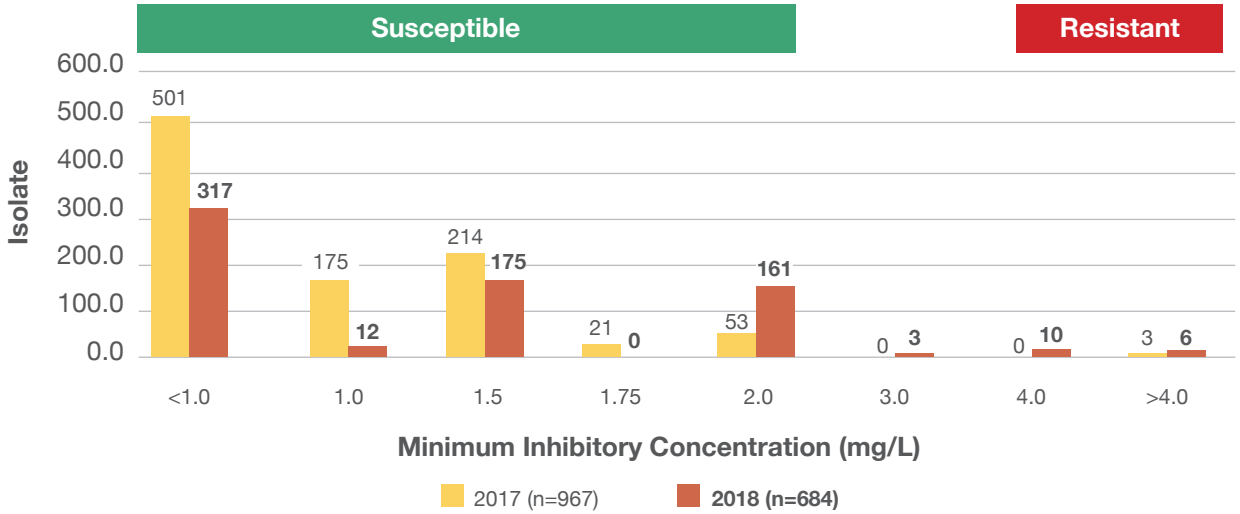
Table 7. The proportion of antimicrobial resistance in *Acinetobacter calcoaceticus-baumannii* complex, 2017-2018, % (total number of isolates tested)

Drug	2017, (n)	2018, (n)
Total number of isolates	**37,465**	**42,212**
Penicillins		
Ampicillin/sulbactam	69.8 (10,260)	69.3 (10,220)
Piperacillin/tazobactam	72.8 (27,671)	71.3 (31,054)
Cephalosporins		
Cefotaxime	97.2 (15,358)	92.3 (18,776)
Cefotaxime*	-	69.7 (587)

Drug	2017, (n)	2018, (n)
Ceftazidime	70.6 (31,795)	69.4 (36,040)
Ceftazidime*	-	58.6 (640)
Ceftriaxone	96.7 (17,457)	94.2 (18,080)
Ceftriaxone*	-	53.7 (784)
Cefepime	69.3 (2,529)	65.2 (4,944)
Carbapenems		
Imipenem	70.4 (23,171)	67.9 (28,378)
Meropenem	69.8 (32,077)	68.2 (36,766)
Fluoroquinolones		
Ciprofloxacin	70.3 (28,942)	67.6 (33,329)
Levofloxacin	71.5 (15,544)	67.4 (18,565)
Aminoglycosides		
Amikacin	52.1 (33,074)	51.8 (36,255)
Gentamicin	62.3 (29,227)	60.3 (31,954)
Miscellaneous		
Sulfamethoxazole/trimethoprim	59.9 (26,275)	56.7 (28,510)
Tetracycline	83.5 (242)	81.5 [u] (184)
Colistin*	0.3 (961)	2.9 (680)

*Interpreting by minimum inhibitory concentration test
U = Urine, Urine Catheter, Urine Clean-Voided

Furthermore, 2.9% of those in 2018 appeared resistant to colistin, exceeding that of 0.3% colistin resistance in 2017. Tested in a small portion of isolates of this bacterium (<1,000 out of ca. 40,000 isolates), the minimum inhibitory concentration 90 (MIC_{90}) of colistin was 2 mg/L that was higher than MIC_{90} in 2017 (1.5 mg/L) (Figure 19).



Colistin MIC by Sensititre® (number of hospitals)	MIC_{50} (mg/L)	MIC_{90} (mg/L)
2017 (7)	≤ 1.0	1.5
2018 (6)	2.0	2.0

Figure 19. MIC distribution of colistin for *Acinetobacter calcoaceticus-baumannii* complex, 2017-2018

2. *Pseudomonas aeruginosa*

Overall, 10.0% of *P. aeruginosa* were resistant amikacin while 15.0% - 20.0% were resistant to other anti-pseudomonal agents including carbapenem, ceftazidime, cefepime, and ciprofloxacin. The prevalence of carbapenem-resistant *P. aeruginosa* (CRPA) were similar between 2017 and 2018, i.e., 24.1 and 23.3%, respectively (Table 8). Additionally, CRPA isolates also showed discordance in susceptibility between meropenem and imipenem. In 2018, 63.3% of CRPA isolates were resistant to both antibiotics, however 11.2% of those remained susceptible to meropenem but were intermediate or resistant to imipenem, and only 7.5% of those remained susceptible to imipenem alone (Figure 20). CRPA isolates in 2018 remained susceptible to ceftazidime, cefepime and piperacillin/tazobactam in around 40.7%, 11.9%, and 40.0%, respectively, which were approximately the same proportion as they were in 2017 (Figure 21).

Table 8. The proportion (%) of antimicrobial resistance in *Pseudomonas aeruginosa*, 2017-2018

Drug	2017, (n)	2018, (n)
Total number of isolates	**34,987**	**36,083**
Penicillins		
Piperacillin/tazobactam	17.9 (27,651)	17.5 (29,311)
Cephalosporins		
Ceftazidime	18.2 (31,266)	17.7 (31,754)
Ceftazidime*	-	27 (575)
Cefepime	13.5 (4,764)	17.4 (7,304)
Carbapenems		
Imipenem	19.6 (23,297)	19.8 (25,387)
Meropenem	19.4 (29,240)	19.0 (30,605)
Fluoroquinolones		
Ciprofloxacin	15.3 (28,363)	14.6 (29,726)
Levofloxacin	17.9 (11,981)	17.0 (14,593)
Norfloxacin	38.6 (3,214)	-
Ofloxacin	15.5 (1,359)	-
Aminoglycosides		
Amikacin	9.7 (30,963)	8.8 (31,602)
Gentamicin	14.8 (28,421)	14.0 (27,290)
Netilmicin	11.7 (6,514)	-
Miscellaneous		
Colistin*	0.5 (409)	5.8 (571)

*Interpreting by minimum inhibitory concentration test

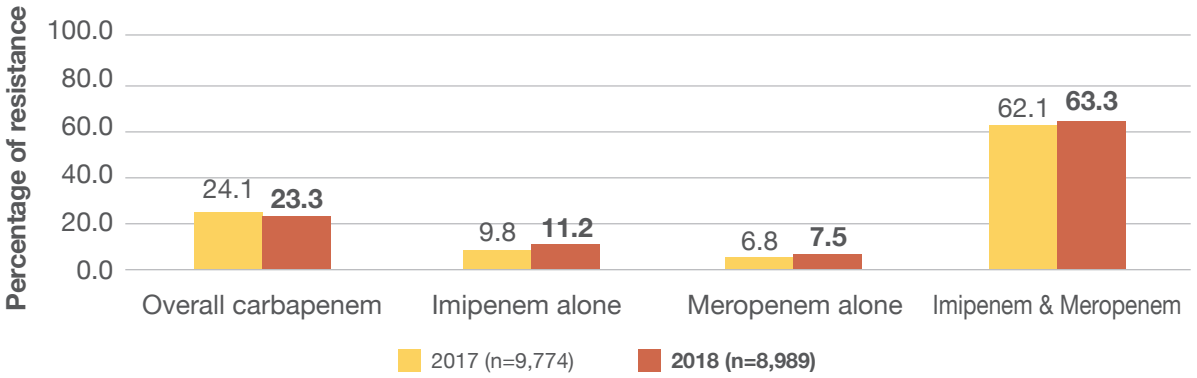


Figure 20. Trend in carbapenem resistance among carbapenem-resistant *Pseudomonas aeruginosa* in 2017-2018 (Carbapenem = carbapenem resistance, Imipenem alone = imipenem monoresistance, Meropenem alone = meropenem monoresistance, Imipenem and meropenem = resistant to both imipenem and meropenem)

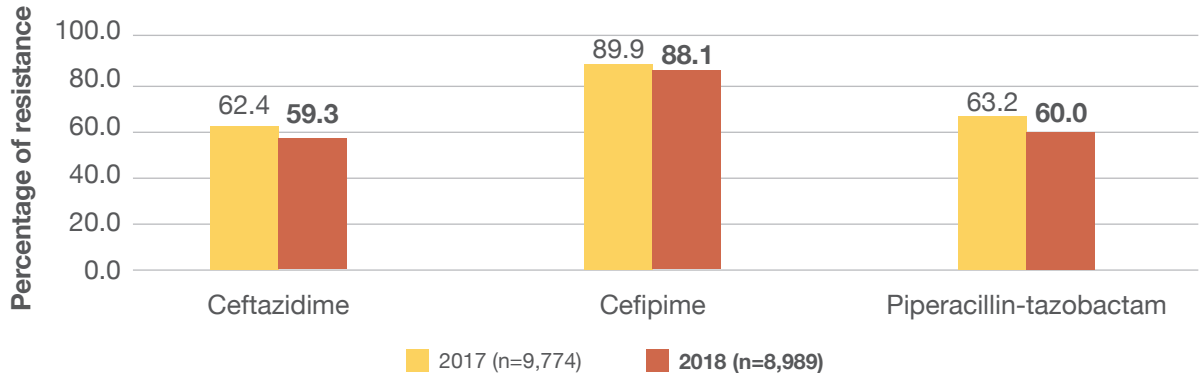
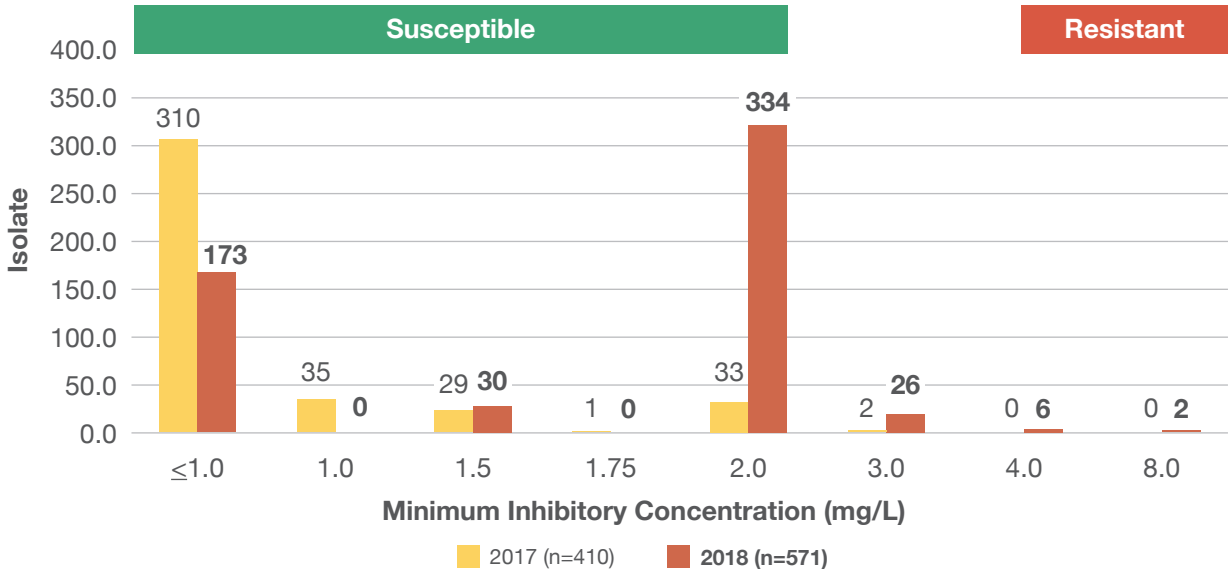


Figure 21. Trend in antimicrobial resistance among carbapenem-resistant *Pseudomonas aeruginosa* in 2017-2018.

A considerably increasing trend in colistin resistance was observed among isolates of *P. aeruginosa* from 0.5% in 2017 to 5.8% in 2018. Moreover, there was also an elevated colistin MIC_{90} value over the two-year period from 1.5 in 2017 to 2.0% in 2018 (Figure 22).



Colistin MIC by Sensititre® (number of hospitals)	MIC_{50} (mg/L)	MIC_{90} (mg/L)
2017 (7)	≤ 1.0	1.5
2018 (6)	2.0	2.0

Figure 22. MIC distribution of colistin for *Pseudomonas aeruginosa*, 2017-2018

3. *Escherichia coli*

Trends in third-generation cephalosporin resistant *E. coli* has not significantly changed during the period. Overall, the percentage of ceftriaxone resistance was between 42.7% and 44.0% and the percentage of ceftazidime resistance was between 34.7% and 36.0%, while the percentage of fluoroquinolone-resistant *E. coli* in 2018 remained about 50.0%, which was somewhat similar to 2017 (Table 9). Noticeably, while prevalence of fluoroquinolone resistance among *P. aeruginosa*, the organism well known for its ease of acquiring resistance, were around 15.0%, resistance of *E. coli* to fluoroquinolones have been around 50.0% for many years and there is no sign of reversion of this phenomenon thus far.

In addition, the percentage of strains susceptible-dose dependent (SDD) to cefepime was around 12.1%. It is recommended that higher doses and/or more frequent doses of up to 2 grams every 8 hours should be used for isolates within this category (Figure 23). Therefore, interpretation of susceptibility test of *E. coli* should be made with cautions in order to optimize the dose of cefepime accordingly to obtain optimal treatment outcomes.

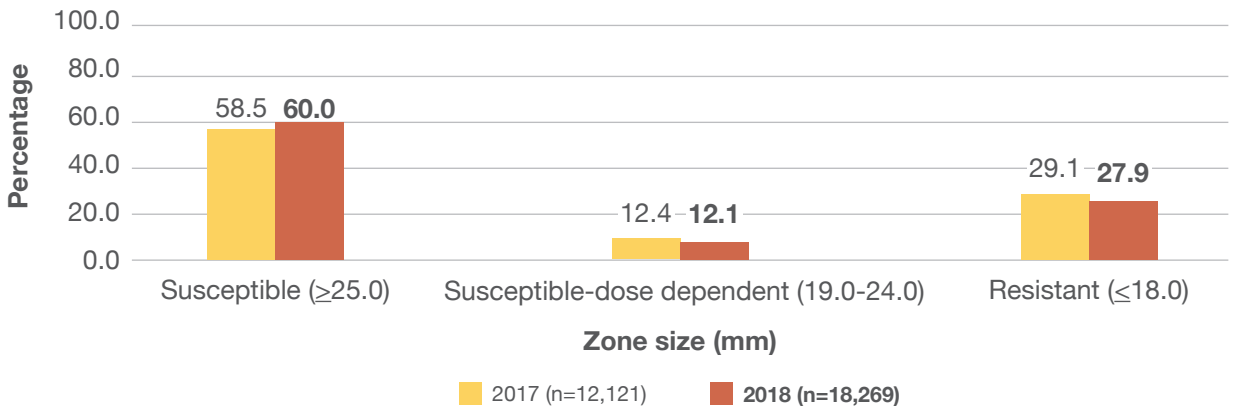


Figure 23. Percentage of susceptible, susceptible-dose dependent and resistance to cefepime among *Escherichia coli*, 2017-2018

Regarding carbapenem-resistant *Enterobacteriaceae* (CRE), *E. coli* resistance rate for carbapenems have remained low at less than 5.0%. However, the proportion of carbapenem-resistant *E. coli* has been slightly increasing over the 2-year period, and the proportion of carbapenem-resistant *E. coli* in 2018 accounted for approximately 2.8%-3.5%. The data are shown in Table 9.

Table 9. The proportion (%) of antimicrobial resistance in *Escherichia coli*, 2017-2018

Drug	2017, (n)	2018, (n)
Total number of isolates	**74,233**	**80,411**
Penicillins		
Ampicillin	86.7 (52,360)	85.7 (49,883)
Amoxicillin/clavulanic acid	33.6 (54,705)	32.3 (58,494)
Ampicillin/sulbactam	43.9 (14,915)	39.6 (13,974)
Piperacillin/tazobactam	8.5 (45,229)	8.9 (55,480)
Cephalosporins		
Cefazolin	67.9 (15,913)	66.9 (15,105)
Cefazolin (U)	49.9 (14,836)	48 (15,436)
Cefuroxime sodium (PARENTERAL)	47.8 (20,529)	45.6 (19,675)
Cefuroxime sodium (ORAL)	64.2 (676)	69.9 (791)
Cefoperazone/sulbactam	10.3 (39,918)	10.3 (40,218)

Drug	2017, (n)	2018, (n)
Cefotaxime	46.2 (54,558)	44.4 (56,133)
Cefotaxime*	-	46.2 (877)
Ceftazidime	36.0 (64,148)	34.7 (66,905)
Ceftazidime*	-	53.3 (1,529)
Ceftriaxone	44.0 (47,405)	42.7 (49,154)
Ceftriaxone*	-	74.7 (1735)
Cefepime	40.0 (9,677)	40.6 (1,5649)
Cefoxitin	12.3 (21,223)	11.8 (20,085)
Carbapenems		
Ertapenem	2.8 (6,795)	3.5 (10,712)
Imipenem	2.6 (46,313)	3.1 (53,860)
Meropenem	2.4 (55,564)	2.8 (62,484)
Fluoroquinolones		
Ciprofloxacin	52.0 (56,661)	50.5 (60,842)
Levofloxacin	50.8 (18,855)	48.8 (25,343)
Norfloxacin	-	57.2 (27,051)
Ofloxacin	53.1 (7,941)	-
Aminoglycosides		
Amikacin	1.5 (61,338)	1.9 (67,558)
Gentamicin	34.3 (61,815)	33 (63,926)
Netilmicin	5.2 (11,956)	-

Drug	2017, (n)	2018, (n)
Miscellaneous		
Fosfomycin (U)	1.9 (10,296)	2.9 (14,147)
Nitrofurantoin (U)	6.9 (3,214)	6.9 (3,699)
Chloramphenicol	23.6 (780)	23.2 (383)
Sulfamethoxazole/trimethoprim	58.4 (58,448)	56.1 (60,355)
Tetracycline	71.8 (5,073)	69 (4,432)
Colistin*	-	3.3 (752)

*Interpreting by minimum inhibitory concentration test

U = Urine, Urine Catheter, Urine Clean-Voided

In the era of antimicrobial resistance, transition to oral therapy is an opportunity for improvement in therapy. For urinary *E. coli* isolates, cefazolin was used as a surrogate for oral antimicrobial agent susceptibilities e.g. cefaclor, cefdinir, cefpodoxime, cefuroxime, cephalexin, etc. In 2018, slightly more than half (54.7%) of urinary *E. coli* isolates remained susceptible to cefazolin (Figure 24).

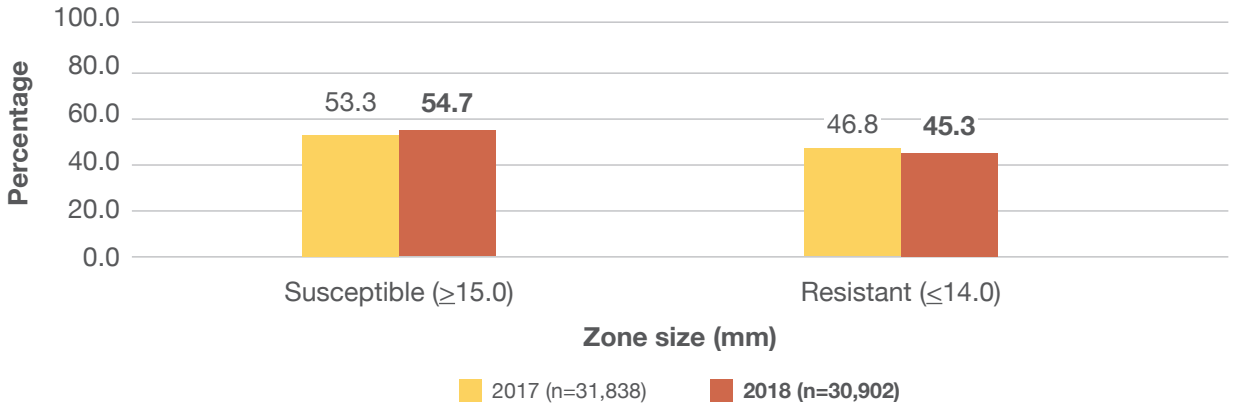
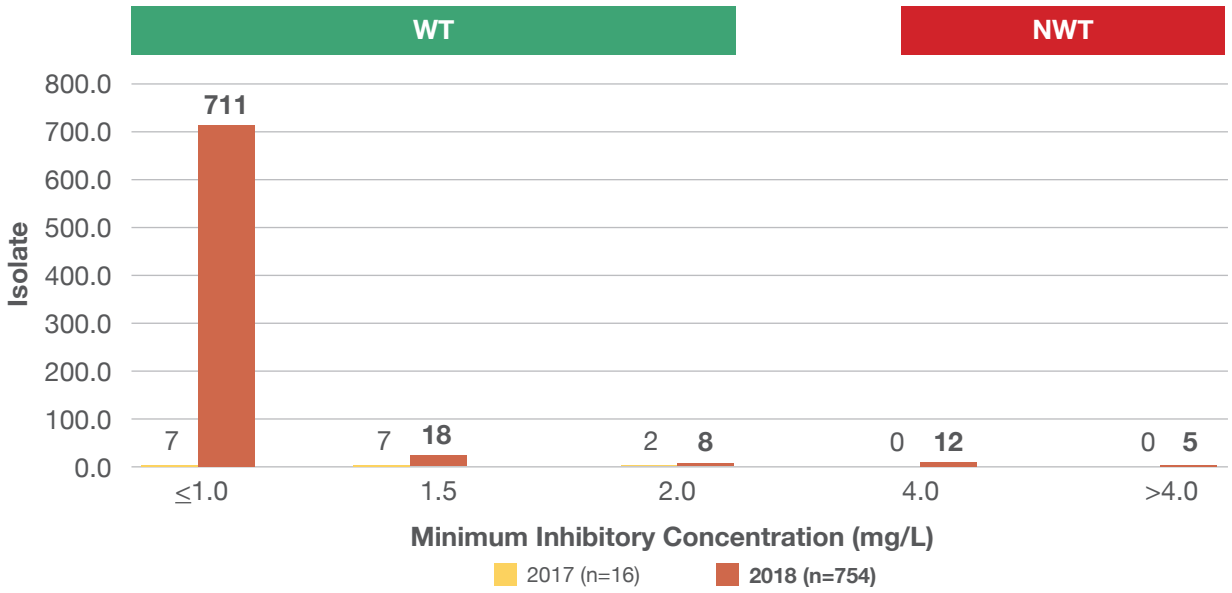


Figure 24. Percentage of susceptible and resistance to cefazolin among urinary isolates of *Escherichia coli* , 2017-2018

The small number of *E. coli* isolates tested in 2017 did not allow for a good comparison in 2018. Over 750 isolates were tested for colistin MIC, which demonstrates that the majority of *E. coli* were still susceptible to colistin, having MIC_{90} of lower than 1 mg/L. However, the proportion of *E. coli* isolates with higher colistin MIC (non-wild type) was 3.3% in 2018 (Figure 25).



Colistin MIC by Sensititre® (number of hospitals)	MIC_{50} (mg/L)	MIC_{90} (mg/L)
2017 (4)	1.5	2.0
2018 (4)	≤ 1.0	≤ 1.0

Figure 25. MIC distribution of colistin for *Escherichia coli*, 2017-2018

4. *Klebsiella pneumoniae*

he proportion of third-generation cephalosporin resistant *K. pneumoniae* in 2018 stayed at the same rate as in 2017 at around 40.0% (Table 10). Furthermore, approximately 33.8% of the isolates appeared resistant to cefepime and 6% of those were susceptible-dose dependent in 2018 (Figure 26).

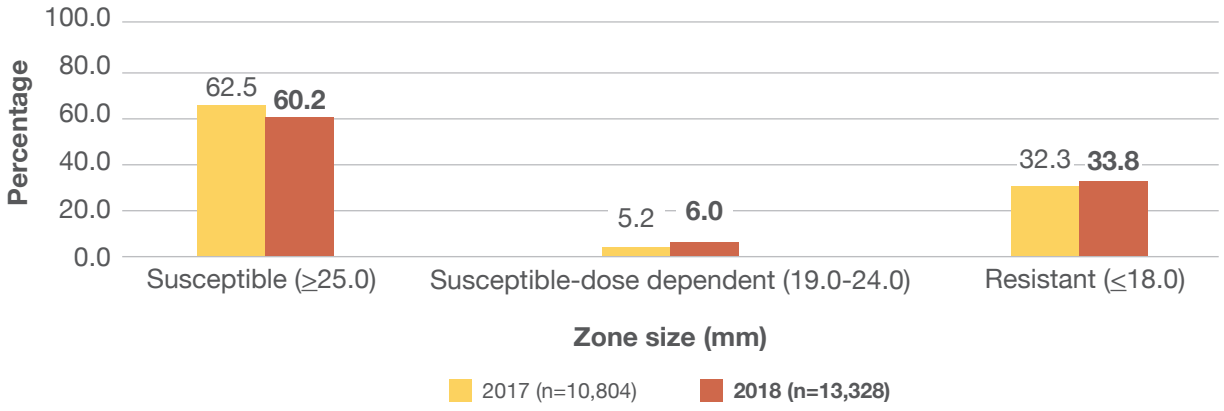


Figure 26. Percentage of susceptible, susceptible-dose dependent and resistance to cefepime among *Klebsiella pneumoniae*, 2017-2018

The overall trend in carbapenem-resistant *K. pneumoniae* (CRKP) has been gradually increased during the two years surveillance. A slightly increased prevalence was seen in 2018 with roughly 12.0% of *K. pneumoniae* being CRKP. Historically, prevalence of CRKP started to rise slowly from 2010 followed by rapidly increased between 2015 and 2016 to almost 10.0% (NARST Data). Percent resistance of *K. pneumoniae* are shown in Table 10.

Table 10. The proportion (%) of antimicrobial resistance in *Klebsiella pneumoniae*, 2017-2018

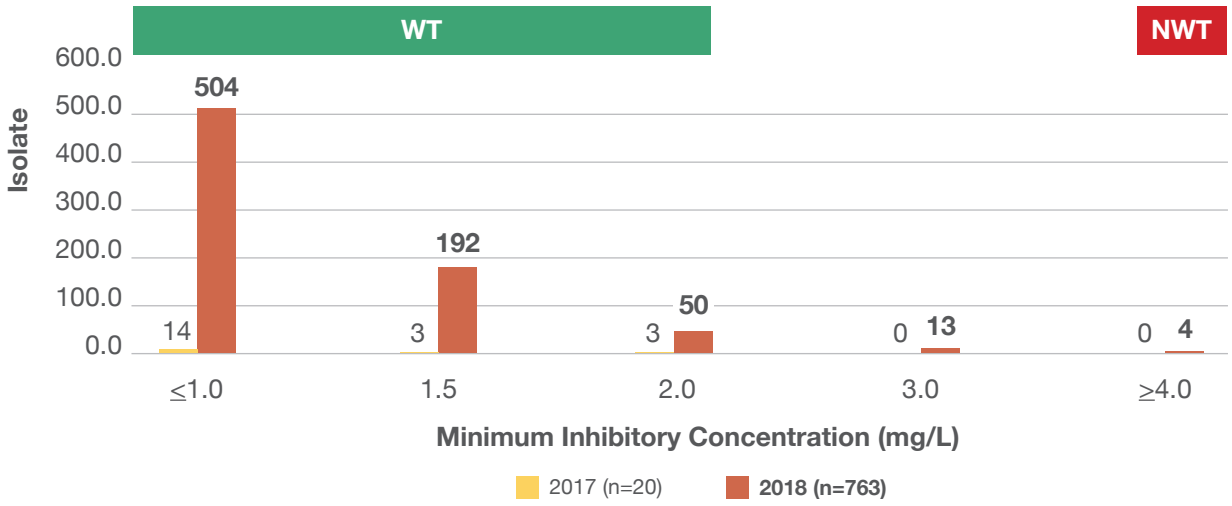
Drug	2017, (n)	2018, (n)
Total number of isolates	**52,906**	**58,273**
Penicillins		
Ampicillin	38.5 (40,752)	38.7 (44,518)
Ampicillin/sulbactam	45.1 (9,857)	46.4 (9,296)
Piperacillin/tazobactam	27.2 (31,444)	29.1 (40,672)
Cephalosporins		
Cefazolin	52.0 (15,505)	50.6 (15,126)
Cefazolin (U)	65.4 (4,001)	57.3 (4,281)
Cefuroxime sodium (PARENTERAL)	46.6 (15,964)	44.2 (14,118)
Cefuroxime sodium (ORAL)	52.5 (505)	61.9 (582)
Cefoperazone/sulbactam	25.9 (29,780)	27.7 (30,885)
Cefotaxime	43.6 (40,646)	42.9 (41,529)
Cefotaxime*	-	42.9 (669)
Ceftazidime	40.6 (46,641)	40.6 (49,872)
Ceftazidime*	-	52.8 (1,226)
Ceftriaxone	42.1 (34,733)	41.9 (36,578)
Ceftriaxone*	-	70.0 (1,635)
Cefepime	33.0 (6,014)	39.3 (11,721)
Cefoxitin	14.9 (16,777)	20.4 (14,586)

Drug	2017, (n)	2018, (n)
Carbapenems		
Ertapenem	11.1 (4,007)	12.6 (7,504)
Imipenem	10.2 (33,180)	12 (39,445)
Meropenem	10.1 (41,043)	12.3 (46,912)
Fluoroquinolones		
Nalidixic acid (U)	56.7 (240)	-
Ciprofloxacin	37.2 (42,293)	36.2 (46,339)
Levofloxacin	26.6 (15,148)	28.1 (20,078)
Norfloxacin	49.8 u (8,434)	51.3 (7,816)
Ofloxacin	31.5 (4,221)	-
Aminoglycosides		
Amikacin	5.5 (44,951)	7.0 (50,395)
Gentamicin	19.3 (44,574)	18.2 (46,076)
Netilmicin	11.0 (10,178)	-
Miscellaneous		
Nitrofurantoin (U)	47.2 (818)	53.4 (1,057)
Chloramphenicol	30.1 (754)	30.0 (293)
Sulfamethoxazole/trimethoprim	42.6 (41,802)	40.9 (43,076)
Tetracycline	38.2 (3,107)	39.3 (2,555)
Colistin*	-	2.4 (788)

*Interpreting by minimum inhibitory concentration test

U = Urine, Urine Catheter, Urine Clean-Voided

The colistin MIC_{90} value of *K. pneumoniae* in 2018 was not different to that in 2017 and it was similar to that of *E. coli*, while the percentage of non-wild type *K. pneumoniae* was 2.4% in 2018 (Figure 27).



Colistin MIC by Sensititre® (number of hospitals)	MIC_{50} (mg/L)	MIC_{90} (mg/L)
2017 (4)	≤ 1.0	2.0
2018 (6)	≤ 1.0	1.5

Figure 27. MIC distribution of colistin for *Klebsiella pneumoniae*, 2017-2018

Gram positive bacteria

1. *Staphylococcus aureus*

The proportion of MRSA has been decreasing from 9.6% in 2017 to 8.1% in 2018. On the other hand, the proportion of MRCNS, which accounted for 55.2% in 2018, was considerably larger than MRSA (Figure 28).

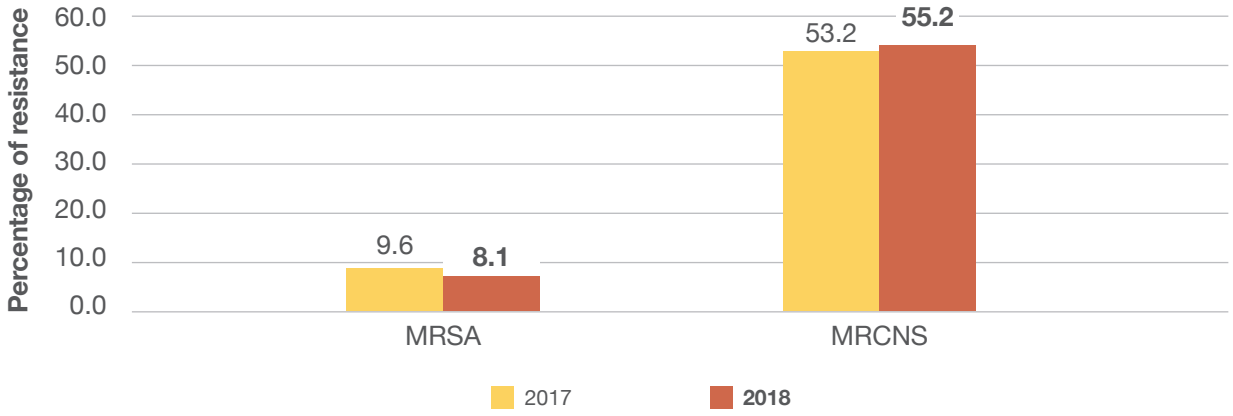


Figure 28. Trend in methicillin resistance among *Staphylococcus aureus* (MRSA) and *Staphylococcus* coagulase negative (MRCNS), 2017-2018

None of the isolates in 2018 was resistant to vancomycin. The data are shown in Table 11.

Table 11. The proportion (%) of antimicrobial resistance in *Staphylococcus aureus*, *Staphylococcus* coagulase negative and *Staphylococcus* coagulase negative (blood), 2017-2018

Drug	*Staphylococcus aureus*, (n)		*Staphylococcus* coagulase negative, (n)		*Staphylococcus*, coagulase negative (blood), (n)	
	2017	2018	2017	2018	2017	2018
Total number of isolates	**31,257**	**33,462**	**28,580**	**32,325**	**19,158**	**22,270**
Penicillins						
Penicillin	92.0 (12,547)	92.0 (11,958)	87.0 (13,732)	88.3 (13,209)	86.2 (9,420)	88.0 (8,981)
Penicillin*	92.0 (450)	91.3 (638)	97.5 (770)	93.7 (990)	97.4 (549)	44.0 (797)
Oxacillin	9.6 (26,584)	8.1 (27,409)	53.2 (25,096)	54.3 (25,279)	51.5 (16,845)	53.4 (17,344)
Cephalosporins						
Ciprofloxacin	14.0 (6,983)	10.8 (10,429)	37.8 (6,009)	38.9 (10,876)	38.6 (3,769)	37.2 (7,504)
Ciprofloxacin*	14.0 (278)	10.1 (437)	41.6 (173)	39.8 (359)	45.5 (121)	39.3 (257)
Levofloxacin	12.0 (4,788)	9.6 (6,194)	37.3 (3,937)	36.4 (9,537)	34.5 (2,553)	35.6 (3,598)
Norfloxacin (U)	15.2 (705)	-	48.0 (1,074)	-	-	-
Ofloxacin	9.8 (663)	-	37.5 (869)	-	37.4 (625)	-
Aminoglycosides						
Amikacin	3.7 (1,098)	-	6.2 (838)	-	6.7 (536)	-
Gentamicin	7.5 (18,653)	5.8 (22,281)	28.0 (15,957)	29 (20,577)	26 (10,128)	28.4 (13,625)
Glycopeptides						
Vancomycin	0.1 (1,176)	-	0.0 (322)	-	0.0 (220)	-
Vancomycin*	-	0.0 (894)	-	0.0 (620)	-	0.0 (474)

Drug	*Staphylococcus aureus*, (n)		*Staphylococcus* coagulase negative, (n)		*Staphylococcus*, coagulase negative (blood), (n)	
	2017	2018	2017	2018	2017	2018
Miscellaneous						
Clindamycin	14.0 (24,651)	13 (26,989)	46.8 (23,082)	50.7 (25,753)	46.4 (15,682)	49.9 (18,430)
Clindamycin*	20.8 (268)	27.9 (617)	54.5 (165)	53.1 (531)	57.0 (121)	51.0 (394)
Erythromycin	17.0 (24,990)	16.0 (27,097)	57.4 (24,178)	60.0 (25,818)	57.7 (16,660)	59.8 (18,589)
Erythromycin*	21.3 (268)	15.2 (467)	61.2 (165)	64.2 (439)	65.3 (121)	63.8 (343)
Nitrofurantoin (U)	2.1 u (47)	0.0 (49)	6.7 (45)	2.5 (40)	-	-
Chloramphenicol	5.1 (3,233)	5.9 (4,388)	9.7 (3,406)	12.8 (4,360)	8.8 (1,901)	11.5 (2,739)
Sulfamethoxazole/ trimethoprim	3.4 (25,483)	2.9 (26,813)	33.7 (24,005)	32.0 (26,002)	34.4 (15,947)	32.1 (17,567)
Tetracycline	42.2 (6,552)	39.5 (7,731)	43.9 (5,717)	45.4 (7,018)	41.2 (3,566)	41.2 (4,626)

*Interpreting by minimum inhibitory concentration test

U = Urine, Urine Catheter, Urine Clean-Voided

2. *Enterococcus* spp.

Ampicillin-resistant *Enterococcus faecalis* was found in around 5.0% of all isolates tested. Because they are naturally susceptible to ampicillin, further study of the underlying mechanisms and epidemiology of this resistant trait may be worth performing. In addition, the percentage of vancomycin-resistant *enterococcus* (VRE) isolates was found in approximately 2.0% of *E. faecalis* and 8.0% of *E. faecium* (Table 12). Since there was a distinct antimicrobial susceptibility among *Enterococcus* species, identifying species of enterococci might be warranted.

Table 12. The proportion (%) of antimicrobial resistance in *Enterococcus faecalis, Enterococcus faecium* and *Enterococcus* spp. 2017-2018

Drug	*E. faecalis*, (n)		*E. faecium*, (n)		*Enterococcus* spp., (n)	
	2017	2018	2017	2018	2017	2018
Total number of isolates	**14,836**	**17,754**	**7,553**	**8,877**	**5,461**	**3,845**
Penicillins						
Penicillin	30.6 (9,064)	30.6 (11,878)	91.1 (4,224)	93.6 (5,518)	55.2 (3,659)	55.7 (2,679)
Penicillin*	-	53.8 (184)	79.3 (87)	78.5 (167)	-	-
Ampicillin	5.2 (12,886)	5.6 (15,599)	90.1 (66,970)	91.7 (7,738)	37.8 (4,891)	41.5 (3,231)
Fluoroquinolones						
Ciprofloxacin (U)	77.1 (2,094)	77.1 (3,731)	96.2 (1,284)	96.0 (2,260)	86.3 (512)	82.0 (478)
Ciprofloxacin* (U)	-	72.3 (119)	-	93.3 (75)	-	-
Levofloxacin (U)	64.1 (1,497)	66.6 (2,263)	93.2 (789)	92.6 (1,251)	77.6 (1,057)	74.6 (787)
Norfloxacin (U)	72.2 (5,909)	-	95.8 (3,506)	-	77.1 (1,557)	-
Aminoglycosides						
Gentamicin 120 mg	45.6 (10,513)	46.3 (12,261)	37.6 (5,720)	34.2 (6,234)	39.6 (4,033)	40.5 (2,818)
Glycopeptides						
Vancomycin (see text for details)	2.3 (13,253)	2.0 (16,031)	8.8 (6,724)	8.4 (7,896)	3.2 (5,203)	3.0 (3,440)
Vancomycin* (see text for details)	-	46.0 (313)	-	48.7 (191)	-	91.9 (124)
Teicoplanin	0.4 (1,872)	1.9 (1,869)	15.8 (877)	12.6 (888)	9.1 (231)	4.1 (98)

Drug	*E. faecalis*, (n)		*E. faecium*, (n)		*Enterococcus* spp., (n)	
	2017	2018	2017	2018	2017	2018
Miscellaneous						
Fosfomycin (U)	8.1 (3,200)	7.3 (3,733)	-	-	-	-
Erythromycin	86.1 (2,664)	84.1 (3,475)	91.4 (1,087)	93.8 (1,259)	78.2 (910)	76.6 (607)
Erythromycin*	-	93.4 (152)	-	96.2 (105)	-	-
Nitrofurantoin (U)	2.0 (549)	3.9 (762)	70.6 (466)	86.9 (594)	32.2 (102)	24.2 (33)
Tetracycline (U)	92.8 (2,658)	92.6 (2,990)	96.0 (1,519)	93.1 (1,587)	90.9 (1,044)	90.4 (480)

*Interpreting by minimum inhibitory concentration test

U = Urine, Urine Catheter, Urine Clean-Voided

Thousands of enterococcal isolates were tested susceptible to vancomycin by disc diffusion method. Those with intermediate susceptibility or resistance were further selected for MIC determination by standard broth microdilution technique. Among 313 isolates of *E. faecalis* and 191 isolates of *E. faecium*, 45.4% and 43.5% were VRE, respectively (Figure 29). As a result, the magnitude of the VRE problem in our healthcare system could not be precisely estimated at this time. In addition, other enterococci were not identified to the species level, thus, they were labeled as *Enterococcus* spp. Among 124 isolates tested, almost 90.0% of "Other enterococci" were resistant to vancomycin. Because species identification was not performed, this data might include enterococcal species with natural resistance to vancomycin.

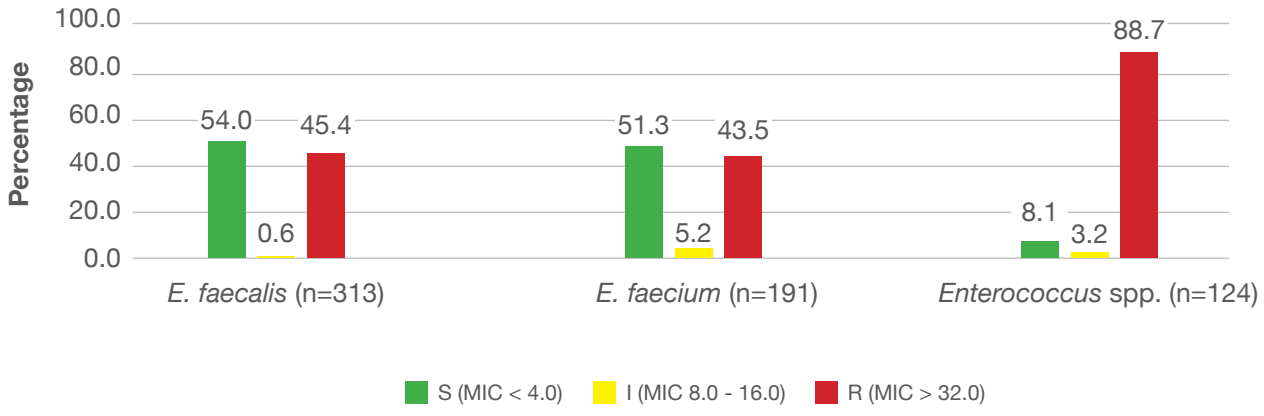


Figure 29. Percentage of susceptible, intermediate and resistance to vancomycin among *Enterococcus*, 2017-2018

3. *Streptococcus pneumoniae*

The proportion of penicillin-resistant *S. pneumoniae* (PRSP) accounted for approximately 50.0%-57.1% of pneumococcal isolates in cerebrospinal fluid (CSF) specimens from meningitis patients. It should be noted that the number of tested isolates was very small. Nonetheless, the proportion of penicillin non-susceptible *S. pneumoniae* (PNSP) including *S. pneumoniae* with intermediate-level of resistance to penicillin remained at about 5.0%-10.0% for non-CSF samples. A worrisome finding is that a large proportion of meningitis are PRSP. Moreover, no cefotaxime-resistant pneumococci was found in meningitis isolates while 1.0% of non-meningitis isolates were cefotaxime-resistant. The data are shown in Table 13. On the other hand, drug-resistant non-meningitis pneumococcal isolates were not that common, which is contradictory to c ommon belief. This issue needs further study since the resistance phenomenon is commonly used commercially to promote sales of antibiotic with broader spectrum of activity and overuse of these agents could further augment the magnitude of the AMR problem in Thailand.

Table 13. The proportion (%) of antimicrobial resistance in *Streptococcus pneumoniae,* 2017-2018

Drug	All isolates, (n)		E-test, (n)			
			Meningitis		Non-meningitis	
	2017	2018	2017	2018	2017	2018
Total number of isolates	**3,842**	**4,318**	**-**	**-**	**-**	**-**
Beta-lactams						
Penicillin*	65.8 (371)	63.4 (366)	50.0 (2)	57.1 (7)	10.0 (369)	5.62 (359)
Cefotaxime*	-	-	0.0 (11)	0.0 (3)	0.0 (144)	0.98 (209)
Fluoroquinolones						
Levofloxacin	0.9 (1,437)	1.0 (1,750)	-	-	-	-
Ofloxacin	0.6 (163)	-	-	-	-	-
Glycopeptides						
Vancomycin	0.2 (3,217)	0.1 (3,434)	-	-	-	-

Drug	All isolates, (n)		E-test, (n)			
			Meningitis		Non-meningitis	
	2017	2018	2017	2018	2017	2018
Miscellaneous						
Clindamycin	30.1 (2,895)	32.2 (3,279)	-	-	-	-
Clindamycin*	-	56.4 (39)	-	-	-	-
Erythromycin	35.6 (3,099)	36.2 (3,621)	-	-	-	-
Chloramphenicol	9.7 (1,356)	11.2 (1,229)	-	-	-	-
Sulfamethoxazole/ trimethoprim	55.7 (2,650)	51.9 (2,785)	-	-	-	-
Tetracycline	72.4 (1,464)	73.4 (1,235)	-	-	-	-

*Interpreting by minimum inhibitory concentration test

Other antimicrobial-resistant bacteria

1. Non-typhoidal *Salmonella* spp.

Determination of ciprofloxacin susceptibility for non-typhoidal *salmonella* from extraintestinal isolates showed that there was ciprofloxacin resistance around 4.2% in recent years (Table 8). However, when the MIC test was performed in selected 49 isolates, we found a dramatic increase in prevalence of this resistant trait, rising from 23.0% in 2017 to 45.0% in 2018 (Figure 30). Because the number of isolates were small and were selected based on availability of Sensititre® antimicrobial susceptibility testing in the institutions, MIC testing in a larger number of isolates to verify this finding is needed. However, the finding suggested that determination of ciprofloxacin MIC may be a better alternative to the conventional disc diffusion test because infections caused by this organism are common and physicians rely on the susceptibility testing results to guide treatment. Due to limited resources, financial support for microbiology laboratory is needed to perform MIC testing.

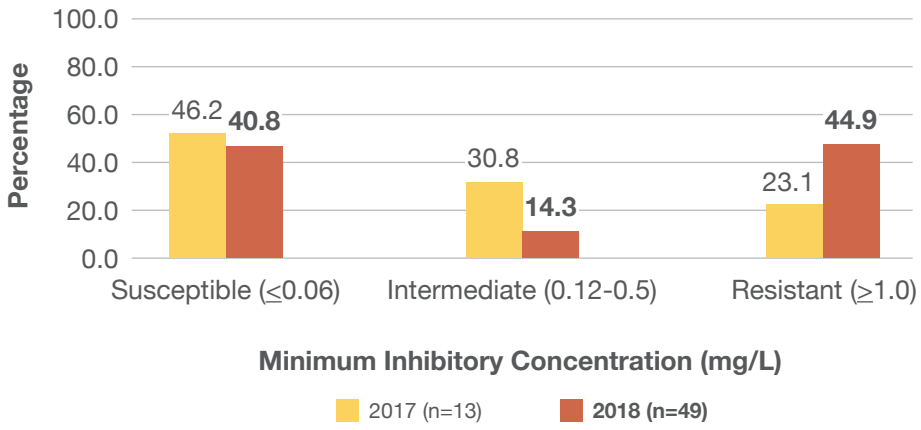


Figure 30. Percentage of susceptible, intermediate and resistance to ciprofloxacin among non-typhoidal *Salmonella* spp., 2017-2018

The overall trends of third-generation cephalosporin resistance in *Salmonella* spp. have been stable around 12.0% -15.0%. The data are shown in Table 14.

Table 14. The proportion (%) of antimicrobial resistance in non-typhoidal *Salmonella* spp. from extraintestinal isolates, 2017-2018

Drug	2017, (n)	2018, (n)
Total number of isolates	**2,668**	**3,354**
Penicillins		
Ampicillin	52.1 (2,197)	50.2 (1,431)
Cephalosporins		
Cefoperazone/sulbactam	0.9 (560)	1.4 (541)
Cefotaxime	15.2 (1,622)	13.9 (1,209)
Ceftazidime	14.3 (1,143)	12.2 (961)
Ceftazidime*	-	30.6 (36)
Ceftriaxone	15.1 (1,306)	12.0 (1,060)
Ceftriaxone*	-	68.1 (66)

Drug	2017, (n)	2018, (n)
Fluoroquinolones		
Nalidixic acid (U)	51.9 (79)	-
Ciprofloxacin	4.6 (1,867)	4.2 (3,085)
Ciprofloxacin*	23.1 (13)	44.9 (49)
Levofloxacin	6.8 (367)	-
Ofloxacin	6.4 (157)	-
Miscellaneous		
Chloramphenicol	22.7 (432)	18.4 (228)
Sulfamethoxazole/trimethoprim	14.3 (2,295)	11.8 (1,663)

*Interpreting by minimum inhibitory concentration test (MIC)

U = Urine, Urine Catheter, Urine Clean-Voided

2. *Neisseria gonorrhoeae*

N. gonorrhoeae isolates showed a high rate of resistance to Penicillin. In addition, about 95.0% of *N. gonorrhoeae* isolates have become non-susceptible to ciprofloxacin and over 90.0% of those have appeared non-susceptible to tetracycline for years. However, no resistance to cefixime or ceftriaxone has been reported. Almost every isolate has remained susceptible to azithromycin except only one isolate with a high MIC value, which was reported in 2017 (Table 15 and Figure 31). There has been a published report of ceftriaxone-resistant *N. gonorrhoeae* in the literature but this case was out of the boundary of the current surveillance scheme. Therefore, the public health sector is now more vigilant in looking into this issue.

Table 15. The proportion (%) of antimicrobial resistance and MIC90 value in *Neisseria gonorrhoeae*, 2017-2018

Drug	% Resistance, (n)		MIC_{90} (mg/L), (n)	
	2017	2018	2017	2018
Total number of isolates	**506**	**592**	**485**	**591**
Penicillins				
Penicillin	99.5 (173)	99.4 (168)	>32.0 (18)	>32.0 (15)
Cephalosporins				
Cefixime	0.0 (496)	0.0 (590)	0.016 (441)	0.016 (510)
Ceftriaxone	0.0 (495)	0.0 (590)	0.008 (484)	0.008 (518)
Fluoroquinolones				
Ciprofloxacin	96.8 (462)	96.4 (523)	8.0 (321)	9.0 (315)
Aminoglycosides				
Gentamicin	0.0 (407)	0.0 (407)	8.0 (407)	8.0 (407)
Spectinomycin	0.0 (174)	0.0 (153)	12.0 (19)	N/A (0)
Miscellaneous				
Tetracycline	94.1 (10)	95.3 (211)	24.0 (171)	16.0 (211)
Azithromycin	0.2 (441)	0.0 (560)	0.25 (441)	0.25 (560)

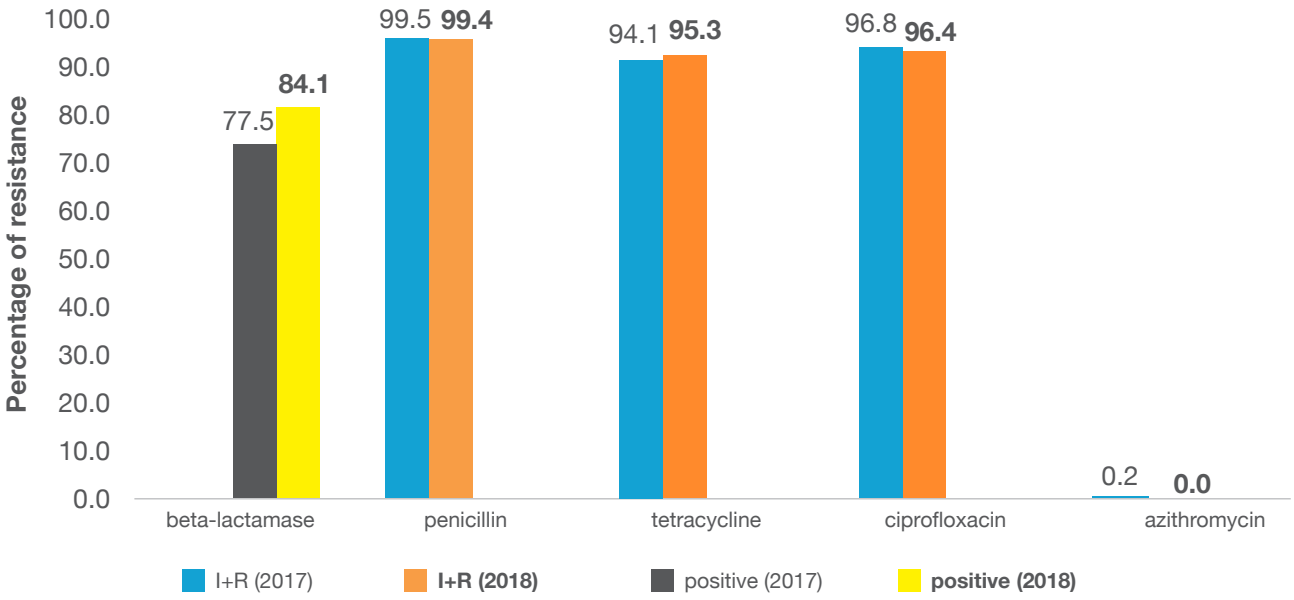


Figure 31. Trend in antimicrobial resistance among *Neisseria gonorrhoeae* in 2017-2018

3.1.4 Limitation

- This report did not identify risk factors linked with baseline characteristics of patients and did not show the distribution of isolates from different hospital levels (primary, secondary or tertiary care).
- For most data in this report, all types of specimen were selected for calculation of resistance rate.
- This report did not divide isolates into those from outpatient or inpatient hospital departments including intensive care units.
- Due to the cost of the MIC test, most of the *Staphylococcus aureus* and coagulase-negative *Staphylococcus* spp. isolates were tested by disk diffusion method, instead of the MIC test for vancomycin that is recommended by the CLSI guideline.
- The limited number of *Acinetobacter* spp., *Pseudomonas aeruginosa*, and *Enterobacteriaceae* isolates were performed with the colistin MIC test.
- A two-year analysis of data is insufficient to draw a conclusion of resistant infectious trends in Thailand.
- The tables in this chapter were illustrated using only the percentage of resistance, while the percentage of intermediate susceptibility are reported as the percentage of resistance, with the exception of Table 14 that shows only percentage of resistance in non-typhoidal *Salmonella*, not including intermediate susceptibility.

3.1.5 Prospect

- The data regarding trends towards antimicrobial resistance should be observed for several years in order to assess their evolution and the overall situation of antimicrobial resistance problems in Thailand. Finding will contribute substantially to addressing the problem of AMU and AMR and support implementation of effective antimicrobial stewardship policies and infection control programmes.
- Time trends analysis using logistic regression models over a longer period are needed in order to understand how significant changes in the past several years have evolved.
- Systematically combining data on antimicrobial consumption and antimicrobial resistance at patient, hospital, and community level should be carried out to allow further analysis of the association between antimicrobial use and the development of resistance.

- Antimicrobial resistance data should be separately analyzed into specimen types (blood, sputum, urine, etc.) or at least sterile and non-sterile sites, and should be stratified by healthcare service sectors, for instance, the proportion of isolates from outpatient departments and inpatient departments including intensive care units.
- Regional antimicrobial resistance rates should be further analyzed and compared.
- Laboratory consideration of MIC testing is very crucial in dose optimization to tackle the antimicrobial resistance problem; thus MIC of antimicrobial agents against certain bacterial species as suggested by international guidelines should be performed and reported in settings with available resources, for example, in vancomycin for *Staphylococcus aureus*.
- Knowledge on type of carbapenemase genes among highly antimicrobial-resistant organisms, e.g. carbapenem-resistant *Enterobacteriaceae* (CRE) may be of value in search of new antimicrobial agents as well as development of treatment guidelines to suggest reasonable therapeutic options on the essential medicines list.
- Data on antimicrobial resistance in viruses, fungi and *Mycobacterium tuberculosis* should be reported in the future.

3.2 Morbidity of AMR in patients with Hospital-Associated Infections

Data source
Surveillance of Hospital-associated Infection,
Bamrasnaradura Infectious Disease Institute, Ministry of Public Health

Authors
Anond Kulthanmanusorn
Weerawat Manosuthi
Visal Moolasart
Varaporn Thienthong

Editors
Kumthorn Malathum
Viroj Tangcharoensathien
Angkana Lekagul
Sunicha Chanvatik
Wanwisa Kaewkhankhaeng

Key summary

From 23 hospitals which provided high quality data; in 2018, the incidence rate and incidence proportion of hospital-associated infections (HAI) were 2.5 per 1,000 patient-days and 0.8% of total discharged patients respectively. Additionally, the incidence rate and incidence proportion of antimicrobial resistance (AMR) in patients with HAI were 1.4 per 1,000 patient-days and 0.5% of total discharged patients respectively. More than half (60.2%) of HAI patients had AMR infections. *Acinetobacter baumannii* (47.2%), *Klebsiella pneumoniae* (21.8%) and *Escherichia coli* (19.1%) were the top-three AMR pathogens in patients with HAI.

3.2.1 General

One of the five goals in the National Strategic Plan on Antimicrobial Resistance 2017-2021 (NSP-AMR 2017-2021) is to reduce AMR morbidity by 50% by 2021 [19]. Currently in Thailand, various departments of the Ministry of Public Health separately host AMR monitoring platforms.

NARST has two decades mature experience of AMR surveillance. However, its laboratory-based approach is not designed to provide clinical information of patients and AMR correlation, which is essential to estimate AMR morbidity.

Currently, there are two potential platforms to monitor AMR morbidity: 1) the Global Antimicrobial Resistance Surveillance System, Thailand (GLASS-Thailand) hosted by the National Institute of Health; and 2) Hospital Associated Infection Surveillance hosted by the Bamrasnaradura Infectious Disease Institute (BIDI's HAI surveillance).

Initiated in 2016, GLASS-Thailand monitors both community- and hospital-acquired AMR infections, however only a small number of hospitals participated and only certain bacterial species obtained from specific clinical specimens are monitored. In contrast, BIDI's HAI surveillance is the largest prospective HAI and AMR case-based surveillance in Thailand involving public and private hospitals and in 2018, 302 hospitals were in the surveillance systems. Since its launch in 2013, the main objective is to identify the incidence of HAI in inpatients; however, since 2017, surveillance has also included pathogens and drug resistant profiles of HAI patients.

This study analyzed the data from BIDI's HAI prospective surveillance and aimed to estimate 2018 baseline AMR morbidity as well as explore a further potential national platform for AMR morbidity monitoring.

3.2.2 Method and data sources

Study design

This study retrospectively analyzed data from BIDI's hospital-wide surveillance, which included all HAI cases entered during January and December 2018.

All HAI occurring in the surveillance hospitals were detected by ICWNs and confirmed by ICNs in each hospital using the definition in the Thai Manual of HAI Diagnosis 2018 [20]. The data of patients with HAI was manually submitted to the surveillance web portal on a monthly basis. To simplify the data entering process, only the susceptibility data (Susceptible, Intermediate or Resistant) of each drug group reported in laboratory results was collected; as a result, there was no zone size or MIC data. As well as HAI patient data, hospital service profiles such as the number of patient-days, the number of discharged patients, the number of operations performed, and the number of ventilator-days were used as a denominator.

In 2018, 302 hospitals participated in the system but only 103 hospitals submitted complete data as well as some hospitals also submitted incomplete drug susceptibility data. As a result, data verification was needed. Therefore, only 23 hospitals from 103 hospitals were included in the study and ICNs in these hospitals were requested to retrospectively review and complete missing data using their hospital database.

Sampling frame and eligible criteria

This study included all hospitals participating in the BIDI's HAI surveillance which submitted adequate data. In this study, we requested that regional and general hospitals must submit at least 100 HAI records per year while other types of hospital (community, other MOPH, other public, and private hospitals) had to submit not fewer than 15 records per year (Figure 32). These numbers were suggested by a group of experts on infectious diseases and AMR during the consultative meeting on 17th June 2019.

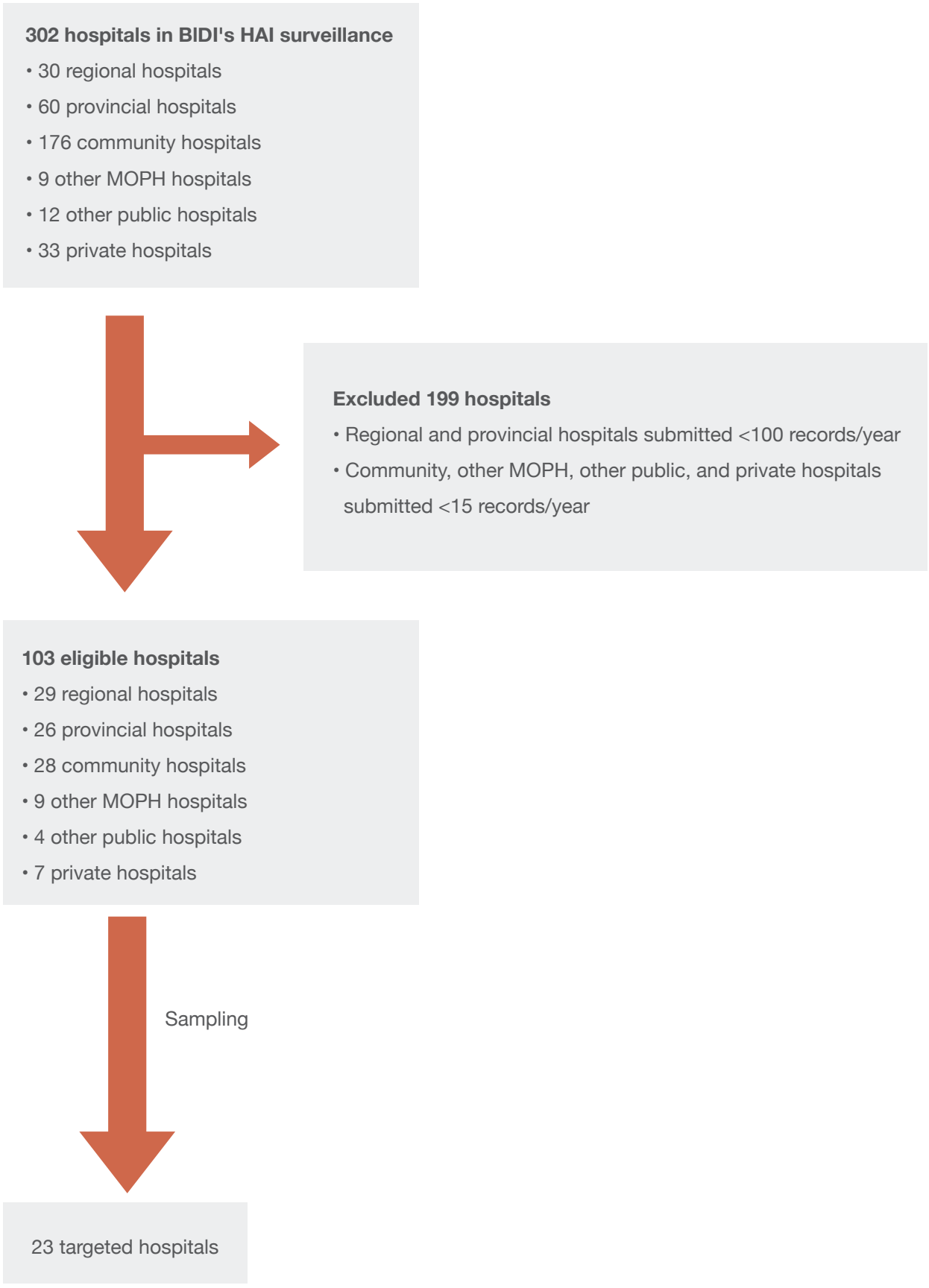


Figure 32. Sampling frame and eligible criteria

Sampling and sample size

A single-stage cluster sampling technique was applied in this study. All inpatients admitted to selected hospitals from January 2018 to December 2018 were included in the surveillance. To take into account different contexts in each hospital, 103 eligible hospitals were divided into six types comprising: 1) referral hospitals at regional level (regional hospital); 2) tertiary-care general hospitals at provincial level; 3) secondary-care community hospitals at district level; 4) other MOPH hospitals - specialty hospitals organized by various departments in the MOPH; 5) other public hospitals owned by other ministries (not MOPH); and 6) private hospitals.

The total patients required for this study were 6,667 per day. To calculate the sample size, several factors were determined including the prevalence of HAI (P = 1.6% - 7.3%) and response rate (= 78.0%) from the previous study [21], acceptable error (d = 1.0%), Z statistic for 95% CI (Z = 2.0) and design effect (=2).

The equation was $n = \frac{z^2 P(1 - P)}{d^2} \times \frac{1}{\text{response rate}} \times \text{deff}$ [22].

The number of samples in each hospital type was individually assigned using a proportional-to-size technique. The number of targeted hospitals was determined by the average number of inpatients per hospital per day. In each hospital type, a systematic random sampling technique was applied to select targeted hospitals. In the case where a selected hospital refused to participate in the survey, it was replaced by the next hospital on the list. A total of 23 targeted hospitals was selected from hospitals participating in BIDI's HAI surveillance (Table 16).

Table 16. Sample size calculation

Hospital types	Number of total hospitals	Number of inpatients/day		Estimated sample size		Average inpatients/ day/ hospital	Number of targeted hospitals
		Number	%	Number	%		
Public hospitals							
• **Regional hospitals**	29	19,339	57.0	3,818	57.0	667	6
• **General hospitals**	26	8,193	24.0	1,617	24.0	315	6
• **District hospitals**	28	2,510	7.0	496	7.0	90	6
• **Other MOPH hospitals**	4	343	1.0	68	1.0	86	1
• **Other public hospitals**	7	1,650	5.0	326	5.0	236	2
Private hospitals	9	1,734	5.0	342	5.0	193	2
Total	**103**	**33,769**	**100**	**6,667**	**100**	**328**	**23**

Definition

The definition of HAI in this study follows the Manual of HAI Diagnosis 2018 published by BIDI and is used as the national HAI definition [20]. This study defined a HAI event using a repeat infection time frame (RIT) definition. Any HAI records at the same anatomical sites of infection within 14 days after the previous infection were excluded. A HAI patient was defined as any patient who was infected with HAI within the one-year study period.

The AMR definition was defined by the NSP-AMR 2017-2021, which covered nine targeted organisms and selected drugs of interest for each pathogen (Table A13) [19]. An AMR infection was defined as an infection of a targeted pathogen with at least one selected drug resistance reported. In terms of an AMR event, the study applied a Repeat Infection Timeframe (RIT) concept. The event was counted when there was an AMR infection but excluded if the infection was caused by a pathogen similar to a previous AMR infection within 14 days. Finally, an AMR patient was defined as any patient who was infected with any AMR pathogens within the one-year study period.

Data collection

Data from 23 sampled hospitals, included both patient records and hospital service profiles, were exported from the database. Then, the verification process was done and records with missing data were verified by local ICNs to fulfill the missing data from their own hospital database. After ICNs fulfilled the missing data, data were rechecked, and the complete data set was analyzed by the research team (Figure 33).

Figure 33. Data collection flow

Data analysis

After a verification process, surveillance data from 23 hospitals were analyzed. Duplicate records and HAI diagnosis without fulfilled diagnostic criteria were removed. The incidence of HAI and AMR was calculated using the data of HAI records as numerators and hospital services profile as denominators (Table 17). In each hospital type, incidences of HAI and AMR were calculated separately. Then the weighted incidences of HAI and AMR were estimated using an inverse probability weighting technique. The total number of patient-days in the selected 103 hospitals, the population of interest, and the number of patient-days in 23 sampling hospitals were used for the weight calculation in each hospital type (Table A14).

Table 17. Numerators and denominators of HAI and AMR incidences

Indicator	Numerator	Denominator
1. HAI incidence rate/ 1,000 patient-days	Total number of HAI events	Total patient-days
2. HAI incidence proportion	Total number of HAI patients	Total number of discharged patients
3. VAP incidence rate/ 1,000 ventilator-days	Total number of VAP event	Total number of ventilator-days
4. CAUTI incidence rate/ 1,000 urinary catheter-days	Total number of CAUTI event	Total number of urinary catheter-days
5. CLABSI incidence rate/ 1,000 central line-days	Total number of CLABSI event	Total number of central line-days
6. SSI incidence proportion/ 100 surgeries	Total number of SSI event	Total number of surgeries
7. AMR incidence rate/ 1,000 patient-days	Total number of AMR events*	Total patient-days
8. AMR incidence proportion	Total number of AMR patients*	Total number of discharged patients
9. Percentage of AMR patient in total HAI patient	Total number of AMR patients*	Total number of HAI patients
10. Resistance percentage	Total number of drug resistance organism	Total number of first isolates organisms

* Note: Patients with AMR colonization were excluded from the study.

Ethical clearance

This study was approved on 22nd January 2019 by the ethical committee of the Institute for the Development of Human Research Protection based on the International Conference on Harmonization of Good Clinical Practice and Ethical Consideration.

3.2.3 Results

Data were collected from 23 hospitals which had implemented hospital-wide HAI surveillance. These were six regional hospitals, six general (provincial) hospitals, six community (district) hospitals, one other MOPH hospital, two other public non-MOPH hospitals including a university hospital, and two private hospitals. Of all 8,683 records submitted, 218 were removed from the study due to duplication or incomplete diagnosis details; for example, lack of microbiological results for diagnoses such as urinary tract infection, bloodstream infection, burn wound infection or bedsore infection. The remaining 8,465 valid records after verification by researchers were included for data analysis. During the one-year study period, there were 2,934,318 patient-days as denominators for this study. The average number of valid records was 368 per hospital while the average number of patient-days was 127,579 patient-days per hospital in 2018 (Table 18).

Hospital-associated infection

Overall in these 23 hospitals, in 2018, there were total 7,275 HAI events reported in 5,688 patients affected by HAI. The incidence rate and incidence proportion of HAI were 2.5 per 1,000 patient-days and 0.8% of total inpatients, respectively. Regional hospitals had the highest HAI incidence rate (3.4 per 1,000 patient-days) and other public hospitals had the highest HAI incidence proportion (1.7% of total inpatients). Data showed the lowest HAI incidence rate and incidence proportion to be in private hospitals at 0.7 per 1,000 patient-days and 0.2% of total inpatients respectively (Table 19).

Table 18. Detail of 23 participating hospitals by type of hospital

Hospital type	Number of hospitals	Submitted records	Verified records	Number of verified records per hospital			Total patient-days	Number of patient-days per hospital		
				mean	max	min		mean	max	min
Regional hospital	6	5,967	5,759	960	430	2,167	1,471,214	245,202	214,683	294,030
General hospital	6	1,260	1,259	210	122	267	853,535	142,256	80,836	214,101
Community hospital	6	250	246	41	20	74	220,453	36,742	27,703	56,522
Other MOPH hospital	1	151	151	151	-	-	44,657	44,657	-	-
Other public hospital	2	981	976	488	82	894	262,077	131,039	59,195	202,882
Private hospital	2	74	74	37	32	42	82,382	41,191	29,819	52,563
Total	**23**	**8,683**	**8,465**	**368**	**20**	**2,167**	**2,934,318**	**127,579**	**27,703**	**294,030**

Table 19. Incidence rate (per 1,000 patient-days) and incidence proportion (%) of HAI by type of hospital

Hospital type	Weight	HAI events	HAI patients	Patient-days	Discharged patients	Weighted HAI incidence rate	Weighted HAI incidence proportion
Regional hospital	4.8	4,964	3,785	1,471,214	315,526	3.4	1.2
General hospital	3.5	1,047	869	853,535	230,608	1.2	0.4
Community hospital	4.2	227	208	220,453	64,000	1.0	0.3
Other MOPH hospital	2.8	128	96	44,657	9,199	2.9	1.0
Other public hospital	2.3	853	678	262,077	40,108	3.3	1.7
Private hospital	7.7	56	52	82,382	24,163	0.7	0.2
Total		**7,275**	**5,688**	**2,934,318**	**683,604**	**2.5**	**0.8**

Most HAI events (5,092 events or 70.0%) occurred in late adults and elderly patients (age ≥ 50 years old). Among pediatric patients with HAI, over half of pediatric HAI events were in newborns (382 of 729 events in pediatric patients or 52.4%) (Figure 34).

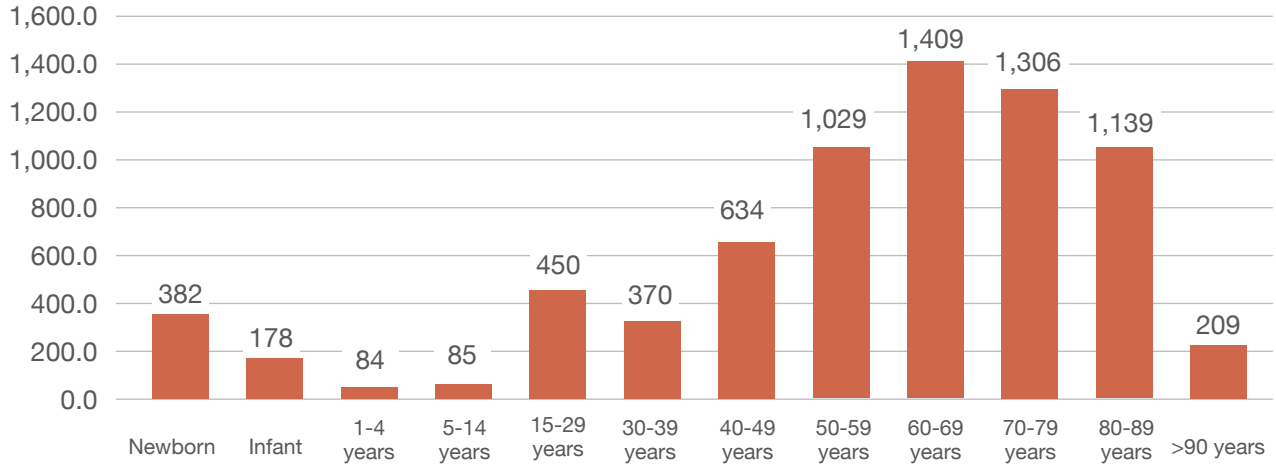


Figure 34. Number of HAI events by age group

Approximately 48.3% of overall HAI events were respiratory tract infections, followed by urinary tract infections (26.3%), and bloodstream infections (8.5%). More specifically, the top-three HAI are ventilator-associated pneumonia (1,747 events), catheter-associated urinary tract infections (1,341 events), and hospital-associated pneumonia not associated with ventilator (1,048 events) (Table 20).

Table 20. Hospital-associated infection by site of infection

Site of infection	Specific site of infection	HAI event	Total	(%)
Respiratory tract	Ventilator-associated pneumonia	1,747	3,514	(48.3)
	Hospital-associated pneumonia, not associated with ventilator	1,048		
	Other lower respiratory tract infection	705		
	Upper respiratory tract infection	14		
Urinary tract	UTI, catheter-associated	1,341	1,911	(26.3)
	UTI, not associated with cath.	570		
Bloodstream	Primary bloodstream infection	394	621	(8.5)
	CLABSI	227		
Surgical site	Surgical site infection	601	601	(8.3)
Skin and soft tissue	Other skin and soft tissue infection	152	255	(3.5)
	Bedsore	76		
	Burn	21		
	Omphalitis	4		
	Newborn circumcision	2		
Gastrointestinal tract	Gastroenteritis	47	100	(1.4)
	Necrotizing enterocolitis	28		
	Other GI tract infection	25		
Cardiovascular system	Phlebitis	85	85	(1.2)
Central nervous system	Meningitis or ventriculitis	27	43	(0.6)
	Subdural infection	4		
	Other CNS infection	4		
	Encephalitis	3		
Eye ear nose and throat	Conjunctivitis	18	38	(0.5)
	Other eye infection	12		
	Oral cavity infection	5		
	Other ear nose and throat infection	4		
	Neonatal Conjunctivitis	2		
	Otitis media	2		
Reproductive system	Episiotomy	24	29	(0.4)
	Other reproductive organ infection	5		
Others	Other infection	77	78	(1.0)
	Disseminated infection	1		
Total			**7,275**	**(100)**

From the total HAI events, the top three causative pathogens were *A. baumannii* (28.6%), *K. pneumoniae* (17.3%), and *E. coli* (13.6%) (Figure 35).

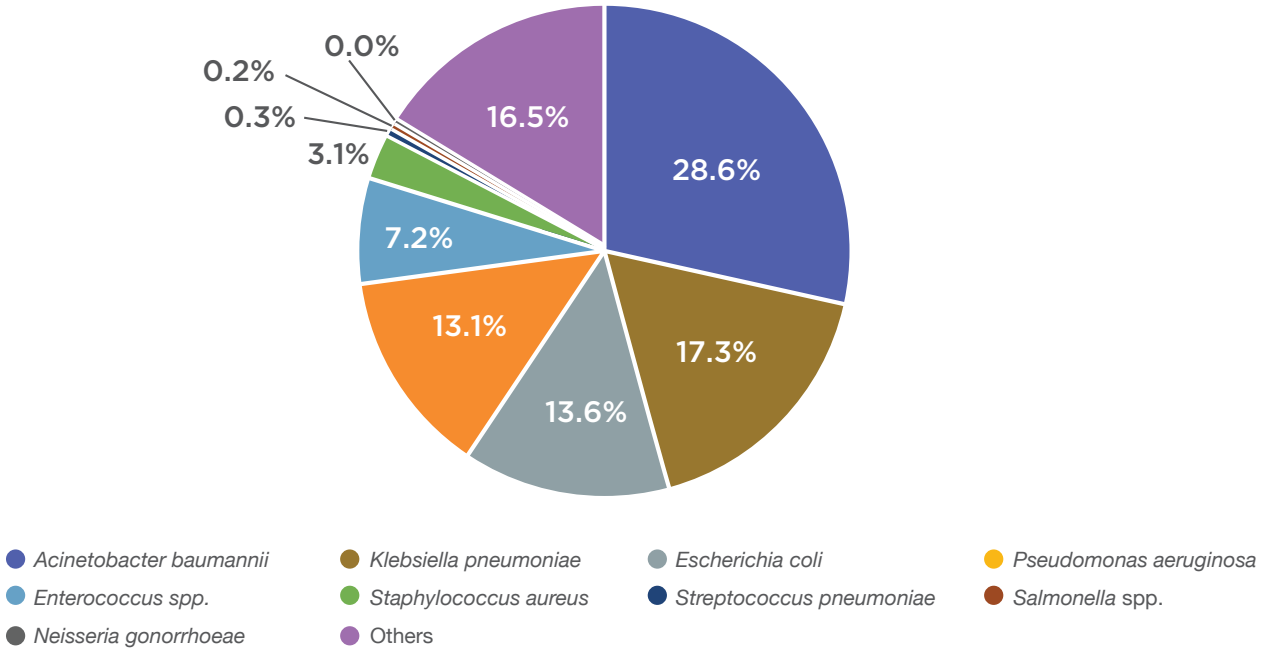


Figure 35. Causative organisms of HAI

The top three invasive device-related HAI were ventilator-associated pneumonia (VAP), catheter-associated urinary tract infections (CAUTI), and central line-associated bloodstream infections (CLABSI). Total incidence rates were 5.5 per 1,000 ventilator-days, 2.1 per 1,000 urinary catheter-days and 2.2 per 1,000 central line-days. The incidence proportion of surgical site infection (SSI) was 0.3 per 100 surgeries (Table 21).

The HAI by hospital types showed interesting findings among the top four HAI. Despite the small number of ventilator-days from community hospitals, they had the highest VAP incidence rate (6.8 per 1,000 ventilator-days). In contrast, other MOPH hospital had the lowest VAP incidence rate (3.3 per 1,000 ventilator-days). This figure was different from CAUTI and CLABSI incidence rates where other MOPH hospitals had the highest incidence rates accounting for 5.1 per 1,000 urinary catheter-days and 3.0 per 1,000 central line-days. General hospitals had the lowest incidence rate of CAUTI (1.3 per 1,000 urinary catheter-days) and there was no report of CLABSI from private hospitals. Finally, the incidence proportion of SSI was highest in regional hospitals and lowest in other MOPH hospital, at 0.4 and 0.1 per 100 surgeries respectively (Table 21).

Table 21. Incidence of invasive device-related HAIs, and surgical site infection by type of hospital

Hospital type	Weight	VAP events	CAUTI events	CLABSI events	SSI events	Ventilator-days	Urinary catheter-days	Central line-days	Number of surgeries	Weighted VAP incidence rate	Weighted CAUTI incidence rate	Weighted CLABSI incidence rate	Weighted SSI incidence proportion
Regional hospital	4.8	1,131	810	189	441	188,966	345,398	70,071	115,816	6.0	2.4	2.7	0.4
General hospital	3.5	409	216	15	86	97,255	172,084	22,299	50,886	4.2	1.3	0.7	0.2
Community hospital	4.2	62	45	1	19	9,059	27,918	838	8,216	6.8	1.6	1.2	0.2
Other MOPH hospital	2.8	7	43	4	4	2,129	8,466	1,330	4,300	3.3	5.1	3.0	0.1
Other public hospital	2.3	118	210	18	43	28,456	54,379	19,237	22,210	4.1	3.9	0.9	0.2
Private hospital	7.7	18	17	-	8	3,266	12,343	660	4,727	5.5	1.4	-	0.2
Total		**1,745**	**1,341**	**227**	**601**	**329,131**	**620,588**	**114,435**	**206,155**	**5.5**	**2.1**	**2.2**	**0.3**

*Note: VAP incidence rate per 1,000 ventilator-days, CAUTI incidence rate per 1,000 urinary catheter-days, CAUTI incidence rate per 1,000 central line-days, SSI incidence proportion per 100 surgeries

Antimicrobial resistance

In 2018, of the total 5,688 HAI patients, there were 3,402 AMR patients and 4,005 AMR reported events. The incidence rate and incidence proportion of AMR infection were 1.4 per 1,000 patient-days and 0.5% of total inpatients, respectively. While regional hospitals had the highest AMR incidence rate (1.8 per 1,000 patient-days), other public hospitals had the highest AMR incidence proportion (0.8% of total inpatients). On the other hand, data showed the lowest AMR incidence rate and incidence proportion in private hospitals at 0.5 per 1,000 patient-days and 0.1% of total inpatients, respectively. Approximately, 60.2% of HAI patients were AMR. This proportion was highest in general hospitals (71.1% of total HAI patients) and lowest in other public hospitals (46.8%) (Table 22).

Table 22. Incidence rate (per 1,000 patient-days) and incidence proportion (%) of AMR by types of hospital

Hospital type	Weight	HAI patient	AMR events	AMR patients	Patient-days	Discharged patients	Weighted AMR incidence rate	Weighted AMR incidence proportion	Weighted percentage of AMR patient in total HAI patient
Regional hospital	4.8	3,785	2,658	2,244	1,471,214	315,526	1.8	0.7	59.3
General hospital	3.5	869	727	618	853,535	230,608	0.9	0.3	71.1
Community hospital	4.2	208	134	127	220,453	64,000	0.6	0.2	61.1
Other MOPH hospital	2.8	96	76	62	44,657	9,199	1.7	0.7	64.6
Other public hospital	2.3	678	370	317	262,077	40,108	1.4	0.8	46.8
Private hospital	7.7	52	40	34	82,382	24,163	0.5	0.1	65.4
Total		**5,688**	**4,005**	**3,402**	**2,934,318**	**683,604**	**1.4**	**0.5**	**60.2**

Most AMR events (2,974 events or 74.3%) occurred in late adult and elderly patients (age ≥50 years old). Among pediatric patients infected with AMR pathogens, half of pediatric HAI events were in newborns (142 of 284 events or 50.0%) (Figure 36).

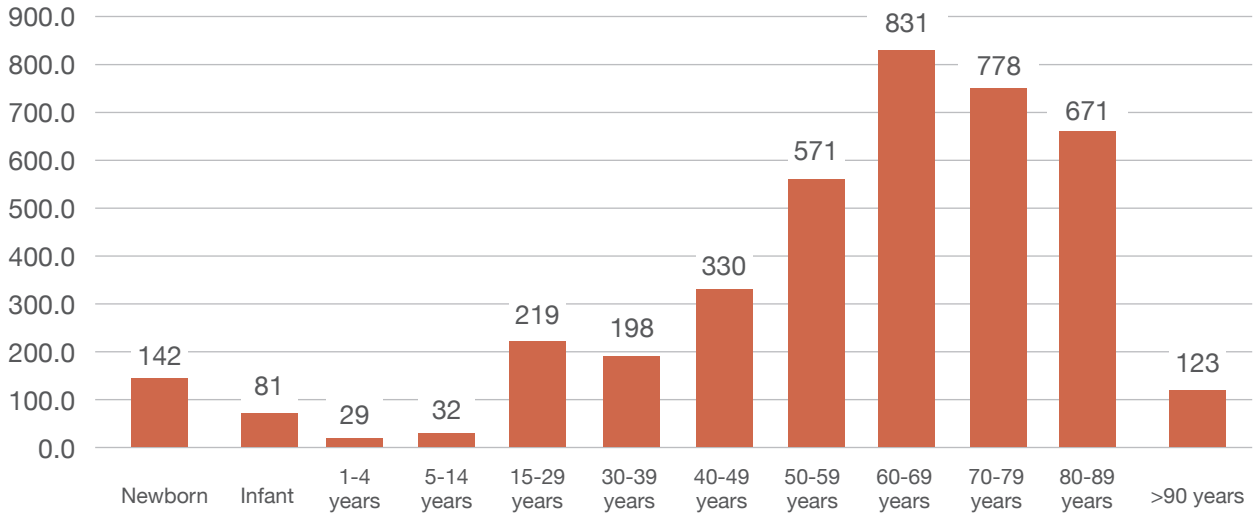


Figure 36. Number of AMR events by age group

Of the total AMR events, *A. baumannii* was the most common pathogen (47.2%), followed by *K. pneumoniae* (21.8%), and *E. coli* (19.1%). However, this report includes all targeted pathogens in NSP-AMR which are either community- or hospital-acquired pathogens. Thus, in this HAI surveillance, there was no report on *N. gonorrhoeae* and few records of *S. pneumoniae* (2 events) and *Salmonella* spp. (4 events) (Figure37).

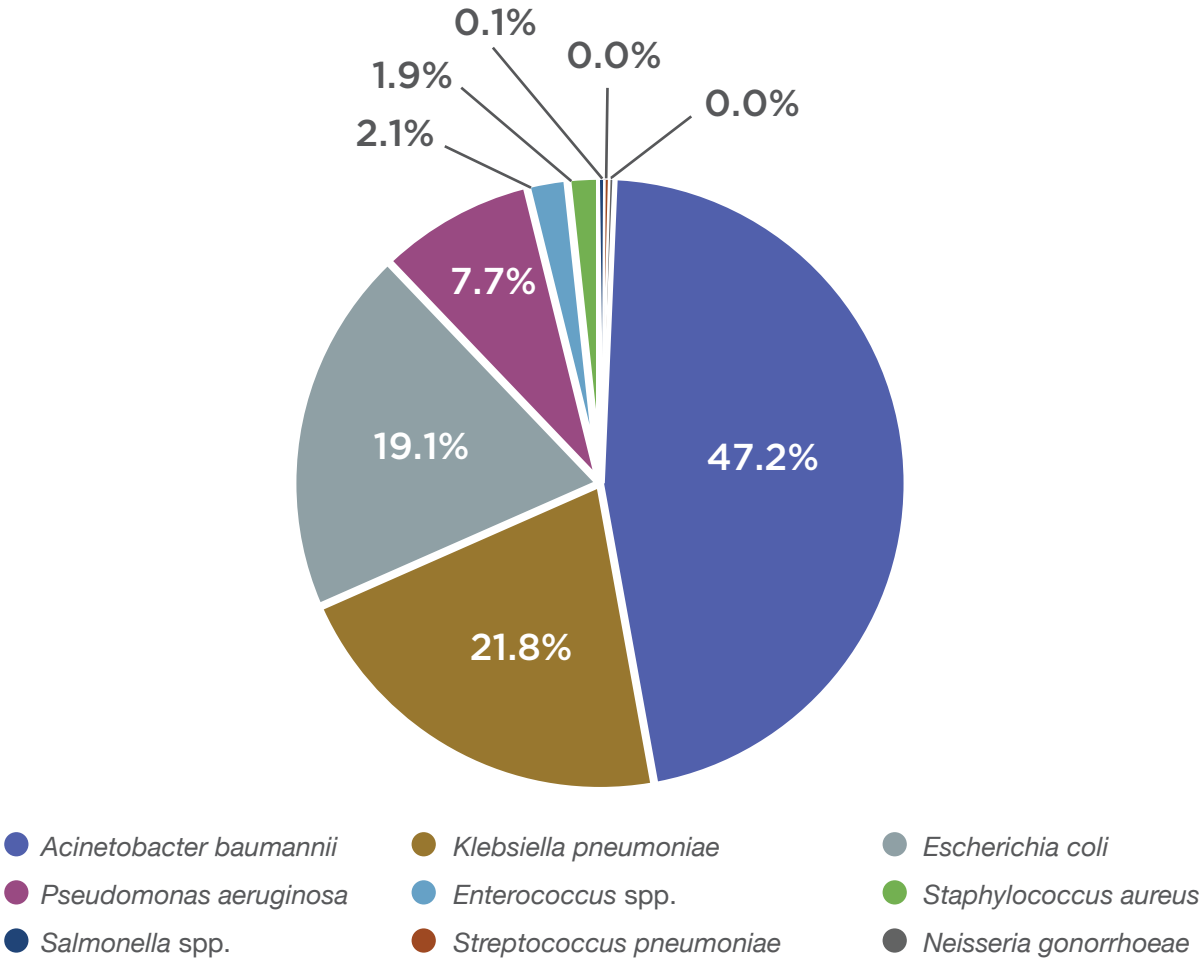


Figure 37. AMR events by targeted pathogen

Regarding the percentage of antibiotic resistance causing HAI, 88.6% of *A. baumannii* isolates were drug resistant (n = 2,028) followed by *E. coli* (73.7%, n = 995), and *K. pneumoniae* (66.6%, n = 1,241). Furthermore, 31.0 % of reported *P. aeruginosa* (n = 914) and 31.6% of *S. aureus* (n = 231) were drug-resistant organisms (Table 23).

Specifically, most of *A. baumannii* were resistant to carbapenems (89.8%, n = 1,999) while carbapenem-resistant *P. aeruginosa* was at 30.0% (n = 887). For third generation cephalosporins, resistance was common in *K. pneumoniae* and *E. coli*, accounting for 67.7% (n = 1,186) and 69.4% (n = 919), respectively. In addition, 33.8% of *S. aureus* was methicillin-resistant *S. aureus* (MRSA) (n = 216). Finally, vancomycin-resistant *Enterococcus* was 16.2% of total reported *Enterococcus* spp. (n = 505) (Table 24).

Table 23. Percentage of drug resistance in targeted pathogens

Pathogen	Total*	AMR	%
1. *A. baumannii*	2,028	1,796	88.6
2. *K. pneumoniae*	1,241	827	66.6
3. *E. coli*	995	733	73.7
4. *P. aeruginosa*	914	283	31.0
5. *Enterococcus* spp.	540	82	15.2
6. *S. aureus*	231	73	31.6
7. *S. pneumoniae*	19	2	21.1
8. *Salmonella* spp.	17	4	23.5
9. *N. gonorrhoeae*	0	-	-

*Include only the first isolated pathogen

Table 24. Percentage of drug resistance in targeted pathogens

AMR target	Drug group	Total*	No result	S	I	R	% resistance
A. baumannii	Carbapenem	2,028	29	195	9	1,795	89.8
	Colistin	2,028	1,328	681	0	19	2.7
K. pneumoniae	Carbapenem	1,241	55	738	11	437	36.9
	Colistin	1,241	979	216	0	46	17.6
	3rd generation cephalosporin	1,241	24	379	14	824	67.7
E. coli	*Carbapenem*	995	76	806	1	112	12.2
	Colistin	995	826	166	0	3	1.8
	Fluoroquinolone	995	98	445	17	435	48.5
	3rd generation cephalosporin	995	31	286	9	669	69.4
P. aeruginosa	Carbapenem	914	27	593	11	283	31.9
	Colistin	914	663	243	1	7	2.8
Enterococcus spp.	Vancomycin	540	35	423	0	82	16.2
S. aureus	Vancomycin	231	165	63	0	3	4.6
	Methicillin	231	15	143	0	73	33.8
S. pneumoniae	Penicillin	19	4	12	1	2	2/15
	3rd generation cephalosporin	19	4	15	0	0	0/15
Salmonella spp.	Colistin	17	17	0	0	0	0/0
	Fluoroquinolone	17	4	10	1	2	2/13
	3rd generation cephalosporin	17	8	6	0	3	3/9
N. gonorrhoeae	3rd generation cephalosporin	0	-	-	-	-	-

*count only first isolate pathogen
S = susceptible
I = intermediate
R = resistance

3.2.4 Limitation

Some limitations were identified. First, despite the fact that BIDI's HAI surveillance is the largest HAI surveillance in Thailand involving all types of hospitals in different regions, the sampling frame applied in this study was limited to those 103 hospitals out of total 1,466 hospitals in Thailand which implemented hospital-wide HAI surveillance and whose data were completely submitted. Hence, despite weighting of samples, using the results as a national representative should be carefully interpreted.

Secondly, this study analyzed data from BIDI's HAI surveillance, which is the most complete AMR case-based surveillance available in Thailand. However, because it is a HAI-focused surveillance approach, the incidence of AMR in this study did not include community-acquired AMR infections. Moreover, AMR target organisms included *S. pneumoniae, Salmonella* spp. and *N. gonorrhoeae* which are community pathogens. Thus, these organisms were rarely reported in the data.

Thirdly, the AMR definition used in this study focused on only nine target pathogens and selected antibiotics for sensitivity tests. Although they were the common AMR pathogens proposed by the National Strategic Plan, the limited scope of pathogens and antibiotics may result in the underestimation of true AMR incidence by all pathogens and all antibiotics.

Fourthly, in terms of drug susceptibility data, the prevalence of drug resistance reported in this study referred to the resistance percentage of each drug class. There is no separate data for resistance in each drug at ATC level 5. Furthermore, resistance percentage in this study is difference from that in the NARST report because of the difference approaches used in each surveillance system [23].

Finally, a lack of standardized laboratory capacity for susceptibility tests of colistin in several hospitals led to just a small number of colistin susceptibility results.

3.2.5 Prospect

In response to meeting the monitoring requirements of AMR morbidity as mandated by the NSP-AMR, Thailand needs to strengthen the BIDI prospective surveillance of HAI and AMR in certain sentinel hospitals. This can be done in 2020 by launching case-based surveillance in 25 hospitals in NARST program and other smaller district hospitals, which are currently not involved. This means BIDI surveillance should focus on high-quality data on case-based HAI and AMR surveillance through the training of ICWN, ICN and infectious disease experts and verification of all HAI and AMR reports with sentinel hospitals.

To ensure quality and accuracy of data, there is a need to:

1. Improve manual and standard operating procedures on surveillance including the definition of HAI, AMR and data entering processes. The BIDI database should include other key data, for example, gender, date of birth, admission number, citizen ID, types of surgery and remove all unnecessary data, for example, uncommon pathogens.
2. Synchronize the NARST database on AMR profiles through linking with citizen ID numbers and maintaining a high standard of confidentiality protection.
3. Ensure the BIDI surveillance system can capture and verify all HAI and AMR events (by local ICWN and ICN), therefore ensuring completeness of records by BIDI, which is the national focal point for infection and prevention control.
4. Strengthen web portal(s) to be user-friendly to encourage ICWN and ICN to submit data.
5. Publish incidence proportion of HAI and AMR per 100 inpatients. There is no need to publish AMR profiles as this duplicates the work done by NARST.

In addition, to encourage HAI and AMR surveillance in other hospitals, the remaining non-sentinel hospitals should participate in surveillance for internal monitoring purposes and timely outbreak control. Finally, monitoring community-acquired AMR infections using case-finding based on clinical specimens, similar to that used by GLASS, should be considered as a complementary action to close the gap in the BIDI HAI-focused approach.

3.3 Antimicrobial resistance in food-producing animals

Data source
Department of Livestock Development, Ministry of Agriculture and Cooperatives

Authors
Watcharachai Narongsak
Sunan Kittijaruwattana
Julaporn Srinha
Thammarath Sujit
Supaporn Wongsricha
Natthapong Supimon
Suchana Sukklad
Thanawan Na Thalang
Somsajee Sivilaikul
Supapat Kirivan

Editors
Saharuetai Jeamsripong
Kumthorn Malathum
Viroj Tangcharoensathien
Angkana Lekagul
Sunicha Chanvatik
Wanwisa Kaewkhankhaeng

Key summary

Escherichia coli

For samples from cecums in both chickens and pigs and from chicken meat collected at slaughterhouses, the highest resistance rate of *E. coli* was found in ampicillin, followed by tetracycline and chloramphenicol. Resistance rates in pork from slaughterhouses were similar to those of meat from retail markets in both species with the highest resistance in ampicillin, followed by tetracycline and trimethoprim/sulfamethoxazole.

***Salmonella* spp.**

For samples from cecums of chickens and pigs and from chicken meat collected at slaughterhouses, the highest resistance rate of *Salmonella* spp. was found in ampicillin, followed by tetracycline and ciprofloxacin. Resistance rates in pork from slaughterhouses were similar to those of meat from retail markets in both species with the highest resistance in ampicillin, followed by tetracycline and trimethoprim/sulfamethoxazole.

Enterococcus faecium* and *Enterococcus faecalis

In cecal samples from chickens and pigs, *E. faecium* and *E. faecalis* were found with highest resistance rate in tetracycline, followed by erythromycin and streptomycin.

Campylobacter coli* and *Campylobacter jejuni

For *C. coli* and *C. jejuni* isolated from cecums of chickens and pigs, the resistance profile in 2018 was between 50.0% to 80.0% including ciprofloxacin, erythromycin, gentamicin, streptomycin and tetracycline.

3.3.1 General

In response to global agenda on AMR and Thailand's National Strategic Plan on AMR 2017-2021, the DLD, who plays an important role in control and regulation on antimicrobial use in animal sector, initiated the surveillance system on AMR in food-producing animals with an aim to monitor the trend of AMR and promote prudent use of antimicrobials in Thailand. In 2016, the National Institute of Animal Health (NIAH), Bureau of Quality Control of Livestock Product, and Regional Veterinary Research and Development Center, have conducted staff training programmes, built laboratory capacities, and implemented standard methods of antimicrobial susceptibility testing AST for AMR prior to the commencement of the national surveillance of AMR in 2017.

3.3.2 Data Sources

The national surveillance of AMR in Thailand in food-producing animals was conducted in two animal species (chickens and pigs) because both of the animal species are the main food-producing animals of Thailand and are potentially raised with antimicrobials. This surveillance included sampling cecums from slaughterhouse, as the representative of healthy animals and meat from slaughterhouses and retail markets. In compliance with the OIE guideline, the sample size was calculated and a total of 5,900 samples were obtained and tested (OIE guidelines) [24]. All samples were transported to laboratories of DLD. The target bacteria of AMR surveillance included zoonotic bacteria (*Salmonella* spp., *Campylobacter coli* and *C. jejuni*) and indicator bacteria (*Enterococcus faecium* and *E. faecalis*, and *Escherichia coli*). AST was performed based on the Clinical and Laboratory Standards Institute (CLSI), ISO 20776-1, and the European Committee on Antimicrobial Susceptibility Testing (EUCAST). The tested antimicrobials were included as follows:

- Polymyxins (colistin)
- Fluoroquinolones (ciprofloxacin)
- 3rd generation cephalosporins (cefotaxime and ceftazidime)
- Antibiotics which have been banned or are not used in livestock, but were included for surveillance purposes, including carbapenems (meropenem), amphenicols (chloramphenicol), glycopeptides and lipoglycopeptide (vancomycin and teicoplanin), oxazolidinones (linezolid) and glycylcyclines (tigecycline).
- Other antibiotic groups used in livestock including sulfonamides, dihydrofolate reductase inhibitors and combinations (sulfamethoxazole and trimethoprim) and aminoglycosides (gentamicin and streptomycin).

Process of sample collection, microbiological testing, and data analysis is shown in Figure 38.

The responsible agency	1. National Institute of Animal Health 2. Bureau of Quality Control of Livestock Product 3. Regional Veterinary Research and Development Center 4. Division of Animal Feed and Veterinary Products Control	
Type of animal	Broiler chickens and pigs	
Target sample and responsible organization	Cecum of chickens and pigs were performed by National Institute of Animal Health, and Regional Veterinary Research and Development Center	Chicken meat and pork were performed by Bureau of Quality Control of Livestock Product, and Regional Veterinary Research and Development Center
Location	Slaughterhouses	Slaughterhouses and retailers
Target bacterial isolates	*E. coli* *Salmonella* spp. *Enterococcus faecium* and *E. faecalis* *Campylobacter coli* and *C. jejuni*	*E. coli* *Salmonella* spp.
Antibiotics Susceptibility Testing (AST)	MIC determination: Broth microdilution Conventional method and Automated MIC device	
Reference	WHO, OIE, FAO, CLSI, EUCAST and ISO 20776-1	
Drug panel for AST	Cover of all class of antibiotics for testing pathogen reference from CLSI, EUCAST and European Food Safety Authority (EFSA)	

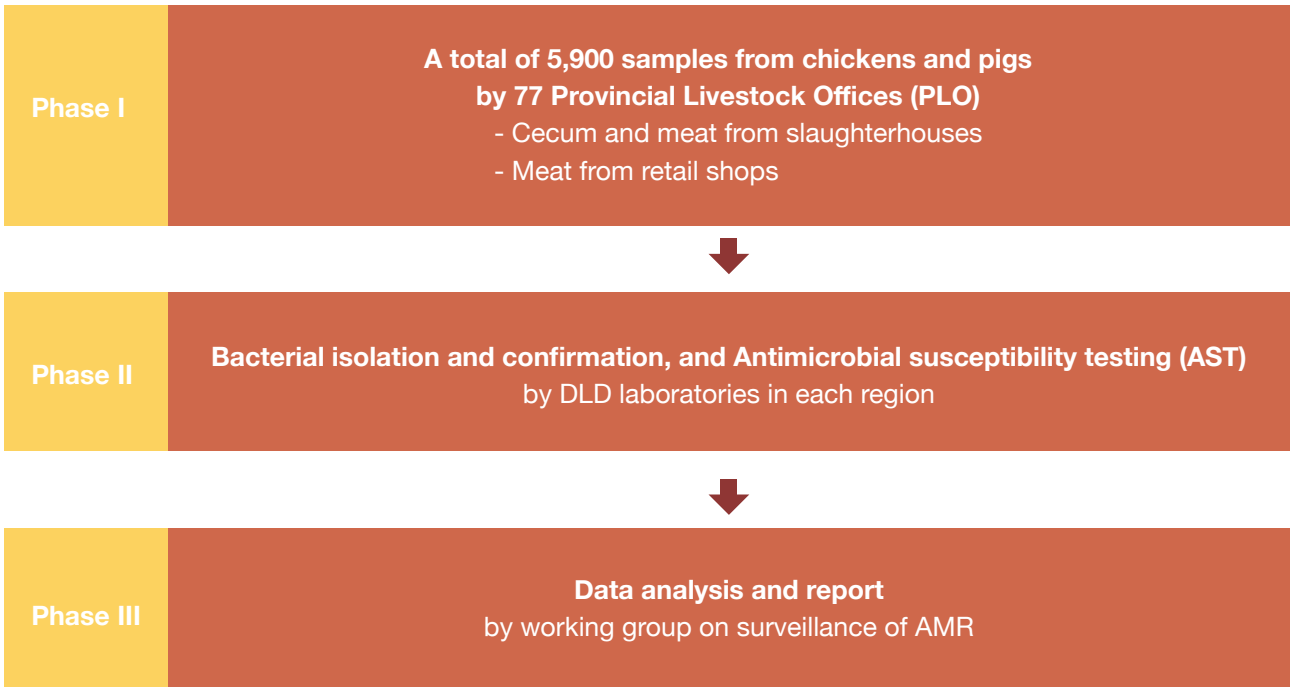


Figure 38. Process of sample collection, microbiological testing, and data analysis

3.3.3 Results

Escherichia coli

- AMR profile of *Escherichia coli* isolates from chickens

Isolates from chickens were commonly resistant against ampicillin in cecums (92.0%), meat from slaughterhouses (78.8%) and meat from retail markets (78.6%) (Figure 39). These results were in line with the findings in 2017 [25]. *E. coli* was resistant to tetracycline in cecum (89.6%), meat from slaughterhouses (66.5%) and meat from retail markets (68.1%). Of cecal and meat samples from slaughterhouses, rate of chloramphenicol-resistant *E. coli* in cecums was 44.7% and that of meats from slaughterhouse was 38.5%, which was in the third rank of resistance rates. However, the third-ranked group of antimicrobials in *E. coli* isolated from meat from retail markets was trimethoprim/sulfamethoxazole (32.8%). Less common resistance rates were observed in third-generation cephalosporins (cefotaxime and ceftazidime), carbapenems (meropenem) and polymyxins (colistin) (Figure 39).

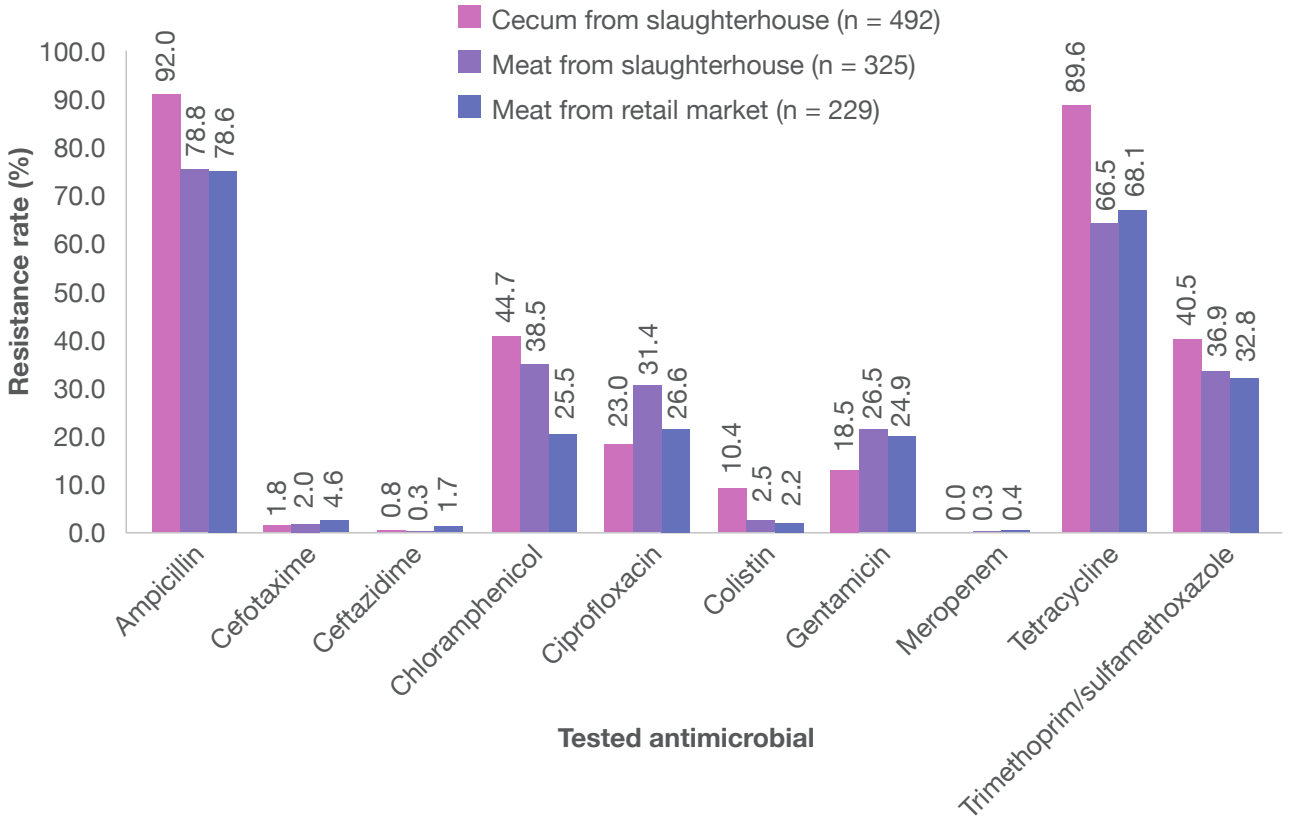


Figure 39. Resistance rate of *E. coli* isolated from chicken cecums and meats in slaughterhouses and retail markets in 2018

- AMR profile of *Escherichia coli* isolates from pigs

The resistance rates in cecums and meat from slaughterhouses and retail markets were different (Figure 40). In 2018, the highest resistance rate to *E.coli* isolates from cecal samples belonged to ampicillin (96.9%), followed by tetracycline (90.4%) and chloramphenicol (63.7%) while the top-three highest rates of resistance in 2017 belonged to ampicillin (93.0%), sulfamethoxazole (83.3%), trimethoprim (73.6%) [25]. For pork samples from slaughterhouses, the highest AMR rate was found in ampicillin (83.2%), followed by tetracycline (72.9%) and trimethoprim/sulfamethoxazole (46.0%). Similarly, the highest percentage of AMR from meats in retail markets was found in ampicillin (84.0%), followed by tetracycline (73.3%), and trimethoprim/sulfamethoxazole (49.3%).

Resistance to chloramphenicol was 63.7% in cecums, 42.5% in meat from slaughterhouses, and 46.8% in meat from retail markets. Similar to *E. coli* isolated from chickens, the less common resistance groups of antimicrobials were third-generation cephalosporins (cefotaxime and ceftazidime), carbapenems (meropenem) and polymyxins (colistin).

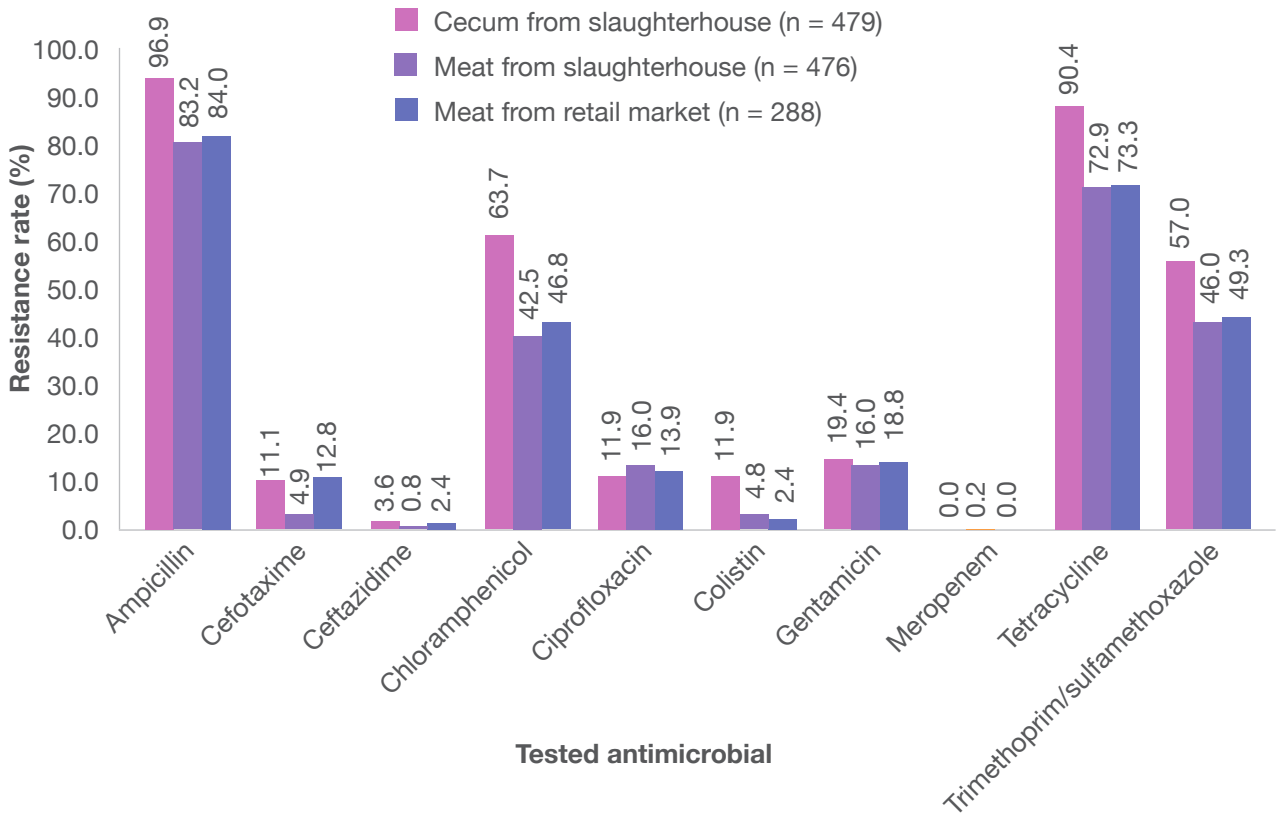


Figure 40. Resistance rate of *E. coli* isolated from porcine cecums and meat in slaughterhouses and retail markets in 2018

***Salmonella* spp.**

- AMR profile of *Salmonella* spp. isolates from chickens

The resistance profile in *Salmonella* spp. isolated from cecums was different from that in meat (Figure 41). In 2018, *Salmonella* spp. isolates from cecums were commonly resistant to three antimicrobials, tetracycline (63.5%), ampicillin (59.9%) and ciprofloxacin (29.3%). The prevalence of AMR in cecums from broilers was different from 2017, in which ampicillin ranked first (78.3%), followed by sulfamethoxazole (77.3%) and trimethoprim (52.3%) [25]. Of meat samples from slaughterhouses in 2018, the highest resistance of *Salmonella* spp. was found in ampicillin (46.9%), followed by tetracycline (41.1%) and ciprofloxacin (19.2%). For meat collected from retail markets, the highest AMR rate was found in ampicillin (53.4%), followed by tetracycline (41.0%) and trimethoprim/sulfamethoxazole (23.6%), which is similar to meat samples from slaughterhouses except for the third rank. The three groups of antimicrobials with the lowest resistance rates were third-generation cephalosporins (cefotaxime and ceftazidime), carbapenems (meropenem) and polymyxins (colistin) (Figure 41).

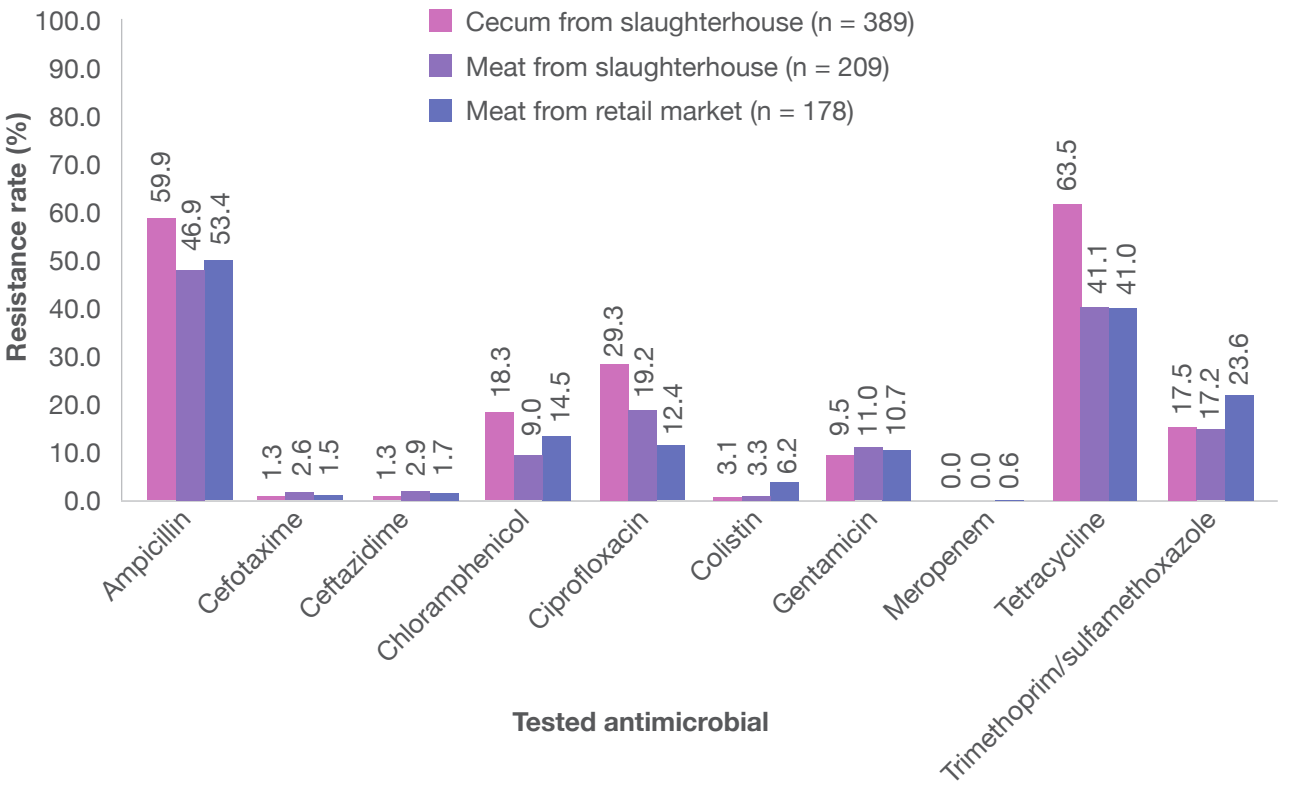


Figure 41. Resistance rate of *Salmonella* spp. isolated from chicken cecums and meat in slaughterhouses and retail markets in 2018

- AMR profile of *Salmonella* spp. isolates from pigs

The resistance rate of *Salmonella* spp. from cecums was different from meat collected from slaughterhouses and retail markets (Figure 42). Of cecal samples collected from slaughterhouses, the highest percentage of resistant *Salmonella* spp. was found in ampicillin (81.8%), followed by tetracycline (73.2%) and chloramphenicol (29.3%), which was different from *Salmonella* isolated from chickens. Compared with *Salmonella* profile of cecal samples in 2017, resistances to ampicillin and tetracycline remained at the highest rank of AMR [25]. Regarding *Salmonella* spp. isolates from meat, the resistance rates between slaughterhouses and retail markets were similar. The highest AMR was found in ampicillin (70.9% for slaughterhouses and 72.1% for retail markets), followed by tetracycline (64.0% for slaughterhouses and 63.0% for retail markets) and trimethoprim/sulfamethoxazole (30.9% for slaughterhouses and 33.4% for retail markets).

The less common resistance groups of antimicrobials (<10.0% resistance in all three sources) were third-generation cephalosporins (cefotaxime and ceftazidime), fluoroquinolone (ciprofloxacin), aminoglycosides (gentamicin), and polymyxins (colistin) (Figure 42). None of *Salmonella* spp. isolates from all three sources of pigs was resistant to meropenem, in contrast to 0.6% of *Salmonella* spp. isolated from chicken meat at retail markets.

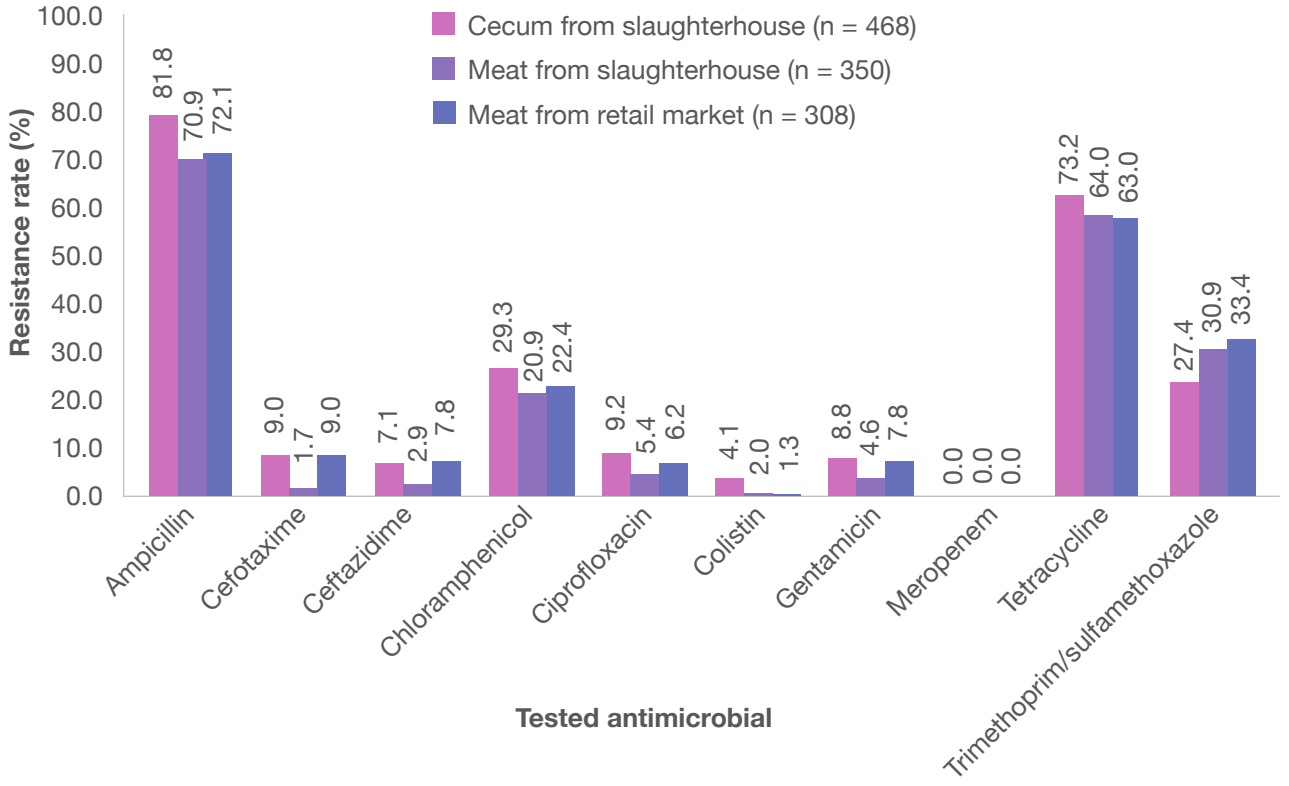


Figure 42. Resistance rate of *Salmonella* spp. isolated from porcine cecums and meat in slaughterhouses and retail markets in 2018

Enterococcus faecium* and *Enterococcus faecalis

- AMR profile of *Enterococcus faecium* and *Enterococcus faecalis* isolates from chickens

In 2018, the trend of AMR rates in *E. faecium* and *E. faecalis* isolated from cecums of broilers was similar to the trend of 2017 (Figure 43) [25]. The highest AMR rate was found in tetracycline (88.9%), which had increased from the rate in 2017 (80.0%). Resistance to erythromycin was found to be 86.7%, which had slightly increased from the rate in 2017 (83.4%). Additionally, resistance to streptomycin was 51.2%, which had increased from the rate in 2017 (39.8%). In 2018, the three antimicrobials with decrease in AMR rates from 2017 were gentamicin (from 18.3% to 16.3%), vancomycin (from 1.9% to 0.3%) and linezolid (1.5% to 0.5%) (Figure 43).

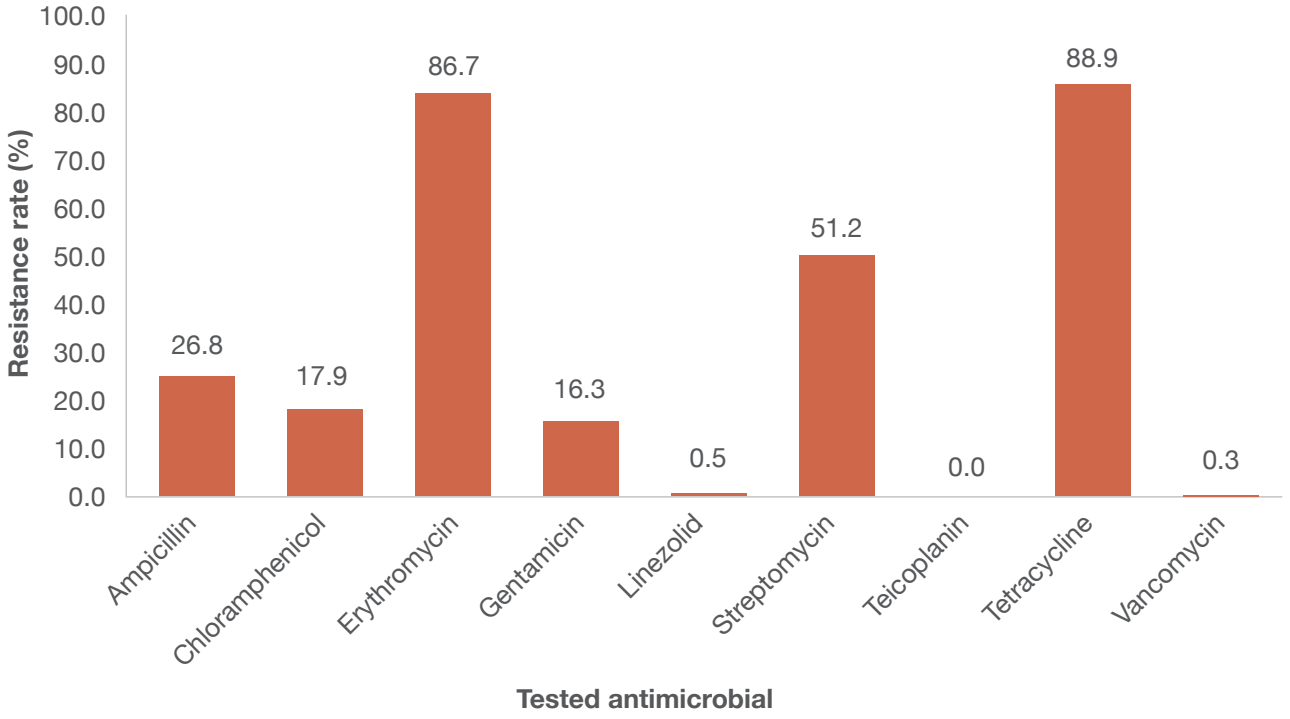


Figure 43. Resistance rate of *E. faecium* and *E. faecalis* isolated from chicken cecums in slaughterhouses in 2018 (n=369)

- AMR profile of *E. faecium* and *E. faecalis* isolates from pigs

The AMR rate of *E. faecium* and *E. faecalis* isolated from cecums of broilers was similar to the trend of 2017 (Figure 44) [25]. The highest AMR rate was found in tetracycline (76.8%), which had increased from the rate in 2017 (65.9%). Ranked second in 2018, the resistance rate to erythromycin was 75.4% resistance, which had slightly increased from 2017 (72.6%). Streptomycin ranked third with 54.6% resistance, which had moderately increased from 2017 (38.1%). None of *E. faecium* and *E. faecalis* isolates was resistant against teicoplanin and vancomycin (Figure 44).

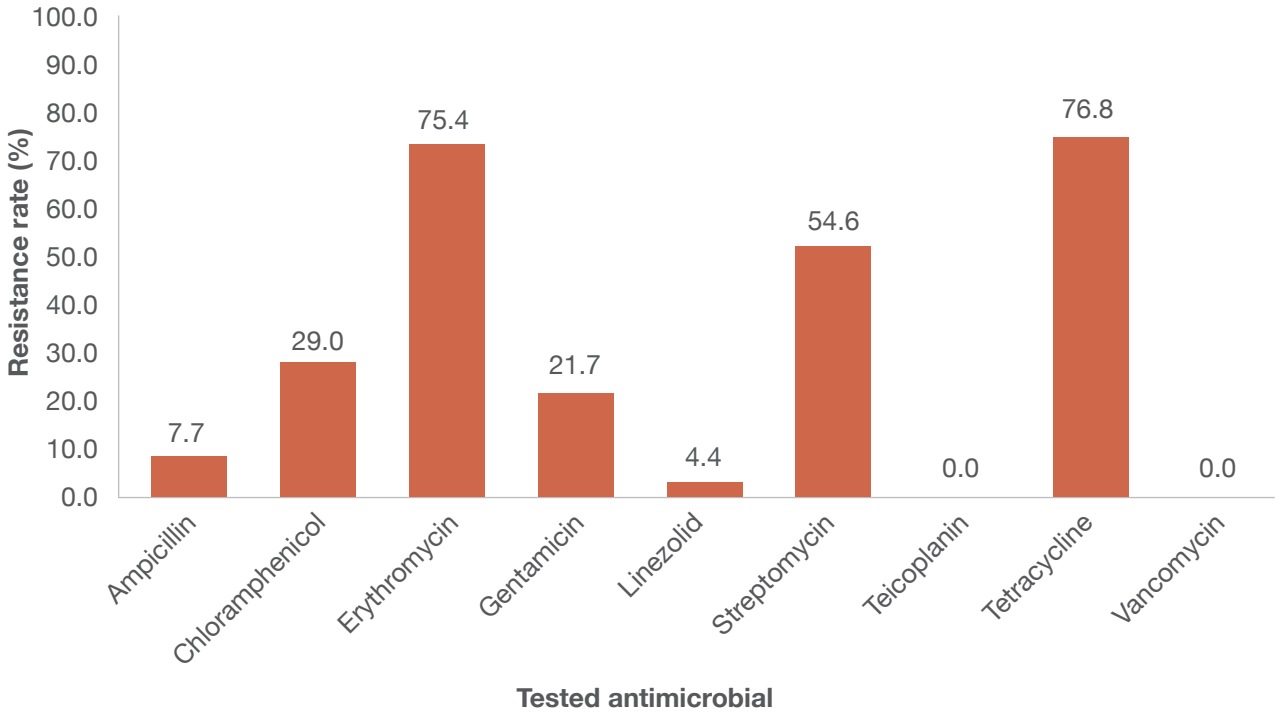


Figure 44. Resistance rate of *E. faecium* and *E. faecalis* isolated from porcine cecums in slaughterhouses, 2018 (n=207)

Campylobacter coli* and *Campylobacter jejuni

- AMR profile of *Campylobacter coli* and *Campylobacter jejuni* isolates from chickens and pigs

For *C. coli* and *C. jejuni* isolated from cecums of chickens and pigs, the resistance profile in 2018 was between 50.0% to 80.0% including ciprofloxacin, erythromycin, gentamicin, streptomycin and tetracycline. However, the number of isolates in some antimicrobials was insufficient to analyze. See 3.3.4 Limitations.

3.3.4 Limitations

As *C. coli* and *C. jejuni* are fastidious bacteria, sample processing and bacterial identification techniques are of importance. As a result, the number of isolates was insufficient to reach the target sample size, affecting AMR patterns.

Moreover, some drugs included in the panel might be found to be resistant, but they have been banned for use in livestock (vancomycin and chloramphenicol), were not available for animals (teicoplanin), or used as a representative drug of an antimicrobial class (ciprofloxacin for fluoroquinolones). Consequently, careful interpretation on AMR results is advised.

Lastly, as the preliminary phase of surveillance system development, this surveillance of AMR in food-producing animals focused only on phenotypic AMR; therefore, genetic resistance determinants were not identified, which is an important consideration in planning and implementing an efficient AMR surveillance system.

3.3.5 Prospect

During the next phase, the DLD plans to include ESBL phenotypic screening in the surveillance panel and improves the quality of sample processing and bacterial identification for *C. coli* and *C. jejuni*, which are important bacteria for public health.

The surveillance of AMR in animals indicated that the results of AST can reflect the current status of AMR in chickens and pigs. For CIA, the use of cephalosporins (3rd and 4th generation), polymyxins and macrolides should be restricted in food-producing animals. Despite a low resistance rate of CIA, the routine surveillance of AMR in chickens and swine should be implemented in order to monitor antimicrobial-resistant bacteria in food-producing animals throughout the food chain. Moreover, the study of resistance determinants is needed to strengthen AMR capacity in Thailand.

In response to AMR, DLD implemented the following key interventions in 2018:

1. Interactive media were created to encourage prudent use of antimicrobials and raise awareness on antimicrobial use and resistance in relevant sectors of food-producing industry.
2. Ministerial Notification pertaining to medicated feed was endorsed in 2018. Under the Notification, activities in relation to medicated feeds need to be authorized by DLD. Regarding the activities, the manufacturers need to follow Good Manufacturing Practice (GMP) and have their own responsible veterinarians at feed mills who have passed training courses conducted by DLD. On top of this, the use of antimicrobials in feed must be approved by responsible veterinarians at farms through prescription.
3. The pilot project “Raised Without Antibiotics or RWA” was initiated in fattening pigs. In this project, the pig farms who want to participate need to follow Good Agricultural Practice (GAP) along with free from beta-agonists. From farm to slaughterhouse, no antibiotics are used. However, if any pigs need to be treated, they are allowed to be treated with antibiotics based on animal welfare, but are then excluded from the project. Any products from the excluded pigs will not be not labeled RWA.
4. Other policies in relation to alternatives for antimicrobials such as herbal products, prebiotics and probiotics are in process of exploration.

3.4 Antimicrobial resistance in food chain

Data source
Food and Drug Administration, Ministry of Public Health

Author
Sayan Ruadrew

Editors
Saharuetai Jeamsripong
Kumthorn Malathum
Viroj Tangcharoensathien
Angkana Lekagul
Sunicha Chanvatik
Wanwisa Kaewkhankhaeng

Key summary

A first step of antimicrobial-risk management is to generate food safety data of resistant bacteria with the potential to contaminate meat. Findings from the isolation of *Salmonella* spp. and *E. coli* in pork and chicken showed that the overall contamination rate of *Salmonella* spp. was higher than that of *E. coli* ($P < 0.0001$). *Salmonella* contamination was higher in pork than in chicken ($P < 0.0001$). In contrast, *E. coli* contamination was higher in chicken than in pork ($P < 0.0001$). All isolates were tested for their antimicrobial susceptibility and extended spectrum beta-lactamases (ESBLs) production. Antimicrobial resistance (AMR) rates varied according to the type of antibiotics. Most *Salmonella* spp. and *E. coli* exhibited multidrug resistance phenotype. The ampicillin resistance rate was highest in *Salmonella* spp. (53.7%) and *E. coli* (60.6%). Colistin resistance rates were found to be approximately 3.0% and none of the isolates was resistant to meropenem. ESBL producing *Salmonella* spp. (8.9%) and *E. coli* (7.1%) were detected. All the ESBL-positive isolates were multidrug-resistant. The results highlighted that pork and chicken play a role as reservoirs of resistant *Salmonella* spp. and *E. coli*. Therefore, appropriate risk control measures are required.

3.4.1 General

AMR has been recognized worldwide as a public health threat that requires all countries to develop and implement national strategies and action plans in order to minimize and contain AMR.

In Thailand, a surveillance system of AMR under the One Health approach was established as one of six strategies under the five-year National Strategic Plan on AMR (2017-2021), which aims to reduce mortality, morbidity and the economic impact from AMR. Monitoring and surveillance of AMR in food sources are important steps to develop AMR control measures. The findings provide food-safety risk managers with vital evidence for managing the risk of AMR in the food supply chain and to foster the prudent use of antimicrobials, in order to prevent and control AMR.

To address the issue of AMR in the food supply chain and put the National Strategic Plan on AMR into action, in 2018 the FDA, with the collaboration of the Faculty of Veterinary Science, Chulalongkorn University has initiated the surveillance programme of AMR in foods at retail markets. The main objective of the surveillance programme is to determine the AMR prevalence in AMR-risk pork, chicken and other foods sold in retail markets.

3.4.2 Data Sources

1. Samples collection

Retail supermarkets located in four provinces in central region of Thailand including Bangkok, Nonthaburi, Pathumtani and Samutprakan were purposively selected based on the averaged quantities of meat sold per day (sale data of meat were kindly provided by the retailers - data not shown). The retailers whose sale quantities contributed to 60.0% of the total daily sale quantity were included in the sampling plan.

All cuts of uncooked pork and chicken samples were randomly collected from selected retail supermarkets. Whenever available, the whole package or 50 grams of unpackaged meat was taken and kept in an ice-box. Then, the samples were delivered within three hours to a laboratory of the Department of Veterinary Public Health, Faculty of Veterinary Sciences, Chulalongkorn University for analysis.

2. Isolation of *Salmonella* spp. and *Escherichia coli*

In this surveillance program, *Salmonella* spp. (pathogenic bacteria) and *E. coli* (commensal bacteria) were investigated. *Salmonella* spp. was isolated from the samples according to ISO 6579-1:2017 [26], and serotyping was carried out according to the methods of the Food and Drug Administration (FDA) Bacteriological Analytical Manual [27] and the Kauffmann-White Scheme of the Pasteur Institute [28]. The isolates of *Salmonella* spp. were kept in 20.0% glycerol solution at -80˚C for further analysis. Isolation of *E. coli* from the samples was carried out using BAM: Enumeration of *E. coli* and the coliform bacteria [29].

3. Identification of Antimicrobial Resistance isolates

AST was performed in accordance with internationally accepted procedures in order to characterize the AMR isolates. These included two-fold agar dilution technique for susceptibility testing against ampicillin, chloramphenicol, ciprofloxacin, colistin, gentamicin, meropenem, streptomycin, sulfamethoxazole, tetracycline and trimethoprim [30]. Disk diffusion technique was used to test susceptibilities of bacteria against cefpodoxime, ceftazidime, cefotaxime and meropenem (CLSI, 2013) and broth microdilution technique was employed for colistin susceptibility testing [31]. The MIC was observed in each test. The isolates were further tested for extended spectrum beta-lactamases production using a method of CLSI (2013).

4. Data Interpretation

In most cases, CLSI-approved clinical breakpoints were used to interpret the AST results (CLSI, 2013), except colistin, where EUCAST breakpoint was used (EUCAST, 2018) (Table 25). The univariate and multivariate logistic regression were performed using Stata version 14.0 (College Station, TX, USA) for analysis of AST data to examine the relationship between parameters of interest and the presence of AMR in samples.

Table 25. Clinical breakpoints of antibiotics used in AST for *E. coli* and *Salmonella* spp. isolates

Antibiotics	Solvents	Concentration range (µg/ml)	Breakpoint* (µg/ml)	
			E. coli	*Salmonella*
Ampicillin	Sterile distilled water	0.25 - 1,024	≥32	≥32
Erythromycin	95% ethanol	0.25-256	Not applicable	≥8
Chloramphenicol	95% ethanol	1 - 512	≥32	≥32
Ciprofloxacin	0.1 N NaOH	0.015 - 64	>1	>1
Colistin	Sterile distilled water	0.125 - 32	>2	>2
Gentamicin	Sterile distilled water	0.125 - 128	≥16	≥16
Streptomycin	Sterile distilled water	1 - 1,024	≥32	≥32
Sulfamethoxazole	0.1 N NaOH	2 - 2,048	≥512	≥512
Tetracycline	70% ethanol	0.0625 - 256	≥16	≥16
Trimethoprim	Dimethyl acetamide	0.25 - 2,048	≥16	≥16

[a] CLSI-approved clinical breakpoints were used to interpret the AST results (CLSI, 2013), except colistin that EUCAST breakpoint was used (EUCAST, 2018).

3.4.3 Results

1. Isolation of *E. coli* and *Salmonella* spp.

A total of 1,141 meat samples were collected, which included pork (n=550) and chicken (n=591) in 2018. Of these samples, 68.3% and 45.7% contained *E. coli* and *Salmonella* spp., respectively (Table 26). Numbers of *E. coli* and *Salmonella* spp. isolates recovered from the samples are shown in Table 27; unexpectedly, contamination of *Salmonella* spp. in pork was significantly higher than in chicken ($p < 0.0001$). On the other hand, contamination of *E. coli* in chicken was significantly higher than in pork ($p < 0.0001$). Serotyping of *Salmonella* spp. revealed a total of 126 serovars of which Rissen (17.3%), Enteritidis (11.8%) and Typhimurium (11.4%) were the predominant serotypes (Data not shown). It is worth noting that contamination of *E. coli* and *Salmonella* spp. was significantly associated with types of meat ($P < 0.0001$) (Table A17-18).

Table 26. Number of meat samples contaminated with *E. coli* and *Salmonella* spp.

Bacteria	Number of positive sample (%)		
	Pork (n = 550)	Chicken meat (n = 591)	Total (n = 1,141)
E. coli	360 (65.5%)	419 (70.9%)	779 (68.3%)
Salmonella spp.	311 (56.5%)	210 (35.5%)	521 (45.7%)

Table 27. Number of *E. coli* and *Salmonella* spp. isolated from pork and chicken samples

Sample	Number of isolate	
	E. coli	*Salmonella* spp.
Pork (n = 550)	360	449
Chicken meat (n = 591)	419	235

2. Antimicrobial susceptibility

E. coli

AST on 779 isolates of *E. coli* recovered from pork and chicken samples showed that 692 isolates (88.8%) were antimicrobial resistant. Resistance rates of *E. coli* isolates had most common resistance to ampicillin, tetracycline, trimethoprim, streptomycin and sulfamethoxazole, whereas meropenem resistance was not identified (Figure 45). Most *E. coli* isolates demonstrated resistance to more than one antimicrobial agent tested (Table A19-20, A23-24).

Taking into consideration 360 isolates of *E. coli* recovered from pork samples, it was found that resistance to ampicillin, tetracycline, trimethoprim, streptomycin and sulfamethoxazole were the most common (Figure 46), whereas 9.7% of *E. coli* isolates (35 isolates) were susceptible strains. A similar trend of resistance was found in *E. coli* isolates from chicken samples (419 isolates) where resistance to ampicillin, tetracycline, streptomycin and trimethoprim were most frequently detected (Figure 47), while 12.4% of the isolates were susceptible (52 isolates).

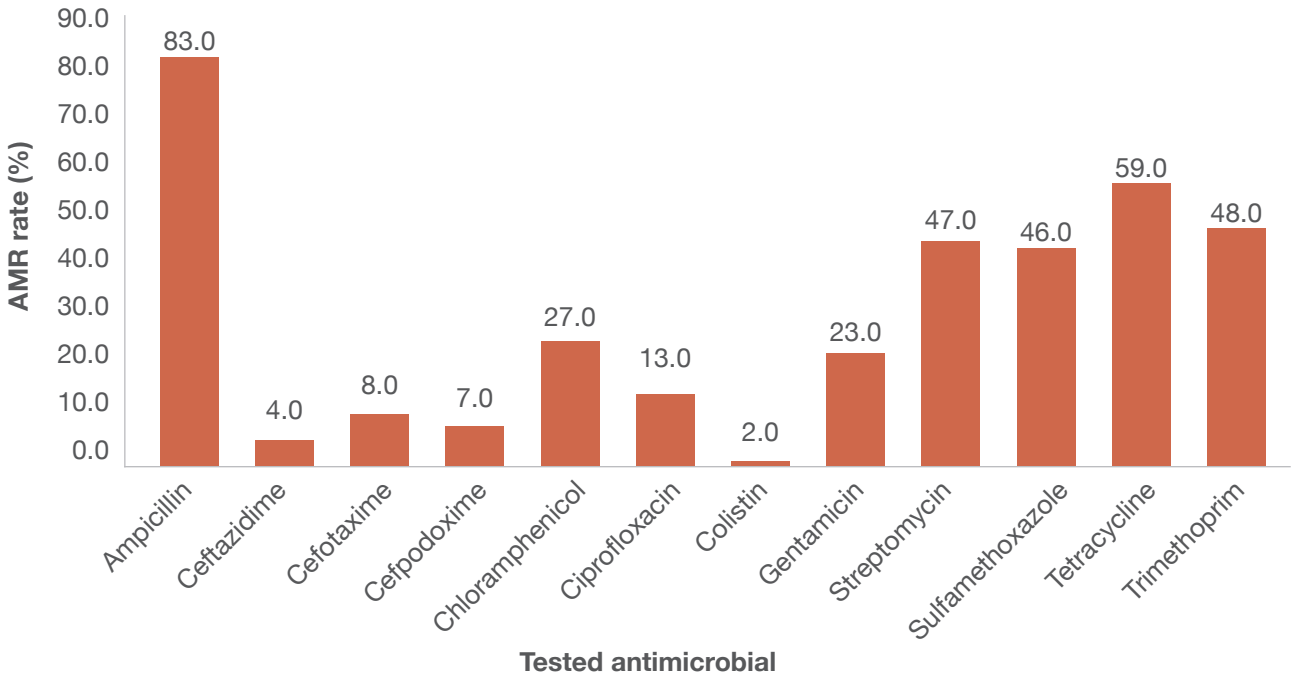


Figure 45. Resistance rate of *E. coli* isolated from pork and chicken samples (n = 779 isolates)

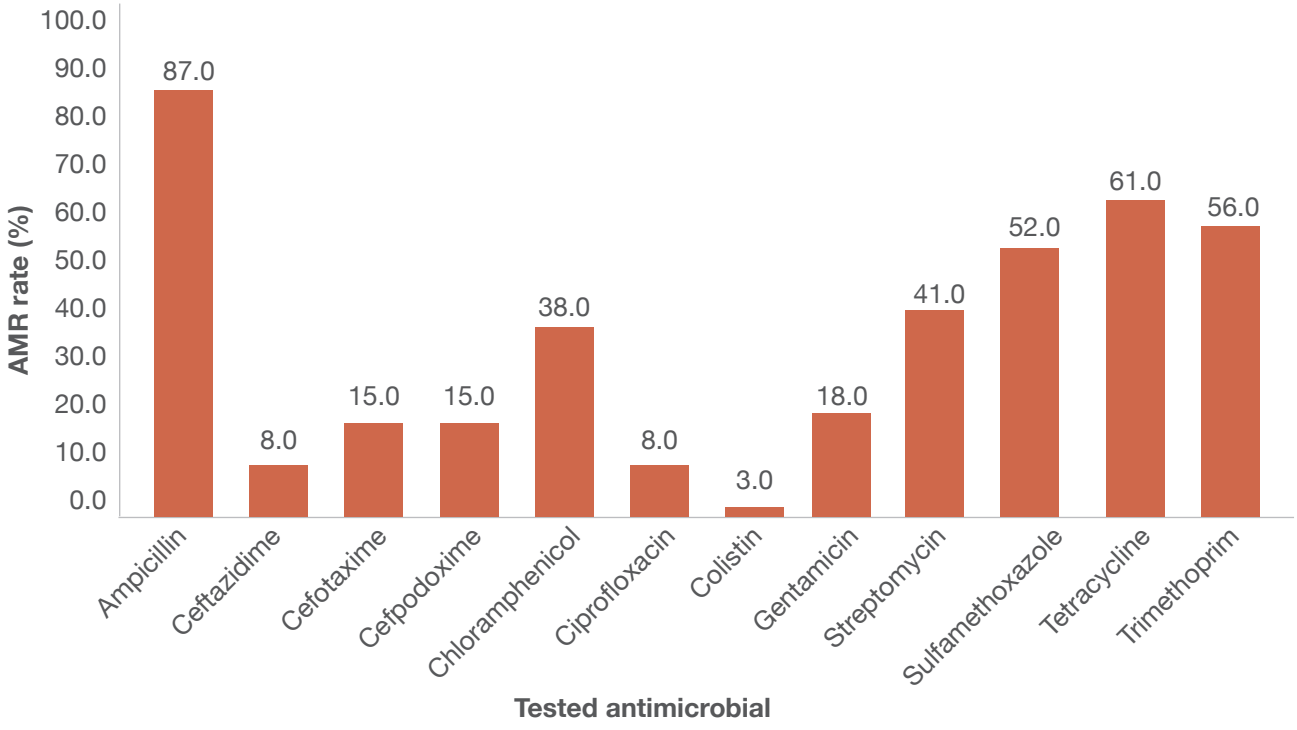


Figure 46. Resistance rate of *E. coli* isolated from pork samples (n = 360 isolates)

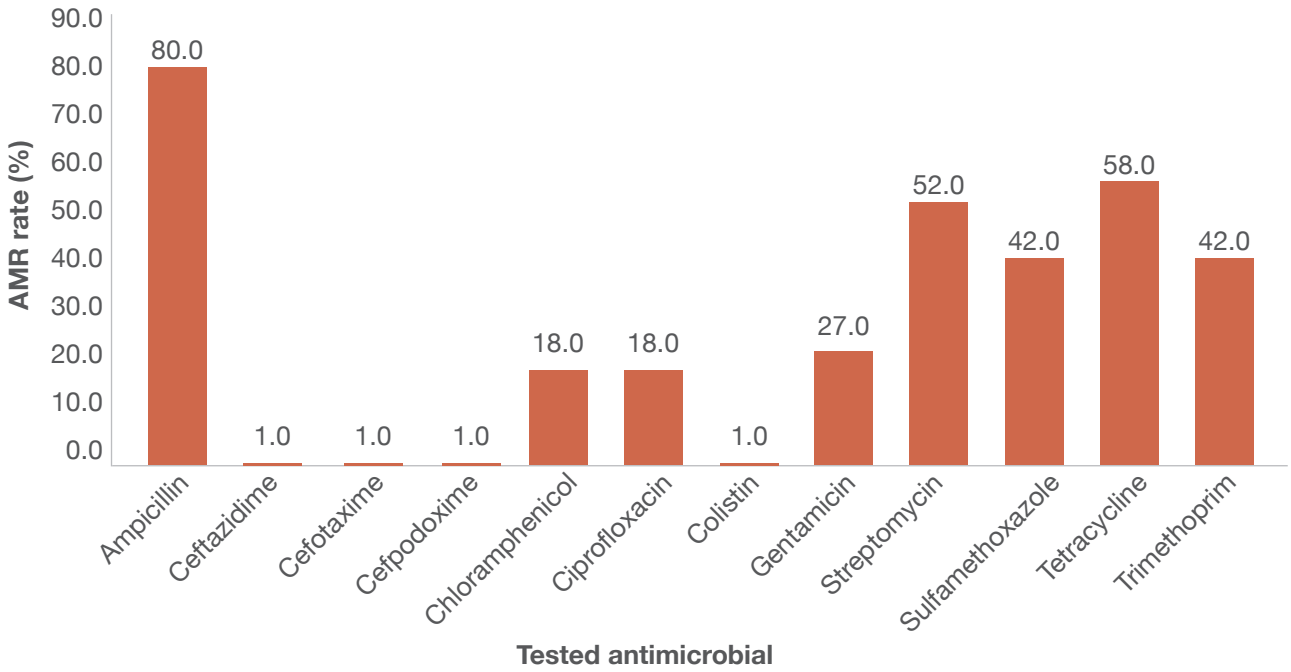


Figure 47. Resistance rate of *E. coli* isolated from pork samples (n = 360 isolates)

***Salmonella* spp.**

AST on 684 isolates of *Salmonella* from meat samples showed 512 isolates of AMR (74.4%). The resistance rates of *Salmonella* isolates which were resistant to ampicillin, erythromycin and tetracycline were the most common, while meropenem resistance was not identified (Figure 48). Most *Salmonella* isolates demonstrated resistance to more than one antimicrobial agent tested (Table A21-22, A25-26).

Of 449 *Salmonella* isolates recovered from pork, resistance to ampicillin, erythromycin and tetracycline were the predominant (Figure 49). Ninety-four isolates (20.4%) were susceptible. Among 235 isolates of *Salmonella* recovered from chicken, 65.5% were AMR of which resistance to ampicillin, tetracycline, and streptomycin were the most common (Figure 50). The *Salmonella* isolates that resistant to colistin were exclusively isolated from chicken samples.

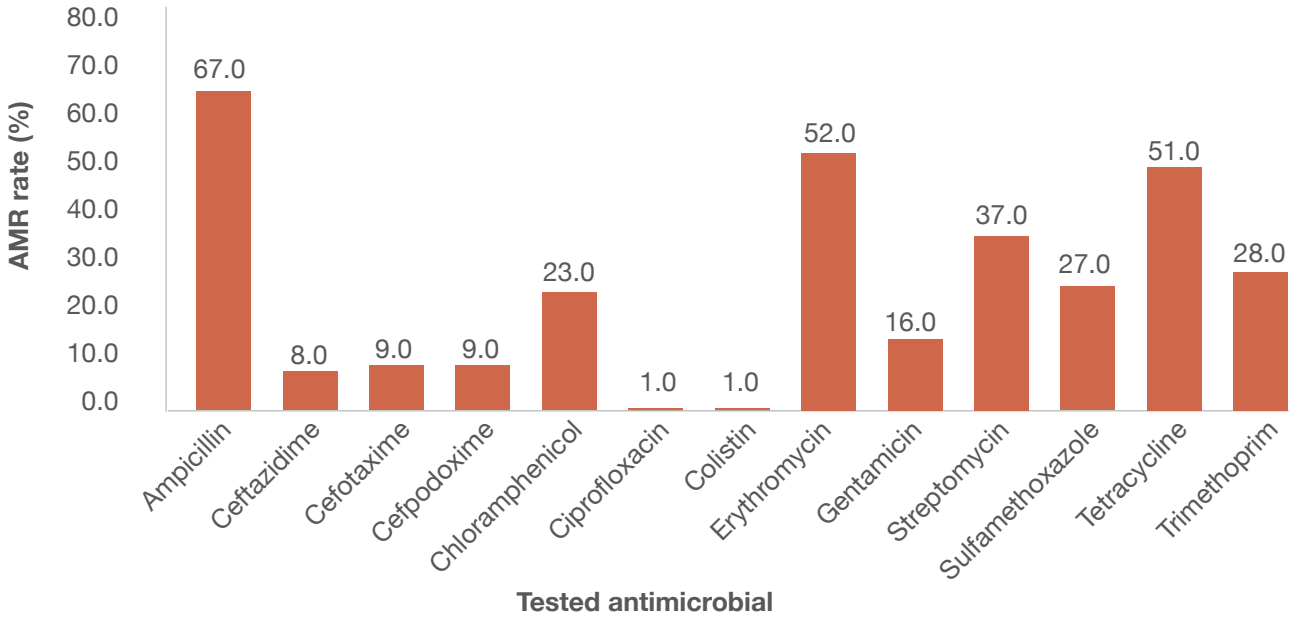


Figure 48. Resistance rate of *Salmonella* spp. isolated from pork and chicken samples (n = 684 isolates)

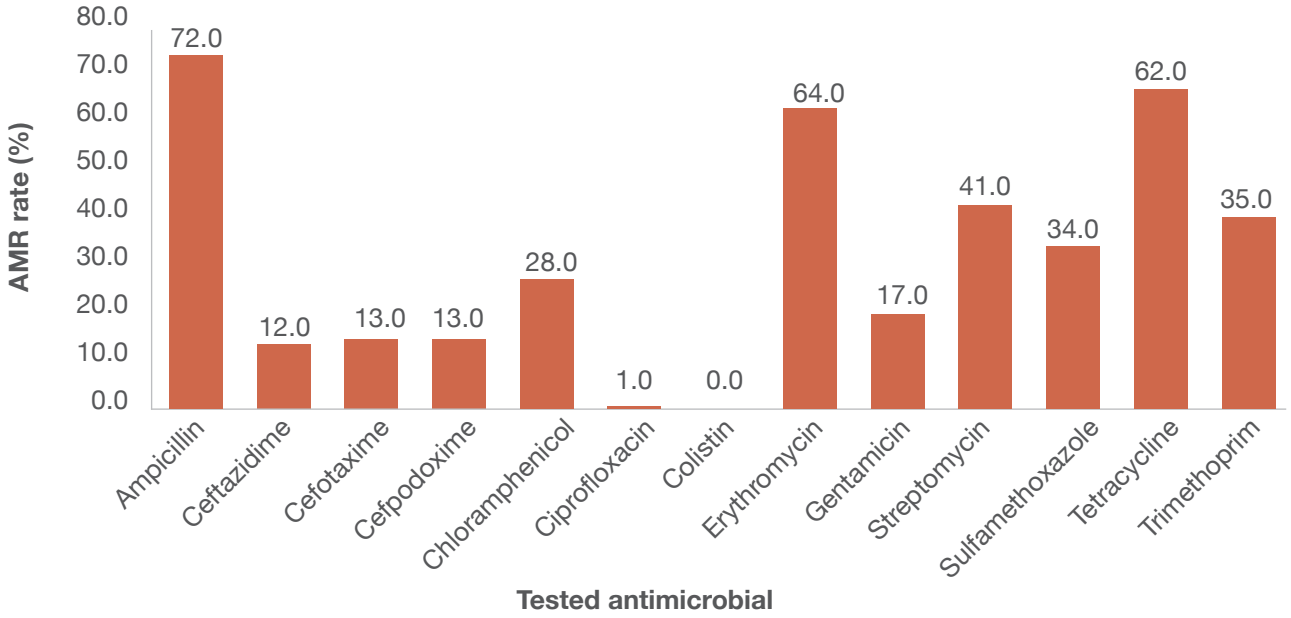


Figure 49. Resistance rate of *Salmonella* spp. isolated from pork samples (n = 449 isolates)

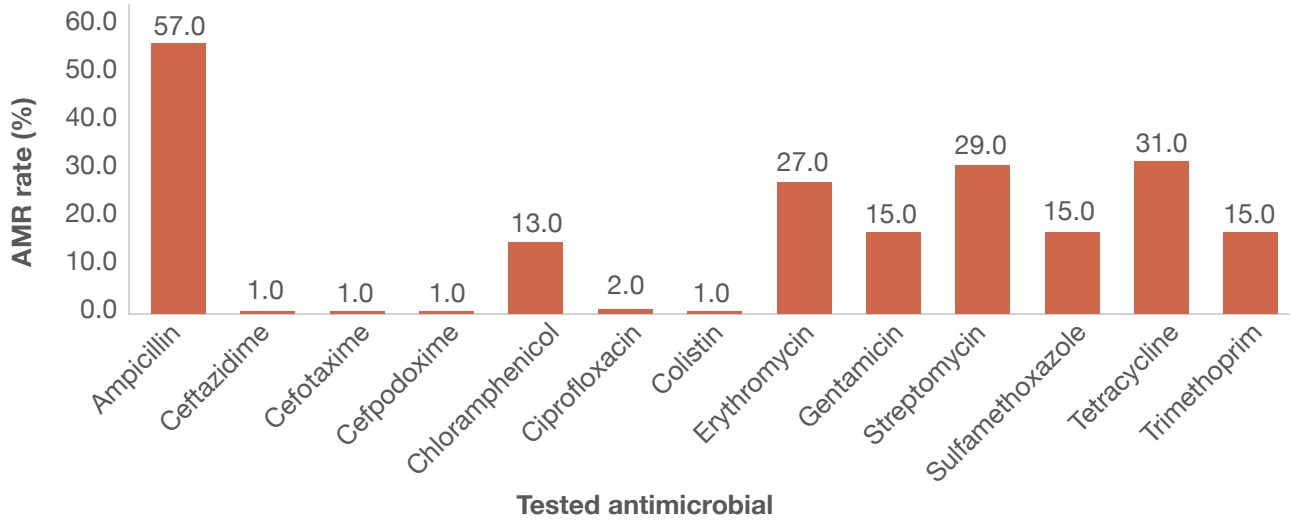


Figure 50. Resistance rate of *Salmonella* spp. isolated from chicken samples (n = 235 isolates)

3. ESBL-producing *E. coli* and *Salmonella* spp.

Examination of ESBL production showed that 7.1% of total *E. coli* isolates (n = 779 isolates) and 8.9% of total *Salmonella* isolates (n=684 isolates) were ESBL-producing strains (Table 28). It was demonstrated that most of ESBL-producing *Salmonella* spp. and *E. coli* were isolated from pork samples. All of ESBL-producing isolates from both sources were multidrug-resistant, of which the patterns are shown in Tables 29-30.

Table 28. Number of ESBL producing isolate recovered from each type of meat

Meat sample	Number of ESBL producing isolates (%)	
	***Salmonella* spp. (n=684)**	***E. coli* (n=779)**
Pork	59 (13.1%)	50 (13.9%)
Chicken	2 (0.8%)	5 (1.2%)
Total	**61 (8.9%)**	**55 (7.1%)**

Table 29. Antimicrobial resistant pattern of ESBL producing *E. coli* isolated from pork and chicken

Antimicrobial resistant pattern	Number of ESBL producing isolate (%)
Ampicillin-Cefotaxime-Cefpodoxime	3 (5.5%)
Ceftazidime-Cefotaxime-Cefpodoxime	1 (1.8%)
Ampicillin-Ceftazidime-Cefotaxime-Chloramphenicol	1 (1.8%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime	1 (1.8%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Streptomycin	1 (1.8%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Tetracycline	2 (3.6%)
Ampicillin-Cefotaxime-Cefpodoxime-Gentamicin-Tetracycline	1 (1.8%)
Ampicillin-Cefotaxime-Cefpodoxime-Streptomycin-Tetracycline	1 (1.8%)
Ampicillin-Cefotaxime-Cefpodoxime-Sulfamethoxazole-Trimethoprim	1 (1.8%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Chloramphenicol-Gentamicin	1 (1.8%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Chloramphenicol-Tetracycline	1 (1.8%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Gentamicin-Tetracycline	2 (3.6%)
Ampicillin-Cefotaxime-Cefpodoxime-Chloramphenicol-Ciprofloxacin-Gentamicin	1 (1.8%)
Ampicillin-Cefotaxime-Cefpodoxime-Chloramphenicol-Ciprofloxacin-Tetracycline	1 (1.8%)
Ampicillin-Cefotaxime-Cefpodoxime-Chloramphenicol-Gentamicin-Tetracycline	2 (3.6%)
Ampicillin-Cefotaxime-Cefpodoxime-Ciprofloxacin-Gentamicin-Tetracycline	1 (1.8%)
Ampicillin-Cefotaxime-Cefpodoxime-Streptomycin-Sulfamethoxazole-Tetracycline	1 (1.8%)
Ampicillin-Cefotaxime-Cefpodoxime-Sulfamethoxazole-Tetracycline-Trimethoprim	1 (1.8%)
Ampicillin-Cefotaxime-Cefpodoxime-Chloramphenicol-Ciprofloxacin-Gentamicin-Tetracycline	1 (1.8%)

Antimicrobial resistant pattern	Number of ESBL producing isolate (%)
Ampicillin-Cefotaxime-Cefpodoxime-Chloramphenicol-Gentamicin-Streptomycin-Tetracycline	1 (1.8%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Streptomycin-Sulfamethoxazole-Tetracycline	1 (1.8%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Chloramphenicol-Gentamicin-Streptomycin	2 (3.6%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Chloramphenicol-Sulfamethoxazole-Tetracycline-Trimethoprim	1 (1.8%)
Ampicillin-Cefotaxime-Cefpodoxime-Chloramphenicol-Gentamicin-Streptomycin-Sulfamethoxazole-Tetracycline	1 (1.8%)
Ampicillin-Cefotaxime-Cefpodoxime-Chloramphenicol-Gentamicin-Streptomycin-Sulfamethoxazole-Trimethoprim	1 (1.8%)
Ampicillin-Cefotaxime-Cefpodoxime-Chloramphenicol-Streptomycin-Sulfamethoxazole-Tetracycline-Trimethoprim	1 (1.8%)
Ampicillin-Cefotaxime-Cefpodoxime-Gentamicin-Streptomycin-Sulfamethoxazole-Tetracycline-Trimethoprim	1 (1.8%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Chloramphenicol-Gentamicin-Streptomycin-Sulfamethoxazole-Tetracycline	1 (1.8%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Chloramphenicol-Gentamicin-Sulfamethoxazole-Tetracycline-Trimethoprim	3 (5.5%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Chloramphenicol-Streptomycin-Sulfamethoxazole-Tetracycline-Trimethoprim	1 (1.8%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Gentamicin-Streptomycin-Sulfamethoxazole-Tetracycline-Trimethoprim	2 (3.6%)
Ampicillin-Cefotaxime-Cefpodoxime-Chloramphenicol-Ciprofloxacin-Gentamicin-Sulfamethoxazole-Tetracycline-Trimethoprim	2 (3.6%)
Ampicillin-Cefotaxime-Cefpodoxime-Chloramphenicol-Ciprofloxacin-Streptomycin-Sulfamethoxazole-Tetracycline-Trimethoprim	1 (1.8%)
Ampicillin-Cefotaxime-Cefpodoxime-Chloramphenicol-Gentamicin-Streptomycin-Sulfamethoxazole-Tetracycline-Trimethoprim	4 (7.3%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Chloramphenicol-Ciprofloxacin-Gentamicin-Sulfamethoxazole-Tetracycline-Trimethoprim	1 (1.8%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Chloramphenicol-Gentamicin-Streptomycin-Sulfamethoxazole-Tetracycline-Trimethoprim	5 (9.1%)
Ampicillin-Ceftazidime-Cefotaxime-Chloramphenicol-Ciprofloxacin-Gentamicin-Streptomycin-Sulfamethoxazole-Tetracycline-Trimethoprim	1 (1.8%)
Total	**55 isolates**

Table 30. Antimicrobial resistant pattern of ESBL producing *Salmonella* spp. isolated from pork and chicken

Antimicrobial resistant pattern	Number of ESBL producing isolate (%)
Ceftazidime-Cefotaxime-Cefpodoxime	1 (1.6%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Erythromycin	2 (3.3%)
Ampicillin-Cefotaxime-Cefpodoxime-Erythromycin-Gentamicin	1 (1.6%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Erythromycin-Gentamicin	4 (6.6%)
Ampicillin-Cefotaxime-Cefpodoxime-Chloramphenicol-Erythromycin-Gentamicin	1 (1.6%)
Ampicillin-Cefotaxime-Cefpodoxime-Erythromycin-Gentamicin-Tetracycline	2 (3.3%)
Cefotaxime-Cefpodoxime-Chloramphenicol-Gentamicin-Streptomycin-Tetracycline	1 (1.6%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Chloramphenicol-Colistin-Tetracycline	1 (1.6%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Chloramphenicol-Erythromycin-Gentamicin	1 (1.6%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Chloramphenicol-Erythromycin-Streptomycin	3 (4.9%)
Ceftazidime-Cefotaxime-Cefpodoxime-Chloramphenicol-Gentamicin-Streptomycin-Tetracycline	4 (6.6%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Chloramphenicol-Erythromycin-Gentamicin-Streptomycin	1 (1.6%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Chloramphenicol-Erythromycin-Streptomycin-Tetracycline	2 (3.3%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Chloramphenicol-Erythromycin-Sulfamethoxazole-Trimethoprim	1 (1.6%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Chloramphenicol-Gentamicin-Streptomycin-Tetracycline	2 (3.3%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Erythromycin-Gentamicin-Streptomycin-Tetracycline	4 (6.6%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Chloramphenicol-Erythromycin-Gentamicin-Streptomycin-Tetracycline	17 (27.9%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Chloramphenicol-Ciprofloxacin-Erythromycin-Gentamicin-Streptomycin-Tetracycline	1 (1.6%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Chloramphenicol-Erythromycin-Gentamicin-Streptomycin-Sulfamethoxazole-Trimethoprim	1 (1.6%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Chloramphenicol-Erythromycin-Streptomycin-Sulfamethoxazole-Tetracycline-Trimethoprim	1 (1.6%)

Antimicrobial resistant pattern	Number of ESBL producing isolate (%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Chloramphenicol-Erythromycin-Gentamicin-Streptomycin-Sulfamethoxazole-Tetracycline-Trimethoprim	7 (11.5%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Chloramphenicol-Ciprofloxacin-Erythromycin-Gentamicin-Streptomycin-Sulfamethoxazole-Tetracycline-Trimethoprim	2 (3.3%)
Ampicillin-Ceftazidime-Cefotaxime-Cefpodoxime-Chloramphenicol-Colistin-Erythromycin-Gentamicin-Streptomycin-Sulfamethoxazole-Tetracycline-Trimethoprim	1 (1.6%)
Total	**61 isolates**

3.4.4 Limitation

Meat samples collected in this surveillance program were not considered to be nationally representative due to the limited samples collected from the specific points in the food chain.

3.4.5 Prospect

The findings in this surveillance program reflect the outcome of the meat industry's past and current antimicrobial stewardship efforts. Further areas for improvement and actions may be identified as follows:

- Sampling should be broadened to be more representative of the target population as well as expanded to a wider scope of bacteria and foods, taking into consideration resource allocation and priorities.
- Molecular genotypic testing of *Salmonella* spp. and *E. coli* should be performed in order to determine the relationship of AMR in food animals, food handlers and environment.
- Priority of AMR food safety hazards should be evaluated and the risk profiles of the prioritized AMR food safety hazard developed.
- There should be a risk assessment conducted based on the priority AMR food safety hazards and further identification of the appropriate risk management interventions.

3.4.6 Acknowledgements

We acknowledge Dr. Rungtip Chuanchuen and Dr. Saharuetai Jeamsripong, Department of Veterinary Public Health, Faculty of Veterinary Science, Chulalongkorn University who carried out samples collection and examination of AMR with the budget support from Thai Food and Drug Administration (Fiscal year 2018).

4

WAY FORWARD

4. Way forward

Author
Viroj Tangcharoensathien

Policy implications on consumption of antimicrobials

The 2018 national report on antimicrobial consumption provides a strong foundation for optimizing consumption in both human and animal sectors. The good news is that consumption in the animal sector reduced by 6.4% (from 557.6 mg/$PCU_{Thailand}$ in 2017 to 522.1 in 2018). However, consumption in the human sector continued to increase by 8.1% (from 68.4 DID in 2017 to 74.4 DID in 2018). This requires serious policy actions to encourage both public and private hospital sectors, which dispense most of the antibiotics (rather than the retail sector) to improve their antibiotics stewardship. There is an urgent need to assess the antibiotics competencies of health professionals and review their in-service professional training.

Most alarming is the high proportion of antibiotics consumed from the CIA list in both highest and high priority groups. We call for immediate action in the human and animal sectors to curb consumption in the CIA group by setting targets of reduction.

Policy implications of AMR in humans

Between 2017 and 2018, there was an increasing trend of AMR especially in Gram-negative bacteria; the largest increase was colistin resistance in *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Enterobacteriaceae*. Steady trends of carbapenem resistance at seriously high rates were reported in *A. baumannii* and *P. aeruginosa*, and the proportion has slightly increased in *E. coli* and *K. pneumoniae*.

Between 2017 and 2018, in relation to Gram-positive bacteria, there was an increasing trend in methicillin-resistant coagulase-negative *Staphylococcus* (MRCNS), while methicillin-resistant *Staphylococcus aureus* (MRSA) rate has gradually declined. A large number of vancomycin-resistant *Enterococcus* (VRE) rate was reported in 2018. A similar rate of penicillin-nonsusceptibility and cefotaxime-nonsusceptibility was observed in the overall *Streptococcus pneumoniae* isolates between 2017 and 2018.

Given these resistance profiles, in particular in the CIA group such as colistin, carbapenaem and vancomycin, efforts to optimize the use of these medicines through improved antibiotics stewardship is the key area for policy attention.

Policy implications on AMR in animal and food chains

Two sets of evidence exist for AMR in the animal sector; a food safety survey by the Food and Drug Administration Bureau of Food in 2018, and two routine rounds of 2017 and 2018 surveillance by the DLD in animals. In the DLD surveillance, samples were collected from poultry, swine caecum and meat in the slaughter houses, and meat from retail markets. The DLD collected 5,900 samples in 2018. Two priority pathogens for surveillance included *E. coli* and *Salmonella* spp.

The FDA reported 68.3% of 550 pork samples and 45.7% of 591 chicken meat samples were contaminated by *E. coli* and *Salmonella* spp. Most *Salmonella* spp. and *E. coli* exhibited multidrug resistance phenotype. Ampicillin resistance rate was highest in *Salmonella* spp. (53.7%) and *E. coli* (60.6%), while resistance to colistin was 3.0% and none of the isolates was resistant to meropenem. ESBL producing *Salmonella* spp. (8.9%) and *E. coli* (7.1%) were detected, and all ESBL-positive isolates were multi-resistant. The FDA report showed that pork and chicken are reservoirs of resistant *Salmonella* and *E. coli*, and appropriate risk-control measures are required.

AMR profiles reported from the DLD surveillance in 2018 showed colistin resistance was found in *E. coli* (10.4% and 11.9% in chicken and swine cecums), but it was low in *Salmonella* spp. (3.1% and 4.1% in chicken and swine cecums). Overall resistance to colistin of *E. coli* and *Salmonella* spp. isolated from chicken and swine cecums was reduced from 2017. The resistance of *E. coli* and *Salmonella* spp. to 3rd generation cephalosporins (cefotaxime and ceftazidime) within three sources of samples ranged between 0.3% to 4.6% in chickens, and 0.8% to 12.8% in pigs. However, none of isolates was resistant to meropenem in *Salmonella* spp. isolated from pigs while very low level of resistance was found in *Salmonella* spp. from chickens and *E. coli* from both chickens and pigs, ranging from 0.0% to 0.6%.

We recommend continuing surveillance of bacterial contamination and AMR in the food chain through effective collaboration between the FDA, DLD and Department of Medical Sciences. Interventions include sampling, standardization of laboratory techniques, reporting, and risk management through food hygiene, inspection and appropriate consumer prevention strategies.

Policy implications on prevalence rate and prevalence ratio of HAI and AMR

The first report of HAI 2018 presented the HAI incidence rate at 2.5 per 1,000 patient days and the incidence proportion at 0.8% of total discharged patients. The AMR incidence rate and incidence proportion in patients with HAI was 1.4 per 1,000 patient-days and 0.5% of total discharged patients. A total of 60.2% of HAI patients were infected by AMR bacteria and *Acinetobacter baumannii* (47.2%), *Klebsiella pneumoniae* (21.8%), and *Escherichia coli* (19.1%) were the top three AMR pathogens in patients with HAI. The 2018 report contributes to baseline morbidity data as mandated by the NSP-AMR in an effort to reduce AMR morbidity by 50.0% by 2021.

This study received contributions from BIDI and IHPP and proves that the BIDI prospective HAI and AMR surveillance is essential. There is a need to strengthen its completeness and accuracy of reporting through the training of ICWNs and ICNs in sentinel hospitals and the linking of databases with the NARST on susceptibility profiles.

5

ANNEXES

5. ANNEXES

Annex 1 Consumption of antibacterial in humans and animals

Table A1. Consumption of antibacterials intended for systemic use in 2018, arranged by ATC level 5 and proportion to overall consumption

ATC level 5	Substance	DDD	DID	Proportion (%)
J01DD04	ceftriaxone	616,642,340.6	23.0	31.0
J01CA04	amoxicillin	248,801,829.7	9.3	12.5
J01AA07	tetracycline	99,162,384.5	3.7	5.0
J01CR02	amoxicillin and beta-lactamase inhibitor	63,250,845.3	2.4	3.2
J01AA02	doxycycline	59,879,500.0	2.2	3.0
J01CA01	ampicillin	57,945,632.1	2.2	2.9
J01FA06	roxithromycin	45,438,305.0	1.7	2.3
J01MA06	norfloxacin	38,636,680.8	1.4	1.9
J01MA02	ciprofloxacin	37,098,251.8	1.4	1.9
J01CF01	dicloxacillin	36,601,100.3	1.4	1.8
J01DD02	ceftazidime	32,577,441.9	1.2	1.6
J01CF02	cloxacillin	20,569,720.8	0.8	1.0
J01EE01	sulfamethoxazole and trimethoprim	20,252,334.3	0.8	1.0
J01FA10	azithromycin	16,268,601.0	0.6	0.8
J01DB01	cefalexin	15,399,106.8	0.6	0.8
J01MA12	levofloxacin	14,506,396.5	0.5	0.7
J01DD01	cefotaxime	13,122,490.8	0.5	0.7
J01FF01	clindamycin	12,945,413.3	0.5	0.6
J01MA01	ofloxacin	11,423,895.0	0.4	0.6
J01CE02	phenoxymethylpenicillin	11,321,625.3	0.4	0.6
J01FA09	clarithromycin	9,914,696.0	0.4	0.5
J01FA01	erythromycin	4,680,686.2	0.2	0.2
J01EA01	trimethoprim	3,278,820.0	0.1	0.2
J01FF02	lincomycin	3,221,442.7	0.1	0.2
J01EC02	sulfadiazine	3,177,839.2	0.1	0.2

ATC level 5	Substance	DDD	DID	Proportion (%)
J01EC01	sulfamethoxazole	3,148,590.0	0.1	0.2
J01DB04	cefazolin	3,104,161.8	0.1	0.2
J01DD08	cefixime	2,827,636.5	0.1	0.1
J01DC02	cefuroxime	2,777,093.1	0.1	0.1
J01DD16	cefditoren	2,667,625.0	<0.1	0.1
J01DH02	meropenem	2,175,121.0	<0.1	0.1
J01DD15	cefdinir	2,152,667.1	<0.1	0.1
J01DC04	cefaclor	1,754,690.5	<0.1	<0.1
J01XD01	metronidazole	1,653,258.3	<0.1	<0.1
J01AA03	chlortetracycline	1,188,890.0	<0.1	<0.1
J01CR05	piperacillin and beta-lactamase inhibitor	1,057,989.7	<0.1	<0.1
J01GB03	gentamicin	804,316.2	<0.1	<0.1
J01GB04	kanamycin	674,838.0	<0.1	<0.1
J01MA14	moxifloxacin	644,635.0	<0.1	<0.1
J01FA03	midecamycin	572,010.7	<0.1	<0.1
J01EB02	sulfamethizole	465,487.5	<0.1	<0.1
J01XX01	fosfomycin	409,534.8	<0.1	<0.1
J01MA21	sitafloxacin	405,000.0	<0.1	<0.1
J01XA01	vancomycin	339,983.3	<0.1	<0.1
J01GB06	amikacin	327,564.8	<0.1	<0.1
J01BA02	thiamphenicol	327,280.0	<0.1	<0.1
J01EB03	sulfadimidine	289,950.0	<0.1	<0.1
J01GA01	streptomycin	289,150.0	<0.1	<0.1
J01CR04	sultamicillin	279,001.0	<0.1	<0.1
J01MA17	prulifloxacin	244,733.3	<0.1	<0.1
J01XB01	colistin	230,793.2	<0.1	<0.1
J01DD62	cefoperazone and beta-lactamase inhibitor	218,054.4	<0.1	<0.1
J01DH03	ertapenem	214,992.0	<0.1	<0.1
J01ED05	sulfamethoxypyridazine	200,000.0	<0.1	<0.1
J01CE01	benzylpenicillin	185,129.6	<0.1	<0.1
J01AA06	oxytetracycline	132,068.5	<0.1	<0.1

ATC level 5	Substance	DDD	DID	Proportion (%)
J01BA01	chloramphenicol	123,670.0	<0.1	<0.1
J01XE01	nitrofurantoin	114,000.0	<0.1	<0.1
J01DB05	cefadroxil	111,898.0	<0.1	<0.1
J01AA04	lymecycline	111,818.0	<0.1	<0.1
J01CR01	ampicillin and beta-lactamase inhibitor	93,175.3	<0.1	<0.1
J01DC01	cefoxitin	84,061.5	<0.1	<0.1
J01CR50	combinations of penicillins	81,000.0	<0.1	<0.1
J01AA08	minocycline	78,200.0	<0.1	<0.1
J01AA12	tigecycline	66,705.0	<0.1	<0.1
J01DH51	imipenem and cilastatin	59,249.3	<0.1	<0.1
J01CG01	sulbactam	53,582.0	<0.1	<0.1
J01DH05	biapenem	41,917.5	<0.1	<0.1
J01DD12	cefoperazone	34,203.8	<0.1	<0.1
J01DE01	cefepime	31,483.5	<0.1	<0.1
J01DH04	doripenem	19,390.0	<0.1	<0.1
J01CE08	benzathine benzylpenicillin	14,000.0	<0.1	<0.1
J01GB07	netilmicin	12,610.7	<0.1	<0.1
J01XX08	linezolid	11,640.0	<0.1	<0.1
J01DI54	ceftolozane and beta-lactamase inhibitor	3,333.3	<0.1	<0.1
J01XA02	teicoplanin	3,018.5	<0.1	<0.1
J01DC03	cefamandole	166.7	<0.1	<0.1
J01CE10	benzathine phenoxymethylpenicillin	37.5	<0.1	<0.1
J01MA15	gemifloxacin	7.0	<0.1	<0.1
J01CA02	pivampicillin	4.6	<0.1	<0.1
J01XX04	spectinomycin	0.7	<0.1	<0.1
	Grand total	**1,529,028,797.3**	**57.1**	**76.8**

Table A2. Consumption of antibiotics for alimentary tract and nitroimidazole derivatives in 2018, arranged by ATC level 5 and proportion to overall consumption

ATC level 5	Substance	DDD	DID	Proportion (%)
Antibiotics for alimentary tract				
A07AA02	nystatin	814,396.4	<0.1	<0.1
A07AA08	kanamycin	568,066.7	<0.1	<0.1
A07AA01	neomycin	103,139.9	<0.1	<0.1
Grand Total		**1,485,603.0**	**2.4**	**<0.1**
Nitroimidazole derivatives				
P01AB01	metronidazole	10,445,333.0	0.4	0.5
P01AB02	tinidazole	712,646.0	<0.1	<0.1
P01AB03	ornidazole	400.0	<0.1	<0.1
Grand total		**11,158,379.0**	**0.4**	**0.6**

Table A3. Consumption of antivirals for systemic use in 2018, classified by ATC level 5 and proportion to overall consumption

ATC level 5	Substance	DDD	DID	Proportion (%)
J05AF05	lamivudine	66,356,249.3	2.5	3.3
J05AR06	emtricitabine, tenofovir disoproxil and efavirenz	48,535,110.0	1.8	2.4
J05AG01	nevirapine	38,380,920.0	1.4	1.9
J05AF01	zidovudine	24,165,781.3	0.9	1.2
J05AG03	efavirenz	22,427,860.0	0.8	1.1
J05AR03	tenofovir disoproxil and emtricitabine	18,150,390.0	0.7	0.9
J05AR10	lopinavir and ritonavir	17,767,987.5	0.7	0.9
J05AF06	abacavir	14,110,171.5	0.5	0.7
J05AR01	zidovudine and lamivudine	7,355,160.0	0.3	0.4
J05AF07	tenofovir disoproxil	5,928,722.4	0.2	0.3
J05AH02	oseltamivir	5,558,532.8	0.2	0.3
J05AF04	stavudine	5,050,732.5	0.2	0.3
J05AB01	aciclovir	4,558,611.9	0.2	0.2
J05AR02	lamivudine and abacavir	2,717,640.0	0.1	0.1

ATC level 5	Substance	DDD	DID	Proportion (%)
J05AP08	sofosbuvir	1,212,092.0	<0.1	<0.1
J05AP51	sofosbuvir and ledipasvir	1,005,592.0	<0.1	<0.1
J05AF11	telbivudine	976,724.0	<0.1	<0.1
J05AE10	darunavir	531,950.0	<0.1	<0.1
J05AR09	emtricitabine, tenofovir disoproxil, elvitegravir and cobicistat	362,820.0	<0.1	<0.1
J05AX08	raltegravir	348,120.0	<0.1	<0.1
J05AR13	lamivudine, abacavir and dolutegravir	313,140.0	<0.1	<0.1
J05AR18	emtricitabine, tenofovir alafenamide, elvitegravir and cobicistat	300,000.0	<0.1	<0.1
J05AF10	entecavir	285,993.0	<0.1	<0.1
J05AF08	adefovir dipivoxil	284,160.0	<0.1	<0.1
J05AX12	dolutegravir	154,230.0	<0.1	<0.1
J05AB11	valaciclovir	102,445.7	<0.1	<0.1
J05AE03	ritonavir	97,665.0	<0.1	<0.1
J05AG04	etravirine	63,150.0	<0.1	<0.1
J05AP01	ribavirin	50,618.4	<0.1	<0.1
J05AB06	ganciclovir	44,163.0	<0.1	<0.1
J05AB14	valganciclovir	27,000.0	<0.1	<0.1
J05AB12	cidofovir	21,300.0	<0.1	<0.1
J05AX05	inosine pranobex	17,500.0	<0.1	<0.1
J05AP54	elbasvir and grazoprevir	16,548.0	<0.1	<0.1
J05AB09	famciclovir	14,000.0	<0.1	<0.1
J05AX09	maraviroc	9,735.0	<0.1	<0.1
J05AR11	lamivudine, tenofovir disoproxil and efavirenz	300.0	<0.1	<0.1
J05AE08	atazanavir	150.0	<0.1	<0.1
J05AF12	clevudine	30.0	<0.1	<0.1
Grand Total		**287,303,295.4**	**10.7**	**14.4**

Table A4. Consumption of antimycotics for systemic use and antifungals for systemic use in 2018, arranged by ATC level 5 and proportion to overall consumption

ATC level 5	Substance	DDD	DID	Proportion (%)
Antimycotics for systemic use				
J02AB02	ketoconazole	54,886,170.0	2.1	2.8
J02AC01	fluconazole	11,487,805.0	0.4	0.6
J02AC02	itraconazole	8,392,385.0	0.3	0.4
J02AA01	amphotericin B	222,641.4	<0.1	<0.1
J02AC03	voriconazole	68,288.3	<0.1	<0.1
J02AC04	posaconazole	22,380.0	<0.1	<0.1
J02AX05	micafungin	14,630.0	<0.1	<0.1
J02AX06	anidulafungin	3,300.0	<0.1	<0.1
J02AX04	caspofungin	2,638.0	<0.1	<0.1
Grand Total		**75,100,237.7**	**2.8**	**3.8**
Antifungals for systemic use				
D01BA01	griseofulvin	12,573,750.0	0.5	0.6
D01BA02	terbinafine	144,200.0	<0.1	<0.1
Grand total		**12,717,950.0**	**0.5**	**0.6**

Table A5. Consumption of drugs for treatment of tuberculosis in 2018, arranged by ATC level 5 and proportion to overall consumption

ATC level 5	Substance	DDD	DID	Proportion (%)
J04AB02	rifampicin	22,772,160.5	0.9	1.1
J04AC01	isoniazid	22,598,634.0	0.8	1.1
J04AK01	pyrazinamide	8,912,323.3	0.3	0.4
J04AK02	ethambutol	7,019,791.7	0.3	0.4
J04AM06	rifampicin, pyrazinamide, ethambutol and isoniazid	467,002.5	<0.1	<0.1
J04AB01	cycloserine	230,400.0	<0.1	<0.1
J04AM02	rifampicin and isoniazid	205,475.0	<0.1	<0.1
J04AD03	ethionamide	126,266.7	<0.1	<0.1
Grand total		**62,334,410.8**	**2.3**	**3.1**

Table A6. Consumption of critically important antimicrobials in humans in 2018, arranged by antimicrobial class and WHO priority

ATC level 5	Substance	DDD	DID	Proportion (%)
P01BA01	chloroquine	7,405,164.0	0.3	0.4
P01BA02	hydroxychloroquine	4,081,953.5	0.2	0.2
P01BA03	primaquine	1,120,500.0	<0.1	<0.1
P01BC01	quinine	347,820.0	<0.1	<0.1
P01BF05	artenimol and piperaquine	32,529.0	<0.1	<0.1
P01BE03	artesunate	8,571.4	<0.1	<0.1
P01BC02	mefloquine	7,676.5	<0.1	<0.1
P01BF01	artemether and lumefantrine	1.7	<0.1	<0.1
Grand total		**13,004,216.1**	**0.5**	**0.7**

Table A7. Consumption of Critically Important Antimicrobials in 2018, arranged by antimicrobial class and WHO priority

Category of human critically important antimicrobials	Consumption	
	DID	Tonne of API
I. Highest priority		
Cephalosporins (3rd and 4th generation)	**25.0**	**1,420.7**
• ceftriaxone	23.0	1,233.3
• ceftazidime	1.2	130.3
• cefotaxime	0.5	52.5
• cefixime	0.1	1.1
• cefditoren	<0.1	1.1
• cefdinir	<0.1	1.3
• cefoperazone and beta-lactamase inhibitor	<0.1	0.9
• cefoperazone	<0.1	0.1
• cefepime	<0.1	0.1
• ceftolozane and beta-lactamase inhibitor	<0.1	<0.1

Category of human critically important antimicrobials	Consumption	
	DID	Tonne of API
Glycopeptides	**<0.1**	**0.7**
• vancomycin	<0.1	0.7
• teicoplanin	<0.1	<0.1
Macrolides and ketolides	**2.9**	**28.9**
• roxithromycin	1.7	13.6
• azithromycin	0.6	4.9
• clarithromycin	0.4	5.0
• erythromycin	0.2	4.7
• midecamycin	<0.1	0.7
Polymyxins	**<0.1**	**0.1**
• colistin	<0.1	0.1
Quinolones	**3.8**	**80.2**
• norfloxacin	1.4	30.9
• ciprofloxacin	1.4	37.0
• levofloxacin	0.5	7.3
• ofloxacin	0.4	4.6
• moxifloxacin	<0.1	0.3
• sitafloxacin	<0.1	<0.1
• prulifloxacin	<0.1	0.1
• gemifloxacin	<0.1	<0.1
Subtotal of highest priority CIA	**31.8**	**1,530.5**
II. High priority		
Aminoglycosides	**0.1**	**3.7**
• kanamycin	<0.1	2.4
• gentamicin	<0.1	0.2
• amikacin	<0.1	0.3
• streptomycin	<0.1	0.3
• neomycin	<0.1	0.5
• netilmicin	<0.1	<0.1

Category of human critically important antimicrobials	Consumption	
	DID	Tonne of API
Ansamycins	**0.9**	**13.7**
• rifampicin	0.9	13.7
Carbapenems and other penems	**<0.1**	**6.9**
• meropenem	<0.1	6.5
• ertapenem	<0.1	0.2
• imipenem and cilastatin	<0.1	0.1
• biapenem	<0.1	<0.1
• doripenem	<0.1	<0.1
Glycylcyclines	**<0.1**	**<0.1**
• tigecycline	<0.1	<0.1
Oxazolidinones	**<0.1**	**<0.1**
• linezolid	<0.1	<0.1
Penicillins (antipseudomonal)	**<0.1**	**15.0**
• piperacillin and beta-lactamase inhibitor	<0.1	14.8
• combinations of penicillins	<0.1	0.2
Aminopenicillins	**11.5**	**491.3**
• amoxicillin	9.3	373.2
• ampicillin	2.2	117.7
• sultamicillin	<0.1	0.4
• pivampicillin	<0.1	<0.1
Aminopenicillins with bela-lactamase inhibitors	**2.4**	**96.8**
• amoxicillin and enzyme inhibitor	2.4	96.2
• ampicillin and enzyme inhibitor	<0.1	0.6
Phosphonic acid derivatives	**<0.1**	**3.1**
• fosfomycin	<0.1	3.1
Drugs used solely to treat tuberculosis or other mycobacterial diseases	**1.5**	**30.8**
• isoniazid	0.8	6.8
• pyrazinamide	0.3	13.4
• ethambutol	0.3	8.4
• rifampicin, pyrazinamide, ethambutol and isoniazid	<0.1	1.7
• cycloserine	<0.1	0.2
• rifampicin and isoniazid	<0.1	0.2

Category of human critically important antimicrobials	Consumption	
	DID	Tonne of API
• ethionamide	<0.1	<0.1
• sodium aminosalicylate	<0.1	<0.1
Subtotal of high priority CIA	**16.4**	**661.3**
Grand total	**48.2**	**2,191.8**

Table A8. Consumption of veterinary antimicrobials for systemic use in 2018, arranged by proportion to overall consumption

ATC vet code	Substance	Consumption ($mg/PCU_{Thailand}$)	Tonne of API	Proportion (%)
QJ01CA04	amoxicillin	210.4	1,538.1	40.3
QJ01XQ01	tiamulin	60.2	440.2	11.5
QJ01AA03	chlortetracycline	42.8	313.2	8.2
QJ01FA91	tilmicosin	16.7	122.4	3.2
QJ01AA02	doxycycline	14.6	106.4	2.8
QJ01FA90	tylosin	14.3	104.5	2.7
QJ01AA06	oxytetracycline	5.8	42.1	1.1
QJ01MA90	enrofloxacin	5.1	37.5	1.0
QJ01FF02	lincomycin	3.5	25.5	0.7
QJ01EQ10	sulfadiazine	3.3	24.4	0.6
QJ01FA93	kitasamycin	2.7	19.8	0.5
QJ01XX04	spectinomycin	2.0	14.7	0.4
QJ01GA90	dihydrostreptomycin	1.9	14.1	0.4
QJ01FA92	tylvalosin	1.8	13.1	0.3
QJ01EQ03	sulfadimidine	1.7	12.4	0.3
QJ01GB03	gentamicin	1.1	7.8	0.2
QJ01CE09	procaine benzylpenicillin	1.1	7.7	0.2
QJ01EA01	trimethoprim	1.0	7.5	0.2
QJ01GB04	kanamycin	0.9	6.6	0.2
QJ01XX01	fosfomycin	0.9	6.2	0.2
QJ01FA01	erythromycin	0.6	4.6	0.1
QJ01CE08	benzathine benzylpenicillin	0.5	3.3	<0.1

ATC vet code	Substance	Consumption (mg/$PCU_{Thailand}$)	Tonne of API	Proportion (%)
QJ01CE02	phenoxymethylpenicillin	0.4	3.3	<0.1
QJ01FA07	josamycin	0.4	2.9	<0.1
QJ01DD90	ceftiofur	0.3	2.0	<0.1
QJ01EQ11	sulfamethoxazole	0.2	1.6	<0.1
QJ01CA01	ampicillin	0.2	1.5	<0.1
QJ01CR02	amoxicillin and beta-lactamase inhibitor	0.1	0.9	<0.1
QJ01GA01	streptomycin	0.1	0.9	<0.1
QJ01EQ17	sulfamerazine	0.1	0.8	<0.1
QJ01EQ16	sulfaquinoxaline	<0.1	0.7	<0.1
QJ01GB90	apramycin	<0.1	0.6	<0.1
QJ01EQ13	sulfadoxine	<0.1	0.4	<0.1
QJ01EQ09	sulfadimethoxine	<0.1	0.4	<0.1
QJ01MA93	marbofloxacin	<0.1	0.4	<0.1
QJ01FA95	gamithromycin	<0.1	0.2	<0.1
QJ01FA94	tulathromycin	<0.1	0.2	<0.1
QJ01XB01	colistin	<0.1	0.2	<0.1
QJ01EQ18	sulfamonomethoxine	<0.1	0.1	<0.1
QJ01AA07	tetracycline	<0.1	<0.1	<0.1
QJ01EQ07	sulfathiazole	<0.1	<0.1	<0.1
QJ01GB05	neomycin	<0.1	<0.1	<0.1
QJ01EQ15	sulfamethoxypyridazine	<0.1	<0.1	<0.1
QJ01FA96	tildipirosin	<0.1	<0.1	<0.1
QJ01MA92	danofloxacin	<0.1	<0.1	<0.1
QJ01DE90	cefquinome	<0.1	<0.1	<0.1
QJ01FF01	clindamycin	<0.1	<0.1	<0.1
QJ01MA97	pradofloxacin	<0.1	<0.1	<0.1
QJ01MA95	orbifloxacin	<0.1	<0.1	<0.1
QJ01DD91	cefovecin	<0.1	<0.1	<0.1
QJ01XQ02	valnemulin	<0.1	<0.1	<0.1
QJ01EA	ormetoprim	<0.1	<0.1	<0.1
QJ01CE90	penethamate hydriodide	<0.1	<0.1	<0.1

ATC vet code	Substance	Consumption (mg/PCU$_{Thailand}$)	Tonne of API	Proportion (%)
QJ01CF01	dicloxacillin	<0.1	<0.1	<0.1
QJ01FA02	spiramycin	<0.1	<0.1	<0.1
QJ01MA	other quinolone	<0.1	<0.1	<0.1
	Grand total	**395.3**	**2,889.5**	**75.7**

Table A9. Consumption of veterinary antimicrobials for intestinal use in 2018, arranged by proportion to overall consumption

ATC vet code	Substance	Consumption (mg/PCU$_{Thailand}$)	Tonne of API	Proportion (%)
QA07AX91	halquinol	80.5	588.5	15.4
QA07AA10	colistin	23.5	172.0	4.5
QA07AA93	bacitracin	14.6	106.9	2.8
QA07AA01	neomycin	7.8	57.0	1.5
QA07AA96	bambermycin	0.2	1.2	<0.1
	Grand total	**126.6**	**925.5**	**24.3**

Table A10. Consumption of veterinary antimicrobials for intrauterine and intramammary use in 2018, arranged by proportion to overall consumption

ATC vet code	Substance	Consumption ($mg/PCU_{Thailand}$)	Tonne of API	Proportion (%)
Antimycotics for systemic use				
QG01AE	sulfamethoxypyridazine	<0.1	0.2	<0.1
QG01AA	trimethoprim	<0.1	<0.1	<0.1
QG51AA05	cefapirin	<0.1	<0.1	<0.1
Grand Total		**0.3**	**<0.1**	**<0.1**
Antifungals for systemic use				
QJ51CF02	cloxacillin	<0.1	0.3	<0.1
QJ51GA90	dihydrostreptomycin	<0.1	0.3	<0.1
QJ51CE09	procaine benzylpenicillin	<0.1	0.2	<0.1
QJ51CA01	ampicillin	<0.1	0.1	<0.1
QJ51GB	neomycin	<0.1	<0.1	<0.1
QJ51DB01	cefalexin	<0.1	<0.1	<0.1
QJ51DB90	cefalonium	<0.1	<0.1	<0.1
QJ51AA07	tetracycline	<0.1	<0.1	<0.1
QJ51GB03	gentamicin	<0.1	<0.1	<0.1
QJ51DD90	ceftiofur	<0.1	<0.1	<0.1
QJ51DE90	cefquinome	<0.1	<0.1	<0.1
QJ51DC02	cefuroxime	<0.1	<0.1	<0.1
QJ51DB08	cefapirin	<0.1	<0.1	<0.1
QJ51XX	bacitracin	<0.1	<0.1	<0.1
QJ51GB	kanamycin	<0.1	<0.1	<0.1
QJ51CF01	dicloxacillin	<0.1	<0.1	<0.1
Grand total		**0.1**	**1.1**	**<0.1**

Table A11. Consumption of veterinary antimicrobials used as premix in 2018, arranged by proportion to overall consumption

ATC vet code	Substance	Consumption ($mg/PCU_{Thailand}$)	Tonne of API	Proportion (%)
QA07AX91	halquinol	80.5	588.5	15.4
QJ01CA04	amoxicillin	59.3	433.6	11.4
QJ01XQ01	tiamulin	58.4	426.7	11.2
QJ01AA03	chlortetracycline	42.2	308.8	8.1
QA07AA10	colistin	20.9	153.1	4.0
QJ01FA91	tilmicosin	16.0	116.9	3.1
QA07AA93	bacitracin	7.3	53.1	1.4
QJ01FA90	tylosin	6.0	44.2	1.2
QJ01AA02	doxycycline	4.0	29.2	0.8
QJ01AA06	oxytetracycline	3.1	22.9	0.6
QJ01FF02	lincomycin	2.3	17.0	0.4
QJ01FA93	kitasamycin	2.0	14.8	0.4
QJ01FA92	tylvalosin	1.7	12.6	0.3
QJ01EQ03	sulfadimidine	1.2	9.0	0.2
QJ01XX01	fosfomycin	0.9	6.2	0.2
QJ01EQ10	sulfadiazine	0.5	3.8	0.1
QJ01CE02	phenoxymethylpenicillin	0.4	3.3	<0.1
QJ01FA07	josamycin	0.4	2.9	<0.1
QA07AA01	neomycin	0.4	2.8	<0.1
QJ01EA01	trimethoprim	0.3	2.4	<0.1
QJ01XX04	spectinomycin	0.2	1.3	<0.1
QA07AA96	bambermycin	0.2	1.2	<0.1
QJ01EQ17	sulfamerazine	0.1	0.8	<0.1
QJ01MA90	enrofloxacin	<0.1	0.6	<0.1
QJ01EQ16	sulfaquinoxaline	<0.1	0.1	<0.1
QJ01EQ18	sulfamonomethoxine	<0.1	0.1	<0.1
QJ01GB90	apramycin	<0.1	0.1	<0.1
QJ01FA01	erythromycin	<0.1	<0.1	<0.1
QJ01GB05	neomycin	<0.1	<0.1	<0.1
QJ01XQ02	valnemulin	<0.1	<0.1	<0.1
Grand total		**308.6**	**2,255.9**	**59.1**

Table A12. Consumption of Critically Important Antimicrobials in animal sector, 2018, arranged by categorization of WHO

Category of human critically important antimicrobials	Consumption	
	Consumption ($mg/PCU_{Thailand}$)	Tonne of API
I. Highest priority		
Cephalosporins (3rd and 4th generation)	**0.3**	**2.1**
• cefovecin	<0.1	<0.1
• cefquinome	<0.1	<0.1
• ceftiofur	0.3	2.
Macrolides and ketolides	**36.6**	**267.7**
• erythromycin	0.6	4.6
• gamithromycin	<0.1	0.2
• josamycin	0.4	2.9
• kitasamycin	2.7	19.8
• spiramycin	<0.1	<0.1
• tildipirosin	<0.1	<0.1
• tilmicosin	16.7	122.4
• tulathromycin	<0.1	0.2
• tylosin	14.3	104.5
• tylvalosin	1.8	13.1
Polymyxins	**23.6**	**172.2**
• colistin	23.6	172.2
Quinolones	**5.2**	**37.9**
• danofloxacin	<0.1	<0.1
• enrofloxacin	5.1	37.5
• marbofloxacin	<0.1	0.4
• orbifloxacin	<0.1	<0.1
• pradofloxacin	<0.1	<0.1
• danofloxacin	<0.1	<0.1

Category of human critically important antimicrobials	Consumption	
	Consumption (mg/$PCU_{Thailand}$)	Tonne of API
• other quinolone	<0.1	<0.1
Subtotal of highest priority CIA	**65.6**	**479.8**
II. High priority		
Aminoglycosides	**12.0**	**87.4**
• apramycin	<0.1	0.6
• dihydrostreptomycin	2.0	14.4
• gentamicin	1.1	7.8
• kanamycin	0.9	6.6
• neomycin	7.8	57.1
• streptomycin	0.1	0.9
Aminopenicillins with beta-lactamase inhibitors	**0.1**	**0.9**
• amoxicillin and enzyme inhibitor	0.1	0.9
Aminopenicillins	**210.6**	**1,539.7**
• amoxicillin	210.4	1,538.1
• ampicillin	0.2	1.6
Phosphonic acid derivatives	**0.9**	**6.2**
• fosfomycin	0.9	6.2
Subtotal of high priority CIA	**223.6**	**1,634.2**
Grand total	**289.2**	**2,114.0**

Annex 2 AMR morbidity in patients with Hospital-Associated Infections

Table A13. Targeted pathogen and drugs

Target pathogen	Drug group	Drug
1 *Acinetobacter baumannii*	Carbapenems	Imipenem Meropenem Doripenem
	Polymyxins	Colistin
2 *Enterococcus* spp.	Glycopeptides	Vancomycin
3 *Escherichia coli*	Carbapenems	Imipenem Meropenem Ertapenem Doripenem
	Polymyxins	Colistin
	3rd generation cephalosporins	Ceftriaxone Cefotaxime Ceftazidime
	Fluoroquinolones	Ciprofloxacin Levofloxacin
4 *Klebsiella pneumoniae*	Carbapenems	Imipenem Meropenem Ertapenem Doripenem
	Polymyxins	Colistin
	3rd generation cephalosporins	Ceftriaxone Cefotaxime Ceftazidime
5 *Neisseria gonorrhoeae*	3rd generation cephalosporins	Cefixime Ceftriaxone
6 *Pseudomonas aeruginosa*	Carbapenems	Imipenem Meropenem Doripenem
	Polymyxins	Colistin

Target pathogen	Drug group	Drug
7 *Salmonella* spp.	Polymyxins	Colistin
	3rd generation cephalosporins	Ceftriaxone Cefotaxime Ceftazidime
	Fluoroquinolones	Ciprofloxacin Levofloxacin
8 *Staphylococcus aureus*	Methicillins (MRSA)	Methicillin (cefoxitin/oxacillin)
	Glycopeptides	Vancomycin
9 *Streptococcus pneumoniae*	3rd generation cephalosporins	Ceftriaxone Cefotaxime
	Penicillins	Oxacillin Penicillin G

Note: adapted from NAP-AMR 2017-2021 [1]

Table A14. Sampling weight computation

Hospital types	Number of hospitals	Total patient-days	Number of targeted hospitals	Total patient-days in targeted hospitals	Weight
Public hospitals					
• Regional hospitals	29	7,058,579	6	1,471,214	4.8
• General hospitals	26	2,990,349	6	853,535	3.5
• District hospitals	28	916,227	6	220,453	4.2
• Other MOPH hospitals	4	125,207	1	44,657	2.8
• Other public hospitals	7	602,190	2	262,077	2.3
Private hospitals	9	633,003	2	82,382	7.7
Total	**103**	**12,325,555**	**23**	**2,934,318**	

Table A15. Incidence of HAI and AMR by hospital

Number	Hospital	Health region	Submitted records	Verified records	HAI event	HAI patient	AMR event	AMR patient	Total patient-days	Total discharged patient	HAI incidence rate	HAI incidence proportion	AMR incidence rate	AMR incidence proportion	Percentage of AMR patient in total HAI patient
1	Regional hospital 1	1	656	639	605	528	423	384	250,484	31,717	2.4	1.7	1.7	1.2	72.7%
2	Regional hospital 2	4	2,241	2,167	1,707	1,161	781	616	227,507	50,660	7.5	2.3	3.4	1.2	53.1%
3	Regional hospital 3	5	1,094	1,064	1,026	799	578	505	243,485	48,674	4.2	1.6	2.4	1.0	63.2%
4	Regional hospital 4	6	871	794	692	543	283	237	241,025	69,767	2.9	0.8	1.2	0.3	43.7%
5	Regional hospital 5	9	430	430	392	333	301	266	294,030	68,283	1.3	0.5	1.0	0.4	79.9%
6	Regional hospital 6	11	675	665	542	421	292	236	214,683	46,425	2.5	0.9	1.4	0.5	56.1%
7	General hospital 1	1	212	212	199	180	137	127	145,806	45,916	1.4	0.4	0.9	0.3	70.6%
8	General hospital 2	4	198	198	187	169	120	114	153,204	33292	1.2	0.5	0.8	0.3	67.5%
9	General hospital 3	5	201	201	192	133	119	94	80,836	24,515	2.4	0.5	1.5	0.4	70.7%
10	General hospital 4	8	123	122	94	86	72	63	135,169	31,265	0.7	0.3	0.5	0.2	73.3%
11	General hospital 5	9	259	259	228	193	173	145	214,101	55,444	1.1	0.4	0.8	0.3	75.1%
12	General hospital 6	12	267	267	147	108	106	75	124,419	40,176	1.2	0.3	0.9	0.2	69.4%
13	Community hospital 1	1	51	51	37	33	22	21	28,934	9,518	1.3	0.4	0.8	0.2	63.6%
14	Community hospital 2	2	27	26	26	24	12	11	29,017	9,504	0.9	0.3	0.4	0.1	45.8%
15	Community hospital 3	4	23	23	23	17	19	16	27,703	6,859	0.8	0.3	0.7	0.2	94.1%
16	Community hospital 4	5	74	74	72	66	30	30	50,420	12,828	1.4	0.5	0.6	0.2	45.5%
17	Community hospital 5	8	55	52	49	48	47	45	56,522	16,339	0.9	0.3	0.8	0.3	93.8%
18	Community hospital 6	11	20	20	20	20	4	4	27,857	8,952	0.7	0.2	0.1	0.0	20.0%
19	Other MOPH hospital	4	151	151	128	96	76	62	44,657	9,199	2.9	1.0	1.7	0.7	64.6%
20	Other public hospital 1	4	84	82	69	64	33	32	59,195	11,240	1.2	0.6	0.6	0.3	50.0%
21	Other public hospital 2	4	897	894	784	614	337	285	202,882	28,868	3.9	2.1	1.7	1.0	46.4%
22	Private hospital 1	4	32	32	25	22	16	13	52,563	16,798	0.5	0.1	0.3	0.1	59.1%
23	Private hospital 2	13	42	42	31	30	24	21	29,819	7,365	1.0	0.4	0.8	0.3	70.0%

Table A16. Incidence of catheter-related HAI and surgical site infection by hospital

Number	Hospital	Health region	VAP	CAUTI	CLABSI	SSI	Respirator-days	Foley catheter-days	Central line-days	Number of surgeries	VAP incidence rate*	CAUTI incidence rate*	CLABSI incidence rate*	SSI incidence proportion*
1	Regional hospital 1	1	202	113	3	57	32,273	62,037	6,510	18,294	6.3	1.8	0.5	0.3
2	Regional hospital 2	4	339	241	38	161	28,091	46,722	11,592	17,526	12.1	5.2	3.3	0.9
3	Regional hospital 3	5	303	151	18	50	41,543	72,864	12,902	21,130	7.3	2.1	1.4	0.2
4	Regional hospital 4	6	99	153	51	98	24,766	50,253	14,616	14,210	4.0	3.0	3.5	0.7
5	Regional hospital 5	9	41	66	19	30	36,737	66,522	9,507	27,805	1.1	1.0	2.0	0.1
6	Regional hospital 6	11	147	86	60	45	25,556	47,000	14,944	16,851	5.8	1.8	4.0	0.3
7	General hospital 1	1	93	23	1	23	15,064	27,164	2,448	10,515	6.2	0.9	0.4	0.2
8	General hospital 2	4	56	65	0	19	22,959	35,014	7,439	12,716	2.4	1.9	0.0	0.2
9	General hospital 3	5	51	46	5	9	4,763	14,764	2,888	5,139	10.7	3.1	1.7	0.2
10	General hospital 4	8	38	13	0	11	14,568	27,999	3,312	9,657	2.6	0.5	0.0	0.1
11	General hospital 5	9	98	41	1	19	28,742	49,359	2,220	9,545	3.4	0.8	0.5	0.2
12	General hospital 6	12	73	28	8	5	11,159	17,784	3,992	3314	6.5	1.6	2.0	0.2
13	Community hospital 1	1	8	9	1	3	991	2,771	86	921	8.1	3.3	11.6	0.3
14	Community hospital 2	2	17	2	0	2	1,160	4,650	28	488	14.7	0.4	0.0	0.4
15	Community hospital 3	4	9	11	0	0	1,938	5,365	0	612	4.6	2.1	-	-
16	Community hospital 4	5	18	17	0	5	1,822	5,589	83	1,263	9.9	3.0	0.0	0.4
17	Community hospital 5	8	10	5	0	7	3,148	8,568	641	4,435	3.2	0.6	0.0	0.2
18	Community hospital 6	11	0	1	0	2	0	975	0	497	-	1.0	-	0.4
19	Other MOPH hospital	4	7	43	4	4	2,129	8,466	1,330	4,300	3.3	5.1	3.0	0.1
20	Other public hospital 1	4	15	15	4	10	5,203	6,914	2,407	3803	2.9	2.2	1.7	0.3
21	Other public hospital 2	4	103	195	14	33	23,253	47,465	16,830	18,407	4.4	4.1	0.8	0.2
22	Private hospital 1	4	14	9	0	1	1,833	7,106	81	2,593	7.6	1.3	0.0	0.0
23	Private hospital 2	13	4	8	0	7	1,433	5,237	579	2134	2.8	1.5	0.0	0.3

* Note: VAP incidence rate per 1,000 ventilator-days, CAUTI incidence rate per 1,000 Foley-days, CAUTI incidence rate per 1,000 central line-days, SSI incidence proportion per 100 surgeries

Annex 3 AMR in food chain

Logistic Regression Model

Logistic regression analysis revealed that the presence of *Salmonella* spp. and *E. coli* is associated with types of meat. Of 1,141 samples, the contamination rate of *Salmonella* spp. in chicken was 63.0% lower than in pork ($e^{-0.99} = 0.37$, $P < 0.0001$); while the contamination rate of *E. coli* in chicken was 13.0% higher than in pork ($e^{0.26} = 1.296$, $P < 0.043$).

Table A17. Logistic Regression of *E. coli* isolated from pork and chicken (n=1,141)

E. coli	Coefficient	S.E.	*P*-value	95% C.I.
Pork	Reference			
Chicken	0.26	0.13	0.043	0.008 to 0.51
Constant	1.01	0.12	<0.0001	0.78 to 1.24

Akaike's information criterion (AIC) = 1,399.93

S.E.= Standard Error; C.I. = Confidence Interval

Table A18. Logistic Regression of *Salmonella* spp. isolated from pork and chicken (n=1,141)

Salmonella spp.	Coefficient	S.E.	*P*-value	95% C.I.
Pork	Reference			
Chicken	-0.99	0.13	<0.0001	-1.24 to-0.74
Constant	0.87	0.11	<0.0001	0.64 to 1.09

Akaike's information criterion (AIC) = 1,406.46

S.E.= Standard Error; C.I. = Confidence Interval

Table A19. Antimicrobial resistant patterns of *E. coli* isolated from pork samples (n=360)

No.	Resistant pattern	Number of Isolates (%)
1	AMP	14 (3.9%)
2	C	1 (0.3%)
3	S	1 (0.3%)
4	TE	1 (0.3%)
5	AMP-C	4 (1.1%)
6	AMP-S	9 (2.5%)
7	AMP-SUL	1 (0.3%)
8	AMP-TE	27 (7.5%)
9	C-CIP	1 (0.3%)
10	C-TE	1 (0.3%)

No.	Resistant pattern	Number of Isolates (%)
11	S-TE	1 (0.3%)
12	AMP-C-SUL	1 (0.3%)
13	AMP-C-TE	7 (1.9%)
14	AMP-C-TMP	1 (0.3%)
15	AMP-CIP-TE	1 (0.3%)
16	AMP-CTX-CPD	3 (0.8%)
17	AMP-GM-S	7 (1.9%)
18	AMP-GM-TE	3 (0.8%)
19	AMP-S-TE	14 (3.9%)
20	AMP-SUL-TE	3 (0.8%)
21	AMP-SUL-TMP	22 (6.1%)
22	CAZ-CTX-CPD	1 (0.3%)
23	AMP-CAZ-CTX-CPD	1 (0.3%)
24	AMP-C-CIP-TE	1 (0.3%)
25	AMP-C-GM-TE	1 (0.3%)
26	AMP-C-S-TE	4 (1.1%)
27	AMP-C-SUL-TMP	7 (1.9%)
28	AMP-C-TE-TMP	2 (0.6%)
29	AMP-CIP-TE-TMP	1 (0.3%)
30	AMP-GM-S-TE	1 (0.3%)
31	AMP-GM-SUL-TMP	1 (0.3%)
32	AMP-S-SUL-TE	6 (1.7%)
33	AMP-S-SUL-TMP	14 (3.9%)
34	AMP-SUL-TE-TMP	20 (5.6%)
35	C-GM-SUL-TMP	1 (0.3%)
36	C-S-SUL-TMP	1 (0.3%)
37	S-SUL-TE-TMP	2 (0.6%)
38	AMP-CAZ-CTX-CPD-TE	2 (0.6%)
39	AMP-C-CIP-CL-S	1 (0.3%)
40	AMP-C-CIP-S-TE	1 (0.3%)
41	AMP-C-CL-S-TE	1 (0.3%)
42	AMP-C-CL-SUL-TMP	1 (0.3%)

No.	Resistant pattern	Number of Isolates (%)
43	AMP-C-S-SUL-TE	1 (0.3%)
44	AMP-C-S-SUL-TMP	6 (1.7%)
45	AMP-C-S-TE-TMP	1 (0.3%)
46	AMP-C-SUL-TE-TMP	24 (6.7%)
47	AMP-CTX-CPD-GM-TE	1 (0.3%)
48	AMP-CTX-CPD-S-TE	1 (0.3%)
49	AMP-CTX-CPD-SUL-TMP	1 (0.3%)
50	AMP-GM-S-SUL-TMP	2 (0.6%)
51	AMP-S-SUL-TE-TMP	13 (3.6%)
52	C-S-SUL-TE-TMP	1 (0.3%)
53	AMP-CAZ-CTX-CPD-C-GM	1 (0.3%)
54	AMP-CAZ-CTX-CPD-C-TE	1 (0.3%)
55	AMP-CAZ-CTX-CPD-GM-TE	2 (0.6%)
56	AMP-C-CIP-GM-S-TE	1 (0.3%)
57	AMP-C-CIP-GM-SUL-TMP	1 (0.3%)
58	AMP-C-CIP-S-SUL-TMP	2 (0.6%)
59	AMP-C-CIP-S-TE-TMP	1 (0.3%)
60	AMP-C-CIP-SUL-TE-TMP	1 (0.3%)
61	AMP-C-GM-S-SUL-TMP	1 (0.3%)
62	AMP-C-S-SUL-TE-TMP	18 (5.0%)
63	AMP-CL-S-SUL-TE-TMP	1 (0.3%)
64	AMP-CTX-CPD-C-CIP-GM	1 (0.3%)
65	AMP-CTX-CPD-C-CIP-TE	1 (0.3%)
66	AMP-CTX-CPD-C-GM-TE	2 (0.6%)
67	AMP-CTX-CPD-C-TE-TMP	1 (0.3%)
68	AMP-CTX-CPD-CIP-GM-TE	1 (0.3%)
69	AMP-CTX-CPD-S-SUL-TE	1 (0.3%)
70	AMP-CTX-CPD-SUL-TE-TMP	1 (0.3%)
71	AMP-GM-S-SUL-TE-TMP	1 (0.3%)
72	AMP-CAZ-CTX-CPD-C-GM-S	1 (0.3%)
73	AMP-CAZ-CTX-CPD-GM-SUL-TE	1 (0.3%)
74	AMP-C-CIP-S-SUL-TE-TMP	1 (0.3%)

No.	Resistant pattern	Number of Isolates (%)
75	AMP-C-GM-S-SUL-TE-TMP	9 (2.5%)
76	AMP-CTX-CPD-C-CIP-GM-TE	1 (0.3%)
77	AMP-CTX-CPD-C-GM-S-TE	1 (0.3%)
78	AMP-CAZ-CTX-CPD-C-CIP-GM-S	1 (0.3%)
79	AMP-CAZ-CTX-CPD-C-GM-S-TE	1 (0.3%)
80	AMP-CAZ-CTX-CPD-GM-S-TE-TMP	1 (0.3%)
81	AMP-C-CIP-CL-GM-SUL-TE-TMP	1 (0.3%)
82	AMP-C-CIP-CL-S-SUL-TE-TMP	2 (0.6%)
83	AMP-C-CIP-GM-S-SUL-TE-TMP	1 (0.3%)
84	AMP-CTX-CPD-C-GM-S-SUL-TE	1 (0.3%)
85	AMP-CTX-CPD-C-S-SUL-TE-TMP	1 (0.3%)
86	AMP-CTX-CPD-GM-S-SUL-TE-TMP	1 (0.3%)
87	AMP-CAZ-CTX-CPD-C-GM-SUL-TE-TMP	3 (0.8%)
88	AMP-CAZ-CTX-CPD-GM-S-SUL-TE-TMP	2 (0.6%)
89	AMP-CTX-CPD-C-CIP-GM-SUL-TE-TMP	2 (0.6%)
90	AMP-CTX-CPD-C-CIP-S-SUL-TE-TMP	1 (0.3%)
91	AMP-CTX-CPD-C-GM-S-SUL-TE-TMP	3 (0.8%)
92	AMP-CAZ-CTX-CPD-C-CIP-GM-SUL-TE-TMP	1 (0.3%)
93	AMP-CAZ-CTX-CPD-C-GM-S-SUL-TE-TMP	5 (1.4%)
94	AMP-CAZ-CTX-CPD-C-CIP-GM-S-SUL-TE-TMP	1 (0.3%)

Table A20. Multidrug-resistant in *E. coli* isolated from pork (n=360)

Resistance	Number of Isolates (%)
No resistance detected	35 (9.7%)
Resistance = 1 CLSI class	22 (6.1%)
Resistance = 2 CLSI Classes	76 (21.1%)
Resistance = 3 CLSI Classes	87 (24.2%)
Resistance = 4 CLSI Classes	77 (21.4%)
Resistance = 5 CLSI Classes	52 (14.4%)
Resistance = 6 CLSI Classes	8 (2.2%)
Resistance = 7 CLSI Classes	3 (0.8%)

Table A21. Antimicrobial resistant patterns of *Salmonella* spp. isolated from pork samples (n=449)

No.	Resistant pattern	Number of Isolates (%)
1	AMP	4 (0.9%)
2	S	1 (0.2%)
3	TE	3 (0.7%)
4	AMP-E	25 (5.6%)
5	AMP-S	3 (0.7%)
6	AMP-TE	2 (0.4%)
7	C-S	1 (0.2%)
8	C-TE	1 (0.2%)
9	E-TE	2 (0.4%)
10	S-TE	6 (1.3%)
11	AMP-C-E	3 (0.7%)
12	AMP-C-TE	1 (0.2%)
13	AMP-E-S	7 (1.6%)
14	AMP-E-TE	9 (2.0%)
15	AMP-E-TMP	1 (0.2%)
16	AMP-GM-S	1 (0.2%)
17	AMP-S-TE	18 (4.0%)
18	CAZ-CTX-CPD	1 (0.2%)
19	C-E-GM	1 (0.2%)
20	E-S-TE	1 (0.2%)
21	GM-S-TE	1 (0.2%)
22	AMP-C-E-TE	9 (2.0%)
23	AMP-C-GM-TE	4 (0.9%)
24	AMP-C-S-TE	1 (0.2%)
25	AMP-E-S-TE	38 (8.5%)
26	AMP-E-SUL-TMP	2 (0.4%)
27	AMP-GM-S-TE	1 (0.2%)
28	AMP-SUL-TE-TMP	3 (0.7%)
29	C-E-S-TE	1 (0.2%)
30	AMP-CAZ-CTX-CPD-E	2 (0.4%)
31	AMP-C-E-GM-S	1 (0.2%)

No.	Resistant pattern	Number of Isolates (%)
32	AMP-C-E-GM-TE	3 (0.7%)
33	AMP-C-E-SUL-TMP	4 (0.9%)
34	AMP-C-SUL-TE-TMP	1 (0.2%)
35	AMP-CTX-CPD-E-GM	1 (0.2%)
36	AMP-E-GM-S-TE	1 (0.2%)
37	AMP-E-S-SUL-TMP	3 (0.7%)
38	AMP-E-S-TE-TMP	3 (0.7%)
39	AMP-E-SUL-TE-TMP	56 (12.5%)
40	AMP-S-SUL-TE-TMP	3 (0.7%)
41	C-E-GM-S-TE	1 (0.2%)
42	GM-S-SUL-TE-TMP	1 (0.2%)
43	AMP-CAZ-CTX-CPD-E-GM	4 (0.9%)
44	AMP-C-CL-E-SUL-TMP	1 (0.2%)
45	AMP-C-E-GM-S-TE	2 (0.4%)
46	AMP-C-E-S-SUL-TMP	1 (0.2%)
47	AMP-C-E-S-TE-TMP	1 (0.2%)
48	AMP-C-E-SUL-TE-TMP	18 (4.0%)
49	AMP-CTX-CPD-C-E-GM	1 (0.2%)
50	AMP-CTX-CPD-E-GM-TE	2 (0.4%)
51	AMP-E-GM-SUL-TE-TMP	1 (0.2%)
52	AMP-E-S-SUL-TE-TMP	19 (4.2%)
53	C-E-S-SUL-TE-TMP	1 (0.2%)
54	CTX-CPD-C-GM-S-TE	1 (0.2%)
55	AMP-CAZ-CTX-CPD-C-E-GM	1 (0.2%)
56	AMP-CAZ-CTX-CPD-C-E-S	3 (0.7%)
57	AMP-CAZ-CTX-CPD-C-GM-TE	1 (0.2%)
58	AMP-C-E-GM-SUL-TE-TMP	1 (0.2%)
59	AMP-C-E-S-SUL-TE-TMP	16 (3.6%)
60	CAZ-CTX-CPD-C-GM-S-TE	4 (0.9%)
61	C-E-GM-S-SUL-TE-TMP	4 (0.9%)
62	AMP-CAZ-CTX-CPD-C-E-GM-S	1 (0.2%)
63	AMP-CAZ-CTX-CPD-C-E-S-TE	2 (0.4%)

No.	Resistant pattern	Number of Isolates (%)
64	AMP-CAZ-CTX-CPD-C-E-SUL-TMP	1 (0.2%)
65	AMP-CAZ-CTX-CPD-C-GM-S-TE	2 (0.4%)
66	AMP-CAZ-CTX-CPD-E-GM-S-TE	2 (0.4%)
67	AMP-C-CIP-E-GM-S-SUL-TMP	1 (0.2%)
68	AMP-C-E-GM-S-SUL-TE-TMP	4 (0.9%)
69	AMP-CAZ-CTX-CPD-C-E-GM-S-TE	16 (3.6%)
70	AMP-CAZ-CTX-CPD-C-CIP-E-GM-S-TE	1 (0.2%)
71	AMP-CAZ-CTX-CPD-C-E-GM-S-SUL-TMP	1 (0.2%)
72	AMP-CAZ-CTX-CPD-C-E-S-SUL-TE-TMP	1 (0.2%)
73	AMP-CAZ-CTX-CPD-C-E-GM-S-SUL-TE-TMP	7 (1.6%)
74	AMP-CAZ-CTX-CPD-C-CIP-E-GM-S-SUL-TE-TMP	2 (0.4%)
75	AMP-CAZ-CTX-CPD-C-CL-E-GM-S-SUL-TE-TMP	1 (0.2%)

Table A22. Multidrug-resistant in *Salmonella* spp. isolated from pork (n=449)

Resistance	Number of Isolates (%)
Resistance = 1 CLSI class	9 (2.0%)
Resistance = 2 CLSI Classes	44 (9.8%)
Resistance = 3 CLSI Classes	53 (11.8%)
Resistance = 4 CLSI Classes	142 (31.6%)
Resistance = 5 CLSI Classes	72 (16.0%)
Resistance = 6 CLSI Classes	32 (7.1%)
Resistance = 7 CLSI Classes	3 (0.7%)
No resistance detected	94 (20.9%)

Table A23. Antimicrobial resistant patterns of *E. coli* isolated from chicken samples (n=419)

No.	Resistant pattern	Number of Isolates (%)
1	AMP	20 (4.8%)
2	S	2 (0.5%)
3	TE	7 (1.7%)
4	AMP-CIP	2 (0.5%)
5	AMP-GM	3 (0.7%)
6	AMP-S	13 (3.1%)
7	AMP-TE	35 (8.4%)
8	C-S	1 (0.2%)
9	CIP-S	3 (0.7%)
10	GM-S	5 (1.2%)
11	S-TE	2 (0.5%)
12	SUL-TMP	2 (0.5%)
13	AMP-C-GM	1 (0.2%)
14	AMP-C-S	2 (0.5%)
15	AMP-C-TE	9 (2.1%)
16	AMP-CIP-GM	2 (0.5%)
17	AMP-CIP-S	1 (0.2%)
18	AMP-CIP-TE	5 (1.2%)
19	AMP-CL-S	1 (0.2%)
20	AMP-GM-S	11 (2.6%)
21	AMP-GM-TE	4 (1.0%)
22	AMP-S-TE	21 (5.0%)
23	AMP-SUL-TMP	10 (2.4%)
24	C-SUL-TMP	1 (0.2%)
25	GM-S-TE	1 (0.2%)
26	SUL-TE-TMP	1 (0.2%)
27	AMP-CAZ-CTX-C	1 (0.2%)
28	AMP-C-S-TE	4 (1.0%)
29	AMP-C-SUL-TMP	1 (0.2%)
30	AMP-CIP-GM-S	10 (2.4%)
31	AMP-CIP-S-TE	4 (1.0%)

No.	Resistant pattern	Number of Isolates (%)
32	AMP-CL-GM-S	2 (0.5%)
33	AMP-GM-S-TE	13 (3.1%)
34	AMP-S-SUL-TMP	8 (1.9%)
35	AMP-SUL-TE-TMP	26 (6.2%)
36	CIP-S-SUL-TMP	1 (0.2%)
37	CIP-SUL-TE-TMP	1 (0.2%)
38	GM-S-SUL-TMP	1 (0.2%)
39	AMP-CAZ-CTX-CPD-S	1 (0.2%)
40	AMP-C-CIP-GM-S	1 (0.2%)
41	AMP-C-CIP-SUL-TMP	1 (0.2%)
42	AMP-C-GM-S-TE	1 (0.2%)
43	AMP-C-S-SUL-TMP	3 (0.7%)
44	AMP-C-SUL-TE-TMP	9 (2.1%)
45	AMP-CIP-GM-S-TE	5 (1.2%)
46	AMP-CIP-S-SUL-TMP	2 (0.5%)
47	AMP-CIP-SUL-TE-TMP	7 (1.7%)
48	AMP-CL-SUL-TE-TMP	1 (0.2%)
49	AMP-GM-S-SUL-TMP	6 (1.4%)
50	AMP-GM-SUL-TE-TMP	1 (0.2%)
51	AMP-S-SUL-TE-TMP	25 (6.0%)
52	CIP-S-SUL-TE-TMP	1 (0.2%)
53	GM-S-SUL-TE-TMP	1 (0.2%)
54	AMP-C-CIP-S-SUL-TMP	1 (0.2%)
55	AMP-C-GM-S-SUL-TMP	3 (0.7%)
56	AMP-C-GM-SUL-TE-TMP	2 (0.5%)
57	AMP-C-S-SUL-TE-TMP	15 (3.6%)
58	AMP-CIP-GM-S-SUL-TMP	3 (0.7%)
59	AMP-CIP-GM-SUL-TE-TMP	1 (0.2%)
60	AMP-CIP-S-SUL-TE-TMP	3 (0.7%)
61	AMP-CL-S-SUL-TE-TMP	1 (0.2%)
62	AMP-GM-S-SUL-TE-TMP	6 (1.4%)
63	AMP-CAZ-CTX-CPD-S-SUL-TE	1 (0.2%)

No.	Resistant pattern	Number of Isolates (%)
64	AMP-C-CIP-S-SUL-TE-TMP	2 (0.5%)
65	AMP-C-GM-S-SUL-TE-TMP	8 (1.9%)
66	AMP-CIP-GM-S-SUL-TE-TMP	8 (1.9%)
67	AMP-CL-GM-S-SUL-TE-TMP	1 (0.2%)
68	AMP-C-CIP-GM-S-SUL-TE-TMP	8 (1.9%)
69	AMP-CTX-CPD-C-GM-S-SUL-TMP	1 (0.2%)
70	AMP-CAZ-CTX-CPD-C-CIP-GM-S-SUL-TE-TMP	1 (0.2%)

Table A24. Multidrug-resistant in *E. coli* isolated from chicken (n=419)

Resistance	Number of Isolates (%)
No resistance detected	52 (12.4%)
Resistance = 1 CLSI class	36 (8.6%)
Resistance = 2 CLSI Classes	86 (20.5%)
Resistance = 3 CLSI Classes	115 (27.4%)
Resistance = 4 CLSI Classes	79 (18.9%)
Resistance = 5 CLSI Classes	40 (9.5%)
Resistance = 6 CLSI Classes	11 (2.6%)

Table A25. Antimicrobial resistant patterns of *Salmonella* spp. isolated from chicken samples (n=235)

No.	Resistant pattern	Number of Isolates (%)
1	AMP	28 (11.9%)
2	C	1 (0.4%)
3	E	6 (2.6%)
4	S	2 (0.9%)
5	TE	3 (1.3%)
6	AMP-C	1 (0.4%)
7	AMP-CL	1 (0.4%)
8	AMP-E	21 (8.9%)
9	AMP-S	7 (3.0%)
10	AMP-SUL	1 (0.4%)
11	AMP-TE	4 (1.7%)
12	AMP-TMP	1 (0.4%)

No.	Resistant pattern	Number of Isolates (%)
13	C-TE	1 (0.4%)
14	CL-TE	1 (0.4%)
15	E-TE	1 (0.4%)
16	S-TE	2 (0.9%)
17	AMP-C-TE	1 (0.4%)
18	AMP-CIP-TE	2 (0.9%)
19	AMP-CL-E	1 (0.4%)
20	AMP-E-S	1 (0.4%)
21	AMP-GM-S	8 (3.4%)
22	AMP-S-TE	11 (4.7%)
23	C-S-TE	1 (0.4%)
24	AMP-C-GM-TE	2 (0.9%)
25	AMP-C-S-TE	3 (1.3%)
26	AMP-CIP-S-TE	2 (0.9%)
27	AMP-E-GM-S	2 (0.9%)
28	AMP-GM-S-TE	2 (0.9%)
29	AMP-C-SUL-TE-TMP	1 (0.4%)
30	AMP-E-GM-S-TE	1 (0.4%)
31	AMP-S-SUL-TE-TMP	2 (0.9%)
32	E-S-SUL-TE-TMP	1 (0.4%)
33	AMP-C-E-SUL-TE-TMP	3 (1.3%)
34	AMP-C-GM-S-SUL-TMP	1 (0.4%)
35	AMP-E-S-SUL-TE-TMP	4 (1.7%)
36	AMP-GM-S-SUL-TE-TMP	1 (0.4%)
37	E-GM-S-SUL-TE-TMP	1 (0.4%)
38	AMP-C-E-GM-SUL-TE-TMP	5 (2.1%)
39	AMP-C-E-S-SUL-TE-TMP	5 (2.1%)
40	AMP-E-GM-S-SUL-TE-TMP	5 (2.1%)
41	AMP-CAZ-CTX-CPD-E-GM-S-TE	2 (0.9%)
42	AMP-C-E-GM-S-SUL-TE-TMP	5 (2.1%)

Table A26. Multidrug-resistant in *Salmonella* spp. isolated from chicken (n=235)

Resistance	Number of Isolates (%)
No resistance detected	81 (34.5%)
Resistance = 1 CLSI class	40 (17.0%)
Resistance = 2 CLSI Classes	49 (20.9%)
Resistance = 3 CLSI Classes	21 (8.9%)
Resistance = 4 CLSI Classes	17 (7.2%)
Resistance = 5 CLSI Classes	12 (5.1%)
Resistance = 6 CLSI Classes	15 (6.4%)

Annex 4 Health Policy and Systems Research on antimicrobial resistance working group members

Ministry of Public Health

International Health Policy Program
Viroj Tangcharoensathien
Angkana Lekagul
Sunicha Chanvatik
Supapat Kirivan
Wanwisa Kaewkhankhaeng
Oranat Rueangna

Food and Drug Administration
Charunee Krisanaphan
Varavoot Sermsinsiri
Kritsada Limpananont
Chutamas Luangaroonchai
Pischa Lusanandana
Chaiporn Pumkam
Sitanan Poonpolsub
Pongsathid Virungrojint

Ministry of Agriculture and Cooperatives

Department of Livestock Development
Thanida Harintharanon
Sasi Jareonpoj
Julaporn Srinha
Suchana Sukklad
Natthapong Supimon
Somsajee Sivilaikul
Thanawan Na Thalang

Department of Fisheries
Janejit Kongkumnerd
Thitiporn Laoprasert
Chanotit Nakmanoc
Narintha Boonkuang
Jutamas Auewongaree
Suppaluck Chambang

Faculty of Pharmaceutical Sciences, Chulalongkorn University
Rungpetch Sakulbumrungsil
Sang Usayaporn

Faculty of Pharmacy, Silpakorn University
Inthira Kanchanaphibool

Faculty of Pharmaceutical Sciences, Khon Kaen University
Nussaraporn Kessomboon

Faculty of Pharmaceutical Sciences, Prince of Songkla University
Khunjira Udomaksorn

Contributors

Faculty of Veterinary Science, Mahidol University
Walasinee Moonarmart
Boonrat Chantong
Sarin Suwanpakdee
Anuwat Wiratsudakul

Thai Feed Mill Association
Boonyita Rujtikumporn
Wichai Thermphonboon
Chaiwat Suwannatad
Sompong Harnuthaikij
Krisada Rithichaidumrongkul
Yamuna Patthong
Sureemas Nitikanchana
Pranee Pirompud
Pattama Sritiangtrong

Animal Health Products Association
Nackanun Chitaroon
Panitan Suwannapetch
Eagaluk Theerakornsakul
Varisara Jirathitivong

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