Nippon AMR One Health Report (NAOR) 2020

January 8, 2021

The AMR One Health Surveillance Committee

TABLE OF CONTENTS

1. Preface

Japan's "National Action Plan on AMR 2016-2020" was published in April 2016, clearly indicating the implementation of integrated one health surveillance regarding antimicrobial-resistant bacteria that are isolated from humans, animals, food and the environment. This one health surveillance is endorsed as an important strategy for correctly identifying the current status and issues related to AMR, which leads to promoting appropriate national AMR policy. In presenting the results of this surveillance, this report aims to identify the current status of and trends in antimicrobial-resistant bacteria and national antimicrobial use in the areas of human health, animals, agriculture, food and the environment, with the objective of assessing measures to combat antimicrobial-resistant bacteria and clarify challenges in this area.

We hope that this report would provide the first step for presenting Japan's effort to fight against AMR with one health approach to both domestic and international stakeholders; moreover, related governmental agencies, organizations/associations, academic societies and other entities, our intended target readers, are welcome to utilize this report in order to accelerate and advance policy and research activities on AMR.

2. Abbreviations

AMED	Japan Agency for Medical Research and Development
AMU	Antimicrobial Use
AMR	Antimicrobial Resistance
AMRCRC	Antimicrobial Resistance Clinical Reference Center
AUD	Antimicrobial Use Density
BP	Break Point
CDI	*Clostridioides* (*Clostridium*) *difficile* Infection
CLSI	Clinical and Laboratory Standards Institute
CRE	Carbapenem-resistant *Enterobacteriaceae*
DID	Defined Daily Dose per 1000 Inhabitants per Day
DDD(s)	Defined Daily Dose(s)
DOT	Days of Therapy
EUCAST	European Committee on Antimicrobial Susceptibility Testing
FAMIC	Food and Agricultural Materials Inspection Center
FAO	Food and Agricultural Organization of the United Nations
GLASS	Global Antimicrobial Resistance Surveillance System
HAI	Healthcare-associated Infection
ICU	Intensive Care Unit
JAMUS	Japan Antimicrobial Use Surveillance
JANIS	Japan Nosocomial Infections Surveillance
J-SIPHE	Japan Surveillance for Infection Prevention and Healthcare Epidemiology
JVARM	Japanese Veterinary Antimicrobial Resistance Monitoring System
MIC	Minimum Inhibitory Concentration
MDRA	Multidrug-resistant *Acinetobacter* spp.
MDRP	Multidrug-resistant *Pseudomonas aeruginosa*
MRSA	Methicillin-resistant *Staphylococcus aureus*
MSSA	Methicillin-susceptible *Staphylococcus aureus*
NDB	National Database of Health Insurance Claims and Specific Health Checkups of. Japan
NESID	National Epidemiological Surveillance of Infectious Disease
OIE	World Organisation for Animal Health
PPCPs	Pharmaceuticals and Personal Products
PRSP	Penicillin-resistant *Streptococcus pneumoniae*
RICSS	Regional Infection Control Support System
SSI	Surgical Site Infection
WHO	World Health Organization
VRE	Vancomycin-resistant *Enterococci*
VRSA	Vancomycin-resistant *Staphylococcus aureus*
DALY(s)	Disability-adjusted life year(s)
PPS	Point Prevalence Survey

3. Types and Abbreviations of Antimicrobials

Type			Nonproprietary name	Abbreviation*
Beta-lactam antibiotics	Penicillins		Benzylpenicillin (penicillin G)	PCG
			ampicillin	ABPC
			ampicillin/sulbactam	ABPC/SBT
			piperacillin	PIPC
			oxacillin	MPIPC
			piperacillin/tazobactam	PIPC/TAZ
			amoxicillin	AMPC
			amoxicillin/clavulanic acid	AMPC/CVA
	Cephalosporins	1st generation	cefazolin	CEZ
			cephalexin	CEX
		2nd generation	cefotiam	CTM
			cefaclor	CCL

			cefmetazole	CMZ
			cefoxitin	CFX
		3rd generation	cefotaxime	CTX
			ceftazidime	CAZ
			ceftriaxone	CTRX
			cefoperazone/sulbactam	CPZ/SBT
			cefdinir	CFDN
			cefcapene pivoxil	CFPN-PI
			cefditoren pivoxil	CDTR-PI
			cefixime	CFIX
		4th generation	cefepime	CFPM
			cefpirome	CPR
			cefozopran	CZOP
	Cephamycins		cefmetazole	CMZ
			cefoxitin	CFX
	Oxacephems		flomoxef	FMOX
			latamoxef	LMOX
	Monobactams		aztreonam	AZT
	Carbapenems		meropenem	MEPM
			doripenem	DRPM
			biapenem	BIPM
			imipenem/cilastatin	IPM/CS
			panipenem/betamipron	PAPM/BP
			tebipenem pivoxil	TBPM-PI
	Penems		faropenem	FRPM
ST			sulfamethoxazole-trimethoprim	ST

Macrolides	erythromycin	EM
	clarithromycin	CAM
	azithromycin	AZM
	tylosin	TS
Ketolides	telithromycin	TEL
Lincomycins	clindamycin	CLDM
	lincomycin	LCM
Streptogramins	quinupristin/dalfopristin	QPR/DPR
	virginiamycin	VGM
Tetracyclines	minocycline	MINO
	tetracycline	TC
	doxycycline	DOXY
	oxytetracycline	OTC
Aminoglycosides	streptomycin	SM
	tobramycin	TOB
	gentamicin	GM
	amikacin	AMK
	arbekacin	ABK
	kanamycin	KM
	spectinomycin	SPCM
	dihydrostreptomycin	DSM
Quinolones (◎fluoroquinolones)	◎ciprofloxacin	CPFX
	◎levofloxacin	LVFX
	◎pazufloxacin	PZFX
	◎norfloxacin	NFLX

	◎prulifloxacin	PUFX
	◎moxifloxacin	MFLX
	◎garenoxacin	GRNX
	◎sitafloxacin	STFX
	◎ofloxacin	OFLX
	◎enrofloxacin	ERFX
	oxolinic acid	OA
	nalidixic acid	NA
Glycopeptides	vancomycin	VCM
	teicoplanin	TEIC
Oxazolidinones	linezolid	LZD
Polypeptides	polymyxin B	PL-B
	colistin	CL
	bacitracin	BC
Lipopeptides	Daptomycin	DAP
Amphenicols	chloramphenicol	CP
	florfenicol	FF

Other antibacterial agents	fosfomycin	FOM
	salinomycin	SNM
	bicozamycin	BCM
	trimethoprim	TMP
Antitubercular antibiotics	isoniazid	INH
	ethambutol	EB
	rifampicin (rifampin)	RFP
	pyrazinamide	PZA
	rifabutin	RBT

* Quoted from the Glossary of Antimicrobial Chemotherapy (Japanese Society of Chemotherapy), the Annual Report of the Japanese Society of Antimicrobials for Animals 36 (2014), and the Guidelines for the Use of Antimicrobial Substances in Cooperative Livestock Insurances (2009, Ministry of Agriculture, Forestry and Fisheries)

[Reference] There are multiple relevant terminologies with different definitions. However, in medical practice, the following four terms are often used interchangeably to refer drugs that act against bacteria: “antimicrobial agents,” “antibiotics,” “antibiotic agents,” and “antibacterial agents.” In the areas of agriculture and livestock, the expressions "antibacterial agents" and "antimicrobial agents" are commonly used, because these agents are not only used for therapeutic purposes, but also in antibiotic feed additives.

Antimicrobial agents or antimicrobials: Antimicrobial agents, or antimicrobials, are active against microorganisms, which are generally categorized into bacteria, fungi, viruses and parasites. These are the general term for drugs to treat and prevent infectious diseases. They contain antibacterial agents, antifungal agents, antiviral agents and antiparasitic agents.

Antibacterial agents: Antimicrobial agents that are active against bacteria.

Antibiotics: informally defined as an agent that is derived from living organisms to inhibit and control cell activities of microorganisms

Antibiotic agents: Another term for drugs that use the antibacterial action of antibiotics

Reference: the Manual of Antimicrobial Stewardship, 1st edition

In terms of active ingredients (veterinary drugs), in terms of effective value (antibiotic feed additives), in terms of active ingredients (agrochemicals), antimicrobial consumption in terms of potency by weight (humans): All these terms refer to active ingredient weight. Quantities in terms of the weight of active ingredients in veterinary drugs are calculated from sales data collected from marketing authorization holders for the volume of each drug sold. When doing so, the marketing authorization holders also submit estimates of the percentage of sales for each species of domestic animal, so the estimated volumes sold are calculated for each species based on those estimated percentages. As with the figures for veterinary drugs, quantities of antibiotic feed additives in terms of effective value, quantities of agrochemicals in terms of active ingredients, and human antimicrobial consumption in terms of potency by weight refer to active ingredient weight

Indicators of antimicrobial use:

・**AUD (antimicrobial use density):** Mainly used to ascertain usage in medical institutions, AUD is calculated by dividing the total titer of antimicrobials in a specified period by defined daily dose (DDD) as defined by the World

Health Organization (WHO), and correcting the result with the total patient-days. The units used for AUD include DDDs per 100 bed-days and DDDs per 1,000 patient-days.

- **DID (DDDs/1,000 inhabitants/day):** Antimicrobial use in a region or country is expressed as DID, which is calculated by dividing the total titer by DDD and correcting the denominator with the number of inhabitants of the region per day.

- **DOT (day of therapy):** DOT is calculated by correcting the total days of therapy (DOTs) using antimicrobials in a specified period with the total patient-days. The units used for DOT include DOTs per 100 bed-days and DOTs per 1,000 patient-days.

4. Executive Summary

Background:

Japan's "National Action Plan on AMR 2016-2020" positions efforts to ascertain the current status of antimicrobial-resistant bacteria and national antimicrobial use in the areas of human health, animals, food and the environment and trends therein as an important strategy for both evaluating current policy and examining future policy. For global monitoring and reporting, WHO has launched the Global Antimicrobial Resistance Surveillance System (GLASS) for the gathering and sharing of trends in resistant bacteria worldwide. Japan contributes to GLASS by providing our national data. In addition, Japan also submits data as part of our assistance with an initiative by the World Organisation for Animal Health (OIE), which uses standardized methods for monitoring the volume of antimicrobial use in animals. Accordingly, it is crucial for Japan to update both domestic and overseas stakeholders about the current status and progress of our AMR policy, in order both to reaffirm Japan's position in the global community and to accelerate and advance AMR policy internationally.

Method:

The AMR One Health Surveillance Committee, comprised of experts on AMR in the areas of human health, animals, food and the environment, discussed current surveillance/monitoring systems and reviewed published research on AMR and antimicrobial use. Data on the proportion of antimicrobial resistance among major pathogens in the human medical setting were derived from the Japan Nosocomial Infections Surveillance (JANIS) program organized by the Ministry of Health, Labour and Welfare of Japan. Data on the proportion of antimicrobial resistance among animals and related antimicrobial sales were derived from the Japanese Veterinary Antimicrobial Resistance Monitoring System (JVARM) implemented by the Ministry of Agriculture, Forestry and Fisheries of Japan (MAFF). We obtained data on sales and consumption of antimicrobials for human use from IQVIA Solutions Japan K.K., the National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB), and Japan Surveillance for Infection Prevention and Health-care Epidemiology (J-SIPHE). Data on the distribution of antimicrobial feed additives were provided by the Food and Agricultural Materials Inspection Center (FAMIC) and the Japan Scientific Feeds Associations (JSFA). Data on the volume of domestic shipments of antimicrobials used as agricultural chemicals was from MAFF.

Data on antimicrobial resistance which are considered pertinent from public health perspective or public awareness toward AMR, but not monitored neither by current suveillance nor monitoring systems were obtained from findings by Health and Labor Sciences Research Groups.

The results of the survey of attitudes among veterinary science students specializing in the animal field are based on responses to a questionnaire conducted in conjunction with a lecture on antimicrobial resistance at 12 universities.

Results:

In Japan, the carbapenem resistance rate in *Enterobacteriaceae*, particularly *Escherichia coli* and *Klebsiella pneumoniae* has remained below 1% during the observed period, despite its global increase in human isolates. Internationally, the increase in vancomycin resistance among enterococci is a problem. While vancomycin resistance among *Enterococcus faecium* in Japan remained less than 1% until 2018, its progress needs to be tracked carefully, as the figure increased to 1.5% in 2019. While the criteria for assessing carbapenem resistance in *Pseudomonas aeruginosa* changed in 2014, the resistance rate appears to be trending downward. The rate of resistance against the third-generation cephalosporins and fluoroquinolones among *Escherichia coli*, however, is increasing. Although the percentage of methicillin-resistant *Staphylococcus aureus* (MRSA) has been declining since 2011, levels remain high. Clear similarities in the pattern of resistance rates to antimicrobials were observed in serotypes of *Salmonella* spp. isolated from food and from humans, strongly suggesting a link between resistant strains derived from food and from humans.

In 2019, useage of antimicrobial agents in Japan based on total yearly sales fell by 10.9% from 2013 to a defined daily dose per 1,000 inhabitants per day (DID) of 13.3. Oral antimicrobial agents accounted for 91.8% of total sales, with cephalosporins, fluoroquinolones, and macrolides accounting for the highest shares. While the trend remained similar in 2019, a further decline in usage from 2018 was observed, with the usage of each agent declining by 22.7%, 18.1%, and 20.6% respectively since 2013. However, use of parenteral antimicrobials saw a 12.7% increase from 2013.

Surveillance of antimicrobial resistance in animals focuses on food-producing animals (cattle, pigs, and chickens), aquatic animals (all farmed fish species), and companion animals (dogs and cats). No *Enterobacteriaceae* resistant to carbapenems, which is one of the most critically important antimicrobial classes for human medicine, or vancomycin-resistant enterococci, which cause major problems including nosocomial infections in humans, were isolated.

Among food-producing animals, while tetracycline resistance in *Escherichia coli* derived from healthy food-producing animals—an outcome index for the Action Plan—fell from 45.2% in 2014 to 39.9% in 2015, the rate has undergone repeated fluctuations since 2016 and has failed to fall, reaching 43.6% in 2018. On the other hand, rates of resistance to third-generation cephalosporins and fluoroquinolones mostly remained below 10% between 2014 and 2018.

Among aquatic animals, lincomycin resistance in *Lactococcus garvieae* derived from diseased fish fell from 61.0% in 2017 to 31.5% in 2018, while no strains resistant to erythromycin or oxytetracycline were found in this bacteria.

Among companion animals, while *Escherichia coli* isolated from diseased dogs and cats demonstrated lower resistance to tetracyclines and aminoglycosides than among food-producing animals, resistance rates to the fluoroquinolones and cephalosporins that are critically important antimicrobials for human medicine tended to be higher. *Escherichia coli* isolated from healthy companion animals (dogs and cats) demonstrated lower resistance to all antimicrobials than in the case of diseased ones, demonstrating that susceptibility is being broadly maintained.

The volume of sales of antimicrobials used for animals (food-producing animals, aquatic animals, and companion animals) was calculated in metric tons (t) of the active ingredients, based on sales reports for antibiotics and synthetic antimicrobials mandated by Article 71-2 of the Regulations for Veterinary Drugs (Ordinance of the Ministry of Agriculture, Forestry and Fisheries No. 107 of 2004). In 2018, tetracyclines represented the largest share of antimicrobial sales, accounting for about 40%. In contrast, third-generation cephalosporins and fluoroquinolones each accounted for less than 1% of the total. The total volume of veterinary antimicrobial sales increased from 780.88 t in 2013 to 872.09 t in 2017, but then fell by around 48 t to 824.56 tons in 2018. Looking at the figures by class, sales of tetracyclines fell by about 36 t, sulfonamide by around 10 t, and aminoglycosides by approximately 9 t. On the other hand, sales of macrolides (erythromycin used in aquatic animals) increased by around 14 t and penicillin derivatives used in food-producing animals by about 8 t, with the rise in erythromycin used in aquatic animals presumed to have been triggered by treatment necessitated by an outbreak of infectious disease caused by *Lactococcus garvieae* of a different serotype from that usually found.

Total usage of antimicrobials in 2018 estimated from the volume of sales in each field was 1,761.4 t, comprising 582.1 t for human use, 646.4 t for food-producing animals, 168.5 t for aquatic animals, 8.6 t for companion animals, 216.7 t for antibiotic feed additives, and 139.1 t for agrochemicals.

Observations:

Figures for 2019 sales of oral antimicrobials, including oral cephalosporins, oral macrolides, and oral fluoroquinolones show that usage of these antimicrobials has fallen overall compared with the data for 2013. However, as the decline is only slight when compared with the 2018 data, better antimicrobial stewardship is required. In addition, a clear downward trend in antimicrobial resistance rates has emerged among a number of bacterial species, thereby demonstrating progress toward achieving the numerical targets in the action plan. However, resistance rates continue to climb, including fluoroquinolone resistance rates among *Escherichia coli*.

The data in this report demonstrate that further promotion of measures against AMR will be required. There are reports of a correlation between fluoroquinolone usage and the frequency of occurrence of fluoroquinolone-resistant *Escherichia coli*. There are also reports of a connection between MRSA and usage of third-generation cephalosporins, fluoroquinolones, and macrolides. Accordingly, unnecessary use of third-generation cephalosporins, fluoroquinolones, and macrolides must be reduced and the Manual of Antimicrobial Stewardship employed to promote the proper use of antimicrobials, primarily in respect of acute respiratory tract infections. As the basic premise underpinning the promotion of antimicrobial stewardship is ensuring that the appropriate antimicrobials can be used when needed, securing a stable supply of basic antimicrobial agents is crucial. In addition, information about resistant bacteria in each region and the status of antimicrobial use is being put in place, as it is desirable to select antimicrobials and promote infection control measures tailored to the situation in each region. Furthermore, it will be necessary to continue using various techniques for education and awareness activities targeting the public and medical professionals, to achieve further progress in antimicrobial stewardship.

Among animals, no *Enterobacteriaceae* resistant to carbapenems, which is one of the most critically important antimicrobial classes for human medicine, or vancomycin-resistant enterococci, which cause major problems including nosocomial infections in humans, were isolated. However, rates of resistance to third-generation cephalosporins and fluoroquinolones in *Escherichia coli* isolated from diseased companion animals, surveillance of which began in 2017, were found to be higher than in *Escherichia coli* isolated from food-producing animals. This demonstrates the necessity of continuing and enhancing measures to combat antimicrobial resistance not only via the measures that have been underway for some time in the field of food-producing animals, but also through the widespread circulation of the guide to prudent use in companion animals launched in 2020.

While rates of resistance to third-generation cephalosporins and fluoroquinolones in *Escherichia coli* isolated from healthy food-producing animals—an outcome index for the Action Plan—have been maintained at a low level, it will be necessary to continue to raise awareness among veterinarians and producers about their prudent use as second-line veterinary drugs in food-producing animals. Although the volume of tetracycline sales fell in 2018, rates of resistance to this class of antimicrobial in *Escherichia coli* isolated from healthy food-producing animals have not declined. Accordingly, greater efforts are required to promote prudent use of these antimicrobials, taking into account the actual state of their use among veterinarians and producers.

The existing Action Plan covers the five-year period up to 2020. Although some indices are improving, there are still many that have seen only scant improvement, added to which a number of new issues have emerged, so it is necessary to continue addressing them in coordination with international trends. As such, industry, academia, and government will work together to promote frameworks for collaboration between the organizations tasked with handling different fields, while also examining the promotion of research that enables cross-cutting evaluation of the risks to humans, animals, and the environment to be conducted.

5. Outcome Indices for the Action Plan

Human-related indices for the Action Plan: proportion (%)[*] of specified antimicrobial-resistant bacteria

	2013	2015	2017	2018	2019	2020 (target value[†])
Proportion of penicillin-non-susceptible *Streptococcus pneumoniae*, CSF specimens[§]	47.4	40.5	29.1	38.3	32.0	15% or lower
Proportion of penicillin-non-susceptible *Streptococcus pneumoniae*, non-CSF specimens[§]	3.2	2.7	2.1	2.2	2.2	
Proportion of fluoroquinolone-resistant *Escherichia coli*	35.5	38.0	40.1	40.9	41.4	25% or lower
Proportion of methicillin-resistant *Staphylococcus aureus*	51.1	48.5	47.7	47.5	47.7	20% or lower
Proportion of carbapenem-resistant *Pseudomonas aeruginosa* (Imipenem)	17.1	18.8	16.9	16.2	16.2	10% or lower
Proportion of carbapenem-resistant *Pseudomonas aeruginosa* (Meropenem)	10.7	13.1	11.4	10.9	10.6	10% or lower
Proportion of carbapenem-resistant *Escherichia coli* (Imipenem)	0.1	0.1	0.1	0.1	0.1	0.2% or lower (maintain at the same level)[¶]
Proportion of carbapenem-resistant *Escherichia coli* (Meropenem)	0.1	0.2	0.1	0.1	0.1	0.2% or lower (maintain at the same level)[¶]
Proportion of carbapenem-resistant *Klebsiella pneumoniae* (Imipenem)	0.3	0.3	0.2	0.3	0.2	0.2% or lower (maintain at the same level)[¶]
Proportion of carbapenem-resistant *Klebsiella pneumoniae* (Meropenem)	0.6	0.6	0.4	0.5	0.4	0.2% or lower (maintain at the same level)[¶]

CSF, cerebrospinal fluid

* Prepared based on JANIS data. Data were provided every two years from 2013, but annual data have been provided since 2017.

† Target values were quoted from the National Action Plan on AMR.[1]

§ The proportion of penicillin-non-susceptible *Streptococcus pneumoniae* in 2014, as indicated in the Action Plan, is based on the CLSI (2007) Criteria where those with penicillin MIC of 0.125 μg/mL or higher are considered resistant. The CLSI Criteria were revised in 2008, applying different standards to CSF and non-CSF specimens. Based on this revision, JANIS has divided data into CSF and non-CSF specimens since 2015.

¶ The National Action Plan on AMR [1] indicates that the respective proportion of carbapenem-resistant *Escherichia coli* and *Klebsiella pneumoniae* were at 0.1% and 0.2% in 2014, and the proportions should be maintained at the same level in 2020.

Human-related indices for the Action Plan: use of antimicrobials (DID) (based on volume of sales)

	2013[†]	2019	Change from 2013	2020 (target value*)
All antimicrobials	14.91	13.28	10.9%↓	33%↓
Oral cephalosporins	3.91	3.02	22.7%↓	50%↓
Oral fluoroquinolones	2.83	2.32	18.1%↓	50%↓
Oral macrolides	4.83	3.84	20.6%↓	50%↓
Intravenous antimicrobials	0.96	1.09	12.7%↑	20%↓

DID: Defined daily dose per 1,000 inhabitants per day

* Target values were quoted from [1].

† Prepared from [2].

Animal-related indices for the Action Plan: proportion (%) of specified antimicrobial-resistant bacteria

	2014*	2015*	2016	2017	2018	2020 (target value**)
Proportion of tetracycline-resistant *Escherichia coli* (farms)	45.2	39.9				33% or lower
(Animal slaughterhouses)		39.8	47.6	40.8	43.6	
Proportion of third-generation cephalosporin-resistant *Escherichia coli* (farms)	1.5	0.9				The same level as in other G7 nations
(Animal slaughterhouses)		0.7	2.4	2.1	1.1	
Proportion of fluoroquinolone-resistant *Escherichia coli* (farms)	4.7	3.8				The same level as in other G7 nations
(Animal slaughterhouses)		2.7	5.0	4.0	4.7	

* Prepared from [3] with partial modification.

JVARM "Results of Monitoring of Antimicrobial Resistant Bacteria Isolated from Food-producing Animals on Farms"

** Target values were quoted from [1].

References

1. Ministerial Conference for the Control of Globally Threatening Infectious Diseases. "The National Action Plan on AMR 2016-2020." 2016.
2. Muraki Y, *et al.* "Japanese antimicrobial consumption surveillance: first report on oral and parenteral antimicrobial consumption in Japan (2009–2013)" J Glob Antimicrob Resist. 2016 Aug 6;7:19-23.
3. National Veterinary Assay Laboratory, Ministry of Agriculture, Forestry and Fisheries. "Monitoring of AMR." https://www.maff.go.jp/nval/yakuzai/yakuzai_p3.html

6. Current Status of Antimicrobial-resistant Bacteria in Japan

(1) Humans

1) Gram-negative bacteria

Source: JANIS

As for the recent status of gram-negative bacteria, despite recent global increase of carbapenem (imipenem (IPM) and meropenem (MEPM))-resistant *Enterobacteriaceae* such as *Escherichia coli* and *Klebsiella pneumoniae*, the proportion of carbapenem-resistant *Escherichia coli* and *Klebsiella pneumoniae* in Japan remained low at less than 1%, as in Tables 1 and 2. However, the rate of resistance against third-generation cephalosporins such as cefotaxime (CTX) and fluoroquinolones such as levofloxacin (LVFX) among *Escherichia coli* continues to increase. The rise in the rate of resistance to third-generation cephalosporins would appear to reflect the increase in bacteria with ESBL genes. As such, there appears to be a particular need for measures targeted at the rise of these resistant bacteria.

The proportion of carbapenem-resistant *Enterobacter cloacae* (Table 3) and *Klebsiella (Enterobacter) aerogenes* (Table 4) remained between around 1% and 2%; and the proportion of carbapenem-resistant *Pseudomonas aeruginosa* (Table 5) and *Acinetobacter* spp. (Table 6) remained at a level equivalent to or even lower than in other countries. In particular, the proportion of carbapenem-resistant *Acinetobacter* spp. remained low between around 1% and 3%.

i. *Escherichia coli*

Table 1. Trends in the proportion (%) of antimicrobial-resistant *Escherichia coli*

	BP (-2013)	BP (2014-)	2011	2012	2013	2014	2015	2016	2017	2018	2019
ABPC	32	32	47.6 (116,097)	49.1 (133,330)	49.4 (150,867)	49.2 (170,597)	50.5 (257,065)	51.2 (288,052)	51.7 (307,143)	52.2 (325,553)	52.6 (336,351)
PIPC	128	128	40.1 (119,843)	41.6 (136,978)	42.5 (155,626)	42.5 (175,763)	44.1 (270,452)	44.9 (305,604)	45.2 (327,773)	46.0 (342,066)	46.4 (343,183)
TAZ/ PIPC	4/128	4/128	-	-	2.2 (51,286)	1.7 (89,442)	1.7 (179,722)	1.8 (218,008)	1.7 (241,519)	1.7 (263,131)	3.2 (285,685)
CEZ*	32	8	24.4 (122,803)	26.2 (141,560)	26.9 (161,397)	33.3 (183,542)	35.8 (268,898)	36.8 (303,608)	37.3 (324,109)	38.7 (347,491)	39.0 (361,167)
CMZ	64	64	-	-	-	1.0 (163,342)	0.9 (260,844)	1.0 (300,089)	0.9 (325,296)	0.9 (348,832)	0.9 (365,259)
CTX*	64	4	14.8 (99,543)	16.6 (113,354)	17.8 (124,473)	23.3 (140,186)	24.5 (209,404)	26.0 (230,911)	26.8 (241,843)	27.5 (251,068)	28.3 (257,856)
CAZ*	32	16	5.2 (123,606)	5.2 (142,440)	5.5 (161,163)	9.5 (183,970)	10.8 (275,671)	11.6 (310,281)	12.0 (330,029)	12.4 (352,819)	14.0 (367,538)
CFPM	32	32	-	-	10.9 (81,456)	12.8 (129,606)	15.0 (236,705)	15.8 (273,587)	16.1 (296,143)	16.7 (321,745)	18.1 (337,526)
AZT*	32	16	8.5 (97,906)	9.4 (111,930)	10.2 (126,777)	16.1 (143,046)	17.6 (216,494)	18.4 (239,952)	18.7 (258,193)	19.3 (273,064)	21.0 (283,965)
IPM*	16	4	0.1 (113,820)	0.1 (128,289)	0.1 (146,007)	0.1 (163,181)	0.1 (251,050)	0.1 (284,316)	0.1 (304,633)	0.1 (321,043)	0.1 (328,665)
MEPM*	16	4	-	-	0.1 (95,180)	0.2 (144,913)	0.2 (269,893)	0.2 (317,987)	0.1 (340,687)	0.1 (365,600)	0.1 (379,637)
AMK	64	64	0.2 (123,464)	0.2 (141,114)	0.2 (161,406)	0.2 (184,788)	0.1 (281,641)	0.1 (317,913)	0.1 (339,871)	0.1 (362,591)	0.1 (374,518)
LVFX	8	8	31.4 (117,292)	34.3 (136,253)	35.5 (155,998)	36.1 (178,497)	38.0 (274,687)	39.3 (310,705)	40.1 (336,310)	40.9 (360,329)	41.4 (374,719)

The unit of BP is μg/mL.

Figures in parentheses indicate the number of bacterial strains that were tested for antimicrobial susceptibility. Data for ST were not calculated.

-: Not under surveillance

* CLSI (2007) (M100-S17) Criteria was applied to determine the BP up to 2013. CLSI (2012) (M100-S22) Criteria was applied to determine BP after 2014.

ii. *Klebsiella pneumoniae*

Table 2. Trends in the proportion (%) of antimicrobial-resistant *Klebsiella pneumoniae*

	BP (-2013)	BP (2014-)	2011	2012	2013	2014	2015	2016	2017	2018	2019
ABPC	32	32	75.9	76.9	77.8	76.3	76.9	76.3	77.4	79.4	80.1
			(65,338)	(73,078)	(80,030)	(90,220)	(131,700)	(147,500)	(152,477)	(158,654)	(159,790)
PIPC	128	128	19.7	20.1	24.3	21.9	21.1	21.8	21.8	22.9	24.5
			(67,548)	(74,878)	(82,608)	(91,761)	(136,347)	(154,260)	(161,254)	(165,430)	(161,590)
TAZ/	4/128	4/128	-	-	2.2	2.0	2.0	2.2	2.2	2.6	3.1
PIPC					(27,279)	(46,941)	(91,503)	(110,189)	(118,796)	(127,778)	(135,732)
CEZ*	32	8	8.8	9.0	9.1	11.7	12.1	13.1	13.4	14.3	15.2
			(68,481)	(76,860)	(85,320)	(94,875)	(135,486)	(152,973)	(157,849)	(166,906)	(170,001)
CMZ	64	64	-	-	-	1.9	1.9	1.7	1.5	1.6	1.5
						(85,749)	(132,163)	(152,086)	(159,375)	(168,787)	(172,912)
CTX*	64	4	5.2	5.4	5.1	8.6	8.0	8.9	8.9	9.4	9.7
			(56,236)	(62,242)-	(66,654)	(73,574)	(107,409)	(118,057)	(119,672)	(122,459)	(122,241)
CAZ*	32	16	3.4	2.9	2.7	3.8	4.0	4.6	5.0	5.7	6.9
			(68,916)	(76,961)	(84,761)	(94,878)	(138,191)	(155,293)	(160,619)	(169,097)	(173,031)
CFPM	32	32	-	-	3.0	3.5	4.0	4.8	5.1	5.8	6.8
					(41,143)	(66,399)	(119,563)	(138,737)	(145,745)	(156,485)	(160,502)
AZT*	32	16	4.1	3.7	3.5	5.1	5.3	5.9	6.2	6.7	8.0
			(54,680)	(60,606)	(67,253)	(75,340)	(110,259)	(122,600)	(127,491)	(133,009)	(135,631)
IPM*	16	4	0.2	0.2	0.1	0.3	0.3	0.2	0.2	0.3	0.2
			(63,825)	(70,284)	(77,193)	(85,253)	(126,997)	(143,813)	(149,546)	(154,879)	(155,242)
MEPM*	16	4	-	-	0.2	0.6	0.6	0.5	0.4	0.5	0.4
					(48,190)	(73,903)	(135,930)	(159.623)	(166,298)	(175,408)	(179,042)
AMK	64	64	0.3	0.2	0.2	0.1	0.1	0.1	0.1	0.1	0.1
			(68,995)	(76,293)	(84,916)	(95,643)	(141,710)	(159,871)	(166.081)	(174,259)	(176,609)
LVFX	8	8	2.7	2.4	2.5	2.4	2.6	2.7	2.8	3.1	3.4
			(66,466)	(74,718)	(83,063)	(92,993)	(138,428)	(156,249)	(163,688)	(172,010)	(175,799)

The unit of BP is μg/mL.

Figures in parentheses indicate the number of bacterial strains that were tested for antimicrobial susceptibility. Not under surveillance

* CLSI (2007) (M100-S17) Criteria was applied to determine the BP up to 2013. CLSI (2012) (M100-S22) Criteria was applied to determine BP after 2014.

iii. *Enterobacter* spp.

Table 3. Trends in the proportion (%) of antimicrobial -resistant *Enterobacter cloacae*

	BP (-2013)	BP (2014-)	2013	2014	2015	2016	2017	2018	2019
ABPC	32	32	80.9	79.0	80.2	79.3	79.8	81.2	81.3
			(35,849)	(39,344)	(55,960)	(61,667)	(61,970)	(64,820)	(64,723)
PIPC	128	128	20.6	20.0	19.8	20.1	20.8	21.2	21.7
			(36,988)	(39,636)	(58,039)	(63,580)	(64,217)	(66,020)	(62,798)
TAZ/	4/128	4/128	10.3	8.6	8.9	8.9	9.4	9.8	10.5
PIPC			(11,895)	(21,091)	(40,315)	(47,390)	(48,775)	(52,186)	(54,305)
CEZ*	32	8	97.2	98.2	98.3	98.3	98.3	98.3	98.2
			(37,359)	(41,422)	(58,637)	(64,634)	(64,693)	(68,017)	(68,074)
CMZ**	-	64	-	83.4	85.4	85.5	86.1	88.0	87.4
				(37,492)	(56,647)	(63,331)	(64,158)	(68,013)	(68,727)
CTX*	64	4	19.2	31.1	31.6	31.2	32.4	32.9	33.7
			(30,106)	(32,718)	(46,727)	(50,311)	(50,022)	(51,470)	(50,606)
CAZ*	32	16	20.6	24.7	25.0	24.9	25.8	26.3	26.8
			(37,202)	(41,456)	(59,533)	(65,317)	(65,027)	(68,737)	(69,265)
CFPM	32	32	4.2	4.2	4.2	4.0	4.0	3.9	4.0
			(17,900)	(29,836)	(52,218)	(58,298)	(59,398)	(64,337)	(65,211)
AZT*	32	16	16.8	23.8	24.0	23.9	24.3	24.9	26.1
			(29,460)	(33,551)	(48,570)	(52,951)	(53,374)	(55,988)	(56,211)
IPM*	16	4	0.4	1.6	1.3	1.2	1.1	1.1	1.2
			(34,403)	(37,396)	(54,926)	(60,602)	(60,689)	(63,611)	(61,918)
MEPM*	16	4	0.6	1.3	1.4	1.2	1.1	1.1	0.9
			(21,164)	(32,589)	(59,009)	(67,250)	(67,392)	(71,119)	(71,548)
AMK	64	64	0.4	0.2	0.2	0.1	0.1	0.1	0.1
			(37,947)	(42,005)	(61,086)	(67,133)	(67,125)	(70,659)	(70,392)
LVFX	8	8	4.2	3.5	3.7	3.4	3.5	3.2	3.1
			(37,274)	(40,942)	(59,393)	(65,161)	(65,690)	(69,392)	(70,034)

The unit of BP is μg/mL.

Figures in parentheses indicate the number of bacterial strains that were tested for antimicrobial susceptibility.

-: Not under surveillance

* CLSI (2007) (M100-S17) Criteria was applied to determine the BP up to 2013. CLSI (2012) (M100-S22) Criteria was applied to determine BP after 2014.

Table 4. Trends in the proportion (%) of antimicrobial -resistant *Klebsiella (Enterobacter)* aerogenes*

	BP (-2013)	BP (2014-)	2013	2014	2015	2016	2017	2018	2019
ABPC	32	32	76.5	77.1	78.9	77.9	79.1	80.3	80.5
			(17,362)	(18,385)	(26,680)	(29,228)	(30,844)	(32,746)	(33,621)
PIPC	128	128	14.5	14.5	14.2	15.8	17.1	17.4	18.9
			(18,029)	(18,550)	(27,189)	(29,852)	(31,802)	(33,048)	(32,497)
TAZ/PIPC	4/128	4/128	6.3	4.9	4.8	4.8	5.7	6.9	6.9
			(5,568)	(9,568)	(18,731)	(21,767)	(24,082)	(26,272)	(28,085)
CEZ**	32	8	90.8	94.0	93.7	94.2	94.5	95.0	94.7
			(17,945)	(19,173)	(27,526)	(30,088)	(31,800)	(33,996)	(35,183)
CMZ	64	64	-	84.8	86.8	87.1	88.0	89.1	89.5
				(17,587)	(26,739)	(29,681)	(31,915)	(34,051)	(35,408)
CTX**	64	4	5.2	28.3	30.7	31.1	32.9	33.4	34.2
			(14,452)	(15,173)	(21,985)	(23,572)	(24,195)	(25,493)	(26,271)
CAZ**	32	16	17.3	24.3	25.2	25.7	26.7	27.8	28.5
			(17,992)	(19,439)	(27,886)	(30,388)	(32,030)	(34,142)	(35,487)
CFPM	32	32	1.0	1.2	1.1	1.1	1.3	1.4	1.5
			(8,909)	(13,499)	(24,302)	(27,146)	(29.464)	(32,216)	(33,583)
AZT**	32	16	7.5	15.8	17.5	17.5	18.0	19.2	20.2
			(14,639)	(15,846)	(23,225)	(25,023)	(26,772)	(28,281)	(29,397)
IPM**	16	4	0.4	1.7	1.9	1.9	1.9	2.6	2.3
			(16,881)	(17,463)	(25,690)	(28,307)	(29,869)	(31,288)	(31,645)
MEPM**	16	4	0.2	0.9	0.8	0.8	0.8	0.8	0.8
			(10,249)	(15,003)	(27,560)	(31,311)	(33,150)	(35,448)	(36,550)
AMK	64	64	0.2	0.2	0.1	0.1	0.1	0.1	0.1
			(18,369)	(19,492)	(28,627)	(31,338)	(33,074)	(35,214)	(36,204)
LVFX	8	8	1.1	1.0	0.9	1.0	0.9	0.9	0.9
			(18,111)	(19,068)	(28,012)	(30,451)	(32,503)	(34,383)	(35,735)

The unit of BP is μg/mL.

Figures in parentheses indicate the number of bacterial strains that were tested for antimicrobial susceptibility.

-: Not under surveillance

**Enterobacter aerogenes* has been renamed *Klebsiella aerogenes* (Int. J. Syst. Evol. Microbiol. 67, 502-504, 2017).

** CLSI (2007) (M100-S17) Criteria was applied to determine the BP up to 2013. CLSI (2012) (M100-S22) Criteria was applied to determine BP after 2014.

iv. *Pseudomonas aeruginosa*

Table 5. Trends in the proportion (%) of antimicrobial-resistant *Pseudomonas aeruginosa*

	BP (-2013)	BP (2014-)	2011	2012	2013	2014	2015	2016	2017	2018	2019
PIPC	128	128	12.1	11.9	11.4	10.8	10.5	10.5	10.3	10.0	10.3
			(114,950)	(118,032)	(122,581)	(125,242)	(181,977)	(201,764)	(205,165)	(206,858)	(214,513)
TAZ/ PIPC	4/128	4/128	-	-	9.0	8.8	8.8	8.4	8.3	8.1	8.4
					(68,686)	(79,574)	(132,769)	(155,724)	(165,402)	(172,748)	(185,720)
CAZ	32	32	11.3	10.9	10.2	9.5	8.6	8.7	8.6	8.4	8.7
			(116,596)	(120,473)	(124,864)	(126,718)	(180,479)	(199,597)	(202,025)	(203,554)	(210,892)
AZT	32	32	16.3	16.7	16.5	14.5	14.0	13.8	13.7	13.1	13.3
			(96,435)	(100,964)	(105,681)	(107,167)	(146,841)	(158,737)	(162,952)	(162,365)	(167,331)
CFPM	32	32	9.7	8.9	8.0	7.5	6.6	6.5	6.3	6.0	5.9
			(91,769)	(99,730)	(106,291)	(113,268)	(166,096)	(185,283)	(191,502)	(194,385)	(200,818)
IPM*	16	8	19.8	18.5	17.1	19.9	18.8	17.9	16.9	16.2	16.2
			(112,596)	(116,193)	(119,979)	(119,323)	(168,471)	(186,380)	(188,981)	(188,778)	(195,183)
MEPM*	16	8	12.4	11.8	10.7	14.4	13.1	12.3	11.4	10.9	10.6
			(109,453)	(113,996)	(119,330)	123,976)	(180,850)	(201,991)	(206,368)	(209,149)	(217,161)
GM	16	16	7.0	6.1	5.3	5.1	4.5	4.1	3.3	2.9	3.1
			(111,137)	(115,612)	(118,592)	(117,421)	(165,777)	(182,343)	(184,453)	(184,135)	(190,296)
AMK	64	64	3.1	2.6	2.1	1.9	1.5	1.3	1.1	0.9	0.9
			(116,876)	(121,289)	(126,023)	(128,923)	(185,327)	(204,892)	(208,098)	(209,413)	(217,512)
LVFX	8	8	16.8	16.3	14.5	13.0	12.0	11.6	10.8	10.2	9.8
			(111,005)	(115,478)	(119,162)	(120,691)	(174,301)	(193,366)	(197,890)	(199,760)	(207,963)

The unit of BP is μg/mL.

Figures in parentheses indicate the number of bacterial strains that were tested for antimicrobial susceptibility.

-: Not under surveillance

* CLSI (2007) (M100-S17) Criteria was applied to determine the BP up to 2013. CLSI (2012) (M100-S22) Criteria was applied to determine BP after 2014.

v. *Acintobacter* spp.

Table 6. Trends in the proportion (%) of antimicrobial-resistant *Acinetobacter* spp.

	BP	2011	2012	2013	2014	2015	2016	2017	2018	2019
PIPC	128	13.2	13.2	12.9	12.4	11.5	10.9	10.9	10.3	10.7
		(19,125)	(19,433)	(20,183)	(20,223)	(27,887)	(29,776)	(27,468)	(27,905)	(26,237)
TAZ/	4/128	-	-	7.8	7.8	8.1	8.6	9.0	9.4	9.0
PIPC				(4,953)	(5,215)	(9,058)	(10,551)	(10,983)	(12,171)	(12,401)
SBT/	16/32	6.5	7.2	5.8	5.2	4.8	5,4	4.7	4.4	4.3
ABPC		(2,942)	(3,601)	(4,498)	(6,462)	(11,356)	(12,831)	(12,241)	(13,111)	(12,769)
CAZ	32	10.3	10.6	10.0	9.3	8.0	7.6	7.9	7.6	8.6
		(19,672)	(20,067)	(20,856)	(20,852)	(28,166)	(29,844)	(27,308)	(28,077)	(26,614)
CFPM	32	10.4	10.5	9.2	7.6	7.2	7.4	7.6	6.8	6.8
		(13,013)	(14,093)	(15,394)	(17,424)	(25,412)	(27,386)	(25,631)	(26,616)	(25,224)
IPM	16	2.2	2.0	2.3	3.6	3.2	3.1	2.5	2.0	1.8
		(18,048)	(18,238)	(16,947)	(11,147)	(13,942)	(15,147)	(14,383)	(16,995)	(19,645)
MEPM	16	2.9	2.4	2.3	2.0	1.8	1.9	1.3	1.5	1.4
		(15,485)	(15,880)	(17,027)	(18,859)	(28,227)	(30,489)	(28,064)	(29,024)	(27,418)
GM	16	9.6	10.2	9.5	8.9	8.5	8.5	8.2	7.8	8.0
		(18,276)	(18,842)	(19,422)	(18,832)	(25,689)	(27,313)	(24,887)	(25,465)	(23,925)
AMK	64	4.5	4.5	3.5	3.6	3.1	2.3	2.3	2.0	2.1
		(19,348)	(19,793)	(20,863)	(20,851)	(28,568)	(30,279)	(27,835)	(28,437)	(26,917)
LVFX	8	9.5	9.8	8.3	8.5	7.7	8.2	8.0	7.0	7.5
		(18,732)	(19,484)	(20,040)	(20,047)	(27,858)	(29,702)	(27,360)	(28,209)	(26,898)

The unit of BP is μg/mL.
Figures in parentheses indicate the number of bacterial strains that were tested for antimicrobial susceptibility.
-: Not under surveillance

2) Gram-positive bacteria

Source: JANIS

Looking at the recent status of gram-positive bacteria, methicillin-resistant *Staphylococcus aureus* (MRSA) accounted for approximately 50% of all *Staphylococcus aureus*. Although the proportion has been declining over the past few years, it remains higher than that seen in other countries. The proportion is higher among medical institutions with fewer than 200 beds than among those with 200 or more (Table 10). In the case of enterococci, rising vancomycin (VCM) resistance is a problem in many countries, but as shown in Tables 11 and 12, levels in Japan are comparatively low, at less than 0.05% in the case of *Enterococcus faecalis* and 1.5% among *Enterococcus faecium*. However, in 2019, the VCM resistance rate among *E. faecium* rose and widespread nosocomial outbreaks of VCM-resistant *E. faecium* have been observed in some regions. Regional changes in resistance rates will need to be kept under close observation. The proportion of penicillin-resistant *Streptococcus pneumoniae* (PRSP) accounted for approximately 40% of all detected pneumococcus in cerebrospinal fluid (CSF) samples, though the figure varies from year to year, because only around 100 CSF samples are tested (Table 13). The proportion of PRSP was low for non-CSF samples at below 1% (Table 14), and below 5% even adding penicillin intermediate resistant bacteria.

i. *Staphylococcus aureus*

Table 7. The proportion (%) of antimicrobial resistance in *Staphylococcus aureus* strains

	BP	2018	2019
PCG	0.25	75.4 (287,805)	75.1 (295,031)
MPIPC	4	47.8 (266,047)	47.7 (265,763)
CFX	8	46.1 (57,604)	46.0 (64,239)
CEZ	32	20.7 (360,772)	19.7 (366,803)
GM	16	30.4 (345,964)	28.9 (350,425)
EM	8	51.7 (325,918)	51.2 (329,090)
CLDM	4	22.0 (340,953)	20.4 (350,136)
MINO	16	12.2 (377,507)	10.5 (385,264)
VCM	16	0.0 (374,982)	0.0 (382,254)
TEIC	32	<0.05 (336,502)	＜0.05 (340,855)
LVFX	4	50.4 (358,941)	51.7 (368,676)
LZD	8	<0.05 (286,366)	＜0.05 (294,735)
DAP	2	0.3 (72,401)	0.3 (98,366)

The unit of BP is μg/mL.

Figures in parentheses indicate the number of bacterial strains that were tested for antimicrobial susceptibility.

*Data collection began in 2018.

-: Not under surveillance

Table 8. The propotion (%) of antimicrobial resistance in methicillin-susceptible *Staphylococcus aureus* (MSSA)

	BP	2011	2012	2013	2014	2015	2016	2017	2018	2019
PCG	0.25	61.1 (68,839)	60.1 (75,025)	59.0 (82,477)	57.7 (86,314)	56.2 (119,343)	55.0 (126,394)	53.9 (129,943)	52.9 (135,360)	52.1 (138,818)
CEZ	32	0.3 (77,483)	<0.05 (84,520)	0.2 (93,945)	0.2 (103,603)	0.1 (146,254)	<0.05 (157,917)	<0.05 (161,831)	<0.05 (164,909)	＜0.05 (167,084)
CVA/ AMPC	4/8	0.3 (11,696)	0.1 (9,466)	0.2 (11,230)	0.2 (11,666)	0.1 (19,163)	0.1 (21,783)	0.1 (24,713)	0.1 (26,376)	0.1 (25,258)
IPM	16	0.3 (74,636)	<0.05 (80,472)	0.2 (88,422)	0.2 (95,951)	<0.05 (136,878)	<0.05 (146,433)	<0.05 (149,014)	<0.05 (149,454)	＜0.05 (150,811)
EM	8	22.7 (72,738)	23.4 (79,683)	24.0 (88,528)	23.8 (96,829)	22.9 (136,763)	23.3 (146,280)	23.5 (148,795)	23.1 (150,809)	22.7 (151,577)
CLDM	4	3.4 (67,523)	3.1 (74,387)	3.2 (83,914)	2.8 (93,467)	2.8 (136,292)	2.9 (148,439)	2.9 (151,841)	2.7 (155,141)	2.9 (157,700)
MINO	16	0.7 (77,872)	0.6 (84,595)	0.5 (94,425)	0.6 (104,145)	0.6 (151,493)	0.5 (163,214)	0.6 (167,178)	0.6 (169,953)	0.5 (171,857)
LVFX	4	9.3 (73,163)	10.2 (79,857)	10.6 (89,641)	10.7 (99,898)	11.6 (144,083)	12.3 (154,868)	13.1 (159,066)	13.8 (161,691)	14.7 (164,665)

The unit of BP is μg/mL.

Figures in parentheses indicate the number of bacterial strains that were tested for antimicrobial susceptibility.

Table 9. The propotion (%) of antimicrobial resistance in methicillin-resistant *Staphylococcus aureus* (MRSA)

	BP (2014-)	2011	2012	2013	2014	2015	2016	2017	2018	2019
EM	8	91.3 (105,936)	90.6 (109,521)	88.4 (108,607)	86.0 (107,836)	84.1 (149,851)	83.8 (155,587)	82.9 (157,708)	81.7 (159,215)	80.7 (161,613)
CLDM	4	76.8 (102,895)	73.5 (106,124)	67.3 (105,503)	60.3 (106,910)	56.0 (153,329)	51.6 (160,500)	46.3 (164,301)	41.7 (169,049)	37.9 (175,081)
MINO	16	48.2 (117,325)	43.7 (120,321)	37.1 (120,300)	35.1 (121,258)	31.7 (173,983)	29.1 (182,306)	27.1 (185,770)	23.7 (189,813)	20.1 (195,422)
VCM	16	0.0 (115,679)	0.0 (119,111)	0.0 (119,441)	0.0 (120,535)	0.0 (172,083)	0.0 (181,288)	0.0 (185,948)	0.0 (189,853)	0.0 (195,332)
TEIC	32	<0.05 (110,380)	<0.05 (113,887)	<0.05 (113,684)	<0.05 (113,749)	<0.05 (158,233)	<0.05 (165,213)	<0.05 (167,342)	<0.05 (169,651)	<0.05 (173,090)
LVFX	4	89.0 (111,598)	88.3 (114,381)	86.8 (114,551)	85.4 (115,586)	85.2 (164,734)	85.8 (172,494)	86.5 (176,790)	86.8 (179,731)	87.8 (186,442)
LZD*	8	0.1 (76,632)	<0.05 (84,550)	<0.05 (85,223)	<0.05 (88,255)	0.1 (127,278)	<0.05 (136,468)	<0.05 (139,785)	<0.05 (144,332)	<0.05 (149,340)
DAP	2	-	-	-	1.1 (3,078)	0.9 (16,648)	0,8 (23,217)	0.7 (26,874)	0.5 (35,618)	0.4 (47,835)

The unit of BP is μg/mL.

Figures in parentheses indicate the number of bacterial strains that were tested for antimicrobial susceptibility.

-: Not under surveillance

As of 2019, no vancomycin-resistant *staphylococcus aureus* strains had been reported.

* CLSI (2007) (M100-S17) Criteria was applied to determine the BP up to 2013. CLSI (2012) (M100-S22) Criteria was applied to determine BP after 2014.

Table 10. The proportion of (%) of patients with MRSA among all patients with *Staphylococcus aureus* (*S. aureus*)

Table 10-1. All participating medical institutions

	2011	2012	2013	2014	2015	2016	2017	2018	2019
Number of participating medical institutions	594	660	745	883	1435	1653	1795	1947	2075
The number of patients with MRSA	114,933	117,209	118,539	120,702	169,528	177,768	182,619	185,709	192,320
The number of patients with *S. aureus*	210,382	221,239	231,909	246,030	349,743	372,787	383,006	391,316	400,094
The proportion of MRSA (%)*	54.6	53.0	51.1	49.1	48.5	47.7	47.7	47.5	48.1

Table 10-2. Participating medical institutions with 200 or more beds

	2011	2012	2013	2014	2015	2016	2017	2018	2019
Number of participating medical institutions	-	-	-	791	1177	1269	1312	1334	1357
The number of patients with MRSA	-	-	-	115,757	157,419	160,060	160,714	159,054	161,159
The number of patients with *S. aureus*	-	-	-	237,343	328,540	341,822	344,543	344,156	345,447
The proportion of MRSA (%)*	-	-	-	48.8	47.9	46.8	46.6	46.2	46.7

Table 10-3. Participating medical institutions with fewer than 200 beds

	2011	2012	2013	2014	2015	2016	2017	2018	2019
Number of participating medical institutions	-	-	-	92	258	384	483	613	718
The number of patients with MRSA	-	-	-	4,945	12,109	17,708	21,905	26,655	31,161
The number of patients with *S. aureus*	-	-	-	8,687	21,203	30,965	38,463	47,160	54,647
The proportion of MRSA (%)*	-	-	-	56.9	57.1	57.2	57.0	56.5	57.0

Those detected in selective media were also included.

* The number of patients with MRSA / The number of patients with *S. aureus*

-: Not under surveillance

ii. *Enterococcus* spp.

Table 11. Trends in the proportion (%) of antimicrobial-resistant *Enterococcus faecalis*

	BP	2011	2012	2013	2014	2015	2016	2017	2018	2019
PCG	16	2.2	2.1	1.8	1.6	1.4	1.1	1.0	0.9	0.9
		(53,290)	(60,342)	(65,220)	(67,324)	(92,132)	(98,465)	(98,478)	(104,023)	(107,021)
ABPC	16	0.4	0.4	0.3	0.3	0.3	0.2	0.2	0.2	0.2
		(60,686)	(68,440)	(72,587)	(77,997)	(107,733)	(115,548)	(116,493)	(119,014)	(121,530)
EM	8	57.8	58.0	57.1	55.5	54.8	54.3	53.8	52.7	51.7
		(53,222)	(60,825)	(64,465)	(69,171)	(95,409)	(101,036)	(101,379)	(102,496)	(102,871)
MINO	16	47.8	47.7	47.7	52.1	49.7	48.9	50.3	50.9	47.2
		(61,549)	(69,421)	(74,880)	(81,925)	(115,648)	(123,860)	(125,728)	(128,160)	(130,729)
VCM	32	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05
		(61,747)	(69,719)	(75,162)	(81,867)	(115,100)	(124,305)	(126,510)	(129,545)	(132,526)
TEIC	32	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05
		(56,591)	(63,747)	(69,500)	(76,160)	(105,403)	(112,636)	(113,501)	(115,397)	(117,097)
LVFX	8	19.3	18.0	15.5	13.7	12.5	11.9	11.2	10.4	10.1
		(58,877)	(65,934)	(70,895)	(77,563)	(109,160)	(117,297)	(120,136)	(122,551)	(125,836)

The unit of BP is μg/mL.

Figures in parentheses indicate the number of bacterial strains that were tested for antimicrobial susceptibility.

Table 12. Trends in the proportion (%) of antimicrobial-resistant *Enterococcus faecium*

	BP	2011	2012	2013	2014	2015	2016	2017	2018	2019
PCG	16	86.9	87.4	87.7	86.9	87.6	88.2	87.8	87.5	87.4
		(17,642)	(21,139)	(23,466)	(24,534)	(34,752)	(38,060)	(39,478)	(42,178)	(46,021)
ABPC	16	86.0	86.2	86.9	86.9	87.6	88.0	87.9	87.6	88.0
		(19,780)	(23,885)	(26,199)	(28,564)	(41,459)	(45,069)	(47,046)	(49,207)	(52,929)
EM	8	87.2	88.1	85.9	84.5	84.5	84.0	83.1	83.0	83.1
		(17,668)	(21,498)	(23,594)	(25,922)	(37,536)	(40,509)	(42,259)	(43,555)	(45,992)
MINO	16	26.9	28.8	29.3	32.2	35.1	34.7	36.2	38.3	33.0
		(21,877)	(25,961)	(28,387)	(31,550)	(46,351)	(50,325)	(52,494)	(54,540)	(58,314)
VCM	32	1.0	0.4	0.7	0.7	0.7	0.9	0.8	0.9	1.5
		(21,782)	(25,787)	(28,334)	(30,996)	(45,514)	(49,618)	(52,127)	(54,279)	(58,377)
TEIC	32	0.4	0.3	0.2	0.2	0.3	0.6	0.4	0.6	1.0
		(20,163)	(23,855)	(26,282)	(29,151)	(41,905)	(45,388)	(47,321)	(48,991)	(52,502)
LVFX	8	82.9	83.4	84.5	84.7	85.8	86.6	86.5	86.7	87.6
		(19,417)	(23,032)	(25,629)	(28,448)	(42,068)	(45,834)	(48.995)	(51,003)	(55,293)
LZD	8	0.0	0.1	<0.05	0.1	0.1	0.1	<0.05	0.1	0.1
		(12,877)	(16,296)	(18,561)	(22,044)	(33,382)	(37,099)	(39,584)	(41.596)	(44,887)

The unit of BP is μg/mL.

Figures in parentheses indicate the number of bacterial strains that were tested for antimicrobial susceptibility.

iii. *Streptococcus pneumoniae*

Table 13. Trends in the proportion (%) of antimicrobial-resistant *Streptococcus pneumoniae* (CSF specimens)

	BP	2012	2013	2014	2015	2016	2017	2018	2019
PCG	0.125	38.6	47.4	47.0	40.5	36.4	29.1	38.3	32.0
		(101)	(97)	(83)	(126)	(140)	(117)	(94)	(100)
CTX	2	3.7	1.2	2.9	2.0	1.0	2.1	4.5	1.2
		(82)	(84)	(69)	(100)	(105)	(97)	(88)	(85)
MEPM	1	4.2	2.2	1.2	4.2	0.7	5.0	2.1	1.0
		(95)	(92)	(83)	(119)	(134)	(120)	(95)	(99)
EM	1	82.5	82.7	92.5	84.9	75.5	82.4	75.0	84.8
		(80)	(81)	(67)	(86)	(98)	(91)	(76)	(79)
CLDM	1	53.8	68.7	65.1	62.7	61.2	49.5	43.7	64.0
		(65)	(67)	(63)	83)	(98)	(91)	(71)	(75)
LVFX	8	0.0	0.0	1.3	0.0	0.0	0.9	2.3	0.0
		(88)	(91)	(76)	(105)	(123)	(111)	(88)	(93)
VCM	2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		(91)	(90)	(82)	(119)	(134)	(116)	(98)	(96)

The unit of BP is μg/mL.

Figures in parentheses indicate the number of bacterial strains that were tested for antimicrobial susceptibility.

CLSI (2012) (M100-S22) Criteria was applied to determine BP.

Table 14. Trends in the proportion (%) of antimicrobial-resistant *Streptococcus pneumoniae* (non-CSF specimens)

	BP	2012	2013	2014	2015	2016	2017	2018	2019
PCG*	4	3.2	2.7	2.5	2.7	2.1	2.1	2.2	2.2
		(24,980)	(26,932)	(27,206)	(36,475)	(35,960)	(34,415)	(33,483)	(31,506)
CTX	4	2.4	2.0	1.8	1.6	1.4	1.6	1.4	1.4
		(21,654)	(23,096)	(23,002)	(30,734)	(29,405)	(27,773)	(27,004)	(26,040)
MEPM	1	6.9	5.1	5.4	5.0	5.7	6.0	6.3	6.4
		(22,989)	(24,986)	(25,760)	(34,461)	(34,885)	(34,011)	(33,115)	(31,489)
EM	1	87.0	86.2	86.7	85.5	84.4	82.4	81.3	81.5
		(21,979)	(22,435)	(22,215)	(30,501)	(30,144)	(28,097)	(27,154)	(26,270)
CLDM	1	56.4	56.1	57.1	56.1	54.1	50.5	49.9	50.9
		(17,513)	(19,719)	(20,296)	(27,555)	(28,541)	(27,536)	(26,459)	(25,404)
LVFX	8	3.0	3.1	3.3	3.5	4.1	4.3	4.4	4.7
		(24,105)	(25,764)	(26,236)	(35,457)	(35,431)	(34,241)	(33,551)	(32,057)
VCM	2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		(24,085)	(25,425)	(25,775)	(33,530)	(33,670)	(32,681)	(31,741)	(30,250)

The unit of BP is μg/mL.

Figures in parentheses indicate the number of bacterial strains that were tested for antimicrobial susceptibility.

* Each figure for PCG represents the sum of resistance (R: 8 μg/mL) and intermediate resistance (I: 4 μg/mL).

CLSI (2012) (M100-S22) Criteria was applied to determine BP.

3) Antimicrobial-resistant bacteria infection

Source: National Epidemiological Surveillance of Infectious Disease (NESID)

The numbers of cases reported under NESID each year through 2018 are publicized as confirmed reported data. Cases reported since 2013 are listed below. The scope of reporting is limited to cases where the isolated bacteria is regarded as the cause of an infectious disease, or cases where it was detected from specimens that normally should be aseptic. Colonization is excluded from the scope of reporting.

Among notifiable diseases (diseases that must be reported to the authorities in all cases), there have been around 80 reports of vancomycin-resistant enterococcal (VRE) infection per year since 2017, representing a slight rise from the trend of 50 to 60 reports per year between 2013 and 2016. No case of vancomycin-resistant *Staphylococcus aureus* (VRSA) infection has been reported since November 5, 2003, when this disease became notifiable. Carbapenem-resistant *Enterobacteriaceae* (CRE) infection became a notifiable disease on September 19, 2014, and an all-time high of 2,289 cases were reported in 2018. Surveillance for multidrug-resistant *Acinetobacter* (MDRA) infection was started in February 2011, with reporting of cases limited at first to designated sentinel sites. It subsequently became a notifiable disease on September 19, 2014, and reports ranged between 20 and 40 cases per year thereafter, with 24 cases reported in 2018.

Under a March 2017 notification issued by the Director of the Tuberculosis and Infectious Diseases Control Division, Health Service Bureau, MHLW, local public health institutes and other organizations are required to use the PCR method to test strains isolated from notified cases of CRE infection for carbapenemase genes and other information. In 2018, results for 1,684 strains thought to be cases notified via the surveillance program were reported. A carbapenemase gene of some kind was detected in 297 strains (17.6%), with IMP variants—the most prevalent carbapenemase genes in Japan—accounting for the majority (254 strains (85.5%)).

Looking at antimicrobial-resistant infections notified by Japan's approximately 500 designated sentinel sites (medical institutions that have 300 or more beds), both the number of reports of MRSA infections and the number of reports per site had been trending downward since 2011. However, this fall bottomed out in 2016 and 16,311 cases of MRSA infection were reported in 2018. Both the total number of reports of penicillin-resistant *Streptococcus pneumoniae* infection (PRSP) and multidrug-resistant *Pseudomonas aeruginosa* infection (MDRP) and the number of reports per site are continuing to trend downward.

i. Diseases subject to notifiable disease surveillance

Table 15. Number of cases reported for diseases subject to notifiable disease surveillance (2013-2018)

	2013	2014	2015	2016	2017	2018
VRE	55	56	66	61	83	80
VRSA	0	0	0	0	0	0
CRE	-	314*	1,673	1,573	1,660	2,289
MDRA	-	15*	38	33	28	24

* Reportable since September 19, 2014.

-: Not under surveillance

ii. Diseases reportable from designated sentinel sites

Table 16. Number of cases reported for diseases reportable from designated sentinel sites (2013-2018)

		2013	2014	2015	2016	2017	2018
PRSP	Cases	3,161	2,292	2,057	2,017	2,001	1,895
	Cases per sentinel site	6.65	4.79	4.29	4.21	4.18	3.94
MRSA	Cases	20,155	18,082	17,057	16,338	16,551	16,311
	Cases per sentinel site	42.43	37.83	35.61	34.11	34.55	33.91
MDRA*	Cases	8	4	-	-	-	-
	Cases per sentinel site	0.02	0.01	-	-	-	-
MDRP	Cases	319	268	217	157	128	121
	Cases per sentinel site	0.67	0.56	0.45	0.33	0.27	0.25

* MDRA became reportable under notifiable disease surveillance on September 19, 2014.

-: Not under surveillance

4) Other antimicrobial-resistant bacteria

i. *Campylobacter* spp.

Source: Tokyo Metropolitan Institute of Public Health

Tokyo Metropolitan Institute of Public Health has conducted trend surveillance concerning the proportion of antimicrobial-resistant *Campylobacter* spp. Among the 119 outbreaks of food-borne illness that occurred in Tokyo in 2019, 36 outbreaks (30.3%) were caused by *Campylobacter* spp., being the largest cause of bacterial food-borne illness.[1] Among the *Campylobacter jejuni* (*C. jejuni*) isolated from patients with diarrhea in 2018, the proportion of ciprofloxacin (CPFX)-resistant strains was 51.8%, higher than 2017. The proportion of CPFX-resistant *Campylobacter coli* (*C. coli*) strains was 37.5%, which was lower than the previous year. Note that, however, the number of tested strains was smaller for *C. coli* and this should be taken into consideration upon interpretation of the result.

Table 17. The proportion (%) of antimicrobial-resistant *Campylobacter jejuni isolated from diarrhea cases**

(Number of samples)	2011 (108)	2012 (83)	2013 (85)	2014 (125)	2015 (116)	2016 (113)	2017 (115)	2018 (110)
EM	3.7	2.4	1.2	0.8	0.9	0.9	1.7	1.8
NA	53.7	62.7	50.6	50.4	37.1	53.1	46.1	51.7
CPFX	53.7	62.7	50.6	50.4	37.1	52.2	43.5	51.8

* Strains isolated from diarrhea cases in Tokyo

Prepared from [5] with partial modification.

Table 18. The proportion (%) of antimicrobial-resistant *Campylobacter coli isolated from diarrhea cases**

(Number of samples)	2011 (8)	2012 (9)	2013 (12)	2014 (7)	2015 (8)	2016 (14)	2017 (8)	2018 (8)
EM	12.5	22.2	16.7	28.6	0.0	14.3	25.0	62.5
NA	87.5	66.7	75.0	57.1	50.0	50.0	62.5	50
CPFX	87.5	66.7	75.0	57.1	50.0	35.7	62.5	37.5

* Strains isolated from diarrhea cases in Tokyo

Prepared from [5] with partial modification.

ii. Non-typhoidal *Salmonella* spp.

Source: Public Health Institutes

The 21 Public Health Institutes across Japan conducted research on the multidrug-resistant status of the 2,338 *Salmonella* strains that were isolated between 2015 and 2019, using standardized methodology.[2] Table 19 lists the key serotypes of human-derived strains and food-derived strains.

In total, 39.8% of the 1,755 human-derived strains and 91.7% of the 586 food-derived strains indicated resistance to one or more antimicrobials (Tables 20 and 21). Although this investigation was not conducted as a routine national surveillance operation, the results here are considered to reflect the current status in Japan, given that the investigation covered all regions of Japan and the proportion of resistant strains isolated between 2015 and 2019 was similar. Table 20 appears to show that rates of resistance to cephalosporins (CTX, CAZ, CFX) rose in strains isolated between 2017 and 2019, but the same trend was seen in 2015 and 2016 when the focus was limited to domestic chicken meat (figures in parentheses), suggesting that the strains isolated between 2017 and 2019 contained a high proportion of strains from foreign chicken meat. As for multidrug resistance, the proportion of three-drug resistance was large both among human-derived strains and among food-derived strains. Thirty-three among human-derived strains, and 50 among food-derived strains, indicated multidrug resistance to as many as six to 11 drugs.

Tables 22 and 23 show antimicrobial resistance in the top two serotypes of food-derived strains (*S.* Infantis and *S.* Schwarzengrund), while Tables 24 to 28 show antimicrobial resistance in the top five serotypes of human-derived strains (*S.* Infantis, *S.* Enteritidis, *S.* Thompson, *S.* 4:i:-, and *S.* Saintpaul). Among food-derived strains, trends in resistance by serotype have many aspects in common, but distinctive features were observed in serotype-specific resistance trends among human-derived strains.

In a comparison of antimicrobial resistance rates between human- and food-derived strains for the three serotypes (*S.* Schwarzengrund, *S.* Infantis, and *S.* Manhattan) appearing in both the top five serotypes among food-derived strains and the top 10 serotypes among human-derived strains (Table 29), clear similarities were observed in the overall trends in resistance rates for each serotype between human-derived strains and food-derived strains, suggesting a strong association between food-derived and human-derived antimicrobial-resistant bacteria.

In addition to antimicrobial susceptibility tests, strains isolated between 2015 and 2018 that demonstrated resistance to one or more of the agents CTX, CAZ, and CFX (26 human-derived strains and 31 food-derived strains) underwent testing to detect extended-spectrum beta-lactamase (ESBL) and AmpC beta-lactamase (AmpC)

producing genes. The CTX-M-1 group was the most common genotype among the ESBL producing genes in human-derived and food-derived strains alike, followed by TEM. CIT was the most common genotype among the AmpC producing genes in human-derived and food-derived strains alike, followed by TEM. These results showed similarities in trends toward the detection of ESBL and AmpC genes in both human-derived and food-derived strains.

Table 19. Serotypes of human- and food-derived non-typhoidal *Salmonella* spp. (2015-2019)

Human-derived strains (n=1,755)	%	Food-derived strains (n=586)	%
4:i:-	12.1	Schwarzengrund	42.0
Enteritidis	11.7	Infantis	28.6
Infantis	9.6	Manhattan	9.7
Thompson	7.5	Agona	2.9
Saintpaul	6.4	Typhimurium	2.6
Typhimurium	5.9	Others	14.2
Schwarzengrund	4.7	Total	100.0
Newport	3.0		
Stanley	2.8		
Manhattan	2.3		
Others	34.0		
Total	100.0		

Table 20. The proportion of antimicrobial-resistant human-derived non-typhoidal *Salmonella* spp. (2015-2019)

	2015 (n=388)	2016 (n=362)	2017 (n=420)	2018 (n=317)	2019 (n=268)	2015-2019 (n=1,755)
ABPC	17.3	18.0	15.5	19.2	14.9	17.0
GM	0.3	0.6	0.7	0.6	1.5	0.7
KM	5.9	11.6	7.1	8.2	5.6	7.7
SM	27.1	29.8	26.0	29.0	23.1	27.1
TC	32.5	28.7	26.4	25.2	21.6	27.3
ST	4.4	6.6	7.9	6.3	3.7	5.9
CP	2.3	6.4	5.2	6.0	5.6	5.0
CTX	0.3	2.8	3.1	3.2	1.9	2.2
CAZ	0.3	2.2	1.7	1.9	1.1	1.4
CFX	0.0	1.4	0.5	0.6	0.0	0.5
FOM	0.0	0.3	0.5	0.3	0.4	0.3
NA	7.0	8.0	10.0	6.0	5.2	7.5
CPFX	0.3	0.8	1.4	0.3	1.5	0.9
NFLX	0.3	0.8	0.5	0.0	0.7	0.5
AMK	0.0	0.0	0.0	0.0	0.0	0.0
IPM	0.0	0.0	0.0	0.0	0.0	0.0
MEPM	0.0	0.0	0.0	0.0	0.0	0.0
Number resistant to one or more antimicrobials	163	162	158	126	90	699
Proportion resistant to one or more antimicrobials	42.0	44.8	37.6	39.7	33.6	39.8

Table 21. The proportion (%) of antimicrobial-resistant food-derived non-typhoidal *Salmonella* spp.* (2015-2019)

	2015 (n=156)	2016 (n=110)	2017 (n=86)	2018 (n=108)	2019 (n=126)	2015-2019 (n=586)
ABPC	17.9	13.6	11.6	12	11.1	13.7
GM	0.0	0.9	1.2	0.0	0.0	0.3
KM	47.4	47.3	45.3	50	57.1	49.7
SM	82.7	70.9	69.8	77.8	64.3	73.7
TC	85.9	76.4	73.3	78.7	70.6	77.6
ST	19.9	16.4	12.8	38	25.4	22.7
CP	7.1	10.0	2.3	8.3	4	6.5
CTX	5.1 (5.6)	5.5(6.3)	8.1(2.6)	6.5(5.6)	6.3(3.8)	6.1(4.9)
CAZ	4.5 (4.9)	6.4(7.4)	8.1(2.6)	6.5(5.6)	4.8(1.9)	5.8(4.5)
CFX	2.6 (2.8)	3.6(4.2)	8.1(2.6)	4.6(3.3)	5.6(2.9)	4.6(3.1)
FOM	0.0	0.9	1.2	0	0	0.3
NA	18.6	18.2	14.0	16.7	27	19.3
CPFX	0.0	0.9	1.2	0.0	0.0	0.3
NFLX	0.0	0.0	0.0	0.0	0.0	0.0
AMK	0.0	0.0	0.0	0.0	0.0	0.0
IPM	0.0	0.0	0.0	0.0	0.0	0.0
MEPM	0.0	0.0	0.0	0	0	0
Number resistant to one or more antimicrobials	143	96	77	98	113	527
Proportion resistant to one or more antimicrobials	91.7	87.3	89.5	90.7	89.7	91.7

Figures in parentheses indicate resistance rate in strains isolated from domestic chicken meat.

Table 22. The proportion (%) of antimicrobial-resistant food-derived *S.* Infantis (2015-2019)

	2015 (n=65)	2016 (n=33)	2017 (n=19)	2018 (n=27)	2019 (n=24)	2015-2019 (n=168)
ABPC	10.8	12.1	5.3	14.8	8.3	10.7
GM	0.0	3.0	0.0	0.0	0.0	0.6
KM	44.6	42.4	15.8	33.3	37.5	38.1
SM	81.5	72.7	68.4	85.2	58.3	75.6
TC	89.2	81.8	68.4	85.2	58.3	80.4
ST	18.5	30.3	0.0	44.4	12.5	22.0
CP	3.1	3.0	0.0	0.0	0.0	1.8
CTX	4.6	6.1	5.3	11.1	8.3	6.5
CAZ	3.1	9.1	5.3	11.1	0.0	5.4
CFX	4.6	9.1	5.3	14.8	8.3	7.7
FOM	0.0	0.0	0.0	0.0	0.0	0.0
NA	3.1	9.1	0.0	3.7	16.7	6.0
CPFX	0.0	0.0	0.0	0.0	0.0	0.0
NFLX	0.0	0.0	0.0	0.0	0.0	0.0
AMK	0.0	0.0	0.0	0.0	0.0	0.0
IPM	0.0	0.0	0.0	0.0	0.0	0.0
MEPM	0.0	0.0	0.0	0.0	0.0	0.0

Table 23. The proportion (%) of antimicrobial-resistant food-derived *S.* Schwarzengrund (2015-2019)

	2015 (n=47)	2016 (n=37)	2017 (n=45)	2018 (n=51)	2019 (n=66)	2015-2019 (n=246)
ABPC	17.0	5.6	0.0	7.8	3.0	6.5
GM	0.0	0.0	0.0	0.0	0.0	0.0
KM	85.1	88.9	77.8	80.4	92.4	85.0
SM	93.6	80.6	82.2	76.5	74.2	80.5
TC	95.7	86.1	80.0	86.3	80.3	85.4
ST	36.2	16.7	24.4	56.9	43.9	37.4
CP	19.1	11.1	4.4	9.8	6.1	9.8
CTX	0.0	0.0	2.2	0.0	0.0	0.4
CAZ	0.0	0.0	2.2	0.0	0.0	0.4
CFX	0.0	0.0	2.2	0.0	0.0	0.4
FOM	0.0	0.0	2.2	0.0	0.0	0.4
NA	25.5	19.4	6.7	23.5	27.3	21.1
CPFX	0.0	0.0	0.0	0.0	0.0	0.0
NFLX	0.0	0.0	0.0	0.0	0.0	0.0
AMK	0.0	0.0	0.0	0.0	0.0	0.0
IPM	0.0	0.0	0.0	0.0	0.0	0.0
MEPM	0.0	0.0	0.0	0.0	0.0	0.0

Table 24. The proportion (%) of antimicrobial-resistant human-derived *S.* Infantis (2015-2019)

	2015 (n=34)	2016 (n=48)	2017 (n=48)	2018 (n=22)	2019 (n=16)	2015-2019 (n=168)
ABPC	0.0	2.1	0.0	9.1	6.3	2.4
GM	0.0	0.0	0.0	0.0	0.0	0.0
KM	20.6	14.6	6.3	22.7	12.5	14.3
SM	29.4	33.3	20.8	50.0	31.3	31.0
TC	47.1	33.3	22.9	54.5	37.5	36.3
ST	14.7	14.6	2.1	18.2	0.0	10.1
CP	0.0	0.0	0.0	9.1	6.3	1.8
CTX	0.0	0.0	0.0	4.5	6.3	1.2
CAZ	0.0	0.0	0.0	0.0	0.0	0.0
CFX	0.0	2.1	0.0	0.0	0.0	0.6
FOM	0.0	0.0	0.0	0.0	6.3	0.6
NA	8.8	4.2	8.3	0.0	12.5	6.5
CPFX	0.0	0.0	0.0	0.0	0.0	0.0
NFLX	0.0	0.0	0.0	0.0	0.0	0.0
AMK	0.0	0.0	0.0	0.0	0.0	0.0
IPM	0.0	0.0	0.0	0.0	0.0	0.0
MEPM	0.0	0.0	0.0	0.0	0.0	0.0

Table 25. The proportion (%) of antimicrobial-resistant human-derived *S.* Enteritidis (2015-2019)

	2015 (n=39)	2016 (n=41)	2017 (n=50)	2018 (n=43)	2019 (n=38)	2015-2019 (n=211)
ABPC	5.1	19.5	6.0	7.0	5.3	8.5
GM	0.0	0.0	0.0	0.0	0.0	0.0
KM	2.6	2.4	0.0	0.0	0.0	0.9
SM	12.8	12.2	14.0	14.0	5.3	11.8
TC	10.3	2.4	6.0	9.3	5.3	6.6
ST	5.1	0.0	0.0	0.0	0.0	0.9
CP	2.6	0.0	0.0	0.0	0.0	0.5
CTX	0.0	2.4	0.0	0.0	0.0	0.5
CAZ	0.0	2.4	0.0	0.0	0.0	0.5
CFX	0.0	0.0	0.0	0.0	0.0	0.0
FOM	0.0	0.0	0.0	2.3	0.0	0.5
NA	10.3	26.8	14.0	25.6	10.5	17.5
CPFX	0.0	0.0	0.0	0.0	0.0	0.0
NFLX	0.0	0.0	0.0	0.0	0.0	0.0
AMK	0.0	0.0	0.0	0.0	0.0	0.0
IPM	0.0	0.0	0.0	0.0	0.0	0.0
MEPM	0.0	0.0	0.0	0.0	0.0	0.0

Table 26. The proportion (%) of antimicrobial-resistant human-derived *S.* Saintpaul (2015-2019)

	2015 (n=27)	2016 (n=26)	2017 (n=42)	2018 (n=10)	2019 (n=8)	2015-2019 (n=113)
ABPC	7.4	7.7	14.3	10.0	0.0	9.7
GM	0.0	0.0	2.4	0.0	0.0	0.9
KM	0.0	3.8	4.8	0.0	0.0	2.7
SM	3.7	3.8	11.9	0.0	0.0	6.2
TC	40.7	15.4	21.4	10.0	12.5	23.0
ST	0.0	11.5	16.7	10.0	12.5	10.6
CP	3.7	0.0	14.3	0.0	12.5	7.1
CTX	0.0	0.0	11.9	0.0	0.0	4.4
CAZ	0.0	0.0	2.4	0.0	0.0	0.9
CFX	0.0	3.8	0.0	0.0	0.0	0.9
FOM	0.0	0.0	2.4	0.0	0.0	0.9
NA	7.4	3.8	19.0	0.0	0.0	9.7
CPFX	3.7	0.0	9.5	0.0	0.0	4.4
NFLX	3.7	0.0	0.0	0.0	0.0	0.9
AMK	0.0	0.0	0.0	0.0	0.0	0.0
IPM	0.0	0.0	0.0	0.0	0.0	0.0
MEPM	0.0	0.0	0.0	0.0	0.0	0.0

Table 27. The proportion (%) of antimicrobial-resistant human-derived *S.* 4:i:- (2015-2019)

	2015 (n=60)	2016 (n=37)	2017 (n=36)	2018 (n=36)	2019 (n=23)	2015-2019 (n=192)
ABPC	71.7	64.9	77.8	86.1	82.6	75.5
GM	1.7	0.0	2.8	0.0	0.0	1.0
KM	3.3	5.4	2.8	8.3	4.3	4.7
SM	73.3	70.3	80.6	91.7	82.6	78.6
TC	85.0	62.2	77.8	80.6	65.2	76.0
ST	5.0	10.8	5.6	8.3	8.7	7.3
CP	3.3	10.8	8.3	13.9	8.7	8.3
CTX	0.0	2.7	2.8	2.8	0.0	1.6
CAZ	0.0	2.7	2.8	0.0	0.0	1.0
CFX	0.0	0.0	2.8	0.0	0.0	0.5
FOM	0.0	2.7	0.0	0.0	0.0	0.5
NA	1.7	2.7	5.6	0.0	0.0	2.1
CPFX	0.0	0.0	0.0	0.0	0.0	0.0
NFLX	0.0	0.0	0.0	0.0	0.0	0.0
AMK	0.0	0.0	0.0	0.0	0.0	0.0
IPM	0.0	0.0	0.0	0.0	0.0	0.0
MEPM	0.0	0.0	0.0	0.0	0.0	0.0

Table 28. The proportion (%) of antimicrobial-resistant human-derived *S.* Thompson (2015-2019)

	2015 (n=28)	2016 (n=28)	2017 (n=30)	2018 (n=29)	2019 (n=27)	2015-2019 (n=142)
ABPC	0.0	10.7	0.0	0.0	7.4	3.5
GM	0.0	0.0	0.0	0.0	0.0	0.0
KM	7.1	0.0	0.0	0.0	0.0	1.4
SM	7.1	7.1	3.3	6.9	0.0	4.9
TC	3.6	7.1	6.7	0.0	0.0	3.5
ST	0.0	7.1	0.0	0.0	0.0	1.4
CP	0.0	7.1	0.0	0.0	0.0	1.4
CTX	0.0	10.7	0.0	0.0	0.0	2.1
CAZ	0.0	7.1	0.0	0.0	0.0	1.4
CFX	0.0	7.1	0.0	0.0	0.0	1.4
FOM	0.0	0.0	0.0	0.0	0.0	0.0
NA	0.0	0.0	0.0	3.4	0.0	0.7
CPFX	0.0	7.1	0.0	0.0	0.0	1.4
NFLX	0.0	7.1	0.0	0.0	0.0	1.4
AMK	0.0	0.0	0.0	0.0	0.0	0.0
IPM	0.0	0.0	0.0	0.0	0.0	0.0
MEPM	0.0	0.0	0.0	0.0	0.0	0.0

Table 29. Resistance rates among *S.* Infantis, *S.* Schwarzengrund, and *S.* Manhattan detected in humans and food (2015-2019) (%)

	Infantis		Schwarzengrund		Manhattan	
	Human (n=168)	Food (n=168)	Human (n=82)	Food (n=246)	Human (n=41)	Food (n=57)
ABPC	2.4	10.7	3.7	6.5	2.4	10.5
GM	0.0	0.6	0.0	0.0	0.0	0.0
KM	14.3	38.1	61.0	85.0	0.0	0.0
SM	31.0	75.6	70.7	80.5	87.8	93.0
TC	36.3	80.4	69.5	85.4	82.9	77.2
ST	10.1	22.0	26.8	37.4	0.0	1.8
CP	1.8	1.8	1.2	9.8	0.0	0.0
CTX	1.2	6.5	2.4	0.4	0.0	10.5
CAZ	0.0	5.4	2.4	0.4	0.0	10.5
CFX	0.6	7.7	0.0	0.4	0.0	0.0
FOM	0.6	0.0	0.0	0.4	0.0	0.0
NA	6.5	6.0	14.6	21.1	9.8	12.3
CPFX	0.0	0.0	0.0	0.0	0.0	0.0
NFLX	0.0	0.0	0.0	0.0	0.0	0.0
AMK	0.0	0.0	0.0	0.0	0.0	0.0
IPM	0.0	0.0	0.0	0.0	0.0	0.0
MEPM	0.0	0.0	0.0	0.0	0.0	0.0

iii. *Neisseria gonorrhoeae*

Source: National Institute of Infectious Diseases

The 618, 675, 982, 1,167, and 1,023 *Neisseria gonorrhoeae* strains that were respectively isolated in 2015, 2016, 2017, 2018, and 2019 were tested for antimicrobial susceptibility (based on EUCAST breakpoints; Table 30). Ceftriaxone (CTRX)-resistant strains respectively accounted for 6.2%, 4.3%, 4.3%, 3.5%, and 5.4%. Strains assessed as resistant based on the CLSI Criteria (MIC ≥ 0.5 μg/mL) accounted for 0.6%, 0.4%, 0.5%, 0.3%, and 0.4%. No spectinomycin (SPCM)-resistant strains were present. On the other hand, the proportion (%) of azithromycin (AZM)-resistant strains increased from 13.0% in 2015 to between 33% and 43.9% since 2016.

The CLSI Criteria do not provide a resistance breakpoint for azithromycin (AZM), but, using the azithromycin (AZM) MIC distribution of strains with the 23S rRNA gene mutation as the basis, strains with a MIC of 2 μg/mL or higher are referred to as "non-wild-type." When we investigated the resistance rate (see Reference (8)), albeit as a reference, we found that, between 2015 and 2019, 3.2%, 4.0%, 4.0%, 6.3%, and 7.5% of strains, respectively, had a MIC of 2 μg/mL or higher, indicating an upward trend. According to clinical assessments in Japan, strains indicating an azithromycin (AZM) MIC of 1 μg/mL or higher can reasonably be regarded as resistant. Under this criterion (R ≥ 1 μg/mL), azithromycin-resistant strains accounted for 11.0%, 9.3%, 11.2%, 15.9%, and 14.9% of strains respectively between 2015 and 2019. Among the other three antimicrobials, the proportion of CFIX-resistant strains accounted for approximately 30-40%, and that of CPFX-resistant strains accounted for approximately 60-80%. Penicillins (PCG) would not have a therapeutic effect on more than 80% of strains.

Table 30. The proportion (%) of antimicrobial-resistant *Neisseria gonorrhoeae*

	2015 (618 strains)	2016 (675 strains)	2017 (982 strains)	2018 (1,167 strains)	2019 (1,023 strains)
CTRX	6.2	4.3	4.3	3.5	5.4
SPCM	0.0	0.0	0.0	0.0	0.0
AZM	13.0	33.5	42.6	43.9	40.1
PCG*	38.4 (96.6)	36.3 (96.9)	37.8(99.0)	31.7(82.5)	35.8(88.5)
CFIX	36.2	43.2	31.0	28.4	33.4
CPFX	79.5	78.0	75.8	66.9	64.6

The EUCAST (Appendix 8) standards were used for susceptibility and resistance assessment.

* Figures in parentheses indicate the sum of resistance and intermediate resistance.

The EUCAST resistance breakpoints are as follows. CTRX (>0.125 μg/mL), SPCM (> 64 μg/mL), AZM (>0.5 μg/mL), PCG (> 1 μg/mL), CFIX (>0.125 μg/mL), CPFX (> 0.06 μg/mL)

iv. *Salmonella* Typhi, *Salmonella* Paratyphi A, *Shigella* spp.
Source: National Institute of Infectious Diseases

The 28-46 *Salmonella* Typhi strains that were isolated between 2015 and 2019 were tested for antimicrobial susceptibility (Table 24). CPFX-non-susceptible strains accounted for 60.7-83.9%, while strains with advanced resistance (MIC ≥ 4) to ciprofloxacin accounted for 5.9-23.9%. During this period, 11 strains of multidrug-resistant *Salmonella* Typhi that indicated resistance to ampicillin (ABPC), CP and ST were isolated, along with two strains of CTX-resistant *Salmonella* Typhi.

The 13-30 *Salmonella* Paratyphi A strains isolated between 2015 and 2019 were tested for antimicrobial susceptibility. CPFX-non-susceptible strains accounted for 76.9-100% and one strain with advanced CPFX resistance (MIC ≥ 4) was isolated. No cefotaxime-resistant strains were isolated among the *Salmonella* Paratyphi A.

The 73-156 *Shigella* spp. strains that were isolated between 2015 and 2019 were tested for antimicrobial susceptibility. ST-resistant strains accounted for 73.6-81.0%; CPFX-non-susceptible strains for 14.3-45.7%; and cefotaxime-resistant strains for 3.3-16.4%.

Table 31. The proportion (%) of antimicrobial-resistant *Salmonella* Typhi

	2015 (32 strains)	2016 (46 strains)	2017 (31 strains)	2018 (34 strains)	2019 (28 strains)
ABPC	5.7	2.2	12.9	2.9	10.7
CP	5.7	2.2	12.9	5.9	10.7
ST	5.7	2.2	12.9	5.9	10.7
NA	68.8	63.0	83.9	61.7	57.1
CPFX	68.8 (12.5*)	63.0 (23.9*)	83.9 (16.1*)	61.7 (5.9*)	60.7 (10.7*)
CTX	0.0	0.0	0.0	2.9	3.6

* Advanced resistance to fluoroquinolone

Table 32. The proportion (%) of antimicrobial-resistant *Salmonella* Paratyphi A

	2015 (30 strains)	2016 (20 strains)	2017 (13 strains)	2018 (21 strains)	2019 (16 strains)
ABPC	0.0	0.0	0.0	0.0	0.0
CP	0.0	0.0	0.0	0.0	0.0
ST	0.0	0.0	0.0	0.0	0.0
NA	80.0	80.0	76.9	100	87.5
CPFX	83.3	83.3	76.9	100	87.5
CTX	0.0	0.0	0.0	0.0	0.0

Table 33. The proportion (%) of antimicrobial-resistant *Shigella* spp.

	2015 (105 strains)	2016 (73 strains)	2017 (91 strains)	2018 (156 strains)	2019 (91 strains)
ABPC	21.9	42.5	31.9	19.2	14.3
CP	11.4	24.7	26.4	9.0	6.6
ST	81.0	80.8	73.6	76.9	76.9
NA	63.8	52.1	52.8	45.5	33.0
CPFX	45.7	35.6	35.2	21.2	14.3
CTX	5.7	16.4	13.2	5.1	3.3

5) *Mycobacterium tuberculosis*

Source: The Research Institute of Tuberculosis, Japan Anti-tuberculosis Association

Looking at major antituberculosis antibiotics—isoniazid (INH), rifampicin (RFP), and ethambutol (EB)—among patients with culture-positive pulmonary tuberculosis who were newly notified between 2011 and 2019, resistance to INH has been on the rise in recent years, while RFP and EB resistance rates have remained mostly at the same level. Although a rise of up to 1.1 percentage points was seen in streptomycin (SM) resistance in 2017, it has mostly remained at the same level since 2018. The number of newly reported cases with multidrug-resistant tuberculosis that are resistant at least to both INH and RFP remained in the range of approximately 50 to 60 (0.4-0.7%) per year.

Table 34. Newly Notified Patients with Culture-positive Pulmonary Tuberculosis: Trends in Drug Susceptibility at the Time of Notification

	2011	2012	2013	2014	2015	2016	2017	2018	2019
Culture-positive patients, N	10,915	11,261	10,523	10,259	10,035	9878	9,580	9,016	8,110
INH-resistant, n	386	380	369	349	372	369	383	377	359
(%)*	(4.8)	(4.6)	(4.8)	(4.6)	(4.9)	(4.8)	(4.9)	(5.0)	(5.4)
RFP-resistant, n	86	73	64	76	77	74	80	87	65
(%)*	(1.1)	(0.9)	(0.8)	(1.0)	(1.0)	(1.0)	(1.0)	(1.1)	(1.0)
INH & RFP-resistant†, n	60	60	47	56	48	49	52	55	44
(%)*	(0.7)	(0.7)	(0.4)	(0.5)	(0.5)	(0.6)	(0.7)	(0.6)	(0.7)
SM-resistant, n	-	509	475	469	476	461	557	471	428
(%)§		(6.1)	(6.2)	(6.2)	(6.3)	(6.0)	(7.1)	(6.3)	(6.5)
EB-resistant, n	-	151	106	130	129	100	106	130	126
(%)¶		(1.8)	(1.4)	(1.7)	(1.7)	(1.3)	(1.3)	(1.7)	(1.9)

* The denominator was defined as the number of patients with recorded INH- and RFP-susceptibility testing results among all culture-positive patients: 8,046 (73.7%) patients in 2011, 8,347 (74.1%) patients in 2012, 7,701 (73.2%) patients in 2013, 7,645 (74.5%) patients in 2014, 7,630 (76.0%) patients in 2015, 7,732 (78.3%) patients in 2016, 7,891 (82.4%) patients in 2017, 7,570 (84.0%) patients in 2018 and 6,658 (82.1%) patients in 2019.

-: Not under surveillance

† INH- and RFP- resistant tuberculosis bacteria are referred to as "multidrug-resistant."

§ The proportion appeared here showed the share in patients with INH- and RFP-susceptibility testing results, excluding those who were not tested for SM-susceptibility or those with the unknown test result: 54 patients in 2012, 48 patients in 2013, 52 patients in 2014, 48 patients in 2015, 47 patients in 2016, 51 patients in 2017, 47 patients in 2018 and 41 patients in 2019.

¶ The proportion appeared here showed the share in patients with INH- and RFP-susceptibility testing results, excluding those who were not tested for EB-susceptibility or those with the unknown test result: 14 in 2012, 13 in 2013, 13 in 2014, 19 in 2015, 17 in 2016, 14 in 2017, 13 in 2018 and 8 in 2019).

6) *Clostridioides (Clostridium) difficile* infection

Clostridioides (Clostridium) difficile is a spore-forming gram-positive anaerobic bacillus that colonizes the intestines of about 10% of healthy adults.[3] CDI is a major healthcare-associated infection that causes diarrhea at hospitals and long-term care facilities for the elderly. In addition, CDI has been recognized as a cause of diarrhea even in the community.[4]

Observational studies in Japan indicate that the CDI incidence rate in Japan is 0.8-4.7 cases per 10,000 patient days, while prevalence is 0.3-5.5 cases per 1,000 admissions.[5] In a multi-institutional prospective study (20 wards at 12 institutions) using toxigenic cultures and nucleic acid amplification tests (NAAT), the CDI incidence rate was 7.4 cases per 10,000 patient days, rising to 22.2 in ICU wards, suggesting that the incidence rate is higher than indicated by existing reports, with a particularly high risk in ICU wards.[6] CDI surveillance was launched in 2019 via Japan Surveillance for Infection Prevention and Healthcare Epidemiology (J-SIPHE).

A 2019 J-SIPHE report on inpatients (all wards at 276 facilities: 253 facilities using immunochromatographic toxin tests, 3 facilities using NAAT testing, and 20 other facilities) found that the CDI incidence rate was 1.38 (IQR: 0.56-2.43) per 10,000 inpatient-days.

In comparisons with other countries, consideration must be given to the impact of such factors as survey subjects, specimen collection methods, testing methods, the definition of recurrence, and differences in the average length of admission.

Additional reference

Japan Surveillance for Infection Prevention and Healthcare Epidemiology (J-SIPHE). Annual Report, 2019.

7) Status of health care associated infection

Source: Japan Nosocomial Infections Surveillance (JANIS)

The number of medical institutions participating in the surgical site infection (SSI) division of JANIS has more than doubled over the past seven years. In 2018, among 305,960 surgical operations undertaken at 802 institutions, SSI were reported in 15,566 cases (5.1%). The number of reported SSI declined from 2012 during the observed period.

In the intensive care unit (ICU) division of JANIS, the incidence of infection by ventilator-associated pneumonia has been 1.3-1.7 per 1,000 days of ICU stay over the past seven years, with a figure of 1.3 per 1,000 days of ICU stay recorded in 2018. While the incidence of urinary tract infection is around 0.5-0.8 per 1,000 days of ICU stay, the figure has shown a slight rise since 2016. Meanwhile, the incidence of catheter related bloodstream infection is around 0.6-0.8 per 1,000 days of ICU stay, but the figure has declined somewhat since 2017. JANIS monitors cases of infections that occurred between 48 hours after admission to ICU and discharge from ICU.

i. Surgical site infection

Table 35. The trend of reported SSI cases

	2011	2012	2013	2014	2015	2016	2017	2018
Total SSI cases per total surgical operations (%)*	**6.0**	**6.8**	**6.5**	**6.0**	**5.8**	**5.7**	**5.4**	**5.1**
Participated medical institutions	333	363	442	552	671	730	772	802
Total surgical operations	127,731	129,825	161,077	207,244	251,832	274,132	292,031	305,960
Total SSI cases	7,719	8,771	10,445	12,508	14,701	15,674	15,889	15,566

* Total SSI cases per total surgical operations (%) = (Total SSI cases at medical facilities participated in JANIS) / (Total surgical operations at medical facilities participated in JANIS) times 100

Prepared from annual reports of the SSI division, JANIS.[7]

ii. Infections at Intensive Care Unit (ICU)

Table 36. Incidence rates of infection at ICU

		2011	2012	2013	2014	2015	2016	2017	2018
Ventilator-associated pneumonia	**Total infection incidence rate***	**1.7**	**1.4**	**1.3**	**1.4**	**1.5**	**1.5**	**1.3**	**1.3**
	Total infections at monitored medical institutions	382	327	324	395	522	499	405	409
Urinary tract infection	**Total infection incidence rate***	**0.5**	**0.5**	**0.6**	**0.5**	**0.5**	**0.6**	**0.7**	**0.8**
	Total infections at monitored medical institutions	111	124	143	148	190	219	213	244
Catheter-related bloodstream infection	**Total infection incidence rate***	**0.7**	**0.7**	**0.8**	**0.7**	**0.7**	**0.8**	**0.7**	**0.6**
	Total infections at monitored medical institutions	168	162	204	205	240	263	213	190

* Total infection incidence rate = (Total infections among applicable patients at medial facilities participated in JANIS) / (Total days of ICU stay of applicable patients medial facilities participated in JANIS) times 1000

Prepared from annual reports of the ICU division, JANIS.[8]

8) Survey of infection treatment and control and the disease burden at hospitals

Source: J-SIPHE, AMR Clinical Reference Center (AMRCRC)

The AMR Clinical Reference Center (AMRCRC) operates the J-SIPHE system, which can be used for AMR measures at hospitals as well as for promoting regional cooperation. The J-SIPHE 2019 Annual Report covers a total of 581 participating medical institutions (449 calculating Infection Prevention and Control Premium 1, 127 calculating Infection Prevention and Control Premium 2, and 5 calculating no premium). The median number of blood cultures submitted at hospitals (n=255) was 23.8/1,000 patients/day (QR: 11.0-34.7), while the median share of multiple sets of blood culture among adults exceeded 90%. The median positive rate of blood culture was within an appropriate indicator range at 13.27 (IQR:11.1-17.2). Consideration needs to be given to the hospitals calculating Infection Prevention and Control Premium 1 forming the majority and the variations in practice between one hospital and another, but overall the results are good.

Looking at occurrences of bloodstream infection, *Escherichia coli* accounted for the highest number, at a total of 2.20/10,000 patients, followed by *S. aureus* at a total of 1.61/10,000 patients, and *Klebsiella pneumoniae* at a total of 0.83/10,000 patients. It would be desirable for infection control measures to primarily target the bacteria accounting for the highest percentages of severe infection.

The overall hand hygiene compliance rate was 57.5%, while the breakdown of the figures by ward function showed that critical care wards had the highest rate of compliance, at 67.0%. The total amount of hand rub consumed was 7.44 mL/1,000 patients overall, while the breakdown of the figures by ward function showed that critical care wards used the most, at 33.7 mL/1,000 patients. Further improvements in hand hygiene practice would be desirable to achieve a hand hygiene compliance target of 70-80%. On the other hand, at facilities with few infection control resources, monitoring of infection control over time would be desirable, using the amount of hand rub consumed as a simple alternative indicator.

The estimated number of deaths in patients with bloodstream infections was published after a study of JANIS data carried out with a Health and Labor Sciences Research Grant. The number of deaths due to MRSA has been declining by the year and was estimated to have reached 4,224 in 2017, while the number of deaths due to fluoroquinolone-resistant Escherichia coli has been on the rise and was estimated at 3,915 in 2017. Research into the disease burden of AMR will continue, with the goal of increasing the number of bacterial strains covered over time and ultimately calculating disability-adjusted life years (DALYs).

Basic information on medical institutions participating in J-SIPHE

	2019
Number of beds (IQR)	340.5 (221.3-525.3)
Average length of hospital stay (IQR)	13.6 (11.7-17.1)

QR (Interquartile range)

Multiple sets of blood culture at hospitals (%) (n=276)

	2019
All patients	90.6 (83.6-95.4)
Patients aged 15 years and older	95.0 (90.8-97.2)
Patients aged under 15 years	4.9 (0.9-16.8)

*Share of submissions of 2 sets or more of blood culture among blood culture submissions

Occurrences of bloodstream infection at hospitals (total number per 10,000 patients) (n=253)

	2019
S. aureus (IQR) *	1.61 (0.86-2.17)
Enterococcus faecalis (IQR) *	0.37 (0.12-0.65)
Escherichia coli (IQR) *	2.20 (1.40-3.37)
Klebsiella pneumoniae (IQR) *	0.83 (0.43-1.29)
Enterobacter spp. (IQR) *	0.32 (0.08-0.61)
MRSA (IQR) *	0.59 (0.26-0.94)
3CRRC (IQR)	0.42 (0.16-0.84)
FQRC (IQR)	0.64 (0.27-1.18)

MRSA; methicillin resistant S. aureus, 3 CREC; 3rd generation Cephalosporine resistant E. coli, FQREC; fluoroquinolone resistant E coli, IQR (Interquartile range)

Hand hygiene compliance rate at hospitals (%)

	2019
Total (IQR) (n=45)	57.5 (45.0-68.3)
Critical care (IQR) (n=22)	67.0 (55.8-75.2)
Medical wards (IQR) (n=35)	60.2 (39.3-72.7)
Surgical wards (IQR) (n=35)	54.1 (48.3-71.4)
Other wards (IQR) (n=40)	54.0 (39.9-71.5)

IQR (Interquartile range)

Total amount of hand rub consumed at hospitals (mL/1,000 patients)

	2019
Total (IQR) (n=189)	7.44 (4.36-11.34)
Critical care (IQR) (n=112)	33.7 (18.4-59.8)
Medical wards (IQR) (n=148)	7.39 (4.62-11.51)
Surgical wards (IQR) (n=137)	6.75 (4.38-11.00)
Other wards (IQR) (n=188)	7.15 (4.54-12.02)

IQR (Interquartile range)

Estimated number of patient deaths from bloodstream infection (people)

	2011	2012	2013	2014	2015	2016	2017
S. aureus (95% CI)	17,412 (13,388-22,119)	16,951 (13,058-21,491)	16,789 (12,962-21,233)	16,517 (12,773-20,856)	16,443 (12,777-20,660)	16,565 (12,883-20,796)	17,157 (13,347-21,533)
MRSA (95% CI)	5924 (3837-8513)	5365 (3478-7702)	4755 (3092-6802)	4380 (2853-6256)	4357 (2852-6190)	4298 (2817-6100)	4224 (2769-5994)
E. coli (95% CI)	9044 (7101-11,335)	9650 (7585-12,080)	10,896 (8594-13,589)	11,621 (9178-14,471)	12,587 (9991-15,595)	13,356 (10,612-16,532)	14,016 (11,140-17,344)
FQREC (95% CI)	2045 (1869-2220)	2317 (2120-2513)	2753 (2532-2970)	3012 (277-3243)	3377 (3126-3619)	3678 (3408-3937)	3915 (3629-4189)

MRSA; methicillin resistant S. aureus, FQREC; fluoroquinolone resistant E. Coli, CI; confidence interval.

9) Survey of infections and antimicrobial use at facilities for the elderly

Source: AMRCRC

Funded by a Health and Labor Sciences Research Grant, the AMRCRC conducted a survey of healthcare-associated infections and antimicrobial use at facilities for the elderly.[9]

i Long-term care facilities for the elderly

The center randomly selected 1,500 facilities from among the members of the Japan Association of Geriatric Health Services Facilities and conducted a PPS. Responses were received from 134 facilities (a response rate of 8.9%). Geriatric health services facilities are classified into five type according to their performance based on their function related to home return. In addition, if previous hospital beds are converted to geriatric health services facility, it is called nursing convalescence type. The majority of responses came from Higher Return-to-home facilities (32.5%) and Conventional facilities (60.3%).

The median number of oral antimicrobials deployed in the facilities was four, while the median number of parenteral antimicrobials was two. The main oral antimicrobials used were quinolones and third-generation cephalosporins, while the main parenteral antimicrobials were third-generation cephalosporins and penicillins.

A total of 10,148 patients were admitted to the facilities on the day the survey was carried out. Of these, 172 (1.7%) were using antimicrobials. The median age of the patients was 86.0 years (IQR: 81-91), while the median age of male patients was 84.0 years (IQR: 75-89) and that of female patients was 87.0 years (IQR: 83-92). The top three medical devices being used by patients were peripheral routes and self-inserted or indwelling bladder catheters, which were both used by 33 people (19.4%), and gastrostomy tubes, which were used by 23 people (13.5%). A total of 86 people (50.6%) were not using any medical devices. The top focus of infection were urinary tract infections, affecting 73 people (47.7%); pneumonia, affecting 31 people (20.3%); and upper respiratory tract infections, affecting 15 people (9.8%). The main antimicrobials used to treat urinary tract infections and pneumonia were fluoroquinolones and third-generation cephalosporins. It is necessary to continue to ascertain the status of infections and antimicrobial use at long-term care facilities for the elderly and to promote antimicrobial stewardship.

Table 37. Facility Types

Higher Return-to-home			**Conventional**	**Minimum function**	**Nursing Convalescent**
Super return to home Addition of return-to-home care / home care support functions II		**Return-to-home** Addition of return-to-home care / home care support functions I			
33 (26.2%)	8 (6.3%)	40 (31.7%)	36 (28.6%)	5 (4.0%)	4 (3.2%)

Table 38. Number of antimicrobial agents deployed at facilities: 4 ATC categories

Number of antimicrobial agents based on the 4 ATC categories	Oral Antimicrobials Number of Institutions	Parenteral Antimicrobials Number of Institutions
None	4	25
1 agent	4	29
2 agents	21	27
3 agents	27	13
4 agents	31	13
5 agents	23	6
6 agents	13	2
7 agents or more	3	11
Total	126	126

Table 39. Usage of medical devices by patients using antimicrobials [Multiple answers] n=170 *Missing values: 2

Type of medical device	Number of people (%)
Peripheral route	33 (19.4%)
Self-inserted/indwelling bladder catheter	33 (19.4%)
Gastrostomy tube	23 (13.5%)
Nasogastric tube	12 (7.1%)
Dialysis catheter	3 (1.8%)
Tracheostomy tube	2 (1.2%)
Colostomy equipment	2 (1.2%)
Nephrostomy/cystostomy tube	1 (0.6%)
Other (sputum suction tube, ureteral stent/enterostomy tube)	3 (1.8%)
Not using a medical device	86 (50.6%)
Total	170

Table 40. Focus of infection undergoing treatment [Multiple answers] n=153 *Missing values: 1

Focus of infection or diagnosis	Number of people (%)
Urinary tract infection	78 (51.0%)
Pneumonia	37 (24.2%)
Upper respiratory tract infection	15 (9.8%)
Bronchitis	9 (5.9%)
Cellulitis	7 (4.6%)
Gastroenteritis	2 (1.3%)
Unknown	7 (4.6%)
Other	12 (7.8%)

Breakdown of the 12 cases listed as “Other”: 2 pharyngitis, 2 epidermal cyst, 2 toe inflammation, 1 pressure ulcers on the right second and third toe joints, 1 vaginitis, 1 inflammation of the remaining dental root, 1 suspected bile duct calculus, 1 suspected palmoplantar pustulosis, 1 details unclear

ii Welfare facilities for the elderly requiring long-term care (special nursing homes for the aged)

The center randomly selected 1,500 welfare facilities for the elderly requiring long-term care from among the members of the Japanese Council of Senior Citizens Welfare Service and conducted a point prevalence survey (PPS). Responses were received from 139 facilities (a response rate of 9.3%). The majority of responses came from conventional facilities with mostly multibed rooms (73.0%) and unit-style facilities where small groups of around 10 people share communal living areas, but have their own rooms (36.5%).

A total of 9,044 patients were admitted to the facilities on the day the survey was carried out. Of these, 94 (1.0%) were using antimicrobials. Individual data was received for 80 patients. The median age of the patients was 90.0 years (IQR: 85, 93), while the median age of male patients was 80.5 years (IQR: 76, 90) and that of female patients was 92.0 years (IQR: 87, 93). The top three medical devices being used by patients were peripheral routes (inserted to treat infection), which were used by 12 people (17.1%), indwelling urethral catheters, which were used by 6 people (8.6%), and gastrostomy tubes, which were used by 4 people (5.7%). A total of 49 people (70.0%) were not using any medical devices.

The top focuses of infection were urinary tract infections, affecting 23 people (31.17%); pneumonia, affecting 11 people (14.9 %); and upper respiratory tract infections, affecting 9 people (12.2%). The main antimicrobials used to treat urinary tract infections were oral quinolones, while the main ones used for pneumonia were injectable third-generation cephalosporins. Residents were being treated for the infection by the physician deployed by the facility (appointed physician) or at outpatient consultations. Going forward, it will be necessary to promote antimicrobial stewardship through the use of the Manual of Antimicrobial Stewardship, among others.

Table 41. Facility Types

Conventional	Unit-style	Community-based	Small transitional	Unit-style small transitional
100 (73.0%)	50 (36.5%)	14 (10.2%)	4 (2.9%)	1 (0.7%)

Table 42. Medical devices used by patients using antimicrobials [Multiple answers] n=70 *Missing values: 10

Type of medical device	Number of people (%)
Peripheral route (inserted for the purpose of treating the infection)	12 (17.1 %)
Indwelling urethral catheter	6 (8.6%)
Gastrostomy tube	4 (5.7%)
Nasogastric tube	3 (4.3%)
Nephrostomy/cystostomy tube	1 (1.4%)
Other (pacemaker)	2 (2.9 %)
Peripheral route (inserted prior to the infection)	0
Self-inserted catheter	0
Colostomy equipment	0
Not using a medical device	49 (70.0%)
Total	70

Table 43. Focus of infection undergoing treatment [Multiple answers] n=74 *Missing values: 2

Focus of infection or diagnosis	Number of people (%)
Urinary tract infection	23 (31.1%)
Pneumonia	11 (14.9%)
Upper respiratory tract infection	9 (12.2%)
Bronchitis	7 (9.5%)
Cellulitis	4 (5.4%)
Gastroenteritis	0
Unknown	6 (8.1%)
Other	14 (18.9%)

Described above) The breakdown of the 14 classed as Other is as follows: bronchitis or pneumonia, 2; pressure ulcers, 2; ingrown nail inflammation, 2; erythroderma, 1; systemic dermatitis, 1; cholecystitis, 1; gallstones, 1; digestive system, 1; upper or lower respiratory tract infection, 1; upper respiratory tract infection or complicated cystitis, 1; pneumonia or urinary tract infection, 1.

Table 44. Main antimicrobials used to treat urinary tract infections and pneumonia [Multiple answers]

	n	Main antimicrobials	Number of people (%)
Urinary tract infection	23	・Fluoroquinolones	12 (52.2%)
		・3rd generation cephalosporins	7 (30.4%)
		・Penicillins	3 (13.0%)
		・2nd generation cephalosporins	1 (4.3%)
Pneumonia	11	・3rd generation cephalosporins	5 (45.5%)
		・Fluoroquinolones	3 (27.3%)
		・Carbapenems	1 (9.1%)
		・Macrolides	1 (9.1%)
		・3rd generation cephalosporins and fluoroquinolones	1 (9.1%)

(2) Animals

1) Bacteria derived from food-producing animals

Source: Japanese Veterinary Antimicrobial Resistance Monitoring System (JVARM)

Under the JVARM, antimicrobial susceptibility tests are performed using the broth microdilution method according to the CLSI guidelines. For agents with a BP established by the CLSI, susceptibility was interpreted using the CLSI Criteria. The BPs of the other antimicrobial agents used EUCAST values or were determined microbiologically (midpoint of a bimodal MIC distribution).

Bacteria derived from diseased animals

Surveys of bacteria derived from diseased animals were carried out using bacteria isolated from food-producing animals which were subjected to pathological appraisal by prefectural livestock hygiene service centers.

i. *Salmonella* spp.

Monitoring of antimicrobial resistance on 11 agents was carried out between 2011 and 2018. ABPC resistance in strains isolated from pigs and TC resistance in strains isolated from pigs and chickens were observed to exceed 50% in 2018, as were KM and sulfamethoxazole-trimethoprim (ST) resistance in chickens. On the other hand, no strains that indicated resistance to CTX, which is a critically important antimicrobial for human medicine, were isolated from any livestock. Resistance to CPFX was less than 5% in strains derived from all livestock, as was resistance to colistin (CL) in cattle-derived strains. It must be noted that the BPs of cefazolin (CEZ), CL, and CPFX have been lowered since 2016 to bring them into line with the CLSI revisions. The most common *Salmonella* serotypes isolated from diseased food-producing animals were *S.* Typhimurium and its monophasic variant *S.* 4:i:- among cattle; *S.* Typhimurium, *S.* 4:i:-, and *S.* Choleraesuis among pigs; and *S.* Schwarzengrund and *S.* Infantis among chickens.

Looking at trends in resistance rates between 2011 and 2018, ongoing upward trends were observed in ABPC resistance among pigs and KM and TC resistance among chickens. In all other cases, while fluctuations in resistance rates could be seen, no definite trends were observed. It will remain necessary to make judgments based on the results of future surveys.

Table 45. The proportion (%) of antimicrobial-resistant *Salmonella* spp. isolated from diseased animals

Agent	BP	Animal	2011	2012	2013	2014	2015	2016	2017	2018
ABPC	32*	Cattle	28.0	32.9	60.7	61.9	56.6	50.0	40.7	36.8
		Pigs	25.4	25.3	45.0	41.4	46.9	41.1	40.9	50.0
		Chickens	12.0	9.4	4.0	3.9	14.3	-	-	4.5
CEZ	32 (8* from 2016)	Cattle	10.0	1.2	8.9	7.9	7.9	22.9	5.1	3.5
		Pigs	0.0	0.0	0.0	0.0	6.1	23.2	6.8	9.4
		Chickens	0.0	3.1	4.0	0.0	0.0	-	-	0.0
CTX	4*	Cattle	10.0	1.2	8.9	7.9	7.9	4.3	1.7	0.0
		Pigs	0.0	0.0	0.0	0.0	4.1	0.0	0.0	0.0
		Chickens	0.0	0.0	4.0	0.0	0.0	-	-	0.0
GM	16*	Cattle	0.0	0.0	0.0	3.2	7.9	4.3	1.7	1.8
		Pigs	6.3	3.6	15.0	15.5	8.2	17.9	15.9	4.7
		Chickens	0.0	0.0	2.0	0.0	0.0	-	-	0.0
KM	64*	Cattle	12.0	3.7	25.0	14.3	21.1	25.7	5.1	0.0
		Pigs	9.5	12.0	6.7	8.6	6.1	10.7	13.6	4.7
		Chickens	24.0	15.6	22.0	29.4	42.9	-	-	63.6
TC	16*	Cattle	30.0	32.9	66.1	50.8	55.3	42.9	39.0	33.3
		Pigs	61.9	53.0	66.7	60.3	61.2	58.9	50.0	50.0
		Chickens	36.0	34.4	30.0	39.2	42.9	-	-	77.3
NA	32*	Cattle	2.0	7.3	1.8	3.2	11.8	5.7	5.1	1.8
		Pigs	15.9	21.7	5.0	15.5	6.1	7.1	9.1	20.3
		Chickens	8.0	6.3	8.0	3.9	28.6	-	-	0.0
CPFX	4 (1* from 2016)	Cattle	0.0	0.0	0.0	0.0	0.0	0.0	1.7	1.8
		Pigs	0.0	0.0	0.0	0.0	0.0	3.6	4.5	4.7
		Chickens	0.0	0.0	0.0	0.0	0.0	-	-	0.0
CL	16 (4* from 2016)	Cattle	0.0	0.0	0.0	0.0	0.0	1.4	5.1	0.0
		Pigs	0.0	0.0	1.7	0.0	0.0	3.6	4.5	6.3
		Chickens	0.0	3.1	2.0	0.0	0.0	-	-	18.2
CP	32*	Cattle	14.0	12.2	10.7	17.5	22.4	12.9	3.4	3.5
		Pigs	12.7	13.3	11.7	25.9	12.2	8.9	18.2	21.9
		Chickens	0.0	6.3	6.0	3.9	14.3	-	-	0.0
ST (TMP from 2012 to 2016)	76/4* (TMP is 16*)	Cattle	2.0	1.2	1.8	6.3	13.2	4.3	3.4	1.8
		Pigs	25.4	21.7	36.7	32.8	22.4	21.4	25.0	12.5
		Chickens	20.0	15.6	14.0	29.4	42.9	-	-	59.1
Strains tested (n)		Cattle	50	82	56	63	76	70	59	57
		Pigs	63	83	60	58	49	56	44	64
		Chickens	25	32	50	51	7	-	-	22

The unit of BP is μg/mL. * BP follows CLSI Criteria.

-: Not under surveillance

Table 46. Number of strains of *Salmonella enterica* isolated from diseased food-producing animals by serotype (FY2014-2018)

Serotypes	Cattle	Pigs	Chickens	Total	(%)
Typhimurium	86	115	2	203	30.0
4:i:-	110	60	0	170	25.1
Choleraesuis	0	30	0	30	4.4
Schwarzengrund	3	1	25	29	4.3
Derby	2	14	0	16	2.4
Infantis	17	5	15	37	5.5
Braenderup	4	4	5	13	1.9
Newport	7	5	1	13	1.9
Mbandaka	6	1	5	12	1.8
Thompson	14	2	2	18	2.7
Enteritidis	1	0	7	8	1.2
Dublin	7	0	0	7	1.0
Rissen	2	6	0	8	1.2
Stanley	18	1	0	19	2.8
Tennessee	0	0	2	2	0.3
Others	48	27	16	91	13.5
Total	325	271	80	676	100

ii. *Staphylococcus aureus*

Monitoring of antimicrobial resistance on 7 agents was carried out between 2011 and 2018. Resistance rates of ABPC, erythromycin (EM) and TC in pig-derived strains were observed to exceed 50% in 2018. Resistance rates to all antimicrobials were observed to be higher in strains isolated from pigs than in those derived from cattle and chickens. Resistance to CPFX, which is a critically important antimicrobial for human medicine, was 23.5% in pig-derived strains, but less than 3% in strains isolated from cattle and chickens.

Table 47. The proportion (%) of antimicrobial-resistant *Staphylococcus aureus* isolated from diseased animal

Agent*	BP	Animal	2011	2012	2013	2014	2015	2016	2017	2018
ABPC	0.5	Cattle	5.5	13.6	11.0	11.1	21.3	7.8	7.4	9.3
		Pigs	-	-	-	-	-	75.6	71.4	82.4
		Chickens	0.0	25.0	0.0	15.4	50.0	3.7	22.6	8.0
SM	64	Cattle	6.4	2.3	2.8	1.1	2.7	1.4	3.4	5.8
		Pigs	-	-	-	-	-	33.3	20.4	39.2
		Chickens	0.0	10.0	0.0	7.7	16.7	3.7	0.0	0.0
GM	16†	Cattle	0.9	2.3	1.8	0.0	1.3	0.0	0.6	0.0
		Pigs	-	-	-	-	-	2.2	14.3	11.8
		Chickens	0.0	15.0	0.0	0.0	0.0	3.7	9.7	4.0
EM	8†	Cattle	1.8	3.4	5.5	0.0	6.7	2.8	1.7	5.8
		Pigs	-	-	-	-	-	37.8	38.8	52.9
		Chickens	50.0	55.0	0.0	15.4	16.7	22.2	6.5	4.0
TC	16†	Cattle	0.0	2.3	8.3	5.5	6.7	0.0	0.0	0.6
		Pigs	-	-	-	-	-	57.8	53.1	60.8
		Chickens	37.5	5.0	0.0	16.7	16.7	33.3	19.4	20.0
CP	32†	Cattle	0.0	0.0	0.9	0.0	1.3	0.0	0.6	0.6
		Pigs	-	-	-	-	-	22.2	30.6	43.1
		Chickens	0.0	0.0	0.0	15.4	33.3	3.7	3.2	8.0
CPFX	4†	Cattle	0.0	0.0	0.9	0.0	1.3	0.7	0.6	0.0
		Pigs	-	-	-	-	-	11.1	8.2	23.5
		Chickens	25.0	0.0	4.2	15.4	33.3	3.7	3.2	2.8
Strains tested (n)		Cattle	109	88	109	91	75	141	175	172
		Pigs	-	-	-	-	-	45	49	51
		Chickens	8	20	24	12	6	27	31	25

The unit of BP is μg/mL.

-: No data for pigs was listed before 2016, because the number of strains was less than five each year.

* While NA was also included in the scope of monitoring, its proportion of NA-resistant strains was not listed because BP could not be established.

† BP follows CLSI Criteria.

iii. *Escherichia coli*

Monitoring of antimicrobial resistance on 12 agents was carried out between 2012 and 2018. In 2018, antimicrobial resistance in excess of 50% was observed among strains isolated from food-producing animals as follows: ABPC, SM and TC resistance among cattle, pigs, and chickens; and CP and ST resistance among pigs. Resistance rates to 8 out of 12 antimicrobials were observed to be higher in strains isolated from pigs than in those derived from cattle and chickens. Resistance to CTX, CPFX, and CL, which are critically important antimicrobials for human medicine, was in the ranges 3.3-11.8%, 11.8-22.3%, and 2.0-35.5%, respectively. It must be noted that the BPs of CEZ and CL are the CLSI's revised figures. As the BP of CL has changed, resistance rates in strains isolated from pigs have been above 50% since 2016, but no upward trend has been observed in resistance rates using the pre-revision BP. As CL was positioned as a second-line veterinary drug in 2018, its designation as a feed additive was revoked and its use prohibited. Accordingly, it will be necessary to check trends in resistance rates resulting from these risk management measures going forward.

Table 48. The proportion (%) of antimicrobial-resistant *Escherichia coli* isolated from diseased animals

Agent	BP	Animal	2012†	2013†	2014†	2015	2016	2017	2018
ABPC	32*	Cattle	-	61.4	57.8	63.8	37.7	50.0	51.7
		Pigs	-	65.2	50.4	57.4	74.5	70.7	62.8
		Chickens	75.6	54.2	-	60.4	43.5	33.3	52.9
CEZ	32 (8* from 2016)	Cattle	-	21.1	6.7	14.9	15.6	15.6	17.2
		Pigs	-	10.1	6.1	9.3	34.3	35.0	21.5
		Chickens	40.2	16.7	-	14.6	15.2	11.1	17.6
CTX	4*	Cattle	-	10.5	6.7	8.5	7.8	8.9	9.2
		Pigs	-	2.5	0.0	3.7	2.9	3.3	3.3
		Chickens	37.8	14.6	-	10.4	6.5	5.6	11.8
SM	32	Cattle	-	-	68.9	78.7	49.4	61.1	57.5
		Pigs	-	-	64.3	66.7	74.5	72.4	54.5
		Chickens	-	-	-	60.4	56.5	38.9	51.0
GM	16*	Cattle	-	17.5	6.7	12.8	10.4	8.9	10.3
		Pigs	-	24.1	8.7	19.4	21.6	22.8	13.2
		Chickens	6.1	3.1	-	2.1	10.9	5.6	2.0
KM	64*	Cattle	-	38.6	26.7	29.8	16.9	26.7	28.7
		Pigs	-	34.2	33.9	31.5	46.1	39.0	32.2
		Chickens	51.2	35.4	-	39.6	50.0	36.1	27.5
TC	16*	Cattle	-	50.9	66.7	66.0	54.5	62.2	58.6
		Pigs	-	79.1	75.7	75.9	87.3	78.9	70.2
		Chickens	74.4	61.5	-	70.8	78.3	55.6	72.5
NA	32*	Cattle	-	29.8	33.3	36.2	18.2	33.3	33.3
		Pigs	-	60.1	52.2	50.0	48.0	50.4	33.1
		Chickens	73.2	59.4	-	52.1	56.5	55.6	35.3
CPFX	4*	Cattle	-	19.3	24.4	34.0	11.7	17.8	21.8
		Pigs	-	36.1	23.5	32.4	24.5	28.5	22.3
		Chickens	22.0	25.0	-	8.3	8.7	11.1	11.8
CL	16 (4* from 2016)	Cattle	-	5.3	6.7	0.0	10.4	20.0	11.5
		Pigs	-	3.2	0.0	2.8	56.9§1	52.0§1	35.5§1
		Chickens	2.4	1.0	-	0.0	8.7	0.0	2.0
CP	32*	Cattle	-	21.1	28.9	46.8	19.5	28.9	31.0
		Pigs	-	64.6	64.3	61.1	69.6	59.3	57.0
		Chickens	22	25	-	16.7	21.7	11.1	21.6
ST (TMP from 2012 to 2017)	ST is 76/4* (TMP is 16*)	Cattle	-	22.8	33.3	44.7	23.4	35.6	42.5
		Pigs	-	49.4	59.1	64.8	62.7	56.9	52.9
		Chickens	31.7	33.3	-	33.3	23.9	13.9	19.6
Strains tested (n)		Cattle	-	57	45	47	77	90	87
		Pigs	-	158	115	108	102	123	121
		Chickens	82	96	-	48	46	36	51

The unit of BP is μg/mL. * BP follows CLSI Criteria.

†-: Not under surveillance.

§1 If the BP of 16 used until 2015 is applied, CL resistance rate in pig-derived strains was 2.9% in 2016, 1.6% in 2017, and 0.8% in 2018.

Bacteria derived from healthy food-producing animals

Surveillance of food-borne pathogenic bacteria and indicator bacteria from healthy food-producing animals was carried out using samples of feces collected at animal and poultry slaughterhouses. When JVARM first began, surveillance was carried out using samples of feces from food-producing animals collected at farms by livestock hygiene service centers. Surveillance at animal and poultry slaughterhouses was added in FY2012, as this facilitated more intensive sampling at a stage closer to the final food product. In FY2016, there was confirmed to be no major difference in the findings of both surveys, so JVARM shifted to surveillance at animal and poultry slaughterhouses for bacteria derived from healthy food-producing animals.

i. *Escherichia coli*

Monitoring of antimicrobial resistance on 12 agents between 2012 and 2017, and 13 agents adding MEPM in 2018 was carried out. In 2018, resistance to SM and TC in pig- and chicken-derived strains was observed to exceed 40%, as was resistance to KM and nalidixic acid (NA) in chicken-derived strains. The rates of resistance to critically important antimicrobials for human medicine CTX, CPFX, and CL were respectively less than 4%, less than 13%, and 6% or less. No MEPM-resistant strains were observed. Looking at trends in resistance rates to each agent between 2012 and 2018, an upward trend was observed in KM resistance among chickens since 2012.

Table 49. The proportion (%) of antimicrobial-resistant *Escherichia coli* derived from animal and poultry slaughterhouses

Agent	BP	Animal	2012	2013	2014	2015	2016	2017	2018
ABPC	32*	Cattle	2.4	6.5	3.0	5.5	7.4	4.8	11.6
		Pigs	32.3	26.0	43.0	34.4	36.7	33.7	34.9
		Chickens	30.8	35.5	40.1	43.5	36.1	39.3	36.1
CEZ	32 (8* from 2016)	Cattle	0.4	0.3	0.0	0.0	1.9	0.8	0.5
		Pigs	1.0	0.8	1.1	1.0	6.7	1.2	2.4
		Chickens	3.0	7.8	5.8	3.8	10.8[§1]	6.7[§1]	7.7[§1]
CTX	4*	Cattle	0.0	0.0	0.4	0.0	0.4	0.4	0.0
		Pigs	0.0	0.0	1.1	0.0	1.1	1.2	0.0
		Chickens	1.5	4.8	4.1	2.2	5.7	4.7	3.2
MEPM	4*	Cattle	–	–	–	–	–	–	0.0
		Pigs	–	–	–	–	–	–	0.0
		Chickens	–	–	–	–	–	–	0.0
SM	32	Cattle	14.9	12.3	17.1	12.4	22.1	19.0	18.5
		Pigs	44.1	44.9	52.7	39.6	50.0	41.0	49.4
		Chickens	39.1	38.6	44.8	41.8	51.3	41.3	48.4
GM	16*	Cattle	0.0	0.3	0.0	0.0	0.8	0.0	0.0
		Pigs	0.5	2.4	6.5	2.1	3.3	3.6	3.6
		Chickens	1.5	1.8	2.9	2.2	5.1	6.0	5.2
KM	64*	Cattle	1.2	1.5	0.4	0.7	4.3	1.2	0.0
		Pigs	9.7	7.9	9.7	8.3	10.0	10.8	8.4
		Chickens	24.1	24.1	33.1	37.5	43.7	36.7	43.9
TC	16*	Cattle	19.0	16.4	19.8	18.6	29.8	21.0	26.5
		Pigs	58.5	62.2	59.1	45.8	56.7	55.4	55.4
		Chickens	49.6	44.0	43.6	54.9	56.3	46.0	49.0
NA	32*	Cattle	2.4	1.8	2.3	2.6	2.3	2.0	2.1
		Pigs	4.1	11.0	9.7	5.2	15.6	12.0	12.0
		Chickens	39.8	36.1	45.3	35.9	35.4	39.3	40.6
CPFX	4*	Cattle	0.0	0.6	0.8	0.0	0.4	0.0	0.5
		Pigs	1.5	0.8	2.2	3.1	4.4	0.0	1.2
		Chickens	6.0	5.4	9.9	4.9	10.1	12.0	12.3
CL	16 (4* from 2016)	Cattle	0.0	0.0	0.8	0.0	0.4	1.2	0.0
		Pigs	0.0	0.0	0.0	0.0	4.4[§2]	2.4[§2]	6.0[§2]
		Chickens	0.8	0.6	0.0	0.5	2.5	3.3	0.0
CP	32*	Cattle	5.2	2.3	3.8	2.9	2.3	2.8	4.8
		Pigs	23.6	23.6	34.4	25.0	25.6	21.7	25.3
		Chickens	11.3	11.4	15.1	9.8	19.6	11.3	17.4
ST	76/4*	Cattle	2.0	2.9	5.3	2.9	0.4	2.0	5.3
		Pigs	23.6	26.8	34.4	30.2	4.4	26.5	32.5
		Chickens	24.8	31.9	30.2	28.3	10.1	34.7	33.5
Strains tested (n)		Cattle	248	341	263	274	258	252	189
		Pigs	195	127	93	96	90	83	83
		Chickens	133	166	172	184	158	150	155

The unit of BP is μg/mL.

* BP follows CLSI Criteria.

[§1] If the BP of 32 used until 2015 is applied, CEZ resistance rate in chicken-derived strains was 7.0% in 2016, 4.7% in 2017, and 3.2% in 2018.

[§2] If the BP of 16 used until 2015 is applied, CL resistance rate in pig-derived strains was 1.1% in 2016, 0.0% in 2017, and 0.0% in 2018.

ii. *Campylobacter jejuni*

Monitoring of antimicrobial resistance on 7 agents between 2012 and 2016, and 8 agents adding AZM since 2017 was carried out. In 2018, resistance to NA, CPFX, and TC in cattle-derived strains exceeded 30%, as did resistance to NA in chicken-derived strains. On the other hand, resistance to SM, EM, and CP was less than 3% in each case. Resistance to CPFX, which is a critically important antimicrobial for human medicine, was 31.4% in cattle-derived strains and 29.8% in chicken-derived strains, while AZM resistance rates in both were less than 3%.

Table 50. The proportion (%) of antimicrobial-resistant *Campylobacter jejuni* derived from animal and poultry slaughterhouses

Agent*	BP	Animal	2012	2013	2014	2015	2016	2017	2018
ABPC	32	Cattle	0.0	9.1	12.9	8.9	7.4	8.2	8.6
		Chickens	19.7	19.8	17.5	19.1	16.2	28.4	14.9
SM	32	Cattle	2.4	3.5	3.8	3.2	6.2	4.1	5.7
		Chickens	1.4	0.0	3.5	2.1	8.8	1.5	0.0
EM	32†	Cattle	0.0	0.7	0.0	1.3	0.0	0.0	2.9
		Chickens	0.0	0.0	0.0	0.0	0.0	1.5	0.0
AZM	4	Cattle	–	–	–	–	–	0.0	2.9
		Chickens	–	–	–	–	–	1.5	0.0
TC	16†	Cattle	45.1	52.4	49.2	52.2	63.0	72.2	62.9
		Chickens	38.0	44.4	38.6	28.7	33.8	46.3	23.4
CP	16	Cattle	0.0	6.3	0.0	1.3	1.2	6.2	2.9
		Chickens	0.0	0.0	1.8	0.0	2.9	0.0	2.1
NA	32	Cattle	34.1	33.6	50.8	42.7	44.4	48.5	31.4
		Chickens	39.4	48.1	29.8	27.7	57.4	46.3	31.9
CPFX	4†	Cattle	34.1	29.4	49.2	40.8	44.4	50.5	31.4
		Chickens	39.4	39.5	29.8	26.6	51.5	44.8	29.8
Strains tested (n)		Cattle	82	143	132	157	81	97	35
		Chickens	71	81	57	94	68	67	47

The unit of BP is μg/mL.

* While GM was also included in the scope of monitoring, the proportion of GM-resistant strains was not listed because BP could not be established.

† BP follows CLSI Criteria.

iii. *Campylobacter coli*

Monitoring of antimicrobial resistance to 7 agents between 2012 and 2016 was carried out, but AZM was added in 2017, taking the total number to 8. In pig-derived strains in 2018, resistance to SM exceeding 60%, resistance to TC exceeding 80%, and resistance to NA and CPFX exceeding 50% was observed. On the other hand, CP resistance was less than 4%. Resistance to CPFX, which is a critically important antimicrobial for human medicine, was 58.6%, while the AZM resistance rate was 20.7%.

Table 51. The proportion (%) of antimicrobial-resistant *Campylobacter coli* derived from animal slaughterhouses

Agent*	BP	Animal	2012	2013	2014	2015	2016	2017	2018
ABPC	32	Pigs	23.3	25.5	36.6	24.6	15.4	29.5	17.2
SM	32	Pigs	67.4	78.3	69.9	72.3	64.1	68.9	69.0
EM	32†	Pigs	32.6	44.3	43.0	26.2	38.5	31.1	20.7
AZM	4	Pigs	–	–	–	–	–	31.1	20.7
TC	16†	Pigs	84.5	93.4	80.6	87.7	89.7	83.6	86.2
CP	16	Pigs	10.9	3.8	7.5	9.2	15.4	1.6	3.4
NA	32	Pigs	46.5	53.8	52.7	47.7	61.5	50.8	58.6
CPFX	4†	Pigs	46.5	46.2	50.5	47.7	59.0	54.1	58.6
Strains tested (n)		Pigs	129	106	93	65	39	61	29

The unit of BP is μg/mL.

* While GM was also included in the scope of monitoring, the proportion of GM-resistant strains was not listed because BP could not be established.

† BP follows CLSI Criteria.

iv. *Enterococcus* spp.

Monitoring of antimicrobial resistance on 10 agents between 2012 and 2014, and 11 agents adding VCM since 2015 was carried out. Resistance to KM, EM, lincomycin (LCM), and tylosin (TS) in strains isolated from chickens was observed to exceed 40% in 2017, as was oxytetracycline (OTC) resistance in pig- and chicken-derived strains. On the other hand, gentamicin (GM) resistance was less than 10% and no resistance to ampicillin (ABPC) was observed. Resistance to enrofloxacin (ERFX)—one of the fluoroquinolones, which are critically important

antimicrobials for human medicine—ranged between 0.0% and 3.7%. No resistance to VCM, which is a critically important antimicrobial for human medicine, was observed.

Among *Enterococcus* spp. in 2017, *E. faecalis* ranged from 4.1% (10 out of 242) of cattle-derived strains to 57.4% (85 out of 148) of chicken-derived strains , and *E. faecium* ranged from 1.7% (4 out of 242) of cattle-derived strains to 14.9% (22 out of 148) chicken-derived strains, which was generally same trend as before. Resistance to (ERFX)—one of the fluoroquinolones, which are critically important antimicrobials for human medicine—was 3.7% in pig-derived and 2.7% in chicken-derived strains of *Enterococcus* spp., but whereas the figure for *E. faecalis* was 0.0%, the figures for *E. faecium* were as high as 27.3% and 18.2%, respectively.

Table 52. The proportion (%) of antimicrobial-resistant *Enterococcus* spp. derived from animal slaughterhouses

Agent*	BP	Animal	2012	2014†	2015	2016	2017
ABPC	16§	Cattle	0.0	0.0	0.0	0.0	0.0
		Pigs	0.0	0.0	0.0	0.0	0.0
		Chickens	0.0	0.6	0.0	0.0	0.0
DSM	128	Cattle	85.6	31.2	14.9	2.9	0.8
		Pigs	82.0	55.7	34.4	29.7	28.0
		Chickens	69.2	30.9	49.2	30.6	27.0
GM	32	Cattle	61.2	4.2	2.2	0.8	0.0
		Pigs	43.3	3.4	3.1	4.4	1.2
		Chickens	29.3	5.5	9.4	4.5	3.4
KM	128	Cattle	55.2	5.0	4.1	1.3	0.8
		Pigs	56.2	20.5	31.3	17.6	22.0
		Chickens	68.4	37.0	47.0	41.4	41.9
OTC	16	Cattle	24.4	21.2	27.1	27.6	26.4
		Pigs	61.9	54.5	59.4	64.8	58.5
		Chickens	72.2	58.0	63.0	66.2	52.0
CP	32§	Cattle	1.5	0.0	0.0	0.4	0.4
		Pigs	17.5	17.0	10.4	15.4	14.6
		Chickens	13.5	8.8	7.2	10.2	8.8
EM	8§	Cattle	5.0	3.8	1.5	2.5	2.1
		Pigs	41.8	28.4	30.2	34.1	26.8
		Chickens	50.4	43.1	42.5	45.2	41.2
LCM	128	Cattle	27.9	3.1	0.7	2.5	2.1
		Pigs	59.8	50.0	34.4	37.4	35.4
		Chickens	52.6	34.3	43.1	47.1	40.5
ERFX	4	Cattle	6.0	1.2	0.4	0.8	0.0
		Pigs	22.7	9.1	2.1	1.1	3.7
		Chickens	9.8	3.9	13.3	3.8	2.7
TS	64	Cattle	2.0	2.3	0.7	2.1	2.5
		Pigs	33.0	21.6	19.8	28.6	24.4
		Chickens	49.6	42.0	35.9	42.7	41.2
VCM	32	Cattle	-	-	0.0	0.0	0.0
		Pigs	-	-	0.0	0.0	0.0
		Chickens	-	-	0.0	0.0	0.0
Strains tested (n)		Cattle	201	260	269	289	242
		Pigs	194	88	96	91	82
		Chickens	133	181	181	157	148

The unit of BP is μg/mL.

* While BC, SNM and VGM were also included in the scope of the survey, as was AZM in 2017, the proportions of BC-, SNM-, VGM- and AZM- resistant strains were not listed because BP could not be established.

† The monitoring was not conducted on *Enterococcus* spp. derived from animal slaughterhouses in FY2013.

§ BP follows CLSI Criteria.

-: Not under surveillance.

Table 53. The proportion (%) of antimicrobial-resistant *Enterococcus faecalis* derived from animal slaughterhouses

Agent*	BP	Animal	2012	2014†	2015	2016	2017
ABPC	16§	Cattle	0.0	0.0	0.0	0.0	0.0
		Pigs	0.0	0.0	0.0	0.0	0.0
		Chickens	0.0	0.6	0.0	0.0	0.0
DSM	128	Cattle	90.6	36.4	35.7	12.5	0.0
		Pigs	88.2	62.5	100.0	43.5	38.5
		Chickens	76.9	53.8	72.4	40.6	38.8
GM	32	Cattle	68.8	27.3	0.0	0.0	0.0
		Pigs	76.5	12.5	15.4	8.7	7.7
		Chickens	35.6	9.9	14.3	6.3	3.5
KM	128	Cattle	71.9	9.1	14.3	0.0	0.0
		Pigs	72.9	12.5	69.2	30.4	30.8
		Chickens	71.2	57.1	66.3	55.2	58.8
OTC	16	Cattle	31.3	27.3	28.6	37.5	10.0
		Pigs	64.7	87.5	92.3	73.9	84.6
		Chickens	75.0	67.0	70.4	83.3	65.9
CP	32§	Cattle	9.4	0.0	0.0	12.5	10.0
		Pigs	30.6	62.5	53.8	39.1	38.5
		Chickens	17.3	13.2	9.2	15.6	12.9
EM	8§	Cattle	21.9	9.1	0.0	0.0	10.0
		Pigs	51.8	62.5	69.2	52.2	61.5
		Chickens	58.7	64.8	60.2	59.4	58.8
LCM	128	Cattle	34.4	9.1	0.0	0.0	10.0
		Pigs	76.5	75.0	92.3	56.5	61.5
		Chickens	57.7	45.1	54.1	59.4	55.3
ERFX	4	Cattle	3.1	0.0	0.0	0.0	0.0
		Pigs	5.9	0.0	7.7	0.0	0.0
		Chickens	2.9	1.1	0.0	2.1	0.0
TS	64	Cattle	6.3	0.0	0.0	0.0	10.0
		Pigs	50.6	62.4	69.2	52.2	61.5
		Chickens	57.7	65.9	53.1	59.4	60.0
VCM	32	Cattle	-	-	0.0	0.0	0.0
		Pigs	-	-	0.0	0.0	0.0
		Chickens	-	-	0.0	0.0	0.0
Strains tested (n)		Cattle	32	11	14	8	10
		Pigs	85	8	13	23	13
		Chickens	104	91	98	96	85

The unit of BP is μg/mL.

* While BC, SNM and VGM were also included in the scope of the survey, as was AZM in 2017, the proportions of BC-, SNM-, VGM- and AZM- resistant strains were not listed because BP could not be established.

† The monitoring was not conducted on *Enterococcus* spp. derived from animal slaughterhouses in FY2013.

§ BP follows CLSI Criteria.

-: Not under surveillance.

Table 54. The proportion (%) of antimicrobial-resistant *Enterococcus faecium* derived from animal slaughterhouses

Agent*	BP	Animal	2012	2014†	2015	2016	2017
ABPC	16§	Cattle	0.0	0.0	0.0	0.0	0.0
		Pigs	0.0	0.0	0.0	0.0	0.0
		Chickens	2.4	0.0	0.0	0.0	0.0
DSM	128	Cattle	22.7	33.3	0.0	25.0	0.0
		Pigs	30.3	58.3	0.0	28.6	27.3
		Chickens	28.6	13.9	16.1	30.0	18.2
GM	32	Cattle	2.3	0.0	0.0	0.0	0.0
		Pigs	0.0	0.0	0.0	0.0	0.0
		Chickens	3.6	2.8	3.2	10.0	9.1
KM	128	Cattle	34.1	33.3	16.7	0.0	50.0
		Pigs	30.3	25.0	72.7	28.6	72.7
		Chickens	34.5	33.3	35.5	40.0	45.5
OTC	16	Cattle	9.1	0.0	16.7	0.0	0.0
		Pigs	42.4	41.7	9.1	42.9	54.5
		Chickens	63.1	58.3	64.5	60.0	31.8
CP	32§	Cattle	0.0	0.0	0.0	0.0	0.0
		Pigs	0.0	25.0	0.0	0.0	9.1
		Chickens	4.8	8.3	6.5	0.0	9.1
EM	8§	Cattle	11.4	0.0	33.3	25.0	0.0
		Pigs	15.2	58.3	54.5	57.1	45.5
		Chickens	32.1	30.6	35.5	20.0	27.3
LCM	128	Cattle	9.1	0.0	0.0	0.0	0.0
		Pigs	39.4	50.0	9.1	28.6	27.3
		Chickens	31.0	19.4	29.0	20.0	27.3
ERFX	4	Cattle	36.4	0.0	16.7	25.0	0.0
		Pigs	45.5	25.0	0.0	0.0	27.3
		Chickens	65.5	13.9	71.0	30.0	18.2
TS	64	Cattle	9.1	0.0	0.0	0.0	0.0
		Pigs	12.1	16.7	0.0	28.6	18.2
		Chickens	26.2	19.4	22.6	20.0	27.3
VCM	32	Cattle	-	-	0.0	0.0	0.0
		Pigs	-	-	0.0	0.0	0.0
		Chickens	-	-	0.0	0.0	0.0
Strains tested (n)		Cattle	44	6	6	4	4
		Pigs	84	12	11	7	11
		Chickens	64	36	31	10	22

The unit of BP is μg/mL.

* While BC, SNM and VGM were also included in the scope of the survey, as was AZM in 2017, the proportions of BC-, SNM-, VGM- and AZM- resistant strains were not listed because BP could not be established.

† The monitoring was not conducted on *Enterococcus* spp. derived from animal slaughterhouses in FY2013.

§ BP follows CLSI Criteria.

-: Not under surveillance.

v. *Salmonella* spp.

Monitoring of 12 agents in chicken-derived strains was carried out between 2012 and 2017, but MEPM was added in 2018, bringing the number monitored to 13. Among chicken-derived strains in 2018, resistance to SM and TC exceeding 70%, resistance to KM exceeding 60%, and resistance to ST exceeding 50% was observed. On the other hand, CEZ or CP resistance was less than 4% and no resistance to GM was observed. In the realm of critically important antimicrobials for human medicine, the rate of resistance to CTX was 2.6%, resistance to CL or CPFX was less than 1%, and no resistance to MEPM was observed. Looking at trends in resistance rates to each agent between 2012 and 2017, while a decline was observed in ABPC and CEZ resistance since 2012, a rise in KM resistance has been observed over the same period.

The *Salmonella* serotypes most commonly isolated from poultry slaughterhouses in FY2015-2018 were *S.* Schwarzengrund, *S.* Infantis, *S.* Typhimurium, and *S.* Manhattan. In a comparison of *Salmonella* serotypes isolated from poultry slaughterhouses with those isolated from food and from humans (source: Nippon AMR One Health Report 2019: Table 19) (Table 57, Figure 1), the same trends were observed in *Salmonella* serotypes isolated from poultry slaughterhouses as in those isolated from food. The top five serotypes isolated from poultry slaughterhouses were the same as those isolated from food, respectively accounting for 97% and 84% of all serotypes from those sources, which suggested a relationship between them. On the other hand, the serotypes isolated from humans were more diverse than those isolated from poultry slaughterhouses and food, with the top five serotypes isolated from poultry slaughterhouses accounting for 24% of human-derived strains, which suggested the possibility that there are variety of origin other than poultry or their food products. In a comparison of resistance rates between *S.* Schwarzengrund and *S.* Infantis, which are the top two serotypes accounting for the majority of strains isolated from poultry slaughterhouses (Table 58, Figure 2) (source: Nippon AMR One Health Report 2019: Table 29), similarities between food-derived and poultry slaughterhouse-derived strains were found in respect of resistance to KM, SM, and TC in *S.* Infantis and resistance to KM and TC in *S.* Schwarzengrund. However, the fact that they showed a different trend from that seen in resistance rates among human-derived strains suggested the possibility that there are sources of these serotypes isolated from humans other than poultry and their food products.

Table 55. The proportion (%) of antimicrobial-resistant *Salmonella* spp. derived from poultry slaughterhouses

Agent	BP	Animal	2012	2013	2014	2015	2016	2017	2018
ABPC	32*	Chickens	31.9	22.9	17.2	13.0	13.5	8.0	6.8
CEZ	32 (8* from 2016)	Chickens	7.4	5.9	3.1	1.6	7.7	2.5	3.4
CTX	4*	Chickens	7.4	5.1	2.3	1.6	1.9	1.8	2.6
MEPM	4*	Chickens	–	–	–	–	–	–	0.0
SM	32	Chickens	77.7	84.7	85.9	76.4	77.9	60.7	77.8
GM	16*	Chickens	0.0	0.0	0.0	0.0	0.0	0.0	0.0
KM	64*	Chickens	31.9	42.4	57.8	69.1	72.1	73.2	66.7
TC	16*	Chickens	74.5	82.2	85.2	83.7	82.7	77.7	77.8
CP	32*	Chickens	0.0	0.8	1.6	1.6	0.0	0.9	1.7
CL	16 (4* from 2016)	Chickens	0.0	0.0	0.0	0.0	0.0	0.0	0.9
NA	32*	Chickens	29.8	19.5	17.2	15.4	12.5	17.0	18.8
CPFX	4 (1* from 2016)	Chickens	0.0	0.0	0.0	0.0	0.0	0.0	0.9
ST	76/4*	Chickens	31.9	48.3	51.6	57.7	56.7	55.4	53.0
Strains tested (n)		Chickens	94	118	128	123	104	112	117

The unit of BP is μg/mL.
* BP follows CLSI Criteria.

Table 56. Serotypes of *Salmonella enterica* derived from poultry slaughterhouses (FY2015-2018)

Serotypes	Number of strains isolated	(%)
Schwarzengrund	326	64.9
Infantis	105	20.9
Typhimurium	35	7.0
Manhattan	12	2.4
Agona	11	2.2
Others	13	2.6
Total	502	100

Table 57. Serotypes of *Salmonella enterica* derived from poultry slaughterhouses, food, and humans (FY2015-2018)

From poultry slaughterhouses (n=502)	%
Schwarzengrund	64.9
Infantis	20.9
Typhimurium	7.0
Manhattan	2.4
Agona	2.2
Others	2.6
Total	100

From food (n=460)*	%
Schwarzengrund	31.3
Infantis	38.7
Typhimurium	2.4
Manhattan	9.1
Agona	2.8
Others	15.7
Total	100

From humans (n=1502)*	%
Schwarzengrund	4.7
Infantis	11.0
Typhimurium	5.7
Manhattan	2.8
Agona	0.0
Enteritidis	11.5
04:i:-	8.4
Thompson	7.9
Saintpaul	6.5
Chester	3.0
Newport	2.7
Others	35.8
Total	100

*Source: Nippon AMR One Health Report 2019: Table 19

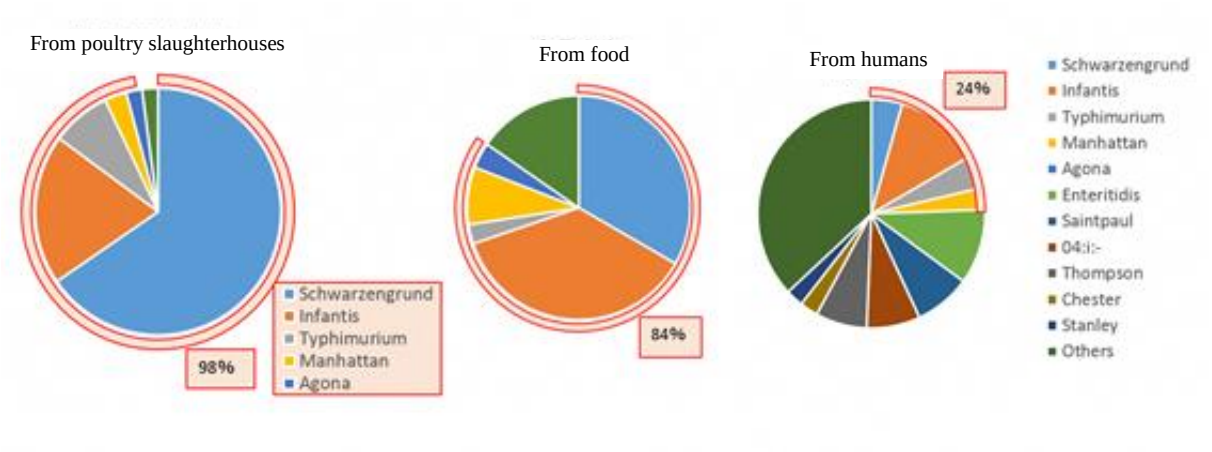


Figure 1. Proportions of the top 5 serotypes of *Salmonella enterica* derived from poultry slaughterhouses isolated in food and humans (2015-2018) (figures for proportions in human-derived and food-derived strains are quoted from Nippon AMR One Health Report 2019: Table 19)

Table 58. Resistance rates among *S*. Infantis and *S*. Schwarzengrund strains isolated from poultry slaughterhouses (chicken), food, and humans (2015-2018)

	Infantis			Schwarzengrund		
	Chicken (n=98)	Food (n=144)*	Humans (n=165)*	Chicken (n=326)	Food (n=178)*	Humans (n=71)*
ABPC	6.1	11.1	1.8	0.9	7.9	4.2
GM	0.0	0.7	0.0	0.0	0.0	0.0
KM	46.9	38.9	15.2	89.6	82.0	60.6
SM	72.4	78.5	30.3	75.2	82.6	70.4
TC	80.6	84.0	35.8	86.5	86.5	69.0
CP	1.0	2.1	1.2	0.9	11.2	1.4
CTX	6.1	6.3	1.2	0.6	0.6	2.8
NA	6.1	4.2	5.5	12.9	18.5	16.9
CPFX	0.0	0.0	0.0	0.3	0.0	0.0

*Source: Nippon AMR One Health Report 2019: Table 29

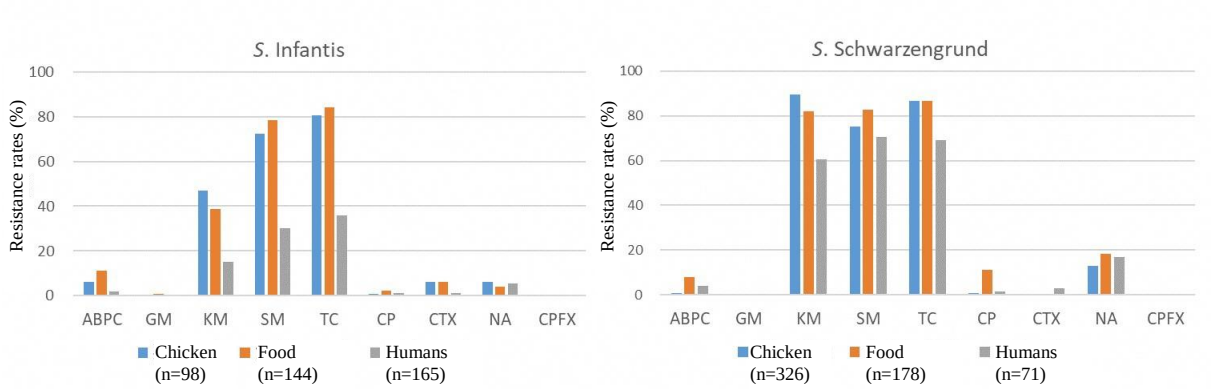


Figure 2. Resistance rates among *S*. Infantis and *S*. Schwarzengrund strains derived from humans, food, and poultry slaughterhouses (2015-2018) (figures for resistance rates in human-derived and food-derived strains are quoted from Nippon AMR One Health Report 2019: Table 29)

2) Aquatic animal farming

Source: Japanese Veterinary Antimicrobial Resistance Monitoring System (JVARM)

For the monitoring and surveillance of antimicrobial resistance in aquaculture under the JVARM, antimicrobial susceptibility monitoring are conducted focusing on *Lactococcus garvieae*, *Photobacterium damselae* subsp. *Piscicida* and *Vibrio* spp. that are derived from diseased fish and on *Vibrio parahaemolyticus* that is derived from aquaculture environment. Strains that were isolated and identified from diseased fish at prefectural fisheries experiment stations were mainly used for testing. Between 2011 and 2016, strains were provided by four to six prefectures per year, increasing to nine in 2017 and 12 in 2018. In antimicrobial susceptibility tests, MIC values were measured using a broth microdilution method or an agar plate dilution method compliant with the CLSI Guidelines. For agents with a BP established by the CLSI, susceptibility was interpreted using the CLSI Criteria. The BPs of the other antimicrobial agents were determined microbiologically (midpoint of a bimodal MIC distribution).

To further enhance surveillance of trends in antimicrobial resistance in aquaculture, the scope of surveillance was expanded to all farmed fishes in FY2017 and antimicrobial susceptibility monitoring of *Lactococcus garvieae* and *Vibrio* spp. is now being carried out.

i. *Lactococcus garvieae* derived from diseased fish

The monitoring of antimicrobial resistance was conducted on 4 agents that had efficacy on the streptococcal diseases from 2011 to 2018. In 2018, resistance to LCM was 31.5%. However, resistance to EM and OTC was maintained at 0%. As the MIC distribution of florfenicol (FF) was not bimodal, the BP could not be established and the resistance rate could therefore not be calculated. However, all strains showed low MIC values (≤4 μg/ml), which suggests that susceptibility to this agent has been maintained (Table 59).

Table 59. The proportion (%) of antimicrobial-resistant *Lactococcus garvieae*

Agent*[1]	BP	2011	2012	2013	2014	2015	2016	2017*[2*3]	2018
EM	8	0.0	10.3	0.0	0.0	3.7	8.0	1.9	0
LCM	4	92.6	76.9	71.4	62.5	59.3	76.0	61.0	31.5
OTC	8	0.0	12.8	0.0	0.0	3.7	8.0	0.0	0
Strains tested (n)		27	39	21	16	27	25	105	149

The unit of BP is μg/mL.

*[1]: While FF was also included in the scope of survey, the proportion of FF-resistant strains was not listed because BP could not be established.

*[2]: Monitoring focused only on *Seriola* until 2016, but was expanded in 2017 to include strains derived from all farmed fish species.

*[3]: An agar plate dilution method was used in monitoring until 2016, but the broth microdilution method has been used since 2017.

ii. *Photobacterium damselae* subsp. *piscicida* derived from diseased fish (Seriola)

The monitoring of antimicrobial resistance was conducted on 5 agents that had efficacy against pseudotuberculosis from 2011 to 2016. The number of tested strains was small, with just 3 being tested in 2015, while no strains were isolated at all in 2016. In strains tested between 2011 and 2014, the resistance rate varied particularly for ABPC and for oxolinic acid (OA). However, the resistance rate remained at 7.1% or lower both for bicozamycin (BCM) and for fosfomycin (FOM). Although the proportion of FF resistant strains was not calculated given that no bimodal MIC distribution was observed, MIC values were low (≤ 1 μg/ml) in all strains, suggesting that the susceptibility was maintained. The strains tested in 2015 showed a low MIC value to all the tested agents (Table 60).

Table 60. The proportion (%) of antimicrobial-resistant pseudotuberculosis-causing bacteria (*Photobacterium damselae* subsp. *piscicida*)

Agent*	BP	2011	2012	2013	2014
ABPC	2	11.8	17.6	7.1	59.4
FOM	32	0.0	0.0	7.1	0.0
BCM	64	0.0	0.0	0.0	0.0
OA	1	100.0	82.4	92.9	3.1
Strains tested (n)		17	17	14	32

The unit of BP is μg/mL.

* While FF was also included in the scope of survey, its resistance proportion is not listed because BP cannot be established.

No data for 2015 are shown, because only three strains were tested.

No strains were isolated at all in 2016.

iii. *Vibrio* spp.

Monitoring of agents effective against vibriosis has been carried out since 2017 in respect of strains derived from diseased fish. In 2018, OTC showed bimodal MIC distribution, with a resistance rate of 15.7%. Although the MIC distribution of FF was not bimodal and almost all strains showed low MIC values (≤2 μg/ml), one strain did show a value of 16 μg/ml. Although the MIC distribution of OA was not bimodal, all strains showed low MIC values (≤1 μg/ml), which suggested that susceptibility to these agents was maintained. Sulfamonomethoxine (SMMX), however, did not show bimodal MIC distribution, so the resistance rate could not be calculated (Table 61).

Table 61. Trends in resistance rates among *Vibrio* spp. (%)

Agent*	BP	2017	2018
OTC	4	12.8	15.7
Strains tested (n)		39	51

The unit of BP is μg/mL.

* While FF, OA and SMMX were also included in the scope of survey, their resistance proportion were not listed because BP cannot be established.

iv. *Vibrio parahaemolyticus* derived from aquaculture environment

Monitoring of five agents approved as aquatic drugs (EM, LCM, OTC, OA and FF) was carried out using the 53 and 50 strains derived from aquaculture environments in 2011 and 2012.

Given that no bimodal MIC distribution was observed for any of these agents, the proportion of the strain that was resistant to those agents was not calculated. MIC values, however, were low (≤ 2 μg/ml for EM, ≤ 1 μg/ml for OTC and FF, and ≤ 0.5 μg/ml for OA) in all strains, excluding lincomycin (≤ 256 μg/ml for LCM), which suggested that the susceptibility was maintained to these agents.

3) Companion animals

Source: Japanese Veterinary Antimicrobial Resistance Monitoring System (JVARM)

Routine monitoring of antimicrobial resistance in bacteria derived from diseased dogs and cats was launched in FY2017, as part of efforts to strengthen monitoring under the AMR Action Plan. Monitoring of antimicrobial resistance in bacteria derived from diseased animals, as opposed to those from healthy animals, has the potential to be affected by the use of antimicrobials in treatment or by the incidence of diseases. As with food-producing animals, obtaining information about antimicrobial resistance trends in healthy companion animals to serve as a baseline is considered important. Accordingly, as well as ongoing monitoring of diseased animals, surveillance of healthy dogs and cats was launched in 2018.

Antimicrobial susceptibility tests measured the MIC values of antimicrobials in respect of the bacterial strains collected, using a broth microdilution method compliant with the CLSI Criteria. For agents with a BP indicated by the CLSI, susceptibility was interpreted using the CLSI Criteria. The BPs of the other antimicrobial agents used EUCAST values or were determined microbiologically (midpoint of a bimodal MIC distribution).

a. Bacterial strains from diseased dogs and cats

Bacterial strains from diseased dogs and cats were collected from small-animal clinical laboratories. The country was divided into six regional blocks—Hokkaido and Tohoku, Kanto, Chubu, Kinki, Chugoku and Shikoku, and Kyushu and Okinawa—and the number of strains allocated on the basis of the number of notifications of veterinary clinic (small animal and other animals) establishment received.

Samples of *Escherichia coli* and *Klebsiella* spp. were collected from urine and reproductive organs, samples of coagulase-positive *Staphylococcus* spp. from urine and skin, and samples of *Enterococcus* spp. from urine and ears.

i. *Escherichia coli*

Monitoring of 14 agents was carried out for strains from dogs and cats. As in 2017 and 2018, rates of resistance to ABPC and NA were high in 2019 at 46.9-60.2%. On the other hand, the rate of resistance to GM, KM, and CP in strains isolated from dogs and cats was less than 20%. The rates of resistance to critically important antimicrobials for human medicine in dog- and cat-derived strains respectively were as follows: 26.4-26.6% to CTX; and 37.5-38.8% to CPFX. No resistance to CL and MEPM was observed.

Table 62. Resistance rates of *Escherichia coli* derived from diseased dogs and cats (%)

Agent	BP	Animal	2017	2018	2019
ABPC	32*	Dogs	55.3	63.0	51.1
		Cats	64.0	65.6	60.2
CEZ	32*	Dogs	31.2	47.4	30.3
		Cats	37.5	49.5	32.0
CEX	32†	Dogs	31.7	42.9	31.5
		Cats	41.9	47.3	31.3
CTX	4*	Dogs	26.1	41.6	26.4
		Cats	33.8	40.9	26.6
MEPM	4*	Dogs	0.0	0.0	0.0
		Cats	0.0	0.0	0.0
SM	32†	Dogs	29.6	29.9	20.2
		Cats	32.4	34.4	28.9
GM	16*	Dogs	14.1	18.8	12.9
		Cats	12.5	15.1	9.4
KM	64*	Dogs	6.5	7.8	5.1
		Cats	8.1	12.9	7.0
TC	16*	Dogs	28.1	27.3	21.3
		Cats	24.3	28.0	26.6
CP	32*	Dogs	12.6	16.9	11.8
		Cats	13.2	15.1	7.8
CL	4*	Dogs	1.0	0.6	0.0
		Cats	0.0	0.0	0.0
NA	32*	Dogs	61.8	72.7	56.2
		Cats	58.8	68.8	46.9
CPFX	4*	Dogs	43.2	55.2	38.8
		Cats	39.0	50.5	37.5
ST	76/4*	Dogs	24.6	27.9	17.4
		Cats	22.1	34.4	22.7
Strains tested (n)		Dogs	199	154	178
		Cats	136	93	128

The unit of BP is μg/mL.
* BP follows CLSI Criteria.
† BP follows EUCAST Criteria.

ii. *Klebsiella* spp.

Monitoring of 13 agents was carried out. Of the *Klebsiella* spp., *K. pneumoniae* was the most commonly collected, followed by *K. oxytoca*. In 2019, resistance to CEZ, CEX, NA, and CPFX was observed to exceed 40% in dog- and cat-derived strains, as was resistance to CTX, SM, GM, TC, and ST in cat-derived strains. On the other hand, resistance to KM was below 20% in strains derived from both dogs and cats. Looking at rates of resistance to critically important antimicrobials for human medicine, resistance to CTX was 34.6-56.8%, and resistance to CPFX was 46.9-75.7%. No resistance to CL and MEPM was observed.

Table 63. Resistance rates of *Klebsiella* spp. derived from diseased dogs and cats (%)

Agent	BP	Animal	2017	2018	2019
CEZ	32*	Dogs	47.2	51.0	42.0
		Cats	84.6	90.0	67.6
CEX	32†	Dogs	44.4	46.9	42.0
		Cats	84.6	80.0	56.8
CTX	4*	Dogs	41.7	38.8	34.6
		Cats	80.8	80.0	56.8
MEPM	4*	Dogs	0.0	0.0	0.0
		Cats	0.0	0.0	0.0
SM	32†	Dogs	26.4	34.7	29.6
		Cats	57.7	55.0	59.5
GM	16*	Dogs	26.4	28.6	21.0
		Cats	61.5	55.0	40.5
KM	64*	Dogs	8.3	12.2	6.2
		Cats	23.1	20.0	13.5
TC	16*	Dogs	33.3	42.9	30.9
		Cats	57.7	65.0	48.6
CP	32*	Dogs	25.0	32.7	19.8
		Cats	26.9	45.0	16.2
CL	4*	Dogs	1.4	0.0	0.0
		Cats	3.8	0.0	0.0
NA	32*	Dogs	51.4	61.2	46.9
		Cats	84.6	95.0	81.1
CPFX	4*	Dogs	44.4	57.1	46.9
		Cats	84.6	90.0	75.7
ST	76/4*	Dogs	41.7	46.9	37.0
		Cats	76.9	70.0	56.8
Strains tested (n)		Dogs	72	49	81
		Cats	26	20	37

The unit of BP is μg/mL.

* BP follows CLSI Criteria.

†EUCAST values were used as the BP for CEX. As EUCAST has not set a BP for SM, the JVARM value (midpoint of a bimodal MIC distribution obtained in FY2001) was used. Surveillance also covered ABPC, but the figures are not given here, due to the intrinsic resistance of *K. pneumoniae* and *K. oxytoca*.

iii. Coagulase-positive *Staphylococcus* spp.

The most common coagulase-positive *Staphylococcus* spp. in both dogs and cats was *S. pseudintermedius*. *S. aureus*, *S. schleiferi* subsp. *coagulans*, and *S. intermedius* were also collected.

In the case of *S. pseudintermedius*, resistance to oxacillin (MPIPC), GM, TC, CP, EM, AZM, and CPFX in dog- and cat-derived strains was observed to exceed 40% in 2019. More than 70% of strains isolated from both dogs and cats were observed to be resistant to AZM and CPFX, which are critically important antimicrobials for human medicine.

In *S. aureus* isolated from cats, resistance to MPIPC, CEZ, CEX, cefoxitin (CFX), CTX, EM, AZM, and CPFX was observed to exceed 60% in 2019. On the other hand, no resistance to SM and CP was observed. Rates of resistance to CTX, AZM, and CPFX, which are critically important antimicrobials for human medicine, were observed to be more than 70%.

Table 64. Resistance rates of *Staphylococcus pseudintermedius* derived from diseased dogs and cats (%)

Agent*	BP	Animal	2017	2018	2019
MPIPC	0.5†	Dogs	58.2	56.6	62.8
		Cats	68.6	81.8	81.0
GM	16†	Dogs	26.2	54.2	64.1
		Cats	13.7	63.6	52.4
TC	16†	Dogs	62.3	67.5	66.7
		Cats	52.9	81.8	85.7
CP	32†	Dogs	43.4	49.4	60.3
		Cats	64.7	72.7	83.3
EM	8†	Dogs	67.2	74.7	79.5
		Cats	70.6	86.4	95.2
AZM	8†	Dogs	67.2	74.7	79.5
		Cats	66.7	86.4	95.2
CPFX	4†	Dogs	64.8	75.9	75.6
		Cats	88.2	100.0	97.6
Strains tested (n)		Dogs	122	83	78
		Cats	51	22	42

The unit of BP is μg/mL.

† BP follows CLSI Criteria.

While ABPC, CEZ, CEX, CFX, CMZ, CTX and SM were also included in the scope of monitoring, the proportion of ABPC-, CEZ-, CEX-, CFX-, CMZ-, CTX- and SM-resistant strains were not listed because BP could not be established.

Table 65. Resistance rates of *Staphylococcus aureus* derived from diseased cats (%)

Agent	BP	Animal	2017	2018	2019
MPIPC	4†	Cats	61.9	70.6	70.0
CEZ	4$	Cats	61.9	64.7	66.7
CEX	16$	Cats	61.9	70.6	70.0
CFX	8$	Cats	61.9	64.7	70.0
CTX	8$	Cats	61.9	64.7	70.0
SM	32$	Cats	4.8	5.9	0.0
GM	16†	Cats	47.6	58.8	36.7
TC	16†	Cats	14.3	41.2	43.3
CP	32†	Cats	0.0	0.0	70.0
EM	8†	Cats	66.7	76.5	70.0
AZM	8†	Cats	66.7	76.5	70.0
CPFX	4†	Cats	61.9	76.5	83.3
Strains tested (n)		Cats	21	17	30

The unit of BP is μg/mL.

† BP follows CLSI Criteria. $ Uses EUCAST's ECOFF value

* While ABPC and CMZ were also included in the scope of monitoring, the proportion of ABPC- and CMZ-resistant strains were not listed because BP could not be established.

iv. *Enterococcus* spp.

The most common *Enterococcus* spp. in both dogs and cats was *E. faecalis*, followed by *E. faecium*. In 2018, rates of resistance to TC were in excess of 60% in both dog- and cat-derived strains, while CP resistance rates was below 20%. Between 31.1% and 43.7% of dog- and cat-derived strains were observed to be resistant to CPFX, a critically important antimicrobial for human medicine. Measurement of VCM as a test drug began in 2019, but no resistant bacteria were found in strains from dogs and cats.

Table 66. Resistance rates of *Enterococcus* spp. derived from diseased dogs and cats (%)

Agent*	BP	Animal	2017	2018	2019
ABPC	16†	Dogs	26.7	20.5	20.0
		Cats	17.3	31.6	33.0
GM	32§	Dogs	22.9	15.4	25.2
		Cats	19.4	24.6	25.2
TC	16†	Dogs	65.6	67.9	68.9
		Cats	70.4	73.7	64.1
CP	32†	Dogs	20.6	14.1	18.5
		Cats	20.4	15.8	8.7
EM	8†	Dogs	61.8	39.7	43.0
		Cats	41.8	54.4	39.8
CPFX	4†	Dogs	42.7	28.2	31.1
		Cats	34.7	49.1	43.7
VCM	32†	Dogs			0.0
		Cats			0.0
Strains tested (n)		Dogs	131	78	135
		Cats	98	57	103

The unit of BP is μg/mL.

* While AZM was also included in the scope of monitoring, the proportion of AZM-resistant strains were not listed because BP could not be established.

† BP follows CLSI Criteria.

§ As EUCAST has not set a BP for GM, the JVARM value (midpoint of a bimodal MIC distribution obtained in FY2002) was used.

b. Bacterial strains from healthy dogs and cats (2018-2019)

Bacterial strains from healthy dogs and cats were collected from veterinary clinics across the country with the cooperation of the Japan Veterinary Medical Association, with the number of strains allocated on the basis of the number of notifications of veterinary clinic (small animal and other animals) establishment received by each prefecture. Rectal swabs were taken from healthy dogs and cats brought to veterinary clinics for health checkups and vaccination. *Escherichia coli* and *Enterococcus* spp. were then isolated from the samples, identified, and sent for antimicrobial susceptibility tests.

i. *Escherichia coli*

Monitoring of 14 agents was carried out. In strains isolated from healthy dogs and cats, the rates of resistance to ABPC and NA were high in both 2018 and 2019, while rates of resistance to the other antimicrobials were less than 20%. The rates of resistance to critically important antimicrobials for human medicine in dog- and cat-derived strains were as follows: 6.4-13.2% to CTX, and 8.8-18.5% to CPFX, while no MEPM- or CL-resistant strains were isolated. In all drugs which resistant strains had been found, resistance rates of *Escherichia coli* derived from healthy dogs and cats were lower than that from diseased dogs and cats collected in same year.

Table 67. Resistance rates of *Escherichia coli* derived from healthy dogs and cats (%)

Agent	BP	Animal	2018	2019
ABPC	32*	Dogs	33.8	23.3
		Cats	28.5	27.1
CEZ	32*	Dogs	19.2	11.4
		Cats	17.1	13.3
CEX	32†	Dogs	17.9	11.4
		Cats	18.4	13.3
CTX	4*	Dogs	13.2	8.8
		Cats	10.8	6.4
MEPM	4*	Dogs	0.0	0.0
		Cats	0.0	0.0
SM	32†	Dogs	19.2	13.0
		Cats	11.4	11.7
GM	16*	Dogs	3.3	2.6
		Cats	2.5	4.3
KM	64*	Dogs	5.3	3.6
		Cats	1.9	3.2
TC	16*	Dogs	16.6	13.0
		Cats	10.8	10.1
CP	32*	Dogs	4.6	5.7
		Cats	1.3	3.7
CL	4*	Dogs	0.0	0.0
		Cats	0.0	0.0
NA	32*	Dogs	27.8	20.7
		Cats	24.7	28.7
CPFX	1*	Dogs	18.5	8.8
		Cats	12.0	13.3
ST	76/4*	Dogs	13.2	7.8
		Cats	12.0	9.6
Strains tested (n)		Dogs	151	193
		Cats	158	188

The unit of BP is μg/mL.

*BP follows CLSI Criteria.

*BP follows EUCAST Criteria.

ii. *Enterococcus* spp.

The most common *Enterococcus* spp. in both dogs and cats were *E. faecalis*. *E. faecium*, *E. gallinarum*, *E. durans*, *E. hirae*, *E. avium*, *E. casseliflavus*, and *E. raffinosus* were also collected. In strains isolated from dogs and cats in both 2018 and 2019, the highest rate of resistance was to TC, followed by EM, while rates of resistance to the other antimicrobials were less than 20%. The rates of resistance to critically important antimicrobial for human medicine CPFX in dog- and cat-derived strains were 5.7-14.4%, while no VCM-resistant strains were isolated.

Table 68. Resistance rates of *Enterococcus* spp. derived from healthy dogs and cats (%)

Agent*	BP	Animal	2018	2019
ABPC	16†	Dogs	6.9	1.9
		Cats	2.2	3.4
GM	32§	Dogs	12.4	7.0
		Cats	11.1	15.7
TC	16†	Dogs	55.9	41.8
		Cats	48.9	61.8
CP	32†	Dogs	15.9	10.1
		Cats	11.1	14.6
EM	8†	Dogs	32.4	23.4
		Cats	34.4	34.8
CPFX	4†	Dogs	13.8	5.7
		Cats	14.4	13.5
VCM	32†	Dogs	0.0	0.0
		Cats	0.0	0.0
Strains tested (n)		Dogs	145	158
		Cats	90	89

The unit of BP is μg/mL.

* While AZM was also included in the scope of monitoring, the proportion of AZM-resistant strains were not listed because BP could not be established.

† BP follows CLSI Criteria.

§ As EUCAST has not set a BP for GM, the JVARM value (midpoint of a bimodal MIC distribution obtained in FY2002) was used.

4) Wild animals

Antimicrobial susceptibility tests were conducted on 963 strains of *Escherichia coli* isolated from 475 wild animals (525 strains from 242 deer; 224 strains from 112 wild boar; 199 strains from 113 small mammals (including brown rats, black rats, large Japanese field mice, and Japanese shrew moles); 10 strains from 4 badgers; 3 strains from 2 feral cattle ((Japanese native cattle *Kuchinoshima-Ushi*); and 2 strains from 2 Amami rabbits) within Japan between 2013 and 2017. Strains isolated from deer and wild boar demonstrated resistance to 8 agents, while those isolated from small mammals showed resistance to 10 agents. Resistant bacteria were observed in 5.9% of strains isolated from deer, with resistance to tetracycline (TC, 4.4%) highest, followed by colistin (1.5%), ABPC, and sulfamethoxazole-trimethoprim (ST, 0.8%). Resistance was observed in 8.0% of strains isolated from wild boar, with resistance to TC (4.0%) highest, followed by ABPC (3.6%), and CP (1.8%). Resistant strains accounted for 18.1% of strains isolated from small mammals, with resistance to ABPC and TC (12.6% in both cases) highest, followed by ST (11.6%). In particular, in the case of small mammals, most of antimicrobial-resistant strains were observed in strains from facilities related to food-producing livestock, with resistance to ABPC, ST, TC, and NA observed to be in excess of 10%. However, resistance to only 2 agents (TC and ST) was found in strains isolated from urban areas and no resistance to any of the 12 agents monitored was found in strains isolated from mountainous areas. Bacteria producing extended-spectrum beta-lactamase (ESBL) were observed in 1 strain isolated from small mammals (livestock facility) and the ESBL was found to be CTX-M-1.

While the effects of antimicrobial-resistant bacteria contamination of habitats can be seen in the distribution of resistant bacteria in land-dwelling wild animals, the rates are low compared with food-producing animals and companion animals. Antimicrobial-resistant bacterial contamination of the mountainous areas that form the main habitat of the deer and wild boar covered by this study appeared to be low.

Table 69. Resistance rates of *Escherichia coli* derived from wild animals (%)

	Deer				Wild boar	Small mammals				Other		
Agent (BP)	Mountains	Shrines	Parks	Subtotal	Mountains	Livestock facilities	Urban areas	Mountains	Subtotal	Badgers	Kuchinoshima cattle	Amami rabbits
Number of strains	327	102	96	525	224	106	47	46	199	10	3	2
Number resistant	15	5	11	31	18	30	6	0	36	4	2	1
Resistance rate (%)	4.6	4.9	11.5	5.9	8.0	28.3	14.0	0	18.1	40.0	66.7	50.0
ABPC (32)	0.6	2.0	0	0.8	3.6	23.6	0	0	12.6	10	0	0
CEZ (32)	0	0	0	0	0	2.8	0	0	1.5	0	0	0
CTX (4)	0	0	0	0	0	1.9	0	0	1.0	0	0	0
MEPM (2)	0	0	0	0	0	0	0	0	0	0	0	0
GM (16)	0.3	0	0	0.2	0.4	2.8	0	0	1.5	0	0	0
KM (64)	0.9	0	0	0.6	1.3	5.7	0	0	3.0	20	0	0
TC (16)	3.1	2.0	11.5	4.4	4.0	17.9	12.8	0	12.6	20	33.3	0
NA (32)	0.9	0	0	0.6	0.9	11.3	0	0	6.0	0	0	0
CPFX (2)	0.3	0	0	0.2	0	0	0	0	0	0	0	0
CL (4)	1.2	2.9	1.0	1.5	1.3	3.8	0	0	2.0	10	33.3	50
CP (32)	0	0	0	0	1.8	1.9	0	0	1.0	0	0	0
ST (76/4)	0.6	2.0	0	0.8	0.9	18.9	6.4	0	11.6	0	0	0

Source: Asai T, Usui M, Sugiyama M, Izumi K, Ikeda T, Andoh M. Antimicrobial susceptibility of Escherichia coli isolates obtained from wild mammals between 2013 and 2017 in Japan. J Vet Med Sci. 82(3):345-349, 2020.

(3) Food

A 2019 research project to promote food safety, which was funded by a Ministry of Health, Labour and Welfare research grant, found that the status of resistance among microbes isolated from food was as follows (FY2019 Health and Labour Sciences Research Grant General Report on the Research Project to Promote Food Safety: Principal Investigator Haruo Watanabe). With the cooperation of 23 local public health institutes across Japan, the research team used standardized methods to isolate strains of *Salmonella* contaminating food (mainly chicken) and to measure their antimicrobial resistance. These results are provided in 4) ii. Non-typhoidal *Salmonella* (local public health institutes) (see Tables 21, 22, 23, and 29). Comparisons of resistance rates among *S*. Infantis and *S*. Schwarzengrund strains isolated from poultry slaughterhouses (chicken), food, and humans (2015-18) can be found in Tables 57 and 58. In summary, the *Salmonella* serotypes and antimicrobial resistance patterns in samples isolated from poultry slaughterhouses were observed to demonstrate the same tendencies as *Salmonella* in samples isolated from food (primarily chicken). However, the *Salmonella* serotypes and antimicrobial resistance patterns in samples isolated from humans (feces) were more diverse than the strains isolated from poultry slaughterhouses and food, suggesting the possibility that there are diverse causes besides poultry and other food products (such as *Salmonella* derived from infections in turtles and other companion animals). In the case of *Campylobacter*, both *C. jejuni* and *C. coli* showed strong similarities in terms of resistance trends between strains derived from human patients and those derived from food, strongly suggesting a relationship between resistant bacteria derived from food and those derived from human patients.

Antimicrobial susceptibility tests conducted on *Escherichia coli* strains isolated from commercially available chicken meat found higher resistance to the following agents in strains isolated from domestic chicken meat: KM (domestic 35.7%, imported 8.3%), TC (domestic 46.9%, imported 19.4%), ABPC (domestic 42.3%, imported 27.8%), CP (domestic 22.8%, imported 5.6%), ST (domestic 29%, imported 19.4%), and SM (domestic 37.3%, imported 30.1%). On the other hand, resistance to NA (domestic 19.9%, imported 36.1%) and GM (domestic 5%, imported 19.4%) was higher in imported chicken meat.

Testing of 311 *Escherichia coli* strains isolated from the feces of healthy individuals for susceptibility to 19 antimicrobial agents found that 39.2% of strains demonstrated resistance to at least 1 agent. The rate of resistance to fluoroquinolones was 10%, while resistance to CTX was around 5%, following the same tendencies seen since 2015. No IPM- or MEPM-resistant strains were observed. Two strains were found to have the plasmid-mediated colistin resistance gene (both were *mcr-1* positive).

With the aim of detecting ESBL-producing Escherichia coli, 129 samples of domestic commercially available chicken meat from FY2019 were selected for CTX resistance on a CTX-containing medium. CTX-resistant *Escherichia coli* was found in 76.7% of chicken thigh meat samples and in 66.0% of chicken breast meat samples. The highest number of CTX-resistant *Escherichia coli* bacteria per sample was approximately 3.0logCFU/g. While it is not necessarily the case that *Escherichia coli* in chicken goes on to become established in the human intestine, the fact that about 5% of *Escherichia coli* isolated from healthy individuals is CTX-resistant (almost all bacteria had the ESBL gene) means one cannot deny the possibility that resistant bacteria or resistance genes are getting into normal human flora via food. In future, it will be necessary to undertake a comparative analysis of resistant bacteria from each source.

(4) Environment

In general, waste resulting from human activities is discharged into the environment (rivers or oceans) after being treated at sewage treatment plants or other household wastewater treatment facilities until it meets effluent standards. Attention to environmental AMR based on the One Health approach focuses on evaluating the risks posed by antimicrobial-resistant bacteria (genes) by determining which antimicrobial-resistant bacteria (genes) exist in environmental water discharged into the environment (rivers and oceans) after waste resulting from human activities (rivers or oceans) is treated at sewage treatment plants or other household wastewater treatment facilities until it meets effluent standards, and considering how those antimicrobial-resistant bacteria (genes) could circulate into our daily lives and pose a risk to human health.

With few quantitative reports available at present concerning the extent to which antimicrobial-resistant bacteria (AMR bacteria: ARB) and the antimicrobial-resistance genes (AMR genes: ARGs) that stem from them are continuing to impose a burden after being excreted into the environment, a systematic nationwide survey is regarded as essential. Accordingly, a research group funded by a Ministry of Health, Labour and Welfare research grant has been formed for the purpose of conducting ongoing environmental AMR surveillance for the Japanese government. Led by Hajime Kanamori, the research group is conducting a study entitled “Research to Establish Methods of Surveying Antimicrobial-resistant Bacteria and Antimicrobials in the Environment” from 2018 to 2020.

In the first two years of the study (FY2018 and FY2019), next-generation sequencers were used to establish a comprehensive technique for sequencing ARGs (metagenomic analysis) in environmental water (Pathogen Genomics Center, National Institute of Infectious Diseases). Metagenomic analysis was then carried out on samples of wastewater from sewage treatment plants provided by 34 local governments (219 samples in total, collected in summer (August) and winter (February) from August 2018 to February 2020). The number of decoded reads of the ARGs in question was detected based on a database of ARG sequences associated with antimicrobials used in clinical settings and food-producing animals. In addition, the Reads Per Kilobase of gene per Million mapped reads (RPKM) method, which normalizes based on ARG base length and total decoded reads in the metagenome, was used to calculate the relative concentration of ARGs and conduct a comparative analysis between samples. Last year's report stated that the ARG levels tended to be slightly higher in winter than in summer, but ongoing surveillance for two years (a total of four occasions) revealed a continued upward trend in ARG levels. The primary cause was the detection of significantly high levels ($p<0.01$) of genes resistant to sulfonamides and quaternary ammonium salts (disinfectant), with the basic component genes of Class 1 integrons (*sul1*, *qacE*delta) known to have been widely acquired and propagated among *Enterobacteriaceae* thought to be a contributory factor in their increased detection. On the other hand, there has been a marked decline in macrolide resistance genes in sewage treatment plants and wastewater, which is a result thought to reflect a fall in the use of macrolides in humans. A similar downward trend was also seen in quinolone resistance genes, suggesting a relationship to a decline in the use of quinolones in humans. However, a deviation was seen from the situation in regard to the isolation of quinolone-resistant *Escherichia coli*. As the research group's metagenomic analysis technique focuses on detecting the externally acquired *oqx* and *qnr* genes, it did not evaluate mutations in the quinolone resistance-determining regions (QRDR) of the *gyrA* and *parC* genes that are the inhibitory targets of quinolones. While the frequency of external acquisition has at least declined and might be approaching a desirable situation, further ongoing surveillance is essential. As the research group's metagenomic analysis technique conforms to metagenomic analysis techniques used globally, the study is believed to have provided information that will be important when comparing reports from different countries. The group plans to continue conducting nationwide surveillance twice a year (in summer and winter) with the assistance of local governments and put in place Japanese environmental AMR (resistome) infrastructure.

In terms of global surveillance, Denmark (The National Food Institute, DTU (WHO Collaborating Centre and European Union Reference Laboratory for Antimicrobial Resistance in Foodborne Pathogens)) is leading a WHO-supported environmental surveillance initiative called the Global Sewage Surveillance Project (GSSP).[1] As this project targets not only environmental AMR, but also contamination with viruses such as the poliovirus, it is focusing primarily on inlet water from sewage treatment plants. The first output from the project provided the results of metagenomic analysis of 79 samples of inlet water from sewage treatment plants (in 60 countries) collected in January and February 2016.[2] The highest level of ARG contamination among these 60 countries was 4616.9 FPKM (fragments per kilobase of exon per million reads mapped) in Brazil and African countries also recorded a high level of ARG contamination, with an average of 2034.3 FPKM. Oceania (New Zealand and Australia) had the lowest level, with an average of 529.5 FPKM. While Asia (excluding Japan) did not have as high a level of ARG contamination as Africa, the ARG composition (resistome) was very similar (27% dissimilarity). ARG FPKM and resistome analysis brought to light results demonstrating a strong correlation between a country's population and economic activity on the one hand and its public health measures on the other. Japan has been involved in this project since 2017, providing pre-treatment inlet water, and a follow-up GSSP report that includes the evaluation of the Japanese samples is awaited. As the GSSP focuses on (untreated) inlet water samples from sewage treatment plants, it is difficult to carry out a comparative analysis based on the same standards as the aforementioned Japanese environmental AMR study, but it does at least provide important quantitative values for determining whether or not the wastewater from Japanese sewage treatment plants, which records levels of up to 100 FPKM, necessitates further environmental purification.

In addition to ARG in wastewater, it is vital to identify the presence of ARB that could potentially exist and proliferate in the environment. Information on the situation within Japan is starting to emerge from the findings of the aforementioned MHLW research group, including reports that, at a water reclamation center in Tokyo Bay, a KPC-2-producing *Klebsiella pneumoniae* strain rarely found in Japan, even in clinical isolates, has been isolated,[3] that KPC-2 was found in *Aeromonas* rarely isolated in wound infections,[4] and that *E. coli* with NDM-5 carbapenemase, which has acquired broader-spectrum activity than NDM-1, has been isolated.[5] A report has also been published on a comprehensive AMR study carried out on hospital wastewater, inlet and outlet water from sewage treatment plants, and river water in the Yodo River basin in Osaka. Its estimates suggest that a diverse array of ARB will be isolated from outlet water from sewage treatment plants and that hospital wastewater will impose an environmental AMR burden unless ozone treatment is carried out.[6] As in the case of the contamination situation overseas, a more extensive field survey would appear to be required in Japan, at least to ascertain the true extent of the isolation of ARB in environmental water, and it will be crucial to develop techniques for intensively eliminating or reducing ARB alone.

Thus, establishing surveillance techniques for monitoring environmental AMR and residual antimicrobials, and actually conducting fact-finding studies are important and it is vital to conduct risk assessments based on both the findings from these studies and literature reviews concerning environmental AMR. To set out the evidence concerning environmental AMR overseas, the research group translated the report Initiatives for Addressing Antimicrobial Resistance in the Environment: Current Situation and Challenges (2018) into Japanese.[7] Its key points regarding measures to combat environmental AMR are as follows. 1) If waste is not treated properly, the environment could be contaminated with antimicrobials and resistant bacteria. 2) The relationship between antimicrobials, resistant bacteria, and waste in the environment and their impact on human health are not well understood. 3) Scientific evidence shows that the risk of infection increases as a result of exposure to resistant bacteria in environmental waters due to the dispersal of antimicrobials and antimicrobial resistance factors into the environment. 4) The amount of resistant bacteria present in environmental waters and their locations will be assessed to understand the risks posed by resistant bacteria to human health. 5) The report also cites the need to assess sampling and testing methods for measuring resistant bacteria in environmental waters and to standardize practices.

In the area of health care associated infections, field epidemiology and molecular epidemiological analysis of isolated strains have, thus far, been used for identifying modes of transmission and quantifying the risk of health effects. However, as described above, research findings indicating that antimicrobial-resistant bacteria derived from the environment affect human and animal health are scarce. Overseas, as the contamination of vegetables believed to result from the use of river water for irrigation [8] and assessments of the risk of exposure through water-based recreation [9] are starting to be reported, albeit only little by little, the risk cycle is being calculated to a certain degree. At this point, it is difficult to set definite standards for discussing environmental risk. However, it is vital to quantitatively monitor and evaluate environmental AMR, conduct research that could assist in appraising health risks, and undertake risk assessments and reviews of major literature from both within Japan and overseas, as shedding light on the major factors contributing to the environmental AMR load and investigating whether it is developing into a risk to human and animal health are matters of urgency.

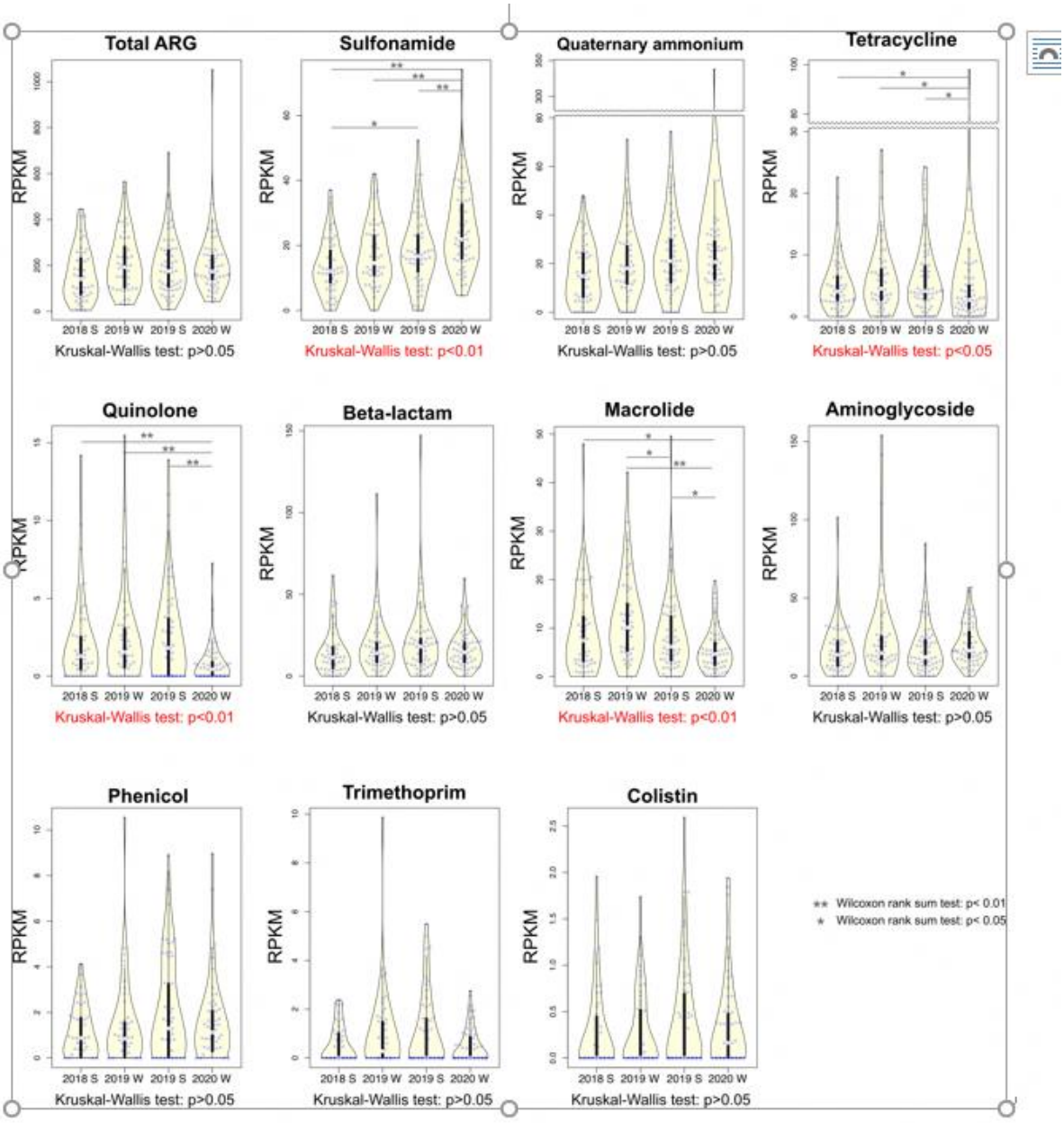


Figure 3. Metagenomic analysis (Metagenomic DNA-Seq) of wastewater discharged from Japanese sewage treatment plants (water reclamation centers)

The quantity of antimicrobial resistant genes in each category detected was standardized using Reads Per Kilobase of gene per Million mapped reads (RPKM).

References

1. Global Sewage Surveillance Project http://www.compare-europe.eu/library/global-sewage-surveillance-project
2. Hendriksen RS, Munk P, Njage P, et al. Global monitoring of antimicrobial resistance based on metagenomics analyses of urban sewage. Nat Commun 2019;10:1124.
3. Sekizuka T, Yatsu K, Inamine Y, et al. Complete Genome Sequence of a blaKPC-2-Positive Klebsiella pneumoniae Strain Isolated from the Effluent of an Urban Sewage Treatment Plant in Japan. mSphere 2018;3.
4. Sekizuka T, Inamine Y, Segawa T, Hashino M, Yatsu K, Kuroda M. Potential KPC-2 carbapenemase reservoir of environmental Aeromonas hydrophila and Aeromonas caviae isolates from the effluent of an urban wastewater treatment plant in Japan. Environ Microbiol Rep 2019;11:589-97.
5. Sekizuka T, Inamine Y, Segawa T, Kuroda M. Characterization of NDM-5- and CTX-M-55-coproducing Escherichia coli GSH8M-2 isolated from the effluent of a wastewater treatment plant in Tokyo Bay. Infect Drug Resist 2019;12:2243-9.

6. Azuma T, Otomo K, Kunitou M, et al. Environmental fate of pharmaceutical compounds and antimicrobial-resistant bacteria in hospital effluents, and contributions to pollutant loads in the surface waters in Japan. Sci Total Environ 2019;657:476-84.
7. Initiatives for Addressing Antimicrobial Resistance in the Environment: Current Situation and Challenges (http://amr.ncgm.go.jp/medics/2-8-1.html#sonota)
8. Van Hoek AH, Veenman C, van Overbeek WM, Lynch G, de Roda Husman AM, Blaak H. Prevalence and characterization of ESBL- and AmpC-producing Enterobacteriaceae on retail vegetables. Int J Food Microbiol 2015;204:1-8.
9. Leonard AFC, Zhang L, Balfour AJ, et al. Exposure to and colonisation by antibiotic-resistant E. coli in UK coastal water users: Environmental surveillance, exposure assessment, and epidemiological study (Beach Bum Survey). Environ Int 2018;114:326-33.

7. Current Volume of Use of Antimicrobials in Japan

(1) Antimicrobials for humans (based on volume of sales)

1) Usage of antimicrobials in Japan

Source: IQVIA Solutions Japan K.K.

Tables 70 and 71 show the usage of antimicrobials in Japan between 2013 and 2019, based on the volume of sales. Overall use of antimicrobials in Japan in 2019 amounted to 13.3 DID. A comparison with DID in major countries in 2018 shows that this was lower than France (25.3 DID), Italy (21.4 DID), and the UK (18.8 DID), but higher than Sweden (12.4 DID), Germany (11.9 DID) and the Netherlands (9.7 DID). No major changes in the use of antimicrobials were observed between 2013 and 2016, but although usage began declining in 2017, the fall abated once more between 2018 and 2019. By 2019, usage had dropped by 10.9% from the 2013 level.

Oral antimicrobial use in 2019 (Table 70) was 12.2 DID, accounting for 91.8% of all antimicrobials. Antimicrobials subject to a reduction target of 50% under Japan's National Action Plan on AMR, namely oral cephalosporins (3.0 DID), oral fluoroquinolones (2.3 DID), and oral macrolides (3.8 DID) together accounted for 75.3% of all oral antimicrobials (the figure for oral cephalosporins is the total for first- (0.1 DID), second- (0.3 DID), and third-generation (2.6 DID) oral cephalosporins). While this trend has not changed since 2013, use of oral cephalosporins, oral fluoroquinolones, and oral macrolides fell by 22.7%, 18.1%, and 20.6% respectively over that period. On the other hand, use of parenteral antimicrobials increased by 12.7% between 2013 and 2019 (Table 71). There are potentially greater opportunities to use parenteral antimicrobials because of the increase in the elderly population. The usage of antimicrobials in 2019 may well have been affected in particular by the shortage of Cefazolin, which resulted in a fall in the use of first-generation cephalosporins and a rise in narrow-spectrum penicillins, penicillins with beta-lactamase inhibitors, and second- and third-generation cephalosporins.

Table 72 shows antimicrobial use based on the AWaRe classification recommended by the WHO as an indicator of antimicrobial stewardship. Carried in the 20th edition of the WHO Model Lists of Essential Medicines, the AWaRe classification is an antimicrobial classification system that is applied as an indicator of antimicrobial stewardship. It classifies antimicrobials into four categories: Access (first- or second-choice antimicrobials used for treating common infections, regarding whose resistance potential there is little concern, and which should be made widely available by all countries in high-quality formulations at a reasonable cost. Examples include ampicillin and cephalexin), Watch (antimicrobials that should be used only for a limited number of conditions or applications, as their resistance potential is a source of concern. Examples include vancomycin, meropenem, levofloxacin, and ceftriaxone), Reserve (antimicrobials that should be used as the last resort when no other alternatives can be used. Examples include tigecycline, colistin, and daptomycin), and Unclassified. This classification was amended in 2019 to add the new category of "discouraged antibiotics," consisting of antimicrobials whose clinical use the WHO does not recommend (for example, cefoperazone-sulbactam). The WHO has set a target of at least 60% of antimicrobial consumption being from medicines in the Access Group. While consumption of antimicrobials in the Access Group as a proportion of total use is lower in Japan than other countries,[6] the figure has risen gradually over the years from 13.0% to 20.4%, with the percentage of antimicrobials in the Watch Group falling from 85.5% to 78.3%. Close scrutiny will continue to be required, due to concerns about the impact of supply shortages and the COVID-19 pandemic.

A survey of oral and parenteral antimicrobial use in terms of potency by weight from a One Health perspective (Table 73) showed no change in overall use. One of the main reasons for the discrepancy between this and the standardized figures expressed as DID is believed to be the effect of the increased parenteral usage of ampicillin/sulbactam, which has a high-potency daily dosage and is used to treat aspiration pneumonia in elderly people.

Factors such as the increasing number of elderly people make it difficult to reduce the use of parenteral antimicrobials in Japan. However, the National Action Plan on AMR has demonstrated some level of effectiveness, as a fall in oral antimicrobial use was observed after its publication. In addition, a system for continuous monitoring of antimicrobial use, which was one of the strategies in the National Action Plan on AMR, has been put in place. While the rate of decline in oral antimicrobial use has slowed, there are limits to the ability to use the volume of sales to forecast the optimal level of antimicrobial use in patients requiring oral antimicrobials in Japan. Ongoing efforts to ascertain the extent of antimicrobial use as part of Japan's measures to combat AMR will continue to be needed to facilitate evaluation of the selective pressure of antimicrobials. In addition, it will be vital to ascertain the purpose of antimicrobial use and implement other new strategies enabling the appropriateness of measures to be assessed.

Table 70. Trends in oral antimicrobial use in Japan based on the volume of sales

	2013	2014	2015	2016	2017	2018	2019
Tetracyclines	0.76	0.75	0.77	0.80	0.81	0.88	0.96
Amphenicols	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	<0.01
Penicillins with extended spectrum	0.88	0.89	0.99	0.97	0.95	1.01	1.13
Beta Lactamase-sensitive penicillins	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01
Combinations of penicillins, including beta lactamase inhibitors	0.21	0.22	0.24	0.25	0.26	0.29	0.33
1st generation cephalosporins	0.07	0.07	0.07	0.07	0.07	0.08	0.09
2nd generation cephalosporins	0.30	0.29	0.29	0.29	0.28	0.28	0.30
3rd generation cephalosporins	3.53	3.41	3.46	3.32	3.08	2.83	2.63
Carbapenems	0.01	0.02	0.02	0.02	0.01	0.01	0.01
Other cephalosporins and penems	0.14	0.14	0.13	0.12	0.12	0.11	0.10
Combinations of sulfonamides and trimethoprim, including derivatives	0.25	0.27	0.29	0.31	0.33	0.36	0.38
Macrolides	4.83	4.50	4.59	4.56	4.18	3.96	3.84
Lincosamides	0.01	0.01	0.02	0.01	0.02	0.02	0.02
Fluoroquinolones	2.82	2.83	2.71	2.75	2.57	2.34	2.32
Other quinolones	0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	<0.01
Other antibacterials	0.10	0.10	0.10	0.10	0.09	0.08	0.08
Total	13.93	13.50	13.67	13.57	12.76	12.25	12.19

* As a unit, defined daily doses (DDDs) per 1,000 inhabitants per day (DID) is used.

* Figures for DDD are those for January 1, 2019.

Table 71. Trends in parenteral antimicrobial use in Japan based on the volume of sales

	2013	2014	2015	2016	2017	2018	2019
Tetracyclines	0.02	0.02	0.02	0.02	0.02	0.02	0.02
Amphenicols	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01
Penicillins with extended spectrum	0.04	0.04	0.04	0.04	0.04	0.05	0.05
Beta Lactamase-sensitive penicillins	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	0.01
Combinations of penicillins, including beta lactamase inhibitors	0.13	0.15	0.16	0.18	0.19	0.21	0.22
1st generation cephalosporins	0.13	0.13	0.14	0.14	0.15	0.15	0.12
2nd generation cephalosporins	0.11	0.11	0.10	0.10	0.10	0.09	0.10
3rd generation cephalosporins	0.18	0.19	0.21	0.22	0.23	0.24	0.27
4th generation cephalosporins	0.06	0.05	0.05	0.05	0.05	0.04	0.04
Monobactams	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01
Carbapenems	0.11	0.11	0.11	0.11	0.11	0.11	0.11
Combinations of sulfonamides and trimethoprim, including derivatives	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01
Macrolides	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01
Lincosamides	0.02	0.02	0.02	0.02	0.02	0.02	0.02
Streptogramins	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01
Streptomycin	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01
Other aminoglycosides	0.05	0.05	0.05	0.04	0.04	0.04	0.03
Fluoroquinolones	0.04	0.04	0.04	0.04	0.04	0.04	0.03
Glycopeptides	0.03	0.03	0.03	0.03	0.03	0.03	0.03
Polymyxins	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01
Metronidazole	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01
Other antibacterials	0.02	0.02	0.02	0.02	0.02	0.02	0.02
Total	0.96	0.96	1.00	1.03	1.05	1.06	1.09

* As a unit, defined daily doses (DDDs) per 1,000 inhabitants per day (DID) is used.

* Figures for DDD are those for January 1, 2019.

Table 72. Trends in antimicrobial use in Japan based on the AWaRe classification

AWaRe classification	2013	2014	2015	2016	2017	2018	2019
Access (%)	1.94 (13.0)	2.00 (13.8)	2.15 (14.7)	2.21 (15.1)	2.27 (16.5)	2.47 (18.4)	2.71 (20.4)
Watch (%)	12.75 (85.5)	12.27 (84.8)	12.32 (83.9)	12.20 (83.5)	11.35 (82.2)	10.75 (80.2)	10.41 (78.3)
Reserve (%)	0.18 (0.01)	0.18 (0.01)	0.18 (0.01)	0.17 (0.01)	0.16 (0.01)	0.15 (0.01)	0.15 (0.01)
Discouraged (%)	0.02 (<0.01)	0.02 (<0.01)	0.02 (<0.01)	0.02 (<0.01)	0.02 (<0.01)	0.02 (<0.01)	0.02 (<0.01)
Unclassified (%)	0.01 (<0.01)	0.01 (<0.01)	0.01 (<0.01)	0.01 (<0.01)	0.01 (<0.01)	<0.01 (<0.01)	<0.01 (<0.01)
Total	14.91	14.48	14.68	14.60	13.81	13.39	13.28

* As a unit, defined daily doses (DDDs) per 1,000 inhabitants per day (DID) is used.

* Figures for DDD are those for January 1, 2019.

Table 73. Trends in oral antimicrobial consumption in Japan in terms of potency by weight based on the volume of sales (t)

	2013	2014	2015	2016	2017	2018	2019
Tetracyclines	7.1	6.9	7.1	7.2	7.0	7.3	7.7
Amphenicols	0.2	0.1	0.1	0.1	0.1	0.1	0.1
Penicillins with extended spectrum	53.7	53.6	57.6	56.3	54.5	57.3	62.6
Beta Lactamase-sensitive penicillins	1.7	1.8	1.7	1.5	1.4	1.3	1.8
Combinations of penicillins, including beta lactamase inhibitors	88.1	95.4	105.8	114.6	124.1	131.9	145.7
1st generation cephalosporins	25.0	24.9	25.2	26.3	27.2	28.4	24.9
2nd generation cephalosporins	28.5	27.4	27.0	26.7	25.9	26.0	28.6
3rd generation cephalosporins	97.7	95.1	97.8	95.9	91.2	86.6	85.3
4th generation cephalosporins	6.6	6.1	6.0	5.7	5.5	4.8	4.5
Monobactams	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Carbapenems	9.9	9.9	10.1	10.2	10.1	9.8	10.0
Other cephalosporins and penems	4.8	4.7	4.6	4.3	4.0	3.8	3.6
Combinations of sulfonamides and trimethoprim including derivatives	45.8	49.9	53.7	58.6	62.1	65.7	71.0
Macrolides	108.0	101.4	103.4	102.9	94.5	89.7	86.8
Lincosamides	2.8	2.7	2.6	2.5	2.4	2.4	2.7
Streptogramins	＜0.1	＜0.1	＜0.1	＜0.1	＜0.1	<0.1	<0.1
Streptomycin	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Other aminoglycosides	1.0	0.9	0.9	0.8	0.8	0.7	0.7
Fluoroquinolones	61.3	60.2	56.6	57.4	53.2	49.7	47.7
Other quinolones	0.5	0.4	0.3	0.3	0.2	0.1	0.1
Glycopeptides	2.2	2.1	2.3	2.4	2.5	2.4	2.6
Polymyxins	＜0.1	＜0.1	＜0.1	＜0.1	＜0.1	<0.1	<0.1
Metronidazole (parenteral)	＜0.1	＜0.1	0.2	0.2	0.2	0.2	0.2
Other antibacterials	17.5	16.5	16.6	16.7	14.3	13.8	13.1
TOTAL	562.6	560.2	579.7	591.0	581.4	582.2	599.6

2) Usage of parenteral antimicrobials in hospitals

Source: J-SIPHE

The 2019 annual report for J-SIPHE system provides a list of parenteral antimicrobials used by 367 institutions (covering only antimicrobials actually used at those institutions), based on information gathered via an app that collates the medical fee statement (receipt) from E-files and F-files.* The most commonly used antimicrobials were penicillins (AUD 3.90, DOT 5.94), followed by third-generation cephalosporins (AUD 3.33, DOT 4.58), first-generation cephalosporins (AUD 1.71, DOT 2.23), and carbapenems (AUD 1.23, DOT 2.05). Trends will continue to need to be checked going forward.

*E-file: Cost data; F-file: Detailed procedure data

Table 74. Use of parenteral antimicrobials at medical institutions (AUD, DOT)

	2019	
	AUD (IQR) (DDDs/100 patient-days)	DOT (IQR) (DOTs/100 patient-days)
Penicillins	3.90 (2.71-5.10)	5.94 (4.15-7.82)
1st generation cephalosporins	1.71 (0.83-2.86)	2.23 (1.21-3.94)
2nd generation cephalosporins	0.18 (0.09-0.41)	0.37 (0.19-0.83)
3rd generation cephalosporins	3.33 (2.18-4.74)	4.58 (3.05-6.30)
4th generation cephalosporins	0.34 (0.14-0.70)	0.53 (0.25-1.01)
Oxacephems	0.30 (0.11-0.70)	0.31 (0.12-0.76)
Cephamycins	0.89 (0.52-1.41)	1.70 (0.99-2.62)
Ceftolozane/tazobactam	0.06 (0.03-0.10)	0.07 (0.03-0.11)
Carbapenems	1.23 (0.63-1.79)	2.05 (1.15-3.00)
Monobactams	0.04 (0.02-0.09)	0.07 (0.03-0.11)
Glycopeptides	0.56 (0.27-0.94)	0.81 (0.46-1.32)
Oxazolidinones	0.11 (0.07-0.16)	0.11 (0.07-0.17)
Arbekacin	0.07 (0.04-0.13)	0.07 (0.04-0.12)
Daptomycin	0.25 (0.14-0.38)	0.17 (0.11-0.28)
Quinolones	0.39 (0.21-0.61)	0.41 (0.23-0.64)
Aminoglycosides	0.10 (0.06-0.18)	0.23 (0.14-0.45)
Tetracyclines	0.14 (0.09-0.26)	0.17 (0.10-0.29)
Lincomycins 系	0.22 (0.13-0.39)	0.32 (0.19-0.55)
Macrolides	0.07 (0.04-0.10)	0.07 (0.04-0.10)
Sulfamethoxazole-trimethoprim	0.07 (0.03-0.11)	0.06 (0.03-0.09)
Metronidazole	0.10 (0.07-0.17)	0.11 (0.07-0.18)

AUD: Antimicrobial Use Density, DOT: Days of Therapy

(2) Veterinary drugs

Source: Japanese Veterinary Antimicrobial Resistance Monitoring System (JVARM)

Based on the volumes of sales of antibiotics and synthesized antimicrobials, as reported under the Veterinary Drug Control Regulations, the amounts of veterinary antimicrobials were calculated in terms of active ingredients (metric tons (t)). In the period from 2013 to 2018, the volume of sales of veterinary antimicrobials ranged between 749.47 t and 872.09 t. The total volume of sales in 2018 was about 48 t lower than in 2017, with falls in the sales of tetracyclines (about 36 t), sulfonamides (about 10 t), aminoglycosides (about 9 t), and peptides (about 8 t) having the greatest impact. This was mainly caused by the decline in the use of these agents in pigs. In contrast, the agents showing an increase in sales were macrolides (approximately 14 t) and penicillins (approximately 6 t), with the rise in macrolides primarily accounted for by erythromycin used in aquatic animals (seawater fish). Tetracyclines represented the largest share of antimicrobial sales over the period monitored, accounting for between 37.7% and 43.6%.

On the other hand, third-generation cephalosporins and fluoroquinolones, which are important antimicrobials for human medicine, accounted for less than 1% of overall volume of sales.

Table 75. Amounts of veterinary antimicrobials in terms of active ingredients by class (t)

	2013	2014	2015	2016	2017	2018
Penicillins	78.17	77.96	83.73	99.75	101.02	107.31
Cephalosporins (total)	5.58	5.50	5.89	6.45	6.65	7.06
1st generation cephalosporins	(4.71)	(4.58)	(4.98)	(5.41)	(5.50)	(5.67)
2nd generation cephalosporins	(0.19)	(0.20)	(0.12)	(0.16)	(0.18)	(0.22)
3rd generation cephalosporins	(0.68)	(0.71)	(0.79)	(0.88)	(0.96)	(1.18)
Aminoglycosides	39.52	40.64	35.47	47.86	44.76	35.61
Macrolides	77.70	70.43	98.41	134.12	140.83	154.72
Lincosamides	38.99	43.26	28.66	21.87	25.26	22.76
Tetracyclines	340.52	324.85	333.86	331.55	347.05	311.18
Peptides	11.78	9.98	14.54	14.02	19.99	12.34
Other antibioitics	25.98	28.85	32.39	31.96	36.19	37.50
Sulfonamides	103.90	97.57	96.67	95.85	99.06	88.77
Quinolones	1.01	1.91	1.71	1.74	1.84	1.48
Fluoroquinolones	5.53	5.63	7.35	6.08	6.83	6.65
Amphenicols	21.53	26.15	29.73	26.49	27.11	24.82
Furan and derivatives	14.46	1.76	1.24	1.57	1.36	1.34
Other synthetic antibacterials	15.02	13.97	13.35	12.12	13.09	11.98
Antifungal antibiotics	1.18	1.03	1.08	1.12	1.07	1.06
Total	780.88	749.47	784.06	832.56	872.09	824.56

* The figures in parentheses are included in the Cephalosporins (total).

The marketing authorization holders also submit the percentage of sales for each species of domestic animal estimated from information on the distributors, so the estimated volumes for each species sold are calculated based on those estimated percentages. In terms of active ingredients, pigs accounted for the largest amount, followed by seawater fish. As described above, fluctuations in amounts for these animal species have a substantial effect on fluctuations in sales volumes.

Animals vary widely in weight, ranging from chicks that weigh just a few dozen grams to dairy cows that weigh more than 600 kg, and the number of animals kept also differs according to the species, so the number of animals and the weight per animal must be taken into account in comparisons by animal species. Accordingly, there is a comparison method which involves using animal weights and numbers to calculate biomass weight (total weight of animals) and expressing figures for antimicrobial use as usage per unit of biomass weight. While there was hitherto no internationally standardized method for calculating biomass weight, the OIE has recently set out a method for calculating biomass weight as part of its collection of veterinary antimicrobial usage data.[14] However, the standard weights for each animal type are calculated on a regional basis and, as the figures have not been published as yet and could vary from year to year, it is not possible to conduct an evaluation using Japanese data alone. The OIE's method will serve as a point of reference in future deliberations concerning evaluation methods, including the possibility of establishing a method specific to Japan.

Table 76. Estimated amounts of veterinary antimicrobials in terms of active ingredients by animal species (t)

	2013	2014	2015	2016	2017	2018
Beef cattle	23.02	20.35	23.77	25.00	25.92	33.17
Dairy cow	31.73	30.45	32.48	35.10	34.55	41.01
Horse	2.18	2.01	2.10	2.31	2.17	3.90
Pig	502.64	490.42	503.13	521.64	551.96	486.01
Broiler	65.90	70.14	62.36	64.79	63.03	64.62
Layer	23.29	23.67	19.36	20.75	16.61	17.69
Fish (Seawater)	112.36	93.41	123.02	143.03	159.07	164.00
Fish (Freshwater)	6.84	5.61	7.28	10.10	9.07	2.91
Ornamental fish	0.72	1.07	1.60	1.95	1.74	1.63
Dog/Cat	9.67	9.13	8.86	7.79	7.97	9.62
Others	2.54	3.22	0.09	0.10	0.00	0.00
Total	780.88	749.47	784.05	832.56	872.09	824.56

1) Food-producing animals

The estimated volumes of veterinary antimicrobials sold for food-producing animals (cattle, pigs, horses, chickens, and others) in terms of active ingredients are listed in Table 77. In the period from 2013 to 2018, the estimated volume of sales ranged between 640.25 t and 694.24 t, with sales in 2018 falling by about 48 t from the 2017 level. Among the factors that had an impact was a fall in sales of tetracyclines (about 29 t) and aminoglycosides (about 10 t), with sales of tetracyclines for pigs declining by about 46 t. Tetracyclines (257.36 tons to 286.74 t) took up the largest share in the overall volume of sales of antimicrobials for food-producing animals, accounting for 39.8 to 44.0%. In contrast, third-generation cephalosporins and fluoroquinolones, which are critically important antimicrobials for human medicine, each accounted for less than 1%

Table 77. The estimated volumes of sales of veterinary antimicrobials for food-producing animals (cattle, pigs, horses, chickens, and others) in terms of active ingredients (unit: metric tons)

	2013	2014	2015	2016	2017	2018
Penicillins	59.50	61.96	67.25	83.56	84.68	92.79
Cephalosporins (total)	3.12	3.06	3.22	3.34	3.44	3.91
1st generation cephalosporins	(2.45)	(2.34)	(2.52)	(2.52)	(2.51)	(2.73)
2nd generation cephalosporins	(0.19)	(0.20)	(0.12)	(0.16)	(0.18)	(0.22)
3rd generation cephalosporins	(0.49)	(0.51)	(0.58)	(0.65)	(0.74)	(0.96)
Aminoglycosides	37.40	38.66	34.07	47.46	44.37	34.69
Macrolides	56.00	53.30	60.36	72.68	71.96	72.09
Lincosamides	35.88	36.61	23.65	15.62	19.39	16.72
Tetracyclines	286.74	275.83	276.24	280.66	286.01	257.36
Peptides	11.77	9.97	14.54	14.01	19.98	12.34
Other antibioitics	25.71	28.43	32.23	31.55	35.72	36.87
Sulfonamides	95.62	88.43	84.40	78.57	84.10	78.59
Quinolones	0.22	0.20	0.20	0.16	0.31	0.01
Fluoroquinolones	4.64	4.73	6.41	5.19	5.93	5.80
Amphenicols	19.66	25.14	27.39	24.82	25.34	23.28
Furan and derivatives	0.00	0.00	0.00	0.00	0.00	0.00
Other synthetic antibacterials	14.98	13.92	13.32	12.07	13.02	11.96
Antifungal antibiotics	0.00	0.00	0.00	0.00	0.00	0.00
Total	651.24	640.25	643.28	669.68	694.24	646.40

* The figures in parentheses are included in the Cephalosporins (total).

2) Aquatic animals

The estimated volumes of veterinary antimicrobials sold for aquatic animals (seawater fish, freshwater fish, and ornamental fish) in terms of active ingredients are summarized in Table 78. In the period from 2013 to 2018, the estimated volume of sales ranged between 100.09 t and 169.88 t, accounting for between 13.4% and 20.4% of the total volume of veterinary antimicrobial sales. Tetracyclines (ranging between 49.01 t and 57.62 t) took up the largest share in the overall volume of sales until 2015 but it has changed to a macrolide (erythromycin) since 2016, with sales totaling between 61.44 t and 82.61 t. The approximately 49 t increase in the volume of sales between 2013 and 2018 was due to a rise in sales of a macrolide (erythromycin), which was attributed to an outbreak of streptococcosis (*Lactococcus garvieae*), for which the agent is indicated.

Third-generation cephalosporins and fluoroquinolones that are important for human health are not approved for aquatic animal use.

Table 78. The estimated volumes of sales of veterinary antimicrobials for aquatic animals (seawater fish, freshwater fish, and ornamental fish) in terms of active ingredients (unit: metric tons)

	2013	2014	2015	2016	2017	2018
Penicillins	16.31	13.87	14.38	14.62	14.66	12.85
Cephalosporins (total)	0.00	0.00	0.00	0.00	0.00	0.00
1st generation cephalosporins	0.00	0.00	0.00	0.00	0.00	0.00
2nd generation cephalosporins	0.00	0.00	0.00	0.00	0.00	0.00
3rd generation cephalosporins	0.00	0.00	0.00	0.00	0.00	0.00
Aminoglycosides	0.00	0.00	0.00	0.00	0.00	0.00
Macrolides	21.70	17.13	38.05	61.44	68.87	82.61
Lincosamides	3.02	6.56	4.90	6.12	5.73	5.91
Tetracyclines	53.78	49.01	57.62	50.89	61.05	52.55
Peptides	0.00	0.00	0.00	0.00	0.00	0.00
Other antibioitics	0.27	0.42	0.16	0.42	0.47	0.63
Sulfonamides	7.68	8.59	11.71	16.74	14.39	9.64
Quinolones	0.79	1.71	1.51	1.58	1.53	1.47
Fluoroquinolones	0.00	0.00	0.00	0.00	0.00	0.00
Amphenicols	1.87	1.01	2.33	1.67	1.77	1.53
Furan and derivatives	14.46	1.76	1.24	1.57	1.36	1.34
Other synthetic antibacterials	0.02	0.04	0.02	0.04	0.06	0.02
Antifungal antibiotics	0.00	0.00	0.00	0.00	0.00	0.00
Total	119.91	100.09	131.91	155.08	169.88	168.54

3) Companion animals

The estimated volumes of veterinary antimicrobials sold for companion animals (dogs and cats) in terms of active ingredients are summarized in Table 79. In the period from 2013 to 2018, the estimated volume of sales ranged between 7.79 t and 9.67 t, accounting for between 0.9% and 1.2 % of the total volume of veterinary antimicrobial sales. Use of human antimicrobials in companion animals was not originally monitored under JVARM and is therefore excluded from the values in the table for 2015 and earlier. Accordingly, with the full cooperation of the Japan Animal Drugs & Instruments Dealers Association and Federation of Japan Pharmaceutical Wholesalers Association, the Ministry of Agriculture, Forestry and Fisheries began monitoring the actual usage of human antimicrobials in 2016 based on the amount sold. The results of its surveillance revealed that the volume of human antimicrobials sold for use in companion animals is about the same as the volume of veterinary antimicrobials sold for that purpose. Including those for human use, the most commonly sold antimicrobials were first-generation cephalosporins and penicillins.

Table 79. The estimated volumes of sales of veterinary and human antimicrobials for companion animals (cats and dogs) in terms of active ingredients (unit: metric tons)

	2013	2014	2015	2016		2017	2018
	Veterinary antimicrobials	Veterinary antimicrobials	Veterinary antimicrobials	Veterinary antimicrobials	Human antimicrobials	Veterinary antimicrobials	Veterinary antimicrobials
Penicillins	2.36	2.13	2.08	1.57	1.93	1.68	1.66
Cephalosporins (total)	2.45	2.44	2.67	3.12	3.23	3.21	3.16
1st generation cephalosporins	(2.26)	(2.23)	(2.46)	(2.89)	(3.12)	(2.99)	(2.93)
2nd generation cephalosporins	(0.00)	(0.00)	(0.00)	(0.00)		(0.00)	(0.00)
3rd generation cephalosporins	(0.20)	(0.20)	(0.21)	(0.23)	(0.11)	(0.22)	(0.22)
Aminoglycosides	2.07	1.97	1.40	0.41	0.02	0.39	0.91
Macrolides	0.00	0.00	0.00	0.00	0.17	0.00	0.02
Lincosamides	0.09	0.09	0.11	0.13	0.10	0.13	0.14
Tetracyclines	0.00	0.00	0.00	0.00	0.28	0.00	1.27
Peptides	0.01	0.01	0.01	0.01	0.00	0.01	0.01
Other antibioitics**	0.00	0.00	0.00	0.00	0.22	0.00	0.00
Sulfonamides	0.60	0.55	0.56	0.53	0.19	0.57	0.53
Quinolones	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Fluoroquinolones	0.90	0.90	0.94	0.89	0.11	0.90	0.84
Amphenicols	0.00	0.00	0.00	0.00	0.12	0.01	0.01
Furan and derivatives	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Other synthetic antibacterials***	0.02	0.01	0.01	0.01	0.08	0.01	0.01
Antifungal antibiotics	1.18	1.03	1.08	1.12	0.00	1.07	1.06
Total	9.67	9.13	8.86	7.79	6.48	7.97	9.62

* The figures in parentheses are included in the Cephalosporins (total).

** Includes fosfomycin and rifamycin.

*** Includes trimethoprim, penems, carbapenems, isoniazid, and ethambutol.

(3) Antimicrobial feed additives

Source: Food and Agricultural Materials Inspection Center (FAMIC) and Japan Scientific Feeds Association

The volumes of distribution of antimicrobial feed additives, based on surveys by the Food and Agricultural Materials Inspection Center and by the Japan Scientific Feeds Association, are indicated in Table 80. While the volume of such additives distributed showed a moderate decline in the period 2013 to 2018, ranging between 235.1 t and 216.7 t, comparisons among the different types of antimicrobials showed an upward trend in the distribution of polyethers (not used in humans), which account for the majority. The designation of the polypeptide colistin as a feed additive was revoked in July 2018, followed by the macrolide tylosin in May 2019 and two tetracyclines in December 2019. Distribution of these antimicrobials ceased from the time their designation was revoked.

Table 80. Volume of distribution of antibiotic feed additives in terms of effective value (unit: metric tons)

	2013	2014	2015	2016	2017	2018
Aminoglycosides	0.0	0.0	0.0	0.0	0.0	0.0
Polypeptides	35.0	28.3	29.6	32.1	15.2	9.4
Tetracyclines	1.6	2.2	2.6	2.0	0.0	0.0
Macrolides	5.6	5.3	5.5	1.4	3.5	0.0
Polysaccharides	0.2	0.0	0.1	0.1	0.1	0.0
Polyethers	136.0	142.5	141.7	159.9	165.5	161.0
Other antimicrobials	20.8	18.3	12.5	14.6	19.8	26.2
Synthetic antimicrobials	35.9	29.3	24.4	18.1	17.1	20.1
Total	235.1	225.9	216.4	228.2	221.2	216.7

Figures do not include antifungal agents.

(4) Agrochemicals

Source: Plant Products Safety Division, Food Safety and Consumer Affairs Bureau, Ministry of Agriculture, Forestry and Fisheries

Table 81 indicates the volume of shipment in Japan of antimicrobials that are used as agrochemicals, in terms of active ingredients (unit: tons). In the period from 2013 to 2017, the volume of shipments of antimicrobials used as agrochemicals remained at around the 150 t mark, ranging between 142.72 t and 153.63 t.

Table 81. The volume of shipment in Japan of antimicrobials that are used as agrochemicals, in terms of active ingredients (unit: metric tons)

	2013	2014	2015	2016	2017	2018
Streptomycin	36.12	36.21	35.49	39.80	45.32	36.19
Oxytetracycline	10.52	12.00	12.54	10.50	9.61	0.13
Kasugamycin	20.53	20.96	21.24	20.56	13.14	21.22
Validamycin	23.11	25.50	24.97	24.80	22.07	23.35
Oxolinic acid	40.08	40.79	41.16	42.17	44.00	44.53
Polyoxins	16.24	15.49	15.25	15.80	8.57	13.65
Total	146.59	150.94	150.66	153.63	142.72	139.07

Figures shown are for the agrochemical year (the 2013 agrochemical year ran from October 2012 to September 2013).
Figures do not include antifungal agents.

(5) Current status of antimicrobial use in Japan

Tables 82 and 83 show the total use of antimicrobials in humans, food producing animals, aquatic animals, companion animals, antimicrobial feed additives, and agrochemicals. Antimicrobial selection pressure in Japan from a One Health perspective is highest among tetracyclines at 19-21%, followed by penicillins at 13-16%, and macrolides at 11-13%. Use of every tetracyclines, penicillins, and macrolides has been growing over recent years, so caution regarding future trends will be required. On the other hand, the fact that barely any changes in cephalosporins and fluoroquinolones were observed is attributed to differences in the antimicrobials that can be used in humans and in non-humans.

Table 82. Current volume of antimicrobial use in Japan (unit: metric tons)

	2013	2014	2015	2016	2017	2018
Penicillins	221.7	228.7	248.7	272.2	281.0	297.8
Cephalosporins	168.3	163.7	166.5	165.6	160.5	156.7
Monobactams	0.1	0.1	0.1	0.1	0.1	0.1
Carbapenems	9.9	9.9	10.1	10.2	10.1	9.8
Aminoglycosides	97.1	98.7	93.1	109.1	104.0	93.7
Macrolides	191.3	177.2	207.3	238.5	238.9	244.4
Lincosamides	41.8	45.9	31.3	24.4	27.7	25.2
Tetracyclines	359.7	346.0	356.1	351.2	363.7	318.6
Peptides and glycopeptides	49.0	40.4	46.5	48.5	37.7	24.2
Sulfonamides*	149.7	147.5	150.4	154.4	161.1	154.5
Fluoroquinolones	66.8	65.8	63.9	63.5	60.1	56.3
Other quinolones	41.5	43.1	43.2	44.2	46.1	46.1
Amphenicols, thiamphenicols and derivatives	21.7	26.3	29.8	26.6	27.2	24.9
Furan and derivatives	14.5	1.8	1.2	1.6	1.4	1.3
Polysaccharides	0.2	0.0	0.1	0.1	0.1	0.0
Polyethers	136.0	142.5	141.7	159.9	165.5	161.0
Polyoxins	16.2	15.5	15.3	15.8	8.6	13.7
Others*	138.3	132.4	124.4	118.5	122.8	133.2
Total	1723.9	1685.5	1729.7	1804.3	1816.2	1761.4

*Sulfonamides used as antimicrobial feed additives and the agrochemical validamycin are included in "Others."

Figures do not include antifungal agents.

Table 83. Changes in the volume of antimicrobial use in Japan by year (unit: metric tons)

	2013						2014						2015					
	Humans	Food-producing animals	Aquatic animals	Companion animals	Antimicrobial feed additives	Agrochemicals	Humans	Food-producing animals	Aquatic animals	Companion animals	Antimicrobial feed additives	Agrochemicals	Humans	Food-producing animals	Aquatic animals	Companion animals	Antimicrobial feed additives	Agrochemicals
Penicillins	143.5	59.5	16.3	2.4	0.0	0.0	150.8	62.0	13.9	2.1	0.0	0.0	165.0	67.3	14.4	2.1	0.0	0.0
Cephalosporins	162.7	3.1	0.0	2.5	0.0	0.0	158.2	3.1	0.0	2.4	0.0	0.0	160.6	3.2	0.0	2.7	0.0	0.0
Monobactams	0.1	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0
Carbapenems	9.9	0.0	0.0	0.0	0.0	0.0	9.9	0.0	0.0	0.0	0.0	0.0	10.1	0.0	0.0	0.0	0.0	0.0
Aminoglycosides	1.0	37.4	0.0	2.1	0.0	56.7	0.9	38.7	0.0	2.0	0.0	57.2	0.9	34.1	0.0	1.4	0.0	56.7
Macrolides	108.0	56.0	21.7	0.0	5.6	0.0	101.4	53.3	17.1	0.0	5.3	0.0	103.4	60.4	38.1	0.0	5.5	0.0
Lincosamides	2.8	35.9	3.0	0.1	0.0	0.0	2.7	36.6	6.6	0.1	0.0	0.0	2.6	23.7	4.9	0.1	0.0	0.0
Tetracyclines	7.1	286.7	53.8	0.0	1.6	10.5	6.9	275.8	49.0	0.0	2.2	12.0	7.1	276.2	57.6	0.0	2.6	12.5
Peptides and glycopeptides	2.2	11.8	0.0	0.0	35.0	0.0	2.1	10.0	0.0	0.0	28.3	0.0	2.3	14.5	0.0	0.0	29.6	0.0
Sulfonamides	45.8	95.6	7.7	0.6	0.0	0.0	49.9	88.4	8.6	0.6	0.0	0.0	53.7	84.4	11.7	0.6	0.0	0.0
Fluoroquinolones	61.3	4.6	0.0	0.9	0.0	0.0	60.2	4.7	0.0	0.9	0.0	0.0	56.6	6.4	0.0	0.9	0.0	0.0
Other quinolones	0.5	0.2	0.8	0.0	0.0	40.1	0.4	0.2	1.7	0.0	0.0	40.8	0.3	0.2	1.5	0.0	0.0	41.2
Amphenicols, thiamphenicols and derivatives	0.2	19.7	1.9	0.0	0.0	0.0	0.1	25.1	1.0	0.0	0.0	0.0	0.1	27.4	2.3	0.0	0.0	0.0
Furan and derivatives	0.0	0.0	14.5	0.0	0.0	0.0	0.0	0.0	1.8	0.0	0.0	0.0	0.0	0.0	1.2	0.0	0.0	0.0
Polysaccharides	0.0	0.0	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0
Polyethers	0.0	0.0	0.0	0.0	136.0	0.0	0.0	0.0	0.0	0.0	142.5	0.0	0.0	0.0	0.0	0.0	141.7	0.0
Polyoxins	0.0	0.0	0.0	0.0	0.0	16.2	0.0	0.0	0.0	0.0	0.0	15.5	0.0	0.0	0.0	0.0	0.0	15.3
Others*	17.5	40.7	0.3	0.0	56.7	23.1	16.5	42.4	0.5	0.0	47.6	25.5	16.8	45.6	0.2	0.0	36.9	25.0
Total	562.6	651.2	119.9	8.5	235.1	146.6	560.2	640.2	100.1	8.1	225.9	151.0	579.7	643.3	131.9	7.8	216.4	150.7
Total for year						1,723.9						1,685.5						1729.7

	2016						2017						2018					
	Humans	Food-producing animals	Aquatic animals	Companion animals	Antimicrobial feed additives	Agrochemicals	Humans	Food-producing animals	Aquatic animals	Companion animals	Antimicrobial feed additives	Agrochemicals	Humans	Food-producing animals	Aquatic animals	Companion animals	Antimicrobial feed additives	Agrochemicals
Penicillins	172.5	83.6	14.6	1.6	0.0	0.0	179.9	84.7	14.7	1.7	0.0	0.0	190.5	92.8	12.9	1.7	0.0	0.0
Cephalosporins	159.1	3.3	0.0	3.1	0.0	0.0	153.8	3.4	0.0	3.2	0.0	0.0	149.6	3.9	0.0	3.2	0.0	0.0
Monobactams	0.1	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0
Carbapenems	10.2	0.0	0.0	0.0	0.0	0.0	10.1	0.0	0.0	0.0	0.0	0.0	9.8	0.0	0.0	0.0	0.0	0.0
Aminoglycosides	0.8	47.5	0.0	0.4	0.0	60.4	0.8	44.4	0.0	0.4	0.0	58.5	0.7	34.7	0.0	0.9	0.0	57.4
Macrolides	102.9	72.7	61.4	0.0	1.4	0.0	94.5	72.0	68.9	0.0	3.5	0.0	89.7	72.1	82.6	0.0	0.0	0.0
Lincosamides	2.5	15.6	6.1	0.1	0.0	0.0	2.4	19.4	5.7	0.1	0.0	0.0	2.4	16.7	5.9	0.1	0.0	0.0
Tetracyclines	7.2	280.7	50.9	0.0	2.0	10.5	7.0	286.0	61.1	0.0	0.0	9.6	7.3	257.4	52.6	1.3	0.0	0.1
Peptides and glycopeptides	2.4	14.0	0.0	0.0	32.1	0.0	2.5	20.0	0.0	0.0	15.2	0.0	2.4	12.3	0.0	0.0	9.4	0.0
Sulfonamides	58.6	78.6	16.7	0.5	0.0	0.0	62.1	84.1	14.4	0.6	0.0	0.0	65.7	78.6	9.6	0.5	0.0	0.0
Fluoroquinolones	57.4	5.2	0.0	0.9	0.0	0.0	53.2	5.9	0.0	0.9	0.0	0.0	49.7	5.8	0.0	0.8	0.0	0.0
Other quinolones	0.3	0.2	1.6	0.0	0.0	42.2	0.2	0.3	1.5	0.0	0.0	44.0	0.1	0.0	1.5	0.0	0.0	44.5
Amphenicols, thiamphenicols and derivatives	0.1	24.8	1.7	0.0	0.0	0.0	0.1	25.3	1.8	0.0	0.0	0.0	0.1	23.3	1.5	0.0	0.0	0.0
Furan and derivatives	0.0	0.0	1.6	0.0	0.0	0.0	0.0	0.0	1.4	0.0	0.0	0.0	0.0	0.0	1.3	0.0	0.0	0.0
Polysaccharides	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Polyethers	0.0	0.0	0.0	0.0	159.9	0.0	0.0	0.0	0.0	0.0	165.5	0.0	0.0	0.0	0.0	0.0	161.0	0.0
Polyoxins	0.0	0.0	0.0	0.0	0.0	15.8	0.0	0.0	0.0	0.0	0.0	8.6	0.0	0.0	0.0	0.0	0.0	13.7
Others*	16.9	43.6	0.5	0.0	32.7	24.8	14.5	48.7	0.5	0.0	36.9	22.1	14.0	48.8	0.7	0.0	46.3	23.4
Total	591.0	669.7	155.1	6.7	228.2	153.6	581.3	694.3	169.9	6.9	221.2	142.7	582.1	646.4	168.5	8.6	216.7	139.1
Total for year						1,804.3						1,816.2						1761.4

*Sulfonamides used as antimicrobial feed additives and the agrochemical validamycin are included in "Others." Antifungal antibiotics used as veterinary drugs are not included in "Others." Figures do not include antifungal agents.

(6) Research into antimicrobial stewardship

The following provides a summary of the progress of studies of antimicrobial stewardship in Japan. It covers only studies using medical insurance claims data for outpatient consultations across the whole of Japan and excludes studies limited to a specific region and studies that analyzed only the amount of antimicrobials used. The medical insurance claims data used includes the NDB[2,3,6] developed by the Ministry of Health, Labour and Welfare, the National Health Insurance database,[4] and commercial databases created by combining medical insurance claims data from multiple health insurance societies (JMDC Inc.'s JMDC Claims Database[1,7,9-15] and IQVIA Inc.'s IQVIA Claims[5]). Unless otherwise indicated, figures in square brackets ([]) in the text show the 95% or 99% confidence interval.

1. Overview of antimicrobial stewardship

[Review of past reports]

Yoshida et al. used the JMDC Claims Database to examine antimicrobials prescribed to pre-school children aged from birth to six years at outpatient consultations between January 2005 and September 2014.[1] Analysis of 1,492,548 consultations for 155,556 children revealed that antimicrobials were most commonly prescribed for acute bronchitis (11.9%), acute upper respiratory tract infection (10.1%), and asthma (7.5%). This study found that risk factors for the prescription of antimicrobials by physicians for nonbacterial upper respiratory tract infections were increasing age, male gender, facility scale (clinic), specialism in a field other than pediatrics, and out-of-hours consultations. Uda et al. conducted a similar study of pediatric patients (aged 15 and under) using the NDB.[2] Analysis of 297,197,328 consultations for infectious diseases between 2013 and 2016 was carried out and the DOT investigated. The results showed that DOT per consultation in 2016 was highest in the case of third-generation cephalosporins (0.545), followed by macrolides (0.517) and penicillins without beta-lactamase inhibitors (0.182). Upper respiratory tract infection (54.6% of the total) and lower respiratory tract infection (26.2%) accounted for about 80% of all conditions for which they were prescribed, followed by otitis media (4.2%), skin infections (4.2%), and gastroenteritis (4.0%). Fosfomycin (41.6%) was the most frequently prescribed antimicrobial for gastroenteritis, with fluoroquinolone (12.7%) the most common choice for otitis media and third-generation cephalosporins (74.1%) for skin infections.

[Information updated in FY2020]

Hashimoto et al. used the NDB to analyze the classes of oral antimicrobial agents prescribed at outpatient consultations in Japan and the conditions for which they were prescribed.[3] This study found that 266,470,173 antimicrobial agents were prescribed at 659,333,605 consultations for infectious diseases between April 1, 2012 and March 31, 2015, and that they were prescribed to 89,600,000 people per year (704 per 1,000 population). The conditions for which antimicrobials were most frequently prescribed were acute bronchitis (184 per 1,000 population), acute upper respiratory tract infection (166), tonsillitis (104), gastroenteritis (41), urinary tract infection (33), and skin and soft tissue infections (31). About 70% of antimicrobials were used for respiratory tract infections and acute diarrhea. The antimicrobials most commonly used were third-generation cephalosporins (36.9%), macrolides (28.8%), and fluoroquinolones (20.3%), together accounting for around 85% of the total, while 56% of all prescriptions for antimicrobials related to infectious diseases for which antimicrobials are not usually used (Table 84). These results did not differ greatly from those of a similar study that the same authors conducted using National Health Insurance data.[4]

Table 84 Annual antimicrobial prescription rate per 1,000 inhabitants (2012-2015)

Diagnosis	All visits (per 1000 population per year	Annual rate of outpatient visits with antibiotic prescription (per 1000 population per year)								
		Any antimicrobials (%)	Penicillins	1st- and 2nd-generation cephalosporins	3rd-generation cephalosporins	Macrolides	Quinolones	ST	Tetracyclines	Other
infections for which antibiotics are usually indicated	103	59 (57.0%)	5	1	17	7	27	1	1	2
Urinary tract infection	48	33 (68.8%)	1	1	10	1	19	0	1	1
Pneumonia	16	9 (56.2%)	0	0	1	2	5	0	0	0
Intra-abdominal infections	4	2 (50.0%)	0	0	1	0	1	0	0	0
Sexually transmitted infections	6	2 (33.3%)	0	0	0	1	0	0	0	1
Other bacterial infections	30	13 (43.3%)	4	0	5	3	1	0	0	0
infections for which antibiotics are potentially indicated	533	248 (46.5%)	21	4	97	59	46	0	7	16
Pharyngitis	177	104 (58.8%)	9	2	48	26	18	0	1	1
Sinusitis	96	52 (54.1%)	5	0	17	20	8	0	0	1
Gastroenteritis	159	41 (25.8%)	3	0	9	5	13	0	0	11
Skin infections	60	31 (51.7%)	1	1	18	3	3	0	2	2
Suppurative otitis media	20	13 (64.3%)	3	0	5	1	4	0	0	1
Acne	22	8 (35.2%)	0	0	1	3	0	0	3	0
infections for which antibiotics are rarely indicated	1090	391 (35.8%)	25	6	##	##	69	0	4	5
Bronchitis	316	184 (58.2%)	9	2	54	79	37	0	2	2
Viral upper respiratory tract infections	410	166 (40.5%)	14	2	71	50	27	0	1	2
External wounds and burns	80	14 (17.5%)	1	1	10	1	1	0	0	0
Eye infections	208	13 (6.2%)	1	1	7	2	2	0	0	0
Influenza	50	6 (11.3%)	0	0	2	3	1	0	0	0
Fever	14	4 (29.4%)	0	0	1	1	1	0	0	0
Nonsuppurative otitis media	10	3 (34.2%)	0	0	1	1	0	0	0	0
Nonbacterial gastroenteritis	3	0.2 (6.7%)	0	0	0	0	0	0	0	0
Viral pneumonia	0	0.01 (10.0%)	0	0	0	0	0	0	0	0

Muraki et al. used IQVIA's database to examine the effects of the antimicrobial stewardship fee introduced in 2018 for outpatient consultations involving pediatric patients, focusing on children under the age of 15.[5] In this study, patients were grouped according to whether or not the facility claimed the fee and changes in the percentage of antimicrobial prescriptions for acute upper respiratory tract infections were observed, looking at 31,137 children seen between April and August 2017 (before the fee's introduction) and 30,502 children seen between April and August 2018 (after its introduction). The study found that although there fewer antimicrobials were prescribed at both facilities that claimed the fee and those that did not after the fee was instituted (a decrease of 6.03 [4.74-7.32] percentage points and 4.84 [3.95-5.73] percentage points, respectively), the percentage of antimicrobial prescriptions at facilities that claimed the fee was lower (23.8% vs 34.7%, respectively, after the fee was instituted) (Table 85). Okubo et al. used the NDB to investigate the relationship between the pediatric primary care physician registration system introduced in April 2016 and the use of antimicrobials.[6] This retrospective cohort study tracked 1,386,313 pediatric patients aged under 2 as of April 2015 through to December 2016. A total of 41,363 patients were registered with a pediatric primary care physician. Difference-in-differences analysis of interventions in the group registered with a pediatric primary care physician and the group that was not found that the number of consultations, the number of days for which antimicrobials were prescribed, and the number of days for which broad-spectrum antimicrobials were prescribed increased (differences 1.11 [1.09-1.12] and 1.19 [1.15-1.23], respectively) among the group registered with a pediatric primary care physician, whereas a decline in out-of-hours consultations (difference 0.89 [0.87-0.90]) was observed in that group (Table 86).

Table 85 The frequency of antibiotic prescription for URIs decreased significantly after the AS fee implementation, regardless of whether the facility claimed the fee

	Before introduction	After introduction	*p*-value*
Medical institutions that claimed antimicrobial stewardship fee	2996 (29.8%)	6345 (70.2%)	<0.001
	2162 (23.8%)	6925 (76.2%)	
Medical institutions that did not claimed antimicrobial stewardship fee	9083 (39.6%)	13880 (60.4%)	<0.001
	7712 (34.7%)	14505 (65.3%)	

*Pearson's chi-squared test was used to verify significance

Table 86 Outcomes of Interest Before and After the Timing of Primary Care Physician Registrations and the Within-Group and Between-Group Differences (Difference-in-Differences [DID] estimate) in the Unadjusted and Adjusted Analyses

	Test Cohort (N=41,362)			Control Cohort (N=1,344,951)			Difference-in-differences estimate exponential coefficients for the interaction term in the model	
	Before (incidence rate per 1000 person-months)	After (incidence rate per 1000 person-months)	Incidence rate ratio (95% confidence interval)	Before (incidence rate per 1000 person-months)	After (incidence rate per 1000 person-months)	Incidence rate ratio (95% confidence interval)	Crude estimation index	Adjusted estimation index
Person-months	496,344	372,258		16,139,412	12,104,559			
Total visits	1,060,700 (2137)	657,544 (1766)	0.83 (0.82-0.83)	29,627,081 (1836)	17,687,323 (1461)	0.79 (0.79-0.80)	1.08 (1.07-1.09)	1.08 (1.07-1.09)
Out-of-hour visits	92,482 (186)	44,736 (120)	0.64 (0.63-0.65)	2,225,802 (138)	1,209,453 (100)	0.73 (0.72-0.73)	0.89 (0.87-0.90)	0.89 (0.87-0.90)
Total DOTs	1,090,213 (2196)	728,279 (1956)	0.89 (0.88-0.89)	31,225,108 (1935)	19,285,233 (1593)	0.82 (0.82-0.82)	1.09 (1.08-1.11)	1.11 (1.09-1.12)
DOTs of extremely broad-spectrum antibiotics	141,310 (285)	100,878 (271)	0.95 (0.94-0.96)	4,067,555 (252)	2,474,883 (204)	0.80 (0.80-0.82)	1.17 (1.14-1.20)	1.19 (1.15-1.23)
Admissions	892 (1.8)	305 (0.8)	0.40 (0.40-0.52)	36,846 (2.2)	12,194 (1.1)	0.44 (0.43-0.45)	1.08 (0.93-1.25)	1.07 (0.92-1.25)

Tatebe et al. used JMDC's database to analyze the relationship between hypoglycemia and pivalate-conjugated antibiotics in pediatric patients aged between 1 month and 5 years during the period January 2011 to December 2013.[7] In this study, 454,153 consultations in the group prescribed pivalate-conjugated antibiotics were analyzed, along with 417,287 consultations of pediatric patients prescribed another antimicrobial. Hypoglycemia was diagnosed in 3,356 consultations (0.74% [0.71-0.76]) and 2,605 consultations (0.62% [0.60-0.65]), respectively. Multivariate logistic regression analysis revealed that the odds of developing hypoglycemia in the pivalate-conjugated antibiotics group were 1.19 [1.13-1.25] times higher than in the group prescribed other antimicrobials (Table 87). The adjusted odds ratios for hypoglycemia risk were 1.17 [1.11-1.24] within 7 days of administration, 1.22 [1.05-1.41] within 8-14 days of administration, and 1.57 [0.90-2.69] 15 days or more after administration.

Table 87 Results of multivariate analysis for risk factors associated with hypoglycemia

Variable	Reference	Odds ratio (95% confidence interval)	Adjusted odds ratio (95% confidence interval)	*p*-value
Antimicrobial				
Administration of pivalate-conjugated antibiotics	Control group	1.19 (1.13-1.25)	1.18 (1.12-1.24)	<0.001
Sex				
Male	Female	1.14 (1.08-1.20)	1.14 (1.08-1.20)	<0.001
Age				
1-2 years	Infants	1.00 (0.90-1.12)	1.00 (0.96-1.10)	0.938
3-4 years	Infants	1.37 (1.23-1.53)	1.36 (1.22-1.52)	<0.001
5 years and older	Infants	1.32 (1.18-1.49)	1.31 (1.17-1.48)	<0.001
Number of days drug supplied				
8-14 days	Up to 7 days	1.05 (0.97-1.13)	1.06 (0.98-1.15)	0.132
15 days or more	Up to 7 days	0.93 (0.71-1.20)	0.96 (0.75-1.28)	0.623

[Summary]

Respiratory tract infections in both children and adults are an important target for antimicrobial stewardship. The usage of third-generation cephalosporins and macrolides in children and adults alike stands out, along with usage of fluoroquinolones in adults, suggesting that efforts to reduce the use of these antimicrobials are required. Two reports have been published that consider the effects of political measures on antimicrobial stewardship; these studies will be important when deciding on future policies. Ongoing investigation will be required, as the age range to which the pediatric outpatient antimicrobial stewardship fee has been extended upward. Furthermore, a report was published on a large study of the risk of hypoglycemia from pivalate-conjugated antibiotics. Most third-generation cephalosporins typically used in Japan contain pivalate-conjugated antibiotics and ascertaining their side-effects is an issue closely related to supporting stewardship. Further research focused on antimicrobial side-effects would be desirable.

2. Antimicrobial stewardship regarding acute respiratory tract infections

[Review of past reports]

Higashi et al. analyzed social insurance billing data from 24,134 consultations between January and March 2005. The analysis revealed that antimicrobials had been prescribed at 60% of the 4,325 consultations in which the patient's diagnosis was a nonbacterial acute upper respiratory tract infection.[8] Teratani et al. used the JMDC Claims Database to investigate antimicrobials prescribed for acute respiratory tract infections in adults and children between January 2013 and December 2015. This study found that 40.7% of all antimicrobial prescriptions were for third-generation cephalosporins, with 32.8% for macrolides and 14.7% for fluoroquinolones.[9] Kimura et al. also used the JMDC Claims Database, extracting information about patients, diagnoses, treatment, and medical facilities for the period April 2012 to July 2017 in order to examine trends in antimicrobial prescriptions and associated factors.[10] The results showed that 17,208,787 consultations for 8,983,098 patients involved cases diagnosed with nonbacterial respiratory tract infections. The mean monthly antibiotic prescribing rate per 100 NB-ARTI consultations during the study period was 31.65, while the monthly antibiotic prescribing rate decreased by 19.2% between the first and last months covered by the study. Examination of the factors in the prescription of antimicrobials revealed that patients in the 13-18, 19-29, and 30-39 age groups were more likely to be prescribed antimicrobials than patients aged 60 and above, and that outpatient clinics whose registered specialism was internal medicine or ear, nose, and throat were more likely to prescribe antimicrobials. In addition, clinics with or without beds prescribed more antimicrobials than other types of medical institution.

[Information updated in FY2020]

Koyama et al. likewise used the JMDC Claims Database to examine antimicrobial prescriptions for acute respiratory tract infections between January 2013 and December 2015.[11] Examination of 8.65 million consultations revealed that the consultation rate and antimicrobial prescription rate per 1000 person-years were 990.6 [989.4-991.7] and 532.4 [531.6-533.3], respectively. The overall proportion of antimicrobial prescriptions was 52.7% (Table 88).

Table 88 Visits with antibiotic prescription and age-standardized annual rate per 1000 person-years with antibiotics prescribed by age and diagnosis during 2013-2015.

Age	Condition	Visit rate (99% confidence interval)	Age-standardized visit rate with acute respiratory tract infection (99% confidence interval)	Annual rate of visits with antibiotics (99% confidence interval)	Age-standardized rate of visits with antibiotics (99% confidence interval)
All ages	All conditions	1150.4 (1149.4-1151.5)	990.6 (989.4-991.7)	606.1 (605.4-606.9)	532.4 (531.6-533.3)
	Nasopharyngitis	365.5 (364.9-366.1)	315.8 (315.1-316.4)	133.6 (133.2-133.9)	118.6 (118.2-119.0)
	Bronchitis	321.9 (321.4-322.4)	273.4 (272.8-274.1)	176.4 (176.0-176.8)	156.3 (155.8-156.7)
	Two or more acute respiratory tract infections	253.5 (253.1-254.0)	225.2 (224.6-225.7)	175.4 (175.0-175.8)	156.6 (156.2-157.1)
	Pharyngitis	138.2 (137.8-138.5)	115.6 (115.2-116.0)	76.1 (75.9-76.4)	63.4 (63.1-63.7)
	Sinusitis	33.7 (33.6-33.9)	28.3 (28.1-28.4)	17.0 (16.9-17.1)	14.0 (13.9-14.1)
	Tonsillitis	31.0 (30.9-31.2)	26.4 (26.3-26.6)	23.9 (23.8-24.0)	20.1 (19.9-20.2)
	Laryngitis	6.6 (6.5-6.7)	5.9 (5.8-6.0)	3.7 (3.7-3.8)	3.4 (3.3-3.5)
0–17	All conditions	2517.3 (2514.4-520.3)	2410.0 (2407.2-2412.9)	1119.6 (1117.0-1121.6)	1093.3 (1091.4-1095.2)
	Nasopharyngitis	823.0 (821.3-824.7)	780.2 (778.6-781.8)	238.6 (237.7-239.5)	233.0 (232.1-233.9)
	Bronchitis	789.3 (787.7-791.0)	752.3 (750.7-753.9)	364.6 (363.5-365.8)	353.6 (352.5-354.7)
	Two or more acute respiratory tract infections	427.0 (425.7-428.2)	417.0 (415.8-418.2)	261.9 (261.0-262.9)	258.7 (257.8-259.7)
	Pharyngitis	336.6 (335.5-337.6)	321.8 (320.8-322.9)	170.1 (169.3-170.8)	165.0 (164.3-165.8)
	Sinusitis	71.5 (71.0-72.0)	70.5 (70.1-71.0)	35.4 (35.1-35.8)	34.9 (34.5-35.2)
	Tonsillitis	58.3 (57.9-58.8)	56.8 (56.4-57.2)	43.3 (42.9-43.7)	42.5 (42.2-42.9)
	Laryngitis	11.7 (11.5-11.9)	11.3 (11.1-11.5)	5.6 (5.5-5.7)	5.5 (5.4-5.6)
18–59	All conditions	688.7 (687.8-689.6)	683.6 (682.7-684.6)	438.9 (438.1-439.7)	434.1 (433.4-434.9)
	Nasopharyngitis	209.1 (208.6-209.7)	208.2 (207.7-208.7)	99.3 (98.9-99.6)	98.4 (98.0-98.7)
	Bronchitis	161.2 (160.7-161.6)	160.9 (160.5-161.4)	112.1 (111.8-112.5)	111.7 (111.4-112.1)
	Two or more acute respiratory tract infections	198.6 (198.1-199.1)	196.0 (195.5-196.5)	149.9 (149.5-150.4)	147.7 (147.2-148.1)
	Pharyngitis	70.9 (70.6-71.2)	70.4 (70.1-70.7)	45.2 (45.0-45.5)	44.7 (44.4-44.9)
	Sinusitis	21.6 (21.4-21.7)	21.2 (21.1-21.4)	11.2 (11.0-11.3)	10.9 (10.8-11.1)
	Tonsillitis	22.4 (22.3-22.6)	22.0 (21.9e-22.2)	18.0 (17.8-18.1)	17.6 (17.4-17.7)
	Laryngitis	4.9 (4.8-4.9)	4.8 (4.7-4.9)	3.2 (3.1-3.2)	3.1 (3.1-3.2)
60–74	All conditions	649.3 (646.4-652.3)	682.1 (678.2-686.0)	353.0 (350.8-355.2)	353.4 (350.7-356.1)
	Nasopharyngitis	216.6 (214.9-218.4)	232.5 (230.2-234.8)	82.7 (81.6-83.7)	82.6 (81.3-84.0)
	Bronchitis	180.0 (178.5-181.6)	191.7 (189.7-193.8)	114.3 (113.1-115.6)	118.0 (116.4-119.6)
	Two or more acute respiratory tract infections	152.2 (150.8-153.7)	152.9 (151.1-154.7)	103.9 (102.8-105.1)	101.8 (100.3-103.3)
	Pharyngitis	67.4 (66.4-68.3)	72.1 (70.8-73.4)	33.3 (32.6-34.0)	33.3 (32.4-34.1)
	Sinusitis	13.7 (13.3-14.1)	13.8 (13.3-14.4)	6.1 (5.8-6.4)	5.9 (5.6-6.3)
	Tonsillitis	14.6 (14.1-15.0)	14.5 (13.9-15.0)	10.0 (9.6-10.4)	9.4 (8.9-9.8)
	Laryngitis	4.8 (4.6-5.1)	4.6 (4.3-4.9)	2.7 (2.5-2.9)	2.4 (2.2-2.7)

[Summary]

Although the antimicrobial usage rate for acute respiratory tract infections differs slightly between studies, these differences are thought to be due to differences in the timing of the studies' implementation and in their definitions of respiratory tract infection. However, as all these studies show usage diminishing over time, the situation in respect of the unnecessary use of antimicrobials for respiratory tract infections is believed to be improving. Nevertheless, given that almost all acute respiratory tract infections are viral infections, further reductions would appear to be possible, so similar studies will continue to be needed. The high prescription rate among patients aged between 13 and 39 could become a target for future efforts to support stewardship.

3. Antimicrobial stewardship regarding acute diarrhea

[Review of past reports]

Okubo et al. used JMDC's database to examine the use of antimicrobials to treat acute diarrhea in children (aged under 18) between April 2012 and December 2015.[12] The study examined medical insurance claims data for 4,493 outpatients suffering from acute diarrhea and found that 29.6% of them had been prescribed antimicrobials of some kind. Fosfomycin was the most commonly prescribed antimicrobial (20.3%), followed by cephalosporins (4.5%), and macrolides (3.5%).

[Information updated in FY2020]

None

[Summary]

This study shows that the unnecessary prescription of antimicrobials for acute diarrhea in children is common. The lack of data on adults means that further consideration is required in the future.

4. Antimicrobial stewardship in other realms

[Review of past reports]

Okubo et al. used JMDC's database to examine the use of antimicrobials to treat group A streptococcal infections (GAS) in children (aged under 18) between April 2012 and December 2015.[13] The study investigated medical insurance claims data for 5,030 outpatients suffering from GAS and found that the most commonly prescribed antimicrobials were third-generation cephalosporins at 53.3% of all prescriptions, followed by penicillins (40.1%) and macrolides (2.6%). Out-of-hours consultation were independently associated with penicillin prescriptions, whereas clinical departments other than pediatrics and internal medicine were related to non-penicillin prescriptions.

Kusama et al. used JMDC's database to examine the use of antimicrobials in 58,380 consultations for acute cystitis in patients aged 15 or over between January 2013 and December 2016.[14] Cephalosporins and faropenem accounted for 40.6% of all antimicrobials prescribed for uncomplicated cystitis, while fluoroquinolones accounted for a further 52.7%, totaling 93.3% overall. Third-generation cephalosporins accounted for 90.9% of prescriptions for cephalosporins and faropenem. The most common duration was 5 days for all antimicrobials except first-generation cephalosporins (7 days), penems (7 days), and ST (3 days).

[Information updated in FY2020]

Teratani et al. used JMDC's database to study the relationship between the use of rapid antigen detection tests to identify GAS and the prescription of antimicrobials for tonsillitis during the period January 2013 to December 2015.[15] Analysis of 1.27 million consultations revealed that 5.6% of patients underwent a rapid antigen detection test to identify GAS. Antimicrobials were prescribed at 59.3% of all consultations, with penicillins accounting for 10.8% of all antimicrobials prescribed. The antimicrobial prescription rate in the group of patients who underwent rapid antigen detection tests was 75.0%, which was higher than in the group who did not (58.4%). On the other hand, the proportion prescribed penicillin was higher among the group who underwent rapid antigen detection tests (25.4% vs 9.7%, odds ratio 1.55 [1.50-1.60]) (Table 89).

Table 89 Factors associated with the use of rapid antigen detection test (RADT) to identify Group A beta-hemolytic *Streptococcus*, using multilevel logistic regression analysis

Diagnostic code	Visits with pharyngitis (%)	Proportion of visits prescribed an antimicrobial			Proportion prescribed penicillins/visits with an antimicrobial	
		Proportion used RADT, %	without RADT, % (95% confidence interval)	with RADT, % (95% confidence interval)	without RADT, % (95% confidence interval)	With RADT, % (95% confidence interval)
Acute pharyngitis, unspecified	1,234,915 (97.5)	3.6	58.4 (58.3-58.5)	63.1 (62.6-63.5)	9.6 (9.6-9.7)	14.8 (14.4-15.2)
Acute pharyngitisdue to other specified	2365 (0.2)	17.7	10.0 (8.7-11.4)	16.5 (12.9-20.0)	10.3 (6.0-14.5)	24.6 (14.5-34.8)
Streptococcal pharyngitis	29,300 (2.3)	88.2	82.7 (81.4-84.0)	96.2 (96.0-96.5)	39.6 (37.8-41.4)	37.3 (36.7-37.9)
Total	1,266,580 (100.0)	5.6	58.4 (58.3-58.5)	75.0 (74.6-75.3)	9.7 (9.7-9.8)	25.4 (25.0-25.8)

[Summary]

GAS infections are one of the most common infections in which the administration of antimicrobials is justified. Appropriate testing and selection of therapeutic drugs are required in the case of GAS infections and these studies showed that they are being carried out appropriately. In particular, given that the use of testing is not yet prevalent, efforts to promote the proper use of testing are required. While cystitis is another infection in which the administration of antimicrobials is justified, there is a tendency to favor third-generation cephalosporins and fluoroquinolones when selecting antimicrobials, due in part to the fact that the antimicrobials available in Japan to treat uncomplicated cystitis are limited (antimicrobials commonly used overseas such as nitrofurantoin, trimethoprim, and pivmecillinam cannot be used in Japan). Accurate diagnosis and efforts to ascertain regional antimicrobial susceptibility are required.

References

1. Yoshida S, Takeuchi M, Kawakami K. Prescription of antibiotics to pre-school children from 2005 to 2014 in Japan: a retrospective claims database study. J Public Health (Oxf). 2018;40:397–403.
2. Uda K, Okubo Y, Kinoshita N, Morisaki N, Kasai M, Horikoshi Y, et al. Nationwide survey of indications for oral antimicrobial prescription for pediatric patients from 2013 to 2016 in Japan. J Infect Chemother. 2019;25:758–63.
3. Hashimoto H, Saito M, Sato J, Goda K, Mitsutake N, Kitsuregawa M, et al. Indications and classes of outpatient antibiotic prescriptions in Japan: A descriptive study using the national database of electronic health insurance claims, 2012-2015. Int J Infect Dis. 2020;91:1–8.
4. Hashimoto H, Matsui H, Sasabuchi Y, Yasunaga H, Kotani K, Nagai R, et al. Antibiotic prescription among outpatients in a prefecture of Japan, 2012–2013: a retrospective claims database study. BMJ Open. 2019;9:e026251.
5. Muraki Y, Kusama Y, Tanabe M, Hayakawa K, Gu Y, Ishikane M, et al. Impact of antimicrobial stewardship fee on prescribing for Japanese pediatric patients with upper respiratory infections. BMC Health Serv Res. 2020;20(1):399.
6. Okubo Y, Michihata N, Uda K, Kinoshita N, Horikoshi Y, Miyairi I. Impacts of Primary Care Physician System on Healthcare Utilization and Antibiotic Prescription: Difference-in-Differences and Causal Mediation Analyses. Pediatr Infect Dis J. 2020:39:937-42.
7. Tatebe Y, Koyama T, Mikami N, Kitamura Y, Sendo T, Hinotsu S. Hypoglycemia associated with pivalate-conjugated antibiotics in young children: A retrospective study using a medical and pharmacy claims database in Japan. J Infect Chemother. 2020;26:86–91.
8. Higashi T, Fukuhara S. Antibiotic prescriptions for upper respiratory tract infection in Japan. Intern Med. 2009;48:1369–75.
9. Teratani Y, Hagiya H, Koyama T, Adachi M, Ohshima A, Zamami Y, et al. Pattern of antibiotic prescriptions for outpatients with acute respiratory tract infections in Japan, 2013–15: a retrospective observational study. Fam Pract. 2019;36:402–9.
10. Kimura Y, Fukuda H, Hayakawa K, Ide S, Ota M, Saito S, et al. Longitudinal trends of and factors associated with inappropriate antibiotic prescribing for non-bacterial acute respiratory tract infection in Japan: A retrospective claims database study, 2012-2017. PLoS One. 2019;14:e0223835.
11. Koyama T, Hagiya H, Teratani Y, Tatebe Y, Ohshima A, Adachi M, et al. Antibiotic prescriptions for Japanese outpatients with acute respiratory tract infections (2013-2015): A retrospective Observational Study. J Infect Chemother. 2020;26:660–6.
12. Okubo Y, Miyairi I, Michihata N, Morisaki N, Kinoshita N, Urayama KY, et al. Recent Prescription Patterns for Children With Acute Infectious Diarrhea. J Pediatr Gastroenterol Nutr. 2019;68:13–6.
13. Okubo Y, Michihata N, Morisaki N, Kinoshita N, Miyairi I, Urayama KY, et al. Recent patterns in antibiotic use for children with group A streptococcal infections in Japan. J Glob Antimicrob Resist. 2018;13:55–9.
14. Kusama Y, Ishikane M, Kihara T, Ohmagari N. Epidemiology of antibiotic treatment for uncomplicated cystitis in adults in Japan. J Infect Chemother. 2010: doi.org/10.1016/j.jiac.2020.09.001 (early view).
15. Teratani Y, Hagiya H, Koyama T, Ohshima A, Zamami Y, Tatebe Y, et al. Association between rapid antigen detection tests and antibiotics for acute pharyngitis in Japan: A retrospective observational study. J Infect Chemother. 2019;25:267–72.

(7) Environment

Pharmaceutical products including antimicrobials, drugs and daily necessities, are collectively referred to as "Pharmaceuticals and Personal Care Products (PPCPs)." PPCPs may have physiological activity even at low concentration, causing concerns about effect on aquatic ecosystems.[10] Regarding antimicrobials as a type of PPCPs, several studies have indicated the measurements of antimicrobial concentrations in the environment (e.g. sewage, treated wastewater, recycled water, environmental water, and sludge).[11]

In some cases, a part of sewage sludge (biomass) that is generated from sewage treatment is reused as agricultural fertilizers through anaerobic digestion and composting. The extent to which PPCPs are degraded in the sewage treatment process or in the sewage sludge digestion process varies by the type of PPCPs. For example, among other antimicrobials, most sulfonamides are decomposed, while fluoroquinolones, such as ofloxacin and norfloxacin, reside in sludge at high concentrations without being degraded.[12] The biodegradation process of PPCPs is affected by water temperature. The removability of PPCPs is affected by treatment conditions in the sewage treatment process, such as hydraulic retention time, the processing concentration and retention time of activated sludge. To further promote removal, research is in progress to improve the removability of antimicrobials using membrane bioreactor.[10] Many research activities are also undertaken both in Japan and overseas to improve efficiency in removing antimicrobials, by introducing ozone and advanced oxidation process. It is required to identify the current status of discharge and developmental trends in Japan.[11]

A study that measured the concentrations of antimicrobials detected in Japanese urban rivers, based on influent sewage at sewage treatment plants, reported that the actual measurements of CPFX and clarithromycin indicated certain similarity to concentrations expected from the volumes of shipment or sales of these antimicrobials, and pointed out that it may be possible to predict sewage concentrations of antimicrobials based on their volumes of shipment or sales.[13] The study reported that, for example, CPFX and clarithromycin were contained in sewage at the respective concentrations of 51 to 442 ng/L and 886 to 1,866 ng/L. However, no research results have been reported that these antimicrobials in the environment are affecting the health of humans and other living things.

References

1. Hashimoto H, Matsui H, Sasabuchi Y, Yasunaga H, Kotani K, Nagai R, et al. Antibiotic prescription among outpatients in a prefecture of Japan, 2012–2013: a retrospective claims database study. BMJ Open [Internet]. 2019 Apr 3
2. Higashi T, Fukuhara S. Antibiotic prescriptions for upper respiratory tract infection in Japan. Intern Med. 2009;48:1369–75.
3. Yoshida S, Takeuchi M, Kawakami K. Prescription of antibiotics to pre-school children from 2005 to 2014 in Japan: a retrospective claims database study. J Public Health (Oxf). 2018;40:397–403.
4. Teratani Y, Hagiya H, Koyama T, Adachi M, Ohshima A, Zamami Y, et al. Pattern of antibiotic prescriptions for outpatients with acute respiratory tract infections in Japan, 2013–15: a retrospective observational study. Fam Pract. 2019;36:402–9.
5. Kimura Y, Fukuda H, Hayakawa K, Ide S, Ota M, et al.. Longitudinal trends of and factors associated with inappropriate antibiotic prescribing for non-bacterial acute respiratory tract infection in Japan: A retrospective claims database study, 2012-2017. PLoS One. 2019; 14(10):e0223835.
6. Tomii K, Matsumura Y, Maeda K, Kobayashi Y, Takano Y, Tasaka Y. Minimal use of antibiotics for acute respiratory tract infections: validity and patient satisfaction. Intern Med. 2007;46:267–72.
7. Okubo Y, Michihata N, Morisaki N, Kinoshita N, Miyairi I, Urayama KY, et al. Recent patterns in antibiotic use for children with group A streptococcal infections in Japan. J Glob Antimicrob Resist. 2018 Jun;13:55–9.
8. Okubo Y, Miyairi I, Michihata N, Morisaki N, Kinoshita N, Urayama KY, et al. Recent Prescription Patterns for Children With Acute Infectious Diarrhea. J Pediatr Gastroenterol Nutr. 2019;68:13–6.
9. Karen E. Jerardi and Elizabeth C. Jackson. Nelson Textbook of Pediatrics, Chapter 553, 2789-2795.e1
10. Tanaka H, *et al.* "Contamination of the Aquatic Environment by PPCPs, and Development of Reducing Technology." Environmental Technology, Vo. 37, No. 12., 2008.
11. Park J, et al. "Removal characteristics of PPCPs: comparison between membrane bioreactor and various biological treatment process." Chemosphere. 2017; 179: 347e358.
12. Narumiya M, et al. "Phase distribution and removal of PPCPs during anaerobic sludge digestion" Journal of Hazardous Materials 2013; 260: 305 - 312.
13. Azuma T, et al. "Evaluation of concentrations of pharmaceuticals detected in sewage influents in Japan by using annual shipping and sales data" Chemosphere. 2015;138 :770 -776.
14. World Organization for Animal Health (OIE), "Monitoring of the Quantities and Usage patterns of Antimicrobial Agents Used in Food-Producing Animal"
    http://www.oie.int/fileadmin/Home/eng/Health_standards/tahc/current/chapitre_antibio_monitoring.pdf

8. Public Awareness regarding Antimicrobial Resistance in Japan

(1) Surveys of the general public

1) Surveys of attitudes among the public

Ohmagari et al. conducted surveys of public awareness concerning antimicrobial resistance in March 2017, February 2018 and September 2019, funded by a Ministry of Health, Labour and Welfare research grant.[1, 2. 3] In these studies, consumers (excluding medical professionals) who had registered with INTAGE Research Inc. to participate in various market research surveys completed an online questionnaire. The 2017 survey had 3,390 respondents, the 2018 survey 3,192 and the 2019 survey 3,218. Women comprised 48.8% of respondents in 2017, 49.7% in 2018 and 52.2% in 2019. More than 40% of all respondents experienced taking antibiotics because of cold. Similarly, approximately 40% of respondents thought that antibiotics were effective for cold and influenza. Approximately 20% discontinued taking antibiotics based on their own judgment; and approximately 10% kept the remaining antibiotics at home. Among the respondents who kept antibiotics at home, approximately 80% used them based on their own judgment. The trends in responses to each survey were more or less the same, so ongoing efforts to raise public awareness using a variety of measures are required in order to change attitudes among the public.

Table 90. Reasons for taking oral antibiotics (%)

n=3,390 (2017), 3,192 (2018), 3,218 (2019) (select all that applied)	2017 (%)	2018 (%)	2019 (%)
Cold	45.5	44.7	41.2
Others/unknown	24.3	21.2	23.2
Influenza	11.6	12.4	12.0
Fever	10.7	11.3	8.5
Nasopharyngitis	9.5	10.8	10.5
Cough	9.0	10.8	6.9
Sore throat	7.7	7.8	8.2
Skin or wound infection	6.5	7.0	9.0
Bronchitis	5.4	6.6	5.1
Headache	4.3	5.0	4.1
Diarrhea	3.1	3.2	2.6
Urinary tract infection	2.3	2.5	2.7
Pneumonia	1.4	1.7	1.3

Table 91. Do you think each of the following statements is correct or incorrect? (%)

		2017 (n=3,390)	2018 (n=3,192)	2019 (n=3,218)
Antibiotics beat viruses	Correct	46.8	46.6	52.4
	Incorrect	21.9	20.3	17.7
	Do not know	31.3	33.0	29.9
Antibiotics have effect on cold and influenza	Correct	40.6	43.8	43.9
	Incorrect	24.6	22.1	22.7
	Do not know	34.8	34.1	33.4
Unnecessary use of antibiotics may result in the loss of their effect	Correct	67.5	68.8	66.4
	Incorrect	3.1	3.7	3.4
	Do not know	29.4	27.5	30.2
Adverse effects are involved in the use of antibiotics	Correct	38.8	41.5	45.7
	Incorrect	12.7	13.4	10.5
	Do not know	48.6	45.0	43.8

Table 92. Do any of the statements below apply to you? (%)

		2017 (n=3,390)	2018 (n=3,192)	2019 (n=3,218)
I have discontinued taking antibiotics, or adjusted a dose or frequency based on my own judgment	Yes	23.6	24.0	24.6
	No	76.4	76.0	75.4
I keep antibiotics in my house	Yes	11.7	11.9	9.8
	No	88.3	88.1	90.2

Table 93. Do any of the statements below apply to you? (%)

		2017 (n=396*)	2018 (n=426*)	2019 (n=3,218)
I have used antibiotics that I kept at home for myself	Yes	75.8	77.5	75.6
	No	24.2	22.5	24.4
I have given antibiotics that I kept at home to my family or friend	Yes	26.5	27.2	28.5
	No	73.5	72.8	71.5

* Only respondents with valid responses that kept antibiotics at home.

(2) Surveys of healthcare providers

1) Survey of attitudes among pharmacists at health insurance pharmacies

Oda et al. conducted a questionnaire among health insurance pharmacies belonging to the Kumamoto City Pharmaceutical Association before and after a January 2018 workshop.[4] The questionnaire sent beforehand in November 2017 (sent to 315 pharmacies, with responses received from 124 pharmacies (39.3% response rate)) contained questions about medical policy relating to measures to combat AMR. 40-50% of responding pharmacies stated that they were aware that antimicrobials were unnecessary for patients with mild symptoms of conditions such as acute diarrhea, with a similar proportion stating that they understood how to give appropriate explanations to patients requesting the prescription of antimicrobials deemed unnecessary. Less than 20% of responding pharmacies stated that they had an understanding of the National Action Plan on AMR and the Manual of Antimicrobial Stewardship. Initiatives to promote awareness activities among health insurance pharmacies would appear to be vital.

2) Survey of attitudes among undergraduate medical students

Hagiya et al. conducted a survey of attitudes among undergraduate students at Okayama University Medical School.[5] This study took the form of a paper-based questionnaire conducted between September 2019 and February 2020, with a response rate of 93.8% (661 responses). While almost all students were familiar with the term "antibiotics," their understanding of it was not necessarily adequate. Although accurate knowledge increased among students in higher years, 26.2% of sixth-year undergraduates (the final year of study) still had incorrect knowledge, responding that antimicrobials could treat the common cold. Education of undergraduate medical students would appear to be vital in promoting antimicrobial stewardship.

Table 94 Do you believe that the following statements are correct? (%)

	1st year undergraduates (n=113)	2nd year undergraduates (n=114)	3rd year undergraduates (n=110)	4th year undergraduates (n=116)	5th year undergraduates (n=105)	6th year undergraduates (n=103)	Total (n=661)
Antimicrobials are effective against viruses	64.6	45.6	27.3	19.8	11.4	7.8	30.0
Antimicrobials are effective against the common cold	77.0	50.9	48.2	49.1	23.8	26.2	46.4
Antimicrobials are effective against influenza	60.2	32.5	25.5	17.2	11.4	9.7	26.5

(3) Survey of veterinary science students

The Ministry of Agriculture, Forestry and Fisheries conducted a survey of attitudes among undergraduate veterinary science students at 12 universities nationwide. The survey took the form of written questionnaire conducted in tandem with a series of lectures about antimicrobial resistance between October 2019 and March 2020. Responses were received from 677 students (431 third-year undergraduates, 199 fourth-year undergraduates, 43 fifth-year undergraduates, and 4 unknown). The results of the study suggest that students were influenced by the lectures conducted in conjunction with the survey. In response to the questions about antimicrobials (Table 95), 4.6% of all students stated that antimicrobials are effective against influenza, whereas 92.9% of the students stated that they are effective against bacterial infections. It is therefore thought that these students have some degree of knowledge about antimicrobials. On the other hand, given that 19.8% of all students thought that they were effective against the common cold, ongoing education about antimicrobial resistance will be vital.

In response to the questions about the use of antimicrobials (Table 96), 9.2% of all students stated that they would use antimicrobials if requested to do so by the farmer/owner, whereas 82.0% of the students stated that they would use them if they judged that antimicrobials would be effective based on the results of antimicrobial susceptibility testing of pathogens, with a higher percentage of students in upper years stating that they would do so in the latter case. From this, it was surmised that undergraduate students gain a certain degree of knowledge about the prudent use of antimicrobials in the course of veterinary science education.

Table 95 Please give your perceptions about antimicrobials (%)

	3rd year undergraduates (n=431)	4th year undergraduates (n=199)	5th year undergraduates (n=43)	Unknown (n=4)	Total (n=677)
Effective against the common cold	17.9	23.1	23.3	25.0	19.8
Effective against influenza	6.0	2.0	2.3	0	4.6
Effective against bacterial infections	91.9	94.5	97.7	75.0	92.9
Used to prevent complications after surgery	45.9	63.8	72.1	50.0	52.9
Used as a feed additive	34.3	46.7	46.5	50.0	38.8
Used in agrochemicals used for vegetables, etc.	34.3	46.7	46.5	50.0	38.8

Table 96 Imagine you had become a veterinarian. In what situations would you use antimicrobials? (%)

	3rd year undergraduates (n=431)	4th year undergraduates (n=199)	5th year undergraduates (n=43)	Unknown (n=4)	Total (n=677)
If I was requested to do so by the farmer/owner	9.5	9.0	2.3	50.0	9.2
If I observed symptoms such as fever or respiratory symptoms	13.7	20.6	27.9	0	16.5
If I suspected a bacterial infection based on test results	72.6	77.4	86.0	50.0	74.7
If I judged antimicrobials would be effective based on the results of antimicrobial susceptibility testing of pathogens	80.5	83.4	93.0	50.0	82.0

References

1. Ohmagari N, *et al.* "'Research on the Public Awareness Concerning Antimicrobial Resistance', under 'Research Concerning the Infection Control of Antimicrobial-Resistant Bacteria in Medical Institutions' (2016- Emg-Adm-General-003), Shared Research Report, Grants for Research from the Ministry of Health, Labour and Welfare of Japan) (Research Project concerning Emerging and Re-emerging Infectious Diseases and Vaccination Policies) FY2016." 2017
2. Ohmagari N, *et al.* "'Research on the Public Awareness Concerning Antimicrobial Resistance: Follow-up Study One Year Later', under 'Research Concerning the AMR Action Plan' (2017- Emg-Adm-Designated-005), Shared Research Report, Grants for Research from the Ministry of Health, Labour and Welfare of Japan) (Research Project concerning Emerging and Re-emerging Infectious Diseases and Vaccination Policies: Measures to Combat Disease and Disability) FY2017." 2019
3. Ohmagari N, et al. "'Research Concerning AMR Countermeasures Education and Awareness', under 'Research Concerning AMR' (2017- Emg-Adm-Designated-005), Shared Research Report, Grants for Research from the Ministry of Health, Labour and Welfare of Japan) (Research Project concerning Emerging and Re-emerging Infectious Diseases and Vaccination Policies: Measures to Combat Disease and Disability) FY2017." 2020
4. Oda K, Katanoda T, Maeda K, Jono H, Kawaguchi T, Saito H. Educational Activities on Measures to Antimicrobial Resistance Based on Questionnaire Investigation for Health Insurance Pharmacists. Journal of Japanese Society of Hospital Pharmacists 2018;54(11):1359-1364.
5. Hagiya H, Ino H, Tokumasu K, Ogawa H, Miyoshi T, Ochi K, Otsuka F. Antibiotic literacy among Japanese medical students. J Infect Chemother. 2020 Jul 16;S1341-321X(20)30212-9. doi: 10.1016/j.jiac.2020.06.021.

9. Way Forward

This document follows on from last year's report in presenting information on the current status of antimicrobial resistance in Japan in the areas of human health, animals, agriculture, food and the environment, as well as the volumes of use (or sales) of human and veterinary antimicrobials. Based on this current report, it is expected that AMR-related measures will be further advanced by promoting multi-disciplinary cooperation and collaboration. It is also considered crucial to continue with advanced surveillance activities, in order to take the leadership in global policy in AMR. Part of this report includes data obtained after Japan's "National Action Plan on Antimicrobial Resistance (AMR) 2016-2020" was published. Following on from 2017, figures for 2018 show that the total usage of all antimicrobials and usage of oral antimicrobials, including oral cephalosporins, oral macrolides, and oral fluoroquinolones, is trending downward compared with the data for 2013. However, further promotion of measures against AMR will be required to achieve the 2020 targets. More specifically, it will be necessary to reduce the unnecessary prescription of antimicrobials, particularly in cases of acute respiratory tract infection, based on the Manual of Antimicrobial Stewardship, among other materials. As the basic premise underpinning the promotion of antimicrobial stewardship is ensuring that the appropriate antimicrobials can be used when needed, securing a stable supply of basic antimicrobial agents is crucial. In addition, information about resistant bacteria in each region and the status of antimicrobial use is being put in place, as it is desirable to select antimicrobials and promote infection control measures tailored to the situation in each region. Furthermore, it will be necessary to continue using various techniques for education and awareness activities targeting the public and medical professionals, to achieve further progress in antimicrobial stewardship.

In animal field, rates of resistance to third-generation cephalosporins and fluoroquinolones in *Escherichia coli* isolated from diseased companion animals, surveillance of which began in 2017, were found to be higher than in *Escherichia coli* isolated from food-producing animals. This demonstrates the necessity of continuing and enhancing measures to combat antimicrobial resistance not only via the measures that have been underway for some time in the field of food-producing animals, but also through the widespread circulation of the guide to prudent use in companion animals launched in 2020. In food-producing animal field, although the volume of tetracycline sales fell in 2018, rates of tetracycline resistance in *Escherichia coli* isolated from healthy food-producing animals—an outcome index for the Action Plan—have not declined. Accordingly, greater efforts are required to promote prudent use of these antimicrobials, taking into account the reality of their use among veterinarians and producers.

Following on from 2019, this report makes comparisons between the volume of antimicrobial use (or sales) in the fields of human medical care, veterinary care, and agriculture. Major progress was thus seen in such areas as the highlighting of differences in the volume of antimicrobial use in each field by type of antimicrobial, the reporting of antimicrobial resistance rates in healthy companion animals to accompany existing reporting on rates in diseased companion animals, and the enhancement of data on trends in antimicrobial-resistant bacteria in food and the environment. Hopes are high that progress in the surveillance of trends in each field will continue next year and beyond. Furthermore, it is hoped that initiatives of the kind spotlighted by the National Action Plan on Antimicrobial Resistance, focusing on linking data from antimicrobial resistance trend surveillance and monitoring in such areas as human health, animals, and food, will contribute to combating antimicrobial resistance in Japan in the future.

The existing Action Plan covers the five-year period up to 2020. Although some indices are improving, there are still many that have seen only scant improvement, added to which a number of new issues have emerged, so it is necessary to continue addressing them in coordination with international trends. As such, industry, academia, and government will work together to promote frameworks for collaboration between the organizations tasked with handling different fields, while also examining the promotion of research that enables cross-cutting evaluation of the risks to humans, animals, and the environment to be conducted.

Appendix

(1) Japan Nosocomial Infections Surveillance (JANIS)

1) Overview

JANIS is conducted for the purpose of having an overview of nosocomial infections in Japan, by surveying the status of health care associated infections at medical institutions in Japan, the isolation of antimicrobial-resistant bacteria, and the status of infections caused by antimicrobial-resistant bacteria, while providing useful information for the control of health care associated infections in medical settings. The aggregated data of information from all medical institutions patriated are published on the website of the National Institute of Infectious Diseases (https://janis.mhlw.go.jp/english/index.asp). A result of the analysis is reported back to each institution so that such a feedback can be utilized for the formulation and evaluation of infection control measures at each institution. JANIS participation is voluntary with approximately 2,000 participating medical institutions at present.

Clinical Laboratory Division of JANIS collects the laboratory data of bacteria that are isolated at hospitals across Japan, and publish aggregated data regarding the proportion of clinically important bacterial species that are resistant to major antimicrobials. In 2018, 1,988 hospitals participated in the laboratory section. The aggregated data include data from hospitals with at least 20 beds, and exclude clinics and facilities for the elderly. Since 2014, figures have also been compiled on the basis of hospital scale, divided into hospitals with 200 or more beds and those with fewer than 200 beds. Only bacteria that are isolated from specimens from hospitalized patients at participating hospitals are included into aggregated data, and specimens from ambulatory sections are excluded. To provide more representative information as a national surveillance system, protocols of sampling including selection of sentinel sites and their stratification need to be improved further. The assessment of antimicrobial susceptibility tests is interpreted based on CLSI Criteria.

Quality control for antimicrobial susceptibility tests depends on medical institutions. To improve the quality of antimicrobial susceptibility tests at hospital laboratories, a quality control program was developed under the leadership of the Japanese Society for Clinical Microbiology and it has been piloted since 2016.

JANIS is a surveillance program regulated by the Statistics Act and it differs from the National Epidemiological Surveillance of Infectious Diseases based on the Infectious Diseases Control Act. While participation is voluntary, from 2014, Premiums for infection control 1 in medical reimbursement requires participation in JANIS or equivalent surveillance programs. JANIS is organized and operated by the Ministry of Health, Labour and Welfare, and its operating policy is determined at the operation council that comprises of experts in infectious diseases, antimicrobial resistance and other relevant professional fields. Section II, Laboratory of Antimicrobial Resistance Surveillance, National Institute of Infectious Diseases functions as a secretariat office for JANIS.

Under the Global Antimicrobial Resistance Surveillance System (GLASS), launched by WHO in 2015, individual countries are encouraged to submit data regarding resistant bacterias in the human health area.[1] Japan has provided necessary data from JANIS and other pertinent monitoring systems to GLASS. Of note, data for 2014 to 2017 have already been submitted. GLASS is calling for the same set of antimicrobials to be used in antimicrobial susceptibility tests at medical institutions subject to monitoring in each country. As JANIS is a voluntary surveillance program, it collects whatever data can be supplied by the participating medical institutions, in whatever form that data emerges from the institutions' routine testing operations. Standardizing the types of antimicrobials tested is therefore difficult. Techniques for compiling data are being considered as part of the JANIS program, to facilitate international cooperation in surveillance. Under GLASS, the expansion of the scope of surveillance to food-producing animal and other areas are discussed.[1] It is expected that the data from this national one health report can be contributed to GLASS.

2) Methods for submission

JANIS consists of five divisions: (1) Clinical Laboratory, (2) Antimicrobial-Resistant Bacterial Infection, (3) SSI, (4) ICU and (5) NICU. Medical institutions select divisions to participate in, in accordance with their purposes and conditions. Among the five divisions, Clinical Laboratory division handles surveillance regarding antimicrobial resistance. In Clinical Laboratory division, all data concerning isolated bacteria are collected from bacteriological examination units installed in the laboratories of medical institutions, computerized systems, and other sources, and converted into the JANIS format before submitted online. The submitted data are aggregated, and the shares of clinically important bacterial species that are resistant to key antimicrobials are calculated, and published as the national data of Japan.

3) Prospects

Most medical institutions participating in JANIS are of a relatively large scale with 200 or more beds. The data in the laboratory division only include specimens from hospitalized patients, and exclude specimens from ambulatory sections. Data are not collected from clinics. The bias based on this sampling policy in JANIS should be addressed.

(2) National Epidemiological Surveillance of Infectious Disease (NESID)

1) Overview

The NESID program collects and publishes domestic information regarding infectious diseases, and monitors the occurrence of and trends in infectious diseases, based on reports from physicians and veterinarians. At present, the NESID program is conducted in accordance with the Act on the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases (hereinafter referred to as "Infectious Diseases Control Law"), which took effect in April 1999. The goal of NESID is to accurately identify and analyze information regarding the occurrence of infectious diseases and to rapidly provide and publish the results to the general public and healthcare practitioners, thereby promoting measures for the effective and adequate prevention, diagnosis and treatment of infectious diseases, and preventing the occurrence and spread of various infectious diseases, while verifying the detection status and characteristics of circulating pathogens, and facilitating appropriate infection control measures, through the collection and analysis of pathogen information.

As of July 2019, the following seven antimicrobial-resistant bacteria infections are designated as reportable under NESID, which are all classified as Category V Infectious Diseases. The four diseases that are subject to notifiable disease surveillance, which requires reporting by all physicians, are vancomycin-resistant enterococcal infection (VRE, designated in April 1999), vancomycin-resistant *Staphylococcus aureus* infection (VRSA, designated in November 2003), carbapenem-resistant *Enterobacteriaceae* infection (CRE, designated in September 2014), and multidrug-resistant *Acinetobacter* infection (MDRA, designated as a disease reportable from designated sentinel sites in February 2011, and changed to a disease reportable under notifiable disease surveillance in September 2014). The three diseases that are reportable from approximately 500 designated sentinel sites (medical institutions that have 300 or more beds, with internal medicine and surgery departments) across Japan are penicillin-resistant *Streptococcus pneumoniae* infection (PRSP, designated in April 1999), methicillin-resistant *Staphylococcus aureus* infection (MRSA, designated in April 1999), and multidrug-resistant *Pseudomonas aeruginosa* infection (MDRP, designated in April 1999).

2) Reporting criteria

A physician who has diagnosed a reportable disease listed above (the manager of a designated notification facility in the case of a disease subject to sentinel surveillance) should report to a Public Health Center using a designated reporting form. The scope of reporting includes cases where bacteria that satisfy the laboratory findings specified in Table A are detected, and the isolated bacteria are regarded as the cause of the relevant infectious disease, or cases where it was detected from specimens that normally should be aseptic. Carriers are excluded from the scope of reporting.

Table A. Reporting criteria

Reportable disease	Summary of reporting criteria
VRE	*Enterococcus* is isolated and identified, and the MIC value of vancomycin is ≥ 16 μg/mL.
VRSA	*Staphylococcus aureus* is isolated and identified, and the MIC value of vancomycin is ≥ 16 μg/mL.
CRE	*Enterobacteriaceae* is isolated and identified, and either A) or B) below is satisfied: A) The MIC value of meropenem is ≥ 2 μg/mL, or the diameter of the inhibition circle of the meropenem susceptibility disk (KB) is ≤ 22 mm. B) It is confirmed that both the following conditions are satisfied: a) The MIC value of imipenem is ≥ 2 μg/mL, or the diameter of the inhibition circle of the imipenem susceptibility disk (KB) is ≤ 22 mm. b) The MIC value of cefmetazole is ≥ 64 μg/mL, or the diameter of the inhibition circle of the cefmetazole susceptibility disk (KB) is ≤ 12 mm.
MDRA	MDRA *Acinetobacter* spp. is isolated and identified, and all three conditions below are satisfied: A) The MIC value of imipenem is ≥ 16 μg/mL, or the diameter of the inhibition circle of the imipenem susceptibility disk (KB) is ≤ 13 mm. B) The MIC value of amikacin is ≥ 32 μg/mL, or the diameter of the inhibition circle of the amikacin susceptibility disk (KB) is ≤ 14 mm. C) The MIC value of ciprofloxacin is ≥ 4 μg/mL, or the diameter of the inhibition circle of the ciprofloxacin susceptibility disk (KB) is ≤ 15 mm.
PRSP	*Streptococcus pneumoniae* is isolated and identified, and the MIC value of penicillin is ≥ 0.125 μg/mL, or the diameter of the inhibition circle of the oxacillin susceptibility disk (KB) is ≤ 19 mm.
MRSA	*Staphylococcus aureus* is isolated and identified, and the MIC value of oxacillin is ≥ 4 μg/mL, or the diameter of the inhibition circle of the oxacillin susceptibility disk (KB) is ≤ 10 mm.
MDRP	*Pseudomonas aeruginosa* is isolated and identified, and all three conditions below are satisfied: A) The MIC value of imipenem is ≥ 16 μg/mL, or the diameter of the inhibition circle of the imipenem susceptibility disk (KB) is ≤ 13 mm. B) The MIC value of amikacin is ≥ 32 μg/mL, or the diameter of the inhibition circle of the amikacin susceptibility disk (KB) is ≤ 14 mm. C) The MIC value of ciprofloxacin is ≥ 4 μg/mL, or the diameter of the inhibition circle of the ciprofloxacin susceptibility disk (KB) is ≤ 15 mm.

3) System

Public Health Centers confirm reported information, and enter the data into NESID. The registered information is further confirmed and analyzed, and additional information is collected, by local infectious disease surveillance centers, the Infectious Diseases Surveillance Center of NIID as the central infectious disease surveillance center, and other relevant bodies. Patient information (e.g. the reported numbers of patients, and trends) that is collected under the Infectious Diseases Control Law, and other related information, are provided to the general public through the Infectious Diseases Weekly Reports (IDWRs) and other media. A March 2017 notification issued by the Director of the Tuberculosis and Infectious Diseases Control Division, Health Service Bureau, MHLW imposed on local public health institutes and other organizations a requirement to test strains isolated from notified cases of CRE infection. Since then, data concerning the detection of major carbapenemase genes in strains isolated from notified cases of CRE infection have been collected and analyzed within the framework of the monitoring of trends in outbreaks of infection and have been published in the Infectious Agents Surveillance Report (IASR), among others.

4) Prospects

A certain level of quality is considered to be guaranteed in the reporting of antimicrobial-resistant bacteria infections under NESID, since reporting is based on case definitions specified by the Infectious Diseases Control Law. Although cases may be underestimated in notifiable disease surveillance, an overall picture of trends in occurrence can be monitored. This surveillance system is also considered useful because, when an unusual trend is observed, it may trigger an intervention (e.g. investigation, guidance) at the relevant medical institution by the Public Health Center. Trends in diseases reportable from designated sentinel sites have been recorded since the launch of the NESID program in 1999, and considered useful for monitoring medium- to long-term trends in the occurrence of the target diseases. In addition, pathogen surveillance focused primarily on CRE was launched in 2017 and, with data on resistance genes set to be gathered and analyzed for VRE and MDRA in due course, it is anticipated that information that will be valuable in devising measures to combat antimicrobial-resistant bacteria will be collected and utilized.

(3) Japan Surveillance for Infection Prevention and Healthcare Epidemiology (J-SIPHE)

1) Overview

The AMR Clinical Reference Center (AMRCRC) operates the J-SIPHE system, which can be used for AMR measures at hospitals as well as for promoting regional partnerships. The J-SIPHE 2019 Annual Report covers a total of 581 participating medical institutions (449 calculating Infection Prevention and Control Premium 1, 127 calculating Infection Prevention and Control Premium 2, and 5 calculating no premium), with the number of participating medical institutions standing at more than 600 as of October 2020.

The purpose of this system is to collate information for use by participating medical institutions and their local communities. It covers such information as the treatment status of infectious diseases at participating institutions nationwide, infection control and antimicrobial stewardship initiatives, the incidence of healthcare-associated infections, the emergence of major bacteria and antimicrobial-resistant bacteria, the incidence of bloodstream infections by such bacteria, and antimicrobial use. It also plays a part in developing benchmarks for measures to combat AMR.

2) System

Participation in this system is based on applications by groups composed of collaborating medical institutions authorized to treat patients with health insurance coverage in Infection Prevention and Control Premium 1 and Infection Prevention and Control Premium 2, and institutions not calculating Infection Prevention and Control Premium 1. Participating institutions may share information within their group based on unified standards, in order to assist in formulating measures to combat AMR that tap into their networks of community relationships. The system is capable of collating and visualizing the necessary data concerning measures to combat AMR in a way that minimizes the burden on participating institutions by making secondary use of existing information such as information fed back to the clinical laboratory division of JANIS and integrated EF files for admissions.

3) Prospects

Most of the institutions participating at present are in the Infection Prevention and Control Premium 1 category, but improvements to develop a system more conducive to community partnerships are required, to build a system that is more accessible for institutions in the Infection Prevention and Control Premium 2 and those calculating no premium, so that use of the system in community cooperation conferences is more meaningful

(4) Trend surveillance of antimicrobial-resistant Mycobacterium tuberculosis

1) Overview

registered tuberculosis patient information system is a part of NESID including: new tuberculosis patients and latent tuberculosis patients who are registered from January 1 to December 31 of a registration year; and all tuberculosis patients who are registered as of December 31 of the calendar year. In principle, information in this system pertains to tuberculosis patients, and focuses on the number of incidence case and incidence rate, the number of patients with tuberoses, treatment status, the number of deaths from tuberculosis, and so on. Information regarding tuberculosis bacillus as the causal bacteria is limited to the smear positive ratio, the number of culture-positive patients, drug-susceptibility testing data, and so on. Though limited, this report exclusively provides routine national information regarding antimicrobial-resistant tuberculosis bacillus.

2) Survey methods

Based on the registered tuberculosis patient information, the results of drug-susceptibility testing in newly registered patients with culture-positive pulmonary tuberculosis are aggregated. The entry of this information item used to be optional, before the Ordinance for the Partial Revision of the Enforcement Regulation of the Act on the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases (MHLW Ordinance No. 101 of 2015, effective May 21, 2015) added "the results of drug-susceptibility testing" under "Conditions of disease" in Item 4, Paragraph 1, Article 27-8.

3) System

When physicians diagnose and report a tuberculosis case to Public Health Center collect, corresponding public health nurses collect detailed information from patients and physicians. Drug-susceptibility testing data are considered to be collected mostly from hospital and commercial laboratories. Those individual data are entered by Public Health Centers across Japan into NESID.

4) Prospects

The surveillance based on the registered tuberculosis patient information system contains the susceptibility results of newly registered patients with culture-positive pulmonary tuberculosis, as reported from all medical institutions. Therefore, data are considered nationally representative. Improvement in the entry rate of drug-susceptibility testing results (approximately 80% at present); the establishment of a system for nationwide quality assurance for drug-susceptibility testing; and the quality control of data entry are warranted.

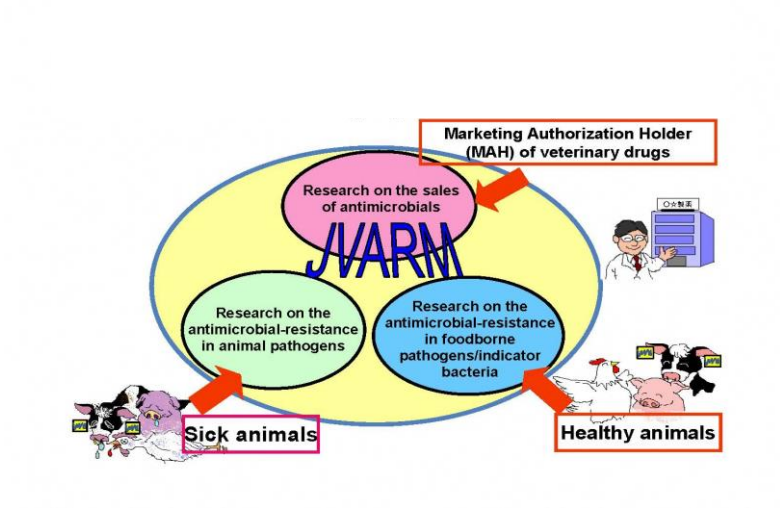
(5) Japanese Veterinary Antimicrobial Resistance Monitoring System (JVARM)

1) Overview

JVARM is a nationwide system for monitoring antimicrobial-resistant bacteria among animals. This monitoring has been conducted by the Ministry of Agriculture, Forestry and Fisheries since 1999 through its network of connections with livestock hygiene service centers across Japan. JVARM provides globally important information and is cited as an example of a monitoring system in the WHO report "Antimicrobial resistance: global report on surveillance 2014."

Under JVARM, three types of monitoring are conducted: (1) monitoring of the volumes of use of antimicrobials (estimated from the volumes of sales); (2) monitoring of antimicrobial resistance among indicator bacteria and foodborne pathogens derived from healthy animals; and (3) monitoring of antimicrobial resistance in pathogenic bacteria (clinical isolates) derived from diseased animals. While verifying the efficacy of veterinary antimicrobials, JVARM also provides basic data for risk assessment and risk management concerning antimicrobial resistance, taking into account influence on human healthcare (Figures 1). The results of JVARM are published on the website of the National Veterinary Assay Laboratory, Ministry of Agriculture, Forestry and Fisheries [2]. In FY2016, reviews were carried out to consider how to strengthen antimicrobial resistance surveillance in aquatic animals and how to conduct antimicrobial resistance surveillance in companion animals, in accordance with the strategies of the National Action Plan on AMR. Antimicrobial resistance surveillance in diseased dogs and cats was launched in FY2017 and in healthy dogs and cats in FY2018.

Figure 1. Overview of veterinary antimicrobial resistance monitoring



2) System for the antimicrobial resistance monitoring

When JVARM first began, surveillance of foodborne pathogenic bacteria and indicator bacteria from healthy animals was carried out using samples of strains isolated and identified from the feces of food-producing animals collected at farms by livestock hygiene service centers. Surveillance using strains isolated and identified by the contracted testing agency from feces collected at animal and poultry slaughterhouses was launched in FY2012, as this facilitated more intensive sampling at a stage closer to the final food product. In FY2016, as it had been confirmed that there was no major difference in the findings of both surveys, JVARM shifted completely from sampling at farms to sampling at animal and poultry slaughterhouses (Figure 2). Bacteria were isolated from feces samples using species-selective media and data are based on one strain per bacterial species per farm (the farm's representative strain).

In the case of clinical isolates from food-producing animals, bacterial strains isolated and identified from materials for pathological appraisal by livestock hygiene service centers across the country were collected. One or two strains isolated from a different individual affected in a single case of infectious disease were collected for the monitoring. The MIC values for these strains are measured by the National Veterinary Assay Laboratory using a broth microdilution method based on the CLSI Criteria (Figure 3). The scope of antimicrobial monitoring includes a broad range of active ingredients that are considered important in antimicrobials used exclusively for animals, antimicrobials used for both animals and humans, and antimicrobial feed additives, among others. Antimicrobial agents subject to monitoring are selected for each bacterial species, according to the past monitoring results and Chapter 6.7 of the OIE Terrestrial Animal Health Code.[3]

The framework for surveillance of companion animals was determinedbased on the results of deliberations by the Working Group for the Surveillance of AMR in Companion Animals. In 2017, bacterial strains isolated from diseased dogs and cats began to be collected from clinical laboratories (Figure 4). Since 2018, samples from healthy dogs and cats have been collected from veterinary clinics across the country with the cooperation of the Japan Veterinary Medical Association (Figure 5). All bacteria were isolated from samples using species-selective media, and adopted one strain per bacterial

species per clinic. The contract laboratories measured MIC by broth microdilution method according to the CLSI guidelines. The antimicrobials for the survey were chosen according to the bacterial species, taking into account the antimicrobials included in the surveillance of food-producing animals and antimicrobials used on companion animals in clinical settings.

Efforts are made to achieve standardization in the isolation and identification of strains and antimicrobial susceptibility testing, by such means as training sessions for the staff of livestock hygiene service centers who carry out this work at the National Veterinary Assay Laboratory each year and checks of quality control at the contracted testing agency. In addition, a parallel survey of the origin of the samples and the date on which they were collected is carried out. Isolated strains collected under JVARM are examined and stocked by the National Veterinary Assay Laboratory, which also performs the analysis of genetic properties and the clarification of antimicrobial resistance mechanism, in order for the molecular epidemiological survey of antimicrobial-resistant strains. Antibiotic feed additives are analyzed by the FAMIC. Data collected through JVARM are published on the website of the National Veterinary Assay Laboratory every year. The data are also utilized for risk assessment by the Food Safety Commission as well as for science-based risk management measures.

Figure 2. System for antimicrobial resistance monitoring in healthy food-producing animals at animal and poultry slaughterhouses

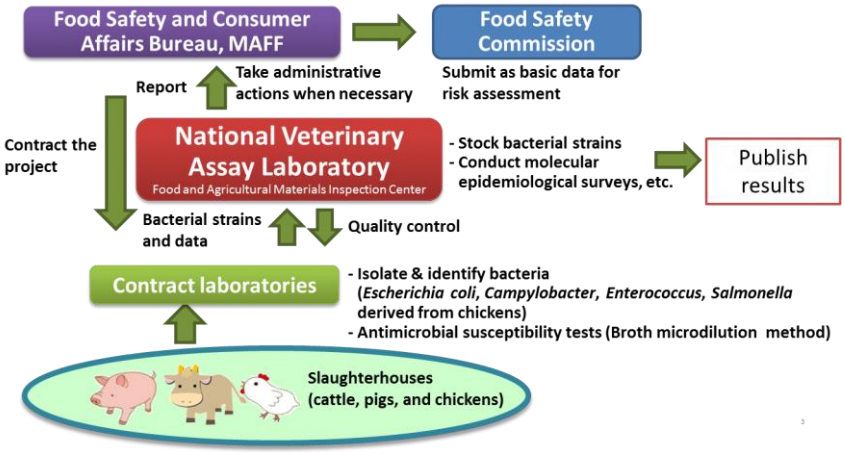


Figure 3. System for antimicrobial resistance monitoring in diseased food-producing animals

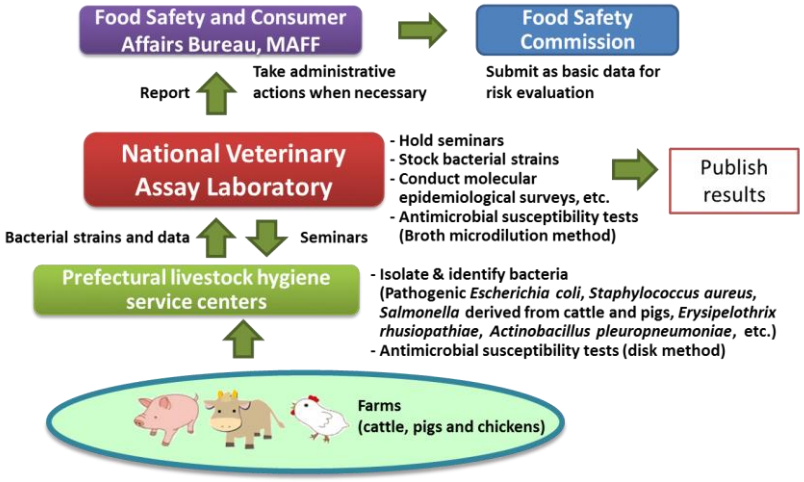


Figure 4. System for antimicrobial resistance monitoring in diseased dogs and cats (from FY2017)

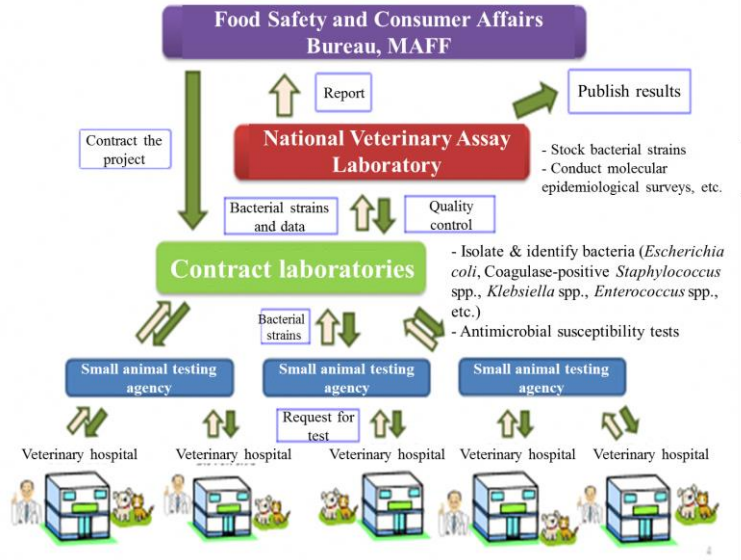
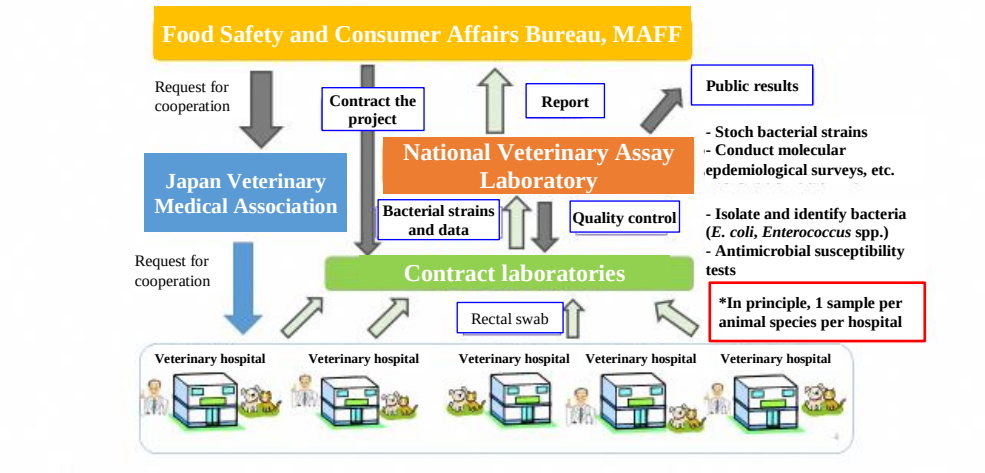


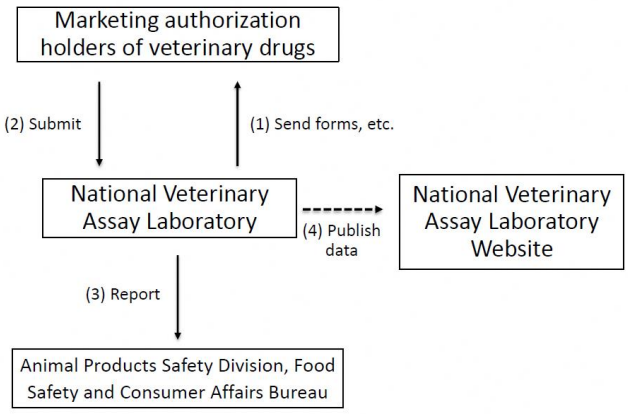
Figure 5. System for antimicrobial resistance monitoring in healthy dogs and cats (from FY2018)



3) Monitoring on the sales volumes of antimicrobials

An annual monitoring is conducted on the volumes of sales of veterinary antimicrobials, based on the reported quantities of veterinary drugs handled by marketing authorization holders, pursuant to Article 71-2 of the Veterinary Drug Control Regulations (MAFF Ordinance No. 107 of 2004) (Figure 6). Starting 2001, the monitoring has included the volume of sales by active pharmaceutical ingredient, and the estimated percentage of sales by animal species, in addition to the volumes of sales by antimicrobial class and route of administration. The data are aggregated and published on the website of the National Veterinary Assay Laboratory as “Annual Report of Sales Amount and Sales Volume of Veterinary drugs, Quasi-drugs and Medical Devices.” Under the OIE Terrestrial Animal Health Code’s section on antimicrobial usage (Chapter 6.8), [4] these data are submitted to the OIE for the activity to understand and compare usage in each country of the world.

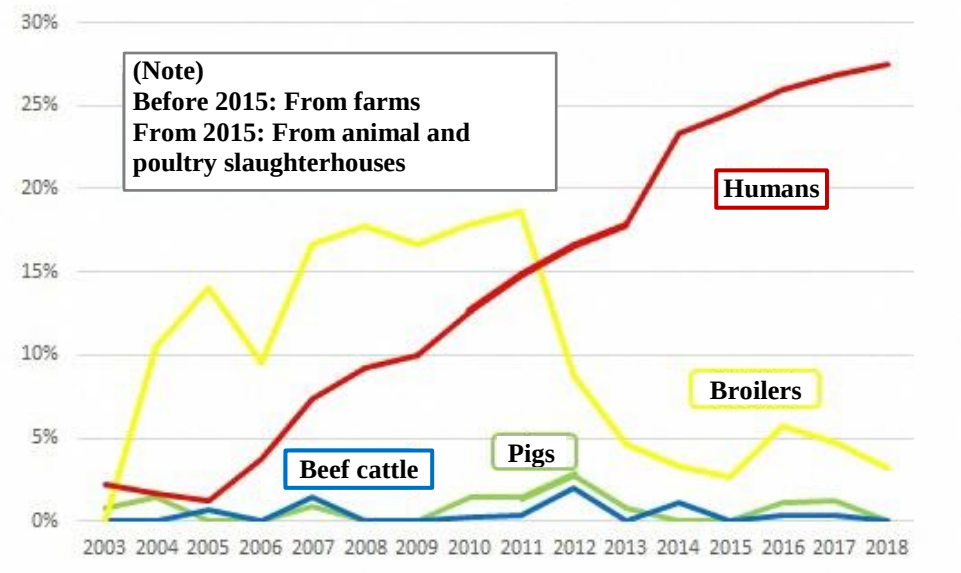
Figure 6. Monitoring on the sales volumes of antimicrobials



4) Collaboration with JANIS

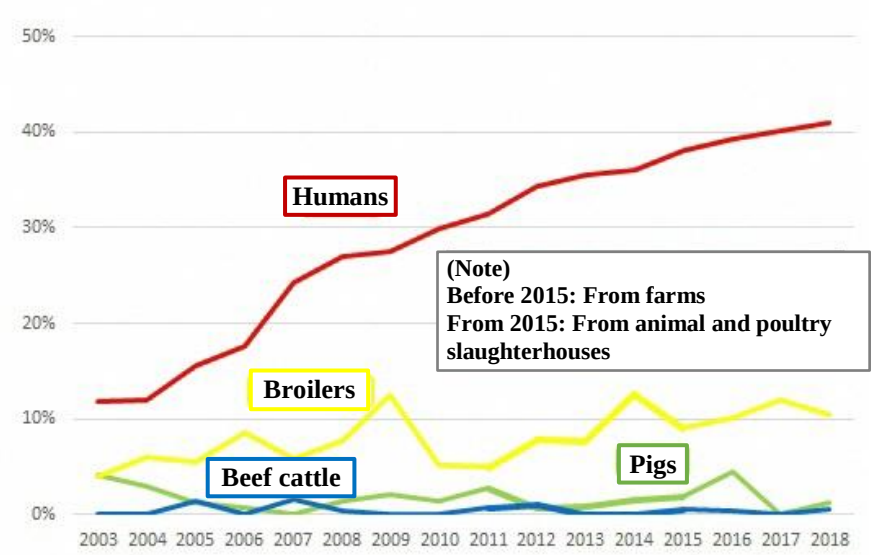
Since FY2012, collaboration has been promoted between JVARM and JANIS (Japan Nosocomial Infections Surveillance). The data of *Escherichia coli* derived from healthy animals collected under JVARM are converted into a format comparable with JANIS data, and the results are published as antibiograms on the website of the National Veterinary Assay Laboratory.[5] These data enable the comparison of trends in antimicrobial-resistant bacteria between humans and animals.

Figure 7. Comparison of the proportion of third-generation cephalosporin-resistant *Escherichia coli* derived from humans and those derived from food-producing animal



The proportion of third-generation cephalosporin-resistant strains derived from humans and those derived from broilers showed an increasing trend until 2011. The key factor behind this is thought to have been the suspension of off-label use of third-generation cephalosporins by certain hatcheries following the presentation of JVARM data and guidance to relevant groups, advising them to halt the use of these agents. On the other hand, the proportion still continues to rise in humans, indicating different trends between humans and broilers.

Figure 8. Comparison of the proportion of fluoroquinolone-resistant *Escherichia coli* derived from humans and those derived from food-producing animal



While a consistent increase was observed in fluoroquinolone-resistant strains derived from humans from 2003, the proportion of fluoroquinolone-resistant strains derived from pigs and beef cattle was below 5%, while the figure for broilers was less than 13%, indicating different trends between humans and food-producing animals.

5) Prospects

JVARM still faces three key tasks: 1) conducting more advanced surveillance and analysis of antimicrobial resistance genes (ARGs) through whole genome analysis of bacteria derived from livestock and from companion animals, and comparing the results with figures for humans; 2) evaluating the volume of use of veterinary antimicrobials with reference to biomass weights calculated using the standardized technique set out by the OIE; and 3) investigating the distribution of antimicrobial-resistant bacteria in environments around sites dealing with food-producing animals. While continuing to carry out monitoring in existing veterinary fields, JVARM will begin working on initiatives in response to these tasks. To further promote One Health monitoring, further collaboration with JANIS will continue to be pursued through comparisons of whole genome analysis data. Those data accumulated will lay the ground for risk assessment and risk management, by clarifying the transmission process of antimicrobial-resistant bacteria, through linkage with other areas.

(6) Japan Antimicrobial Use Surveillance (JAMUS)

1) Overview

Surveillance of antimicrobial use (AMU) in Japan began in April 2015 with the establishment of Japan Antimicrobial Consumption Surveillance (JACS), funded by a research grant from the Ministry of Health, Labour and Welfare (principal investigator: Muraki Yuichi). JACS used sales data purchased from IQVIA concerning all antimicrobials, derived from the company's databases of information about parenteral antimicrobials gathered from medical institutions and drug distribution information obtained from wholesalers. In December 2018, JACS transitioned to Japan Surveillance for Infection Prevention and Health-care Epidemiology (J-SIPHE (coordinating director: Matsunaga Nobuaki)) and Japan Antimicrobial Use Surveillance (JAMUS (coordinating director: Kusama Yoshiki)), which are run by the AMRCRC. JAMUS uses the NDB and the aforementioned sales data to investigate and publish data on AMU in humans at the national and prefectural levels. In this report, AMU is based on the sales data.

2) Monitoring methods

The sales data purchased from IQVIA is used to calculate the titer for overall use and for each agent by dosage form (oral and parenteral), and figures are collated based on either the ATC or AWaRe classification advocated by the WHO. In the case of AMU in humans, these figures are shown over time, adjusted by defined daily dose (DDD) as defined by the WHO, then adjusted by population to calculate DID. To monitor AMU from a One Health perspective, figures converted into titer values are summarized by weight for each ATC category and are then shown totaled with AMU elsewhere. Figures shown for AMU at medical institutions are the results from J-SIPHE monitoring.

3) Prospects

The establishment of Japan's first AMU surveillance programs in the form of JAMUS and J-SIPHE put in place a system that enables trends in AMU over time to be fed back to the public. While sources of AMU information include both data on the volume of sales and insurance billing data, this report focuses on sales data. This is because: 1) it is an international standard; 2) using different sources of information to show information for the same purpose, namely AMU, will confuse the reader; and 3) the outcome indices in the National Action Plan on AMR are based on the results of surveillance of sales volumes. The sources of information used and the way in which they are presented need to be altered according to their purpose and further consideration is required regarding the form in which they should be collated and fed back on an ongoing basis.

(7) Monitoring on the antimicrobial-resistant Campylobacter spp. isolated from humans

1) Overview

Currently the monitoring regarding the emergence of antimicrobial-resistant *Campylobacter* spp. derived from humans is undertaken as research activities by the Tokyo Metropolitan Institute of Public Health, as part of the food safety assurance and promotion research project, with grants for research from the Ministry of Health, Labour and Welfare of Japan.[9]

2) Survey methods

Antimicrobial susceptibility tests were conducted by the disk method, in accordance with the CLSI standards in US.[9] The 110 *C. jejuni* strains and 8 *C. coli* strains that were isolated from the stool of diarrhea cases at hospitals in Tokyo in 2018 were tested using antimicrobials such as TC, NA, CPFX, norfloxacin (NFLX), ofloxacin (OFLX), and EM.

3) Prospects

To identify the emergence of antimicrobial-resistant *C. jejuni /C. coli* on a wide-area basis, it is required to standardize tested antimicrobials, implementation methods, assessment criteria, and other details. While tests were conducted using the disk method, in accordance with U.S. CLSI standards, judgment criteria are provided for only three agents, namely CPFX and EM. Accordingly, other agents were assessed in accordance with standards unified as part of a Ministry of Health, Labour and Welfare-funded research project concerning the promotion of food safety, with reference to EUCAST breakpoints and various literature. It is required to conduct antimicrobial susceptibility tests using common methods not only for strains isolated from humans, but also for strains isolated from food, in order to know the emergence of antimicrobial-resistant bacteria nationwide.

(8) Monitoring on the antimicrobial-resistant non-typhoidal Salmonella spp. isolated from humans and from food

1) Overview

Many Public Health Institutes conducted resistance monitoring regarding antimicrobial-resistant bacteria derived from food. Several Public Health Institutes were organized to undertake the monitoring of antimicrobial-resistant bacteria derived from food as research activities, as part of the food safety assurance and promotion research project, with Grants for research from the Ministry of Health, Labour and Welfare of Japan.[10] This is likely the first monitoring in Japan regarding antimicrobial-resistant bacteria derived from food on a nationwide scale, conducted by standardized methods. The collected data were also reported to GLASS, which was launched by WHO.

2) Methods

With cooperation from 21 Public Health Institutes across Japan, an antimicrobial resistance monitoring was conducted using the common protocol, antimicrobials, instruments, etc., concerning bacteria, particularly *Salmonella* spp., derived from human patients and from food, as collected by these Public Health Institutes.[10] The monitoring was targeted at *Salmonella* spp. strains that were isolated from human patients and from food in 2015 and 2019. Strains derived from humans included those isolated from specimens of patients with infectious gastroenteritis or with food poisoning. For each strain derived from food, the type of source food and the date of isolation were identified. When the source food was chicken meat, information was collected concerning the country of production (domestic, imported (country name), and unknown). The 21 cooperating Public Health Institutes performed antimicrobial susceptibility tests by the CLSI disk diffusion method, in accordance with the Public Health Institute Group Protocol for Antimicrobial Susceptibility Tests, using strains that were assessed as *Salmonella* spp. All Public Health Institutes used common reagents (e.g. susceptibility disks) and instruments (e.g. disk dispensers, vernier calipers) for the tests. Susceptibility disks were laid out on an agar plate as indicated in the layout drawing in the protocol, so that inhibition circles would not be coalesced. The diameters of inhibition circles were measured, and the measurements were assessed based on the susceptibility assessment chart in the protocol.

3) Prospects

Clear similarity was observed in the proportion of antimicrobial-resistant strains derived from humans and of those derived from food. As these data are vital to the One Health approach, which covers the environment, animals, food, and humans, a system has been established that uses conversion software to integrate the data with JANIS and JVARM data to facilitate integrated evaluation of all three.

(9) Monitoring on the antimicrobial-resistant Neisseria gonorrhoeae

1) Overview

In the diagnosis of gonococcal infection, the utilization of nucleic acid testing has been promoted. Isolation culture is only implemented for some patients. Because antimicrobial susceptibility tests for *Neisseria gonorrhoeae* cannot be easily implemented in general laboratories or laboratory companies, it is difficult for JANIS to monitor trends in these bacteria. Therefore, a monitoring on the antimicrobial-resistant *Neisseria gonorrhoeae* has been undertaken as research activities at AMED since 2015. The collected data are also reported to GLASS, which is operated by WHO.

2) Survey methods

More than 40 cooperating clinics are designated across Japan. Antimicrobial susceptibility tests were performed at five facilities capable of testing across Japan, after collecting specimens from the cooperating clinics, or collecting strains through laboratory companies. Antimicrobial susceptibility tests were performed using an agar plate dilution method, recommended by CLSI or EUCAST, or using Etest. MIC values were measured for CTRX and spectinomycin (SPCM) as recommended agents; for AZM, which was used as part of the two-drug combination therapy overseas; and for PCG, CFIX, and CPFX, which had been used as recommended agents in the past. The EUCAST standards were used for susceptibility and resistance assessment (Table A). For reference, the proportion of resistant strain based on CLSI Guidelines (M100-S25) (Table B) is indicated in Table C. The figures for AZM in the tables are based on the MIC distribution of strains that have antimicrobial-resistant gene, as indicated by CLSI Guideline (M100-S27).

3) Prospects

Physicians need to empirically choose therapeutic agents for gonococcal infection according to the result of the monitoring given the difficulty in routinely performing antimicrobial susceptibility tests.

For empiric treatment, it is recommended to use an agent with the potential success rate of 95% or higher. At present, ceftriaxone and spectinomycin are the only recommendable agents in Japan. Because *Neisseria gonorrhoeae* that are present in the pharynx are an important source of infection, *Neisseria gonorrhoeae* in pharynx should be treated. Due to its *in vivo* pharmacokinetics, spectinomycin does not have effect on *Neisseria gonorrhoeae* present in the pharynx. Therefore, ceftriaxone is the only practically recommendable agent.

In sporadic cases, strains isolated in Japan indicate the ceftriaxone MIC of 0.5 μg/mL in antimicrobial susceptibility tests. Ceftriaxone is administered by intramuscular injection overseas, and therefore subject to dose limitation. Therefore, if strains that indicate the ceftriaxone MIC of 0.5 μg/mL are transmitted to overseas, it is likely that ceftriaxone loses its effect. Hence, it is required to continue with the careful monitoring of isolated strains in coming years. Reports of the isolation of strains with the same resistance gene as the resistant strain isolated in Osaka in 2015 [7] have been received from across the globe since 2017.[8]

Table A. Antimicrobial susceptibility assessment criteria based on EUCAST (μg/mL) for *Neisseria gonorrhoeae*

	Susceptible		Resistant
PCG	≤ 0.06	0.125–1	> 1
CFIX	≤ 0.125	-	> 0.125
CTRX	≤ 0.125	-	> 0.125
SPCM	≤ 64	-	> 64
AZM	≤ 0.25	0.5	> 0.5
CPFX	≤ 0.03	0.06	> 0.06

Table B. Antimicrobial susceptibility assessment criteria based on CLSI (μg/mL) for *Neisseria gonorrhoeae*

	Susceptible		Resistant
PCG	≤ 0.06	0.125–1	≧ 2
CFIX	≤ 0.25	-	-
CTRX	≤ 0.25	-	-
SPCM	≤ 32	64	≧ 128
AZM*	-	-	-
CPFX	≤ 0.06	0.12-0.5	≧ 1

* Epidemiological cutoff value indicated in CLSI Standards (M100-S27): wild type (WT) ≤ 1; non-WT ≥ 2

Table C. The proportion (%) of antimicrobial-resistant *Neisseria gonorrhoeae* based on the CLSI (M100-S25)

	2015	2016	2017
CTRX[$]	0.6	0.4	0.5
SPCM	0	0	0
AZM*	3.2	4.0	4.0
PCG[†]	36.0 (96.1)	35.8 (96.7)	37.8(99.0)[†]
CFIX[$]	16.1	11.0	10.0
CPFX[†]	79.0 (79.4)	77.9 (78.3)	74.2(75.8)

[$] Non-susceptibility rate

* The figures are based on the epidemiological cutoff value (non-WT ≥ 2 μg/mL) indicated in CLSI Standards (M100-S27), and differ from resistance proportion.

[†]*Figures in parentheses indicate the sum of resistance and intermediate resistance.

(10) Monitoring on the antimicrobial-resistant *Salmonella* Typhi, *Salmonella* Paratyphi A, and *Shigella* spp.

1) Overview

For typhoid, paratyphoid, and shigellosis, definitive diagnosis is undertaken based on bacterial isolation. Given there is no routine antimicrobial resistance monitoring regarding *Salmonella* Typhi, *Salmonella* Paratyphi A, and *Shigella* spp., susceptibility tests are performed at the National Institute of Infectious Diseases, using strains submitted based on the Notification for Epidemiological Surveillance. Antimicrobial resistance information concerning *Shigella* spp. is also used as data reported to GLASS.

2) Methods

Antimicrobial susceptibility tests are performed using strains that are submitted based on the Notification for Epidemiological Surveillance (HSB/TIDCD Notification No. 100901, PFSB/ISD Notification No. 100902). In antimicrobial susceptibility tests, assessment was performed in accordance with CLSI standards, using a broth microdilution method for *Salmonella* Typhi and *Salmonella* Paratyphi A, and using a disk diffusion method for *Shigella* spp.

3) Prospects

Treatment with antimicrobials is essential for typhoid and paratyphoid. To enable the proper selection of effective therapeutic agents, it is necessary to conduct continuous monitoring. The proportion of strains that are resistant to quinolones and other commonly used antibacterials are high in *Shigella* spp., and therefore recurrence is also possible even after administering antimicrobials. Careful monitoring is required to prevent possible spread of infection in Japan.

References

1. World Health Organization. "Global Antimicrobial Resistance Surveillance System. Manual for Early implementation" http://www.who.int/antimicrobial-resistance/publications/surveillance-system-manual/en/
2. National Veterinary Assay Laboratory, Ministry of Agriculture, Forestry and Fisheries. “Monitoring of AMR.” from http://www.maff.go.jp/nval/yakuzai/yakuzai_p3.html
3. World Organization for Animal Health (OIE),"Harmonisation of National Antimicrobial Resistance Surveillance and Monitoring Programmes." http://www.oie.int/fileadmin/Home/eng/Health_standards/tahc/current/chapitre_antibio_harmonisation.pdf
4. World Organization for Animal Health (OIE),"Monitoring of the Quantities and Usage patterns of Antimicrobial Agents Used in Food-Producing Animal" http://www.oie.int/fileadmin/Home/eng/Health_standards/tahc/current/chapitre_antibio_monitoring.pdf
5. National Veterinary Assay Laboratory, Ministry of Agriculture, Forestry and Fisheries. “Antibiograms of Escherichia coli Surveyed under JVARM.” from http://www.maff.go.jp/nval/yakuzai/yakuzai_p3-1.html
6. Hiki M, *et al.* “Decreased Resistance to Broad-Spectram Cephalosporin in Escherichia coli from Healthy Broilers at Farms in Japan After Voluntary Withdrawal of Ceftiofur,” Foodborne Pathogens Dis. 2015; 12:639-643.
7. Nakayama SI, et al. “New ceftriaxone- and multidrug-resistant Neisseria gonorrhoeae strain with a novel mosaic penA gene isolated in Japan,” Antimicrob Agents Chemorher 2016; 60; 4339-4341.
8. Lahra MM, et al. “Cooperative recognition of internationally disseminated ceftriaxone-resistant Neisseria gonorrhoeae strain,” Emerg Infect Dis 2018; 24; 735-740.
9. Konishi N. et al. “‘Understanding the Emergence of Antimicrobial-Resistant Strains of *Campylobacter* and *Escherichia coli* Derived from Food and Humans,’ Shared Research under ‘Research for Surveillance of Antimicrobial-resistant Bacteria Derived from Food,’ Shared Research Report, Grants for Research from the Ministry of Health, Labour and Welfare of Japan) (Research Project concerning the Assurance and Promotion of Food Safety) FY2019.” 2020
10. Shinomiya H, *et al.* “‘Establishment of Information Collection Systems concerning Antimicrobial-resistant Bacteria Isolated at Public Health Institutes across Japan,’ Shared Research under ‘Research concerning Trends and Hygienic Control of Antimicrobial-resistant Bacteria Derived from Food,’ Shared Research Report, Grants for Research from the Ministry of Health, Labour and Welfare of Japan) (Research Project concerning the Assurance and Promotion of Food Safety) FY2016.” 2018.

Websites of Key Trend Surveys

AMR Clinical Reference Center
http://amrcrc.ncgm.go.jp/

Nippon AMR One Health Report
https://amr-onehealth.ncgm.go.jp/

JANIS
https://janis.mhlw.go.jp/

National Epidemiological Surveillance of Infectious Disease (NESID)
https://www.niid.go.jp/niid/ja/allarticles/surveillance/2270-idwr/nenpou/6980-idwr-nenpo2015.html

Japanese Veterinary Antimicrobial Resistance Monitoring System (JVARM)
http://www.maff.go.jp/nval/yakuzai/yakuzai_p3.html

The Tuberculosis Surveillance Center, The Research Institute of Tuberculosis, Japan Antituberculosis Association
http://www.jata.or.jp/rit/ekigaku/

Japan Antimicrobial Consumption Surveillance (JACS)
https://www.jacs.asia/

The Antimicrobial Resistance One health Surveillance Committee: Terms of References

February XX, 2020

1. Objective

As a sentiment is being elevated to promote AMR-related measures, an integrated AMR trend surveillance with human health, animals, food, and the environment is regarded as important.

The National Action Plan on AMR, enacted on April 5, 2016, also requires establishing systems for such one health AMR surveillance.

Under these circumstances, the Antimicrobial Resistance One health Surveillance Committee (hereinafter referred to as "Committee") is to be held, requesting the participation of experts under the Director-General of the Health Service Bureau, Ministry of Health, Labour and Welfare (MHLW), in order to review necessary technical matters that pertain to one health AMR surveillance.

2. Structure of the Committee

(1) The Committee should consist of experienced experts and other stakeholders.
(2) The Chair should be elected from members by mutual voting.
(3) The Committee should be presided over by the Chair.
(4) The Director-General of the Health Service Bureau may request non-member experts to participate at Committee when necessary.

3. Term of office

(1) In principle, the term of office of a member should be two years. The term of office of a member elected to fill a vacancy should be the remaining term of his/her predecessor.
(2) A member may be re-elected.

4. Others

(1) Sessions of the Committee should be held by the Director-General of the Health Service Bureau, MHLW.
(2) Clerical affairs for the Committee should be handled by the Tuberculosis and Infectious Diseases Control Division, Health Service Bureau, MHLW, with cooperation from the Animal Products Safety Division, Food Safety and Consumer Affairs Bureau, Ministry of Agriculture, Forestry and Fisheries, and from the General Affairs Division, Environmental Management Bureau, Ministry of the Environment.
(3) Sessions of the Committee should be held openly in principle.
(4) Necessary matters concerning the operation of the Committee, other than those specified in this Overview, should be determined at the Committee.

The Process of Preparation of This Report

This report was drafted through discussion at a series of the AMR One Health Surveillance committee in cooperation with additional experts and cooperating governmental agencies:1st meeting on 2/3/2017, 2nd meeting on 3/8/2017, 3rd meeting on 8/21/2017, 4th meeting on 10/2/2017, 5th meeting on 9/5/2018, 6th meeting on 10/22/2018, 7th meeting on 10/17/2019, and 8th meeting on 11/6/2020.

Members of the Antimicrobial Resistance (AMR) One Health Surveillance Committee

ASAI Tetsuo, D.V.M., Ph.D.	United Graduate School of Veterinary Science, Gifu University
KATSUDA Ken	Department of Animal Disease Control and Prevention, National Institute of Animal Health, National Agriculture and Food Research Organization
KANAMORI Hajime	Department of Infection Control and Laboratory Diagnostics, Internal Medicine, Tohoku University Graduate School of Medicine
KAMAYACHI Satoshi, M.D.	Japan Medical Association
KURODA Makoto, Ph.D.	Pathogen Genomics Center, National Institute of Infectious Diseases
SAKAI Masato, D.V.M., M.S.	Japan Veterinary Medical Association
SHINOMIYA Hiroto, M.D., Ph.D.	Ehime Prefectural Institute of Public Health and Environmental Science
SHIBAYAMA Keigo, M.D., Ph.D.	Department of Bacteriology II, National Institute of Infectious Diseases
SUGAI Motoyuki	Antimicrobial Resistance Research Center, National Institute of Infectious Diseases
SEKIYA Tatsuro, D.V.M	Assay Division II, National Veterinary Assay Laboratory, Ministry of Agriculture, Forestry & Fisheries
TANAKA Hiroaki, Ph.D.	Research Center for Environmental Quality Management, Graduate School of Engineering, Kyoto University
TAMURA Yutaka, D.V.M., Ph.D.	Center for Veterinary Drug Development, Rakuno Gakuen University
FUJIMOTO Shuhei, M.D., Ph.D.	Appointed Physician, Hananosono Special Nursing Home; Gunma University; National Institute of Infectious Diseases
MATSUNAGA Nobuaki M.D., MPH, Ph.D.	Clinical surveillance division, AMR Clinical Reference Center, National Center for Global Health and Medicine
MITARAI Satoshi, M.D., Ph.D.	Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association
MURAKI Yuichi, Ph.D.	Department of Clinical Pharmacoepidemiology, Kyoto Pharmaceutical University
YANO Sayoko, D.V.M., Ph.D.	Livestock Technology Department, Kyoto Prefectural Agriculture, Forestry and Fisheries Technology Center
WATANABE Haruo, M.D., Ph.D.*	National Institute of Infectious Diseases; Kurozumi Medical Foundation

(*Chair)

Additional experts who contributed to this report

IZUMIYA Hidemasa	Department of Bacteriology I, National Institute of Infectious Diseases
OHNISHI Makoto, M.D., Ph.D.	National Institute of Infectious Diseases
OHMAGARI Norio	AMR Clinical Reference Center, National Center for Global Health and Medicine
KAWANISHI Michiko, D.V.M., Ph.D.	Animal Products Safety Division, Food Safety and Consumer Affairs Bureau, Ministry of Agriculture, Forestry and Fisheries
KONISHI Noriko, Ph.D.	Division of Food Microbiology, Tokyo Metropolitan Institute of Public Health
KUSAMA Yoshiki	Epidemiology division, AMR Clinical Reference Center, National Center for Global Health and Medicine
GU Yoshiaki	Information and Education Division, AMR Clinical Reference Center, National Center for Global Health and Medicine
SHIMAZAKI Yohko, D.V.M., Ph.D.	Assay Division II, National Veterinary Assay Laboratory, Ministry of Agriculture, Forestry and Fisheries
SUZUKI Satowa	Anthibicrobiarl Resistance Research Center, National Institute of Infectious Diseases
SUZUKI Motoi	Infectious Disease Surveillance Center, National Institute of Infectious Diseases
SUNAGAWA Tomimasa	Infectious Disease Surveillance Center, National Institute of Infectious Diseases
NAKAMIZO Mari	Animal Products Safety Division, Food Safety and Consumer Affairs Bureau, Ministry of Agriculture, Forestry and Fisheries
FUJIYOMO Yumiko	AMR Clinical Reference Center, National Center for Global Health and Medicine
YAHARA Koji	Anthibicrobiarl Resistance Reserch Center, National Institute of Infectious Diseases
YAMAGISHI Takuya	Anthibicrobiarl Resistance Reserch Center, National Institute of Infectious Diseases

Cooperating governmental agencies

Food Safety Commission Secretariat

Ministry of Agriculture, Forestry and Fisheries

Ministry of the Environment

Mnistry of Land, Infrastructure, Transport and Tourism

Secretariat (Tuberculosis and Infectious Diseases Control Division, Health Service Bureau, Ministry of Health, Labour and Welfare)

ENAMI Takeshi	Director, Tuberculosis and Infectious Diseases Control Division
UMEDA Hiroshi	Director, Infectious Diseases Information Management Office
KATO Takuma	Deputy Director
NAKAYAMA Mie	Deputy Director
FUKUTA Keiko	Information Analysis Officer
WATARAI Kazuki	Unit Chief

Nippon AMR One Health Report (NAOR) 2020

Published on: January 8, 2021
Partially revised: January 17, 2022

Published by:
Tuberculosis and Infectious Diseases Control Division, Health Service Bureau, Ministry of Health, Labour and Welfare
Address: 1-2-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-8916, Japan

Suggested citation: The AMR One Health Surveillance Committee. Nippon AMR One Health Report (NAOR) 2020. Tokyo: Infectious Diseases Control Division, Health Service Bureau, Ministry of Health, Labour and Welfare