Nippon AMR One Health Report (NAOR) 2023

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The AMR One Health Surveillance Committee

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1. Preface

Japan's "National Action Plan on Antimicrobial Resistance (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 circumstances 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 circumstances of and trends in antimicrobial-resistant bacteria and national antimicrobial amount used (or sold) in the areas of human health, animals, food and the environment, with the objective of assessing measures to combat antimicrobial-resistant bacteria and clarify challenges in this area.

In 2023, an updated National Action Plan on Antimicrobial Resistance (AMR) (2023-2027) was developed based on the achievements and experiences of the previous Action Plan. The new plan proposes updated goals and strategies to strengthen and promote AMR control further, reemphasizing the importance of the One Health approach to the AMR challenge and promoting measures that consider the close relation of human, animal, food and environmental health. It also emphasizes the importance of updating methodologies for data collection and analysis on trends in antimicrobial resistance and antimicrobial use in Japan and abroad, as well as international collaboration and joint efforts to combat AMR.

This report has demonstrated Japan's efforts in the One Health approach to AMR both domestically and internationally, and has been utilized by relevant government ministries, agencies, organizations, and academic societies to promote countermeasures and research on AMR.

Future efforts under the new Action Plan are expected to contribute to the further development of Japan's AMR control measures and support effective responses to the AMR challenge in Japan and abroad. We hope that the data and analyses provided by this report will serve as a basis for strengthening AMR measures, promoting new research, and formulating policies by domestic and international stakeholders. Ultimately, we hope that these efforts will result in a more comprehensive and effective approach to the challenge of AMR and contribute to improving people's health and public health of the nation.

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	Breakpoint
CDI	*Clostridioides* (*Clostridium*) *difficile* Infection
CLSI	Clinical and Laboratory Standards Institute
CRE	Carbapenem-resistant *Enterobacterales*
DID	Defined Daily Dose per 1000 Inhabitants per Day
DDD(s)	Defined Daily Dose (s)
DOT	Days of Therapy
DOTID	Days of therapy per 1000 Inhabitants per Day
ESBL	Extended-spectrum β-lactamase
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 and Use Surveillance System
HAI	Healthcare-associated Infection
ICU	Intensive Care Unit
JANIS	Japan Nosocomial Infections Surveillance
JSAC	Japan Surveillance of Antimicrobial Consumption
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
PID	Number of patients per 1000 Inhabitants per Day
PPCPs	Pharmaceuticals and Personal Products
PRSP	Penicillin-resistant *Streptococcus pneumoniae*
SSI	Surgical Site Infection
WHO	World Health Organization
VRE	Vancomycin-resistant *Enterococcus* spp.
WOAH	World Organisation for Animal Health
VRSA	Vancomycin-resistant *Staphylococcus aureus*
DALY(s)	Disability-adjusted life year(s)
PPS	Point Prevalence Survey

3. Classes and Abbreviations of Antimicrobials

Class			Nonproprietary name	Abbreviation*
β-lactam antibiotics	Penicillins		benzylpenicillin (penicillin G)	PCG
			ampicillin	ABPC
			sulbactam/ampicillin	SBT/ABPC
			piperacillin	PIPC
			oxacillin	MPIPC
			tazobactam/piperacillin	TAZ/PIPC
			amoxicillin	AMPC
			clavulanic acid/amoxicillin	CVA/AMPC
	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
			sulbactam/cefoperazone	SBT/CPZ
			cefdinir	CFDN
			cefcapene pivoxil	CFPN-PI
			cefditoren pivoxil	CDTR-PI
			cefixime	CFIX
		4th generation	cefepime	CFPM
			cefpirome	CPR
			cefozopran	CZOP
		Cephalosporins combined with β-lactamase inhibitor	tazobactam/ceftolozane	TAZ/CTLZ
	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
			sulfamonomethoxine	SMMX

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
	◎ lascufloxacin	LSFX
	◎ 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
	tedizolid	TZD
Polypeptides	polymyxin B	PL-B
	colistin	CL
	bacitracin	BC
Lipopeptides	daptomycin	DAP
Amphenicols	chloramphenicol	CP
	florfenicol	FF

Class	Nonproprietary name	Abbreviation*
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 agents 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 terms for agents 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: Chemical substances that inhibit or control the cell activities of microorganisms and other living cells (referred to as antimicrobial activity) and are, strictly speaking, produced by microorganisms.

Antibiotic agents: Used as a generic term for antimicrobial agents that act against bacteria.

Reference: The Manual of Antimicrobial Stewardship, 1st edition

In terms of active ingredients (veterinary agents), 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 agents are calculated from sales data collected from marketing authorization holders for the volume of each agent 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 agents, 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 (Antibiotics Usage 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.
- **DOT (Days of Therapy):** DOT is a unit mainly used to grasp the usage in medical institutions. It 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.
- **DID (DDDs/1,000 inhabitants/day)**: DID is a unit of measurement of use, mainly in a region or country; DID is expressed per 1,000 inhabitants as the total titre over a period of time divided by DDD, with the denominator corrected for the number of inhabitants per day in the region ('inhabitants'). The DID is expressed as a value per 1,000 inhabitants, corrected for the number of inhabitants per day.
- **DOTID (DOTs/1,000 inhabitants/day)**: DOTID is a unit that uses claims information to determine usage in a region or country. It is expressed per 1,000 inhabitants as the total number of days of antimicrobial treatment (DOTs) over a period of time in the numerator, with the denominator corrected for the number of inhabitants per day in the region.
- **PID (number of patients/1,000 inhabitants/day)**: PID is a unit that uses insurance claims information to determine usage in a region or country. It is expressed as a value per 1,000 inhabitants with the total number of people using antimicrobials over a period of time as the numerator and the denominator corrected for the number of inhabitants per day in the region.

4. Executive Summary

Background:

Japan's "National Action Plan on Antimicrobial Resistance (AMR) (2016-2020)" positioned efforts to ascertain the current status of antimicrobial-resistant bacteria and national antimicrobial use (AMU) 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.

In 2023, the Action Plan on AMR (2023-2027) was developed, setting updated goals and strategies. The plan emphasizes the importance of the One Health approach to the AMR challenge and calls for the promotion of measures that including the interconnectedness of human, animal, and environmental health. It also emphasizes the importance of international cooperation and joint efforts to combat AMR.

Internationally, Japan contributes to and cooperates with the Global Antimicrobial Resistance and Use Surveillance System (GLASS) established by the World Health Organization (WHO) by providing our national data. In addition, the World Organisation for Animal Health (WOAH) monitors the use of antimicrobial agents in animals by standardized method, and Japan has cooperated with this effort and submitted data.

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. The data and analyses provided by this report are intended to serve as a basis for strengthening AMR control, promoting new research, and formulating policy by national and international stakeholders.

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 AMU. 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 sales of antimicrobials in animals were obtained from the National Veterinary Assay Laboratory, Ministry of Agriculture, Forestry and Fisheries. 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 obtained from MAFF, while information on outbreaks of infectious diseases and the implementation of infection control measures was obtained from the National Epidemiological Surveillance of Infectious Diseases (NESID), JANIS, and J-SIPHE.

Data on the antimicrobial resistance of microorganisms that are considered pertinent from public health perspective and the public awareness toward AMR, which, however, are not monitored either by current surveillance or monitoring systems were obtained from findings by Health and Labor Sciences Research Groups.

In the animal field, the results of the survey of attitudes of veterinary students at 12 universities towards antimicrobial resistance were used.

Results:

In Japan, the carbapenem resistance rate in *Enterobacterales*, particularly *Escherichia coli* and *Klebsiella pneumoniae* has remained below 1% during the observed period, despite its global increase in human isolates. While the resistance rates to third-generation cephalosporins and fluoroquinolones in *E. coli* were on the increase in Japan, but in 2021 they declined slightly for the first time, and in 2022, the resistance rate to third-generation cephalosporins remained flat and that to fluoroquinolones in *E. coli* declined. On the other hand, the resistance rate of third-generation cephalosporins in *K. pneumoniae* remained on the rise. Although the criteria for carbapenem resistance in *Pseudomonas aeruginosa* were changed in 2014, we think that the resistance rate is on a decreasing trend. Internationally, the increase in vancomycin resistance among *Enterococcus* spp. is a problem. In Japan, although VCM resistance in *Enterococcus faecium* was 2.6% in 2022, a relatively low level compared to other countries, it has been increasing in recent years, and widespread, multi-center associated hospital outbreaks due to VCM-resistant *E. faecium* were observed in some regions.

Although the percentage of methicillin-resistant *Staphylococcus aureus* (MRSA) had been in an increasing trend again since 2019, started to decrease in 2021. The trend remained the same in 2022, but it is still high compared to other countries. Clear similarities in the pattern of resistance rates to antimicrobials were observed in serotypes of *Salmonella* spp. isolated from food and humans, strongly suggesting a link between resistant strains derived from food and humans.

AMU based on human antimicrobial sales in Japan was 9.78 DID in 2022, a 3.9% decrease compared to 2020. Oral antimicrobial agents accounted for 90.4% of total sales, with third-generation cephalosporins, fluoroquinolones, and macrolides accounting for the highest shares. The three most frequently used antimicrobial classes in 2022 have also decreased in use by 11.9%, 8.4%, and 9.2%, respectively, compared to 2020. Injectable carbapenems have increased by 2.9% compared to 2020. The proportion of "Access" in the AWaRe classification, has gradually increased since 2013, from 11.0% to 20.9% in 2020 and 23.8% in 2022, while the proportion of "Watch" has decreased from 87.6% to 74.9%.

Surveillance of antimicrobial resistance in animals focuses on food-producing animals (cattle, swine, and chickens), aquatic animals (all farmed fish species), and companion animals (dogs and cats). The resistance rate of *Enterobacterales* to carbapenems, an important antimicrobial class in human medicine, and that of *Enterococcus* spp. to VCM, a major problem in human nosocomial infections, were both 0.0%.

Among food-producing animals, while tetracycline resistance in *E. coli* derived from healthy food-producing animals—an outcome index for the Action Plan (2016-2020)—fell from 45.2% in 2014 to 39.9% in 2015, the rate has undergone repeated fluctuations since 2016 and in 2021, it was 40.7%. On the other hand, rates of resistance to third-generation cephalosporins and fluoroquinolones mostly remained below 10% between 2014 and 2021.

Among aquatic animals, resistance rates to lincomycin remained at 61.0% in 2017, 31.5% in 2018, 55.2% in 2019, 53.8% in 2020, and 66.2% in 2021 in the causative agent of α-hemolytic *Streptococcous* spp. (*Lactococcus garvieae*) from diseased fish. Resistance rates to EM and OTC remained low, at 14.5% and 1.0%, respectively, in 2021, but the former showed an increasing trend from 0.6% in 2020. A pilot study of Vibrio and pathogenic strains of α-hemolytic *Streptococcous* spp. from healthy cultured yellowtail was initiated in 2021.

Among companion animals, while *E. coli* isolated from diseased dogs and cats demonstrated lower resistance rate to tetracyclines and aminoglycosides than among food-producing animals, resistance rates to the fluoroquinolones and third-generation cephalosporins that are critically important antimicrobials for human medicine tended to be higher. *E. coli* isolated from healthy companion animals (dogs and cats) demonstrated a lower resistance rate to all antimicrobials than in the case of diseased ones, indicating that they generally remained susceptible to all antimicrobials.

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 Agents (Ordinance of the Ministry of Agriculture, Forestry and Fisheries No. 107 of 2004). In 2021, as in before, tetracyclines represented the largest share of antimicrobial sales, but their sales volume has been declining in recent years, falling below 40% of the total. Third-generation cephalosporins and fluoroquinolones accounted for 0.1% and around 1% of the total, respectively. The total volume of veterinary antimicrobial sales remained around 800 t, with 800.9 t in 2021, down 42 t from 842.9 t in 2020. Looking at the figures by class, macrolides decreased by about 16 t, largely due to the decline in erythromycin used in aquatic animals. Sulfa drugs also decreased by about 17 t, which was largely due to the impact of the use in chickens. There was no increase of more than 2 t by class or animal species.

The estimated use (or sales) of antimicrobials in 2021, based on sales volumes and other data for each sector, were 507.0 t for humans, 598.1 t for livestock, 194.7 t for aquatic animals, 8.1 t for pets, 211.1 t for antimicrobial feed additives, and 133.2 t for agrochemicals, totaling 1,652.2 t.

Observations:

In the human sector, AMU based on sales of oral antimicrobials, including oral third-generation cephalosporins, oral macrolides, and oral fluoroquinolones in 2022 has been on a downward trend since 2020. The resistance rates in MRSA and *E. coli* to third-generation cephalosporins and fluoroquinolones have decreased slightly, while the resistance rate to third-generation cephalosporins in *K. pneumoniae* has been increasing and should continue to be monitored closely. On the other hand, VCM-resistant *E faecium* has been observed in widespread hospital outbreaks involving multiple facilities, with high numbers reported following 2022. Continued comprehensive outbreak response in the region is required. The Impact of novel coronavirus Infections on antimicrobial use and antimicrobial resistance rates will also be considered. As the effects of COVID-19 on AMU and AMR rates in Japan are also to be considered, they need to be carefully monitored and their impact assessed in the future, given the increase in antimicrobial sales in many countries in the post-coronavirus period. The data in this report demonstrate that further promotion of measures against AMR will be required.

Unnecessary use of third-generation cephalosporins, fluoroquinolones, and macrolides must be continuously reduced, and the Manual of Antimicrobial Stewardship employed to promote the proper use of antimicrobials, primarily in respect of acute respiratory tract infections. In November 2023, the Manual of Antimicrobial Stewardship was updated to include a section on the appropriate use of antimicrobial agents in hospitalized patients. This edition is expected to improve patient outcomes and promote the proper use of antimicrobial agents in hospitals. When promoting the appropriate use of antimicrobials, it is essential that appropriate antimicrobials are available when needed, and it is important to ensure a stable supply of essential antimicrobials.

Strengthening educational and awareness-raising activities and the use of monitoring systems are also important in AMR control. The new Action Plan calls for the formulation of effective countermeasures through a detailed analysis of information on AMR and AMU in each region. Systems such as JANIS, NESID, J-SIPHE, J-SIPHE for clinics, or OASCIS (Online monitoring system for antimicrobial stewardship at clinics) and the AMR One Health Platform should be used to promote antimicrobial selection and infection control measures according to local conditions. Furthermore, in promoting the appropriate use of antimicrobials, it is necessary to continue education and awareness-raising activities using various methods for the public and healthcare professionals.

Among animals, the rate of *Enterobacterales* resistant to carbapenems, an important antimicrobial class for human medicine, and that of *Enterococcus* spp. to VCM, a major problem in nosocomial infections in humans, were 0.0% for any bacterial species derived from any livestock species. However, rates of resistance to third-generation cephalosporins and fluoroquinolones in *E. coli* isolated from diseased companion animals, surveillance of which began in 2017, were found to be higher than in *E. coli* isolated from food-producing animals. Therefore, in addition to the measures against antimicrobial resistance in the food-producing animals that have been implemented, it is necessary to continue and strengthen measures against antimicrobial resistance through the dissemination of the "Guide for Prudent Use in Companion Animals" which was published in 2020.

The resistance rates of *E. coli* from healthy food-producing animals to third-generation cephalosporins and fluoroquinolones, an outcome indicator of the National Action Plan on AMR (2016-2020), have been maintained at below 10% and are expected to meet their targets. It is important to continue to educate veterinarians and producers to use these agents with caution as second-line agents. On the other hand, the resistance rate to tetracyclines was higher than its target. The same antimicrobials as in the National Action Plan on AMR (2016-2020) were set as outcome indicators for the National Action Plan on AMR (2023-2027). In addition, the resistance rate for each livestock species was set as an outcome indicator so that the results of individual actions in line with the issues for each livestock species could be confirmed. In addition, the total amount of veterinary antimicrobials used and the total amount of second-line antimicrobials used in the livestock sector are newly set as outcome indicators.

Japan's AMR response has been conducted in coordination with international movements. Stronger international collaboration and a stronger approach from a One Health perspective will be key to the success of AMR control measures. In addition, it is important to strengthen educational and awareness-raising activities to raise awareness and encourage behavior change among the public, which has not been sufficiently effective; disseminate guidelines to support the appropriate use of antimicrobial agents; and strengthen surveillance systems to measure and evaluate the effectiveness of AMR control measures.

In response to these challenges, the new National Action Plan emphasizes collaboration with various stakeholders and cooperation within the international community. It is essential to build and strengthen these cooperative frameworks to achieve Japan's AMR control goals. The effective response to the AMR challenge by sharing knowledge and experience domestically and internationally, and by promoting research that can assess risks in humans, animals, and the environment in a cross-sectional manner, is critical to the future success of AMR control. These efforts will support effective responses to the AMR challenge both in Japan and overseas and could contribute to strengthening Japan's role in the international community. Efforts should be directed toward achieving a more comprehensive and effective approach to the AMR challenge, to improve the health and public health of the people. The new Action Plan continues to call for government-wide education and awareness-raising activities, but it is important to further explore effective methods that are needed.

5. Outcome Indices for the National Action Plan on AMR

Human-related indices for the National Action Plan on AMR (2016-2020): proportion (%)[*] of specified antimicrobial-resistant bacteria

	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2020 (target value[†])
Proportion of penicillin-non-susceptible *Streptococcus pneumoniae*, CSF specimens[§]	47.4	47.0	40.5	36.4	29.1	38.3	32.0	33.3	59.5	50.9	15% or lower
Proportion of penicillin-non-susceptible *Streptococcus pneumoniae*, non-CSF specimens[§]	3.2	2.5	2.7	2.1	2.1	2.2	2.2	3.5	3.4	3.8	
Proportion of fluoroquinolone-resistant *Escherichia coli*	35.5	36.1	38.0	39.3	40.1	40.9	41.4	41.5	40.4	39.6	25% or lower
Proportion of methicillin-resistant *Staphylococcus aureus*	51.1	49.1	48.5	47.7	47.7	47.5	47.7	47.5	46.0	45.5	20% or lower
Proportion of carbapenem-resistant *Pseudomonas aeruginosa* (Imipenem)	17.1	19.9	18.8	17.9	16.9	16.2	16.2	15.9	15.8	14.8	10% or lower
Proportion of carbapenem-resistant *Pseudomonas aeruginosa* (Meropenem)	10.7	14.4	13.1	12.3	11.4	10.9	10.6	10.5	10.3	9.5	10% or lower
Proportion of carbapenem-resistant *Escherichia coli* (Imipenem)	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.04	0.2% or lower (maintain at the same level) [¶]
Proportion of carbapenem-resistant *Escherichia coli* (Meropenem)	0.1	0.2	0.2	0.2	0.1	0.1	0.1	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	0.3	0.2	0.2	0.3	0.2	0.2	0.2	0.1	0.2% or lower (maintain at [¶]
Proportion of carbapenem-resistant *Klebsiella pneumoniae* (Meropenem)	0.6	0.6	0.6	0.5	0.4	0.5	0.4	0.4	0.4	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] Comparison to 2013.

[§] 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 number of specimens is around 100 (42 in 2021), therefore assessment of the resistance rate should be done with caution.

[¶] 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 National Action Plan on AMR (2023-2027): proportion (%) of specified antimicrobial-resistant bacteria[*1]

	2020	2021	2022	2027 (target value[†])
Number of vancomycin-resistant *Enterococcus* spp. infections	136	124	-	80 or less (maintained 2019 level)
Proportion of methicillin resistant *Staphylococcus aureus* (blood)[*2]	35.9	35.1	33.9	20% or less
Proportion of fluoroquinolone resistant in *Escherichia. coli* (urine)[*3]	35.4	34.6	34.0	30% or less (maintained)
Proportion of carbapenem (meropenem) resistant *Pseudomonas aeruginosa* (blood)*2	7.1	7.0	6.3	3% or less
Proportion of carbapenem (meropenem) resistant *Escherichia coli*	0.1	0.1	0.1	0.2 or less [§]
Proportion of Carbapenem (meropenem) resistant *Klebsiella pneumoniae*	0.4	0.4	0.4	0.2% or less [§]

[*]1Compiled from JANIS data (partly cited from AMED Research on Enhancing Surveillance of Antimicrobial Resistance and Promotion of Comprehensive Countermeasures against Antimicrobial Resistance) and from NESID (National Epidemiological Surveillance of Infectious Diseases).

[†]Target values are taken from AMR Action Plan Reference 7. Comparison to 2020.

[*]2Bloodstream infections contribute significantly to the disease burden, and with the intent of excluding the effects of bacterial carriage, blood samples are taken.

[*]3Urine specimens are used to target urinary tract infections in outpatient settings where drug-resistant bacteria are directly related to treatment.

[§] The AMR Action Plan (Ref. 1) states that the carbapenem resistance rates for *E. coli* and *Klebsiella pneumoniae* in 2014 were 0.1% and 0.2%, and that the resistance rates in 2020 will be maintained at the same level.

Human-related indices for the National Action Plan on AMR (2016-2020): use of antimicrobials (DID) (based on volume of sales)

	2013	2014	2015	2016	2017	2018	2019	2020	Change form 2013	2020 (Target[*])
All antimicrobials	14.52	14.08	14.23	14.15	13.36	12.91	12.75	10.18	29.9%↓	33%↓
Oral cephalosporins	3.91	3.78	3.82	3.68	3.43	3.19	3.02	2.24	42.7%↓	50%↓
Oral fluoroquinolones	2.83	2.83	2.71	2.75	2.57	2.42	2.32	1.66	41.4%↓	50%↓
Oral macrolides	4.83	4.5	4.59	4.56	4.18	3.96	3.84	2.93	39.4%↓	50%↓
Intravenous antimicrobials	0.9	0.9	0.94	0.96	0.98	0.99	1.01	0.87	3.3%↓	20%↓

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

[*]Target values were quoted from [1].

[†] Prepared from [2] and [3].

Human-related indices for the National Action Plan on AMR (2023-2027): use of antimicrobials (DID) [†] (based on volume of sales)

	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	Change from 2020	2027 (Target*)
All antimicrobials	14.52	14.08	14.23	14.15	13.36	12.91	12.75	10.18	9.77	9.78	3.9%↓	15%↓
Oral third-generation cephalosporins	3.54	3.41	3.46	3.32	3.08	2.83	2.63	1.85	1.7	1.63	12.1%↓	40%↓
Oral fluoroquinolones	2.83	2.83	2.71	2.75	2.57	2.42	2.32	1.66	1.48	1.52	8.4%↓	30%↓
Oral macrolides	4.83	4.5	4.59	4.56	4.18	3.96	3.84	2.93	2.72	2.66	9.2%↓	25%↓
Intravenous antimicrobials	0.09	0.08	0.08	0.08	0.08	0.08	0.08	0.07	0.07	0.07	2.9% ↑	20%↓

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

[*]Target values were quoted from [7].

[†] Prepared from [2] and [3].

Animal-related indices for the National Action Plan on AMR (2016-2020): proportion (%) of specified antimicrobial-resistant bacteria

		2014*	2015*	2016	2017	2018	2019	2020	2021	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	44.3	45.0	40.7	
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	2.1	1.4	1.4	
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	5.1	5.2	4.2	

* Prepared from [4] with partial modification. JVARM "Results of Monitoring of Antimicrobial-resistant Bacteria Isolated from Food-producing Animals on Farms"

** Target values for 2020 were quoted from [1].

*** See [4] and [5].

**** MICs greater than 16 μg/mL for tetracyclines, 4 μg/mL for third-generation cephalosporins, and 4 μg/mL for fluoroquinolones are considered resistant.

Animal-related indices for the National Action Plan on AMR (2023-2027): proportion (%) of specified antimicrobial-resistant bacteria

		2021	2027 (Target[§])
Proportion of tetracycline-resistant *Escherichia coli*[*]	Cattle	23.8	Cattle 20% or less Swine 50% or less Chicken 45% or less
	Swine	52.0	
	Chicken	46.2	
Proportion of third-generation cephalosporin-resistant *Escherichia coli*[*]	Cattle	0.0	Cattle 1% or less Swine 1% or less Chicken 5% or less
	Swine	2.0	
	Chicken	2.1	
Proportion of fluoroquinolone-resistant *Escherichia coli*[*]	Cattle	0.0	Cattle 1% or less Swine 2% or less Chicken 15% or less
	Swine	2.0	
	Chicken	14.5	

[§]Target values for 2027 were quoted from [7].

*MICs greater than 16 μg/mL for tetracyclines, 4 μg/mL for third-generation cephalosporins, and 1 μg/mL for fluoroquinolones are considered resistant.

Animal-related indices for the National Action Plan on AMR (2023-2027): use of antimicrobials (t) (based on volume of sales)

	2020	2021	2027 (Target[†]) (Change from 2020)
Total use of veterinary antimicrobials in the livestock sector	626.8	598.1	15%↓
Total use of second-line[※] veterinary antimicrobials in the livestock sector	26.7 t	27.6	Maintain below 27 t

† Target values for 2027 were quoted from [7].

※Third-generation cephalosporins, 15-membered ring macrolides (tulathromycin, gamithromycin), fluoroquinolones, colistin

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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 the recent global increase of carbapenem (IPM and MEPM)-resistant *Enterobacteriales* such as *Escherichia coli* and *Klebsiella pneumoniae*, the proportion of carbapenem-resistant *E. coli* and *K. pneumoniae* in Japan remained low at less than 1%, as in Tables 1 and 2. Resistance rates to third-generation cephalosporins such as CTX and fluoroquinolones such as LVFX in *E. coli*, which had been increasing up until 2020, showed a slight decrease for the first time in 2021 and remained flat and decreased in 2022. 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. It is too early to determine immediately whether the observed decrease in the resistance rate of *E. coli* to third-generation cephalosporins after 2021 is transient or the result of a genuine decline. On the other hand, third-generation cephalosporin-resistant *K. pneumoniae* continues to increase and behaves differently from third-generation cephalosporin-resistant *E. coli*. Both species should continue to be monitored closely for future trend.

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. Resistance rates (%) of *Escherichia coli*

	BP (-2013)	BP (2014-)	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
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)	51.9 (337,433)	50.4 (340,248)	49.9 (358.902)
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)	45.6 (339,444)	44.0 (338,450)	43.5 (352,001)
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)	2.8 (290,567)	2.6 (303,907)	2.6 (326,287)
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)	38.7 (360,415)	37.4 (363,330)	37.2 (379,774)
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)	0.8 (372,259)	0.8 (376,435)	0.7 (398,172)
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)	28.3 (257,134)	26.8 (251,869)	26.8 (258,317)
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)	13.9 (369,898)	13.0 (372,255)	12.8 (390,324)
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)	17.5 (341,664)	16.8 (344,555)	16.2 (362,758)
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)	20.4 (284,169)	19.2 (286,755)	19.1 (301,651)
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)	0.1 (328,031)	0.1 (330,003)	0.04 (342,379)
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)	0.1 (383,513)	0.1 (387,094)	0.1 (407,162)
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)	0.1 (378,104)	0.1 (380,774)	0.1 (400,312)
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)	41.5 (379,538)	40.4 (381,447)	39.6 (398,196)

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. Resistance rates (%) of *Klebsiella pneumoniae*

	BP (-2013)	BP (2014-)	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
ABPC	32	32	75.9 (65,338)	76.9 (73,078)	77.8 (80,030)	76.3 (90,220)	76.9 (131,700)	76.3 (147,500)	77.4 (152,477)	79.4 (158,654)	80.1 (159,790)	79.7 (157,459)	77.7 (160,188)	77.5 (174,552)
PIPC	128	128	19.7 (67,548)	20.1 (74,878)	24.3 (82,608)	21.9 (91,761)	21.1 (136,347)	21.8 (154,260)	21.8 (161,254)	22.9 (165,430)	24.5 (161,590)	25.1 (156,799)	26.7 (158,472)	27.6 (169,964)
TAZ/PIPC	4/128	4/128	-	-	2.2 (27,279)	2.0 (46,941)	2.0 (91,503)	2.2 (110,189)	2.2 (118,796)	2.6 (127,778)	3.1 (135,732)	3.2 (136,696)	3.6 (145,033)	3.6 (160,489)
CEZ*	32	8	8.8 (68,481)	9.0 (76,860)	9.1 (85,320)	11.7 (94,875)	12.1 (135,486)	13.1 (152,973)	13.4 (157,849)	14.3 (166,906)	15.2 (170,001)	16.5 (166,842)	18.2 (170,103)	18.8 (183,757)
CMZ	64	64	-	-	-	1.9 (85,749)	1.9 (132,163)	1.7 (152,086)	1.5 (159,375)	1.6 (168,787)	1.5 (172,912)	1.5 (173,615)	1.5 (177,579)	1.4 (193,632)
CTX*	64	4	5.2 (56,236)	5.4 (62,242)-	5.1 (66,654)	8.6 (73,574)	8.0 (107,409)	8.9 (118,057)	8.9 (119,672)	9.4 (122,459)	9.7 (122,241)	11.0 (119,269)	11.7 (117,676)	12.6 (124,914)
CAZ*	32	16	3.4 (68,916)	2.9 (76,961)	2.7 (84,761)	3.8 (94,878)	4.0 (138,191)	4.6 (155,293)	5.0 (160,619)	5.7 (169,097)	6.9 (173,031)	8.6 (171,425)	9.5 (174,262)	10.3 (189,618)
CFPM	32	32	-	-	3.0 (41,143)	3.5 (66,399)	4.0 (119,563)	4.8 (138,737)	5.1 (145,745)	5.8 (156,485)	6.8 (160,502)	7.7 (160,138)	8.5 (163,139)	9.1 (177,866)
AZT*	32	16	4.1 (54,680)	3.7 (60,606)	3.5 (67,253)	5.1 (75,340)	5.3 (110,259)	5.9 (122,600)	6.2 (127,491)	6.7 (133,009)	8.0 (135,631)	9.1 (133,016)	10.2 (134,988)	11.0 (146,557)
IPM*	16	4	0.2 (63,825)	0.2 (70,284)	0.1 (77,193)	0.3 (85,253)	0.3 (126,997)	0.2 (143,813)	0.2 (149,546)	0.3 (154,879)	0.2 (155,242)	0.2 (151,882)	0.2 (154,691)	0.1 (165,377)
MEPM*	16	4	-	-	0.2 (48,190)	0.6 (73,903)	0.6 (135,930)	0.5 (159.623)	0.4 (166,298)	0.5 (175,408)	0.4 (179,042)	0.4 (178,240)	0.4 (182,018)	0.4 (197,801)
AMK	64	64	0.3 (68,995)	0.2 (76,293)	0.2 (84,916)	0.1 (95,643)	0.1 (141,710)	0.1 (159,871)	0.1 (166.081)	0.1 (174,259)	0.1 (176,609)	0.1 (175,742)	0.1 (179,422)	0.1 (194,640)
LVFX	8	8	2.7 (66,466)	2.4 (74,718)	2.5 (83,063)	2.4 (92,993)	2.6 (138,428)	2.7 (156,249)	2.8 (163,688)	3.1 (172,010)	3.4 (175,799)	4.2 (175,200)	4.6 (178,138)	5.2 (192,244)

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. Resistance rates (%) of *Enterobacter cloacae*

	BP (-2013)	BP (2014-)	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
ABPC	32	32	80.9 (35,849)	79.0 (39,344)	80.2 (55,960)	79.3 (61,667)	79.8 (61,970)	81.2 (64,820)	81.3 (64,723)	81.4 (62,954)	80.4 (62,121)	82.0 (66,059)
PIPC	128	128	20.6 (36,988)	20.0 (39,636)	19.8 (58,039)	20.1 (63,580)	20.8 (64,217)	21.2 (66,020)	21.7 (62,798)	21.6 (60,369)	21.3 (58,758)	21.7 (61,527)
TAZ/PIPC	4/128	4/128	10.3 (11,895)	8.6 (21,091)	8.9 (40,315)	8.9 (47,390)	9.4 (48,775)	9.8 (52,186)	10.5 (54,305)	10.3 (54,675)	10.1 (56,350)	10.6 (59,998)
CEZ*	32	8	97.2 (37,359)	98.2 (41,422)	98.3 (58,637)	98.3 (64,634)	98.3 (64,693)	98.3 (68,017)	98.2 (68,074)	98.2 (67,036)	98.2 (66,201)	98.3 (69,693)
CMZ**	-	64	-	83.4 (37,492)	85.4 (56,647)	85.5 (63,331)	86.1 (64,158)	88.0 (68,013)	87.4 (68,727)	88.1 (68,183)	87.9 (67,430)	88.1 (71,629)
CTX*	64	4	19.2 (30,106)	31.1 (32,718)	31.6 (46,727)	31.2 (50,311)	32.4 (50,022)	32.9 (51,470)	33.7 (50,606)	34.0 (49,402)	34.1 (47,591)	34.9 (48,848)
CAZ*	32	16	20.6 (37,202)	24.7 (41,456)	25.0 (59,533)	24.9 (65,317)	25.8 (65,027)	26.3 (68,737)	26.8 (69,265)	27.4 (67,922)	27.7 (67,174)	28.5 (71,014)
CFPM	32	32	4.2 (17,900)	4.2 (29,836)	4.2 (52,218)	4.0 (58,298)	4.0 (59,398)	3.9 (64,337)	4.0 (65,211)	3.7 (65,110)	3.5 (64,286)	3.6 (67,964)
AZT*	32	16	16.8 (29,460)	23.8 (33,551)	24.0 (48,570)	23.9 (52,951)	24.3 (53,374)	24.9 (55,988)	26.1 (56,211)	26.3 (55,380)	26.5 (54,810)	27.4 (58,130)
IPM*	16	4	0.4 (34,403)	1.6 (37,396)	1.3 (54,926)	1.2 (60,602)	1.1 (60,689)	1.1 (63,611)	1.2 (61,918)	1.0 (61,234)	0.9 (59,721)	0.9 (62,027)
MEPM*	16	4	0.6 (21,164)	1.3 (32,589)	1.4 (59,009)	1.2 (67,250)	1.1 (67,392)	1.1 (71,119)	0.9 (71,548)	1.0 (70,910)	0.8 (70,077)	0.7 (74,210)
AMK	64	64	0.4 (37,947)	0.2 (42,005)	0.2 (61,086)	0.1 (67,133)	0.1 (67,125)	0.1 (70,659)	0.1 (70,392)	0.1 (69,812)	0.1 (68,955)	0.1 (73,178)
LVFX	8	8	4.2 (37,274)	3.5 (40,942)	3.7 (59,393)	3.4 (65,161)	3.5 (65,690)	3.2 (69,392)	3.1 (70,034)	2.9 (69,816)	2.6 (68,752)	2.5 (71,907)

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. Resistance rates (%) of *Klebsiella* (*Enterobacter*)* *aerogenes*

	BP (-2013)	BP (2014-)	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
ABPC	32	32	76.5 (17,362)	77.1 (18,385)	78.9 (26,680)	77.9 (29,228)	79.1 (30,844)	80.3 (32,746)	80.5 (33,621)	80.8 (33,862)	79.6 (35,315)	81.0 (38,564)
PIPC	128	128	14.5 (18,029)	14.5 (18,550)	14.2 (27,189)	15.8 (29,852)	17.1 (31,802)	17.4 (33,048)	18.9 (32,497)	18.6 (32,139)	17.5 (32,962)	17.5 (35,871)
TAZ/PIPC	4/128	4/128	6.3 (5,568)	4.9 (9,568)	4.8 (18,731)	4.8 (21,767)	5.7 (24,082)	6.9 (26,272)	6.9 (28,085)	7.2 (29,124)	7.0 (30,954)	7.4 (34,399)
CEZ**	32	8	90.8 (17,945)	94.0 (19,173)	93.7 (27,526)	94.2 (30,088)	94.5 (31,800)	95.0 (33,996)	94.7 (35,183)	95.1 (35,448)	95.0 (36,851)	94.8 (40,246)
CMZ	64	64	-	84.8 (17,587)	86.8 (26,739)	87.1 (29,681)	88.0 (31,915)	89.1 (34,051)	89.5 (35,408)	89.9 (36,068)	90.0 (37,881)	89.7 (41,502)
CTX**	64	4	5.2 (14,452)	28.3 (15,173)	30.7 (21,985)	31.1 (23,572)	32.9 (24,195)	33.4 (25,493)	34.2 (26,271)	35.4 (26,655)	35.2 (27,111)	35.9 (28,608)
CAZ**	32	16	17.3 (17,992)	24.3 (19,439)	25.2 (27,886)	25.7 (30,388)	26.7 (32,030)	27.8 (34,142)	28.5 (35,487)	29.6 (35,985)	29.7 (37,638)	30.1 (41,161)
CFPM	32	32	1.0 (8,909)	1.2 (13,499)	1.1 (24,302)	1.1 (27,146)	1.3 (29.464)	1.4 (32,216)	1.5 (33,583)	1.4 (34,454)	1.5 (36,047)	1.6 (39,114)
AZT**	32	16	7.5 (14,639)	15.8 (15,846)	17.5 (23,225)	17.5 (25,023)	18.0 (26,772)	19.2 (28,281)	20.2 (29,397)	20.8 (30,056)	20.4 (31,103)	20.8 (34,014)
IPM**	16	4	0.4 (16,881)	1.7 (17,463)	1.9 (25,690)	1.9 (28,307)	1.9 (29,869)	2.6 (31,288)	2.3 (31,645)	2.2 (32,050)	1.7 (33,173)	1.3 (35,870)
MEPM**	16	4	0.2 (10,249)	0.9 (15,003)	0.8 (27,560)	0.8 (31,311)	0.8 (33,150)	0.8 (35,448)	0.8 (36,550)	0.9 (37,291)	0.9 (38,989)	0.9 (42,475)
AMK	64	64	0.2 (18,369)	0.2 (19,492)	0.1 (28,627)	0.1 (31,338)	0.1 (33,074)	0.1 (35,214)	0.1 (36,204)	0.05 (36,866)	0.05 (38,542)	0.04 (41,981)
LVFX	8	8	1.1 (18,111)	1.0 (19,068)	0.9 (28,012)	1.0 (30,451)	0.9 (32,503)	0.9 (34,383)	0.9 (35,735)	0.9 (36.768)	1.0 (38.092)	0.9 (41,329)

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. Resistance rates (%) of *Pseudomonas aeruginosa*

	BP (-2013)	BP (2014-)	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
PIPC	128	128	12.1 (114,950)	11.9 (118,032)	11.4 (122,581)	10.8 (125,242)	10.5 (181,977)	10.5 (201,764)	10.3 (205,165)	10.0 (206,858)	10.3 (214,513)	10.0 (211,455)	9.8 (214,729)	9.7 (223,807)
TAZ/ PIPC	4/128	4/128	-	-	9.0 (68,686)	8.8 (79,574)	8.8 (132,769)	8.4 (155,724)	8.3 (165,402)	8.1 (172,748)	8.4 (185,720)	7.8 (185,847)	7.8 (191,294)	7.8 (201,973)
CAZ	32	32	11.3 (116,596)	10.9 (120,473)	10.2 (124,864)	9.5 (126,718)	8.6 (180,479)	8.7 (199,597)	8.6 (202,025)	8.4 (203,554)	8.7 (210,892)	8.6 (207,738)	8.7 (211,983)	8.7 (221,033)
CFPM	32	32	9.7 (91,769)	8.9 (99,730)	8.0 (106,291)	7.5 (113,268)	6.6 (166,096)	6.5 (185,283)	6.3 (191,502)	6.0 (194,385)	5.9 (200,818)	5.7 (198,849)	5.5 (202,904)	5.3 (212,498)
AZT	32	32	16.3 (96,435)	16.7 (100,964)	16.5 (105,681)	14.5 (107,167)	14.0 (146,841)	13.8 (158,737)	13.7 (162,952)	13.1 (162,365)	13.3 (167,331)	13.6 (164,518)	13.4 (166,971)	13.0 (176,832)
IPM*	16	8	19.8 (112,596)	18.5 (116,193)	17.1 (119,979)	19.9 (119,323)	18.8 (168,471)	17.9 (186,380)	16.9 (188,981)	16.2 (188,778)	16.2 (195,183)	15,9 (191,793)	15,8 (194,826)	14.8 (202,639)
MEPM*	16	8	12.4 (109,453)	11.8 (113,996)	10.7 (119,330)	14.4 123,976)	13.1 (180,850)	12.3 (201,991)	11.4 (206,368)	10.9 (209,149)	10.6 (217,161)	10.5 (214,691)	10.3 (218,610)	9.5 (228,253)
GM	16	16	7.0 (111,137)	6.1 (115,612)	5.3 (118,592)	5.1 (117,421)	4.5 (165,777)	4.1 (182,343)	3.3 (184,453)	2.9 (184,135)	3.1 (190,296)	3.0 (184,307)	2.8 (184,581)	2.5 (193,104)
AMK	64	64	3.1 (116,876)	2.6 (121,289)	2.1 (126,023)	1.9 (128,923)	1.5 (185,327)	1.3 (204,892)	1.1 (208,098)	0.9 (209,413)	0.9 (217,512)	0.8 (214,949)	0.7 (219,053)	0.6 (228,023)
LVFX	8	8	16.8 (111,005)	16.3 (115,478)	14.5 (119,162)	13.0 (120,691)	12.0 (174,301)	11.6 (193,366)	10.8 (197,890)	10.2 (199,760)	9.8 (207,963)	9.5 (204,829)	8.9 (207,311)	8.1 (216,226)

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. *Acinetobacter* spp.

Table 6. Resistance rates (%) of *Acinetobacter* spp.

	BP	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
PIPC	128	13.2 (19,125)	13.2 (19,433)	12.9 (20,183)	12.4 (20,223)	11.5 (27,887)	10.9 (29,776)	10.9 (27,468)	10.3 (27,905)	10.7 (26,237)	10.2 (23,018)	11.0 (22,399)	10.8 (22,002)
TAZ/PIPC	4/128	-	-	7.8 (4,953)	7.8 (5,215)	8.1 (9,058)	8.6 (10,551)	9.0 (10,983)	9.4 (12,171)	9.0 (12,401)	8.2 (11,478)	9.5 (11,275)	9.0 (11,305)
SBT/ABPC	16/32	6.5 (2,942)	7.2 (3,601)	5.8 (4,498)	5.2 (6,462)	4.8 (11,356)	5,4 (12,831)	4.7 (12,241)	4.4 (13,111)	4.3 (12,769)	3.4 (12,047)	3.6 (11,982)	4.3 (11,708)
CAZ	32	10.3 (19,672)	10.6 (20,067)	10.0 (20,856)	9.3 (20,852)	8.0 (28,166)	7.6 (29,844)	7.9 (27,308)	7.6 (28,077)	8.6 (26,614)	8.4 (23,626)	9.1 (23,064)	9.4 (22,645)
CFPM	32	10.4 (13,013)	10.5 (14,093)	9.2 (15,394)	7.6 (17,424)	7.2 (25,412)	7.4 (27,386)	7.6 (25,631)	6.8 (26,616)	6.8 (25,224)	7.0 (22,400))	7.2 (22,002)	6.9 (21,702)
IPM	16	2.2 (18,048)	2.0 (18,238)	2.3 (16,947)	3.6 (11,147)	3.2 (13,942)	3.1 (15,147)	2.5 (14,383)	2.0 (16,995)	1.8 (19,645)	1.1 (21,381)	1.1 (21,243)	1.0 (20,627)
MEPM	16	2.9 (15,485)	2.4 (15,880)	2.3 (17,027)	2.0 (18,859)	1.8 (28,227)	1.9 (30,489)	1.3 (28,064)	1.5 (29,024)	1.4 (27,418)	1.2 (24,163)	1.2 (23,500)	1.3 (23,196)
GM	16	9.6 (18,276)	10.2 (18,842)	9.5 (19,422)	8.9 (18,832)	8.5 (25,689)	8.5 (27,313)	8.2 (24,887)	7.8 (25,465)	8.0 (23,925)	7.7 (20,853)	8.6 (20,174)	8.1 (19,819)
AMK	64	4.5 (19,348)	4.5 (19,793)	3.5 (20,863)	3.6 (20,851)	3.1 (28,568)	2.3 (30,279)	2.3 (27,835)	2.0 (28,437)	2.1 (26,917)	2.0 (23,697)	2.4 (23,217)	2.4 (22,835)
LVFX	8	9.5 (18,732)	9.8 (19,484)	8.3 (20,040)	8.5 (20,047)	7.7 (27,858)	8.2 (29,702)	8.0 (27,360)	7.0 (28,209)	7.5 (26,898)	7.8 (23,650)	8.7 (22,998)	8.6 (22,546)

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 *S. aureus*. Although the proportion has been declining over the past few years, it remains higher than that seen in other countries. The proportion was higher among medical institutions with fewer than 200 beds than among those with 200 or more (Table 10). In the case of *Enterococcus* spp., rising VCM-resistance was a problem in many countries, but as shown in Tables 11 and 12, levels in Japan were comparatively low, at less than 0.05% in the case of *Enterococcus faecalis* and 2.6% in *Enterococcus faecium*. However, also in 2021, the VCM-resistance rate among *E. faecium* significantly increased and widespread, nosocomial outbreaks of VCM-resistant *E. faecium* involving multiple facilities 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 *S. pneumoniae* in cerebrospinal fluid (CSF) samples, though the figure varies from year to year, because only around 100 CSF samples were 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. Resistance rates (%) of total *Staphylococcus aureus**

	BP	2018	2019	2020	2021	2022
PCG	0.25	75.4 (287,805)	75.1 (295,031)	74.3 (281,583)	73.3 (277,317)	72.8 (288,253)
MPIPC	4	47.8 (266,047)	47.7 (265,763)	47.5 (243,162)	46.0 (237,103)	45.5 (243,386)
CFX	8	46.1 (57,604)	46.0 (64,239)	46.1 (61,811)	45.2 (62,331)	43.6 (65,031)
CEZ	32	20.7 (360,772)	19.7 (366,803)	19.3 (339,052)	17.8 (334,737)	16.2 (346,659)
GM	16	30.4 (345,964)	28.9 (350,425)	27.5 (325,197)	26.1 (317,744)	25.1 (330,361)
EM	8	51.7 (325,918)	51.2 (329,090)	50.5 (302,105)	48.4 (297,317)	46.6 (308,701)
CLDM	4	22.0 (340,953)	20.4 (350,136)	18.9 (325,568)	17.3 (319,298)	15.7 (331,565)
MINO	16	12.2 (377,507)	10.5 (385,264)	9.7 (360,076)	8.9 (353,680)	8.0 (365,963)
VCM	16	0.0 (374,982)	0.0 (382,254)	0.0 (356,747)	0.0 (347,976)	0.0 (358,032)
TEIC	32	<0.05 (336,502)	<0.05 (340,855)	<0.05 (314,742)	<0.05 (308,176)	＜0.05 (318,317)
LVFX	4	50.4 (358,941)	51.7 (368,676)	52.3 (344,943)	51.3 (339,292)	51.3 (349,500)
LZD	8	<0.05 (286,366)	<0.05 (294,735)	<0.05 (276,069)	<0.05 (268,079)	< 0.05 (277,713)
DAP	2	0.3 (72,401)	0.3 (98,366)	0.3 (108,416)	0.3 (116,811)	0.3 (128,962)

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. Resistance rates (%) of Methicillin-susceptible *Staphylococcus aureus* (MSSA)

	BP	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
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)	51.1 (133,767)	50.7 (135,944)	50.2 (143,105)
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)	<0.05 (155,735)	<0.05 (159,135)	<0.05 (167,376)
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)	0.1 (24,967)	0.1 (26,846)	0.1 (28,097)
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)	<0.05 (138,998)	<0.05 (137,863)	<0.05 (141,411)
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)	22.6 (139,415)	21.5 (142,251)	20.5 (149,705)
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)	3.0 (147,257)	2.9 (150,416)	2.8 (158,285)
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)	0.6 (161,001)	0.6 (164,230)	0.5 (172,471)
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)	15.5 (154,754)	15.9 (158,287)	16.4 (165,426)

The unit of BP is μg/mL.

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

Table 9. Resistance rates (%) of Methicillin-resistant *Staphylococcus aureus* (MRSA)

	BP (2014-)	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
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)	79.8 (147,736)	78.6 (140,331)	76.8 (143,415)
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)	35.1 (161,937)	33.1 (153,027)	30.2 (156,646)
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)	18.7 (181,557)	17.7 (172,374)	16.0 (175,443)
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)	0.0 (181,671)	0.0 (171,879)	0.0 (174,187)
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)	<0.05 (158,930)	<0.05 (150,589)	<0.05 (153,290)
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)	88.5 (173,610)	88.9 (164,814)	89.4 (166,997)
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)	<0.05 (137,980)	<0.05 (129,420)	<0.05 (132,000)
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)	0.5 (51,671)	0.5 (53,782)	0.5 (58,616)

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 2020, no VRSA 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*

Table 10-1. All participating medical institutions

	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Number of medical institutions	594	660	745	883	1,435	1,653	1,795	1,947	2,075	2,167	2,220	2,289
Number of patients with MRSA	114,933	117,209	118,539	120,702	169,528	177,768	182,619	185,709	192,320	176,848	167,858	168,718
Number of patients with *S. aureus*	210,382	221,239	231,909	246,030	349,743	372,787	383,006	391,316	400,094	367,976	360,912	370,067
MRSA (%)*	54.6	53.0	51.1	49.1	48.5	47.7	47.7	47.5	48.1	48.1	46.5	45.6

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

	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Number of medical institutions	-	-	-	791	1,177	1,269	1,312	1,334	1,357	1,364	1,378	1,386
Number of patients with MRSA	-	-	-	115,757	157,419	160,060	160,714	159,054	161,159	144,828	135,984	135,670
Number of patients with *S. aureus*	-	-	-	237,343	328,540	341,822	344,543	344,156	345,447	312,738	305,116	311,251
MRSA (%)*	-	-	-	48.8	47.9	46.8	46.6	46.2	46.7	46.3	44.6	43.6

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

	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Number of medical institutions	-	-	-	92	258	384	483	613	718	803	842	903
Number of patients with MRSA	-	-	-	4,945	12,109	17,708	21,905	26,655	31,161	32,020	31,874	33,048
Number of patients with *S. aureus*	-	-	-	8,687	21,203	30,965	38,463	47,160	54,647	55,238	55,796	58,816
MRSA (%)*	-	-	-	56.9	57.1	57.2	57.0	56.5	57.0	58.0	57.1	56.2

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. Resistance rates (%) of *Enterococcus faecalis*

	BP	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
PCG	16	2.2 (53,290)	2.1 (60,342)	1.8 (65,220)	1.6 (67,324)	1.4 (92,132)	1.1 (98,465)	1.0 (98,478)	0.9 (104,023)	0.9 (107,021)	0.9 (111,226)	0.9 (114,014)	0.8 (117,159)
ABPC	16	0.4 (60,686)	0.4 (68,440)	0.3 (72,587)	0.3 (77,997)	0.3 (107,733)	0.2 (115,548)	0.2 (116,493)	0.2 (119,014)	0.2 (121,530)	0.2 (123,238)	0.2 (125,752)	0.2 (129,563)
EM	8	57.8 (53,222)	58.0 (60,825)	57.1 (64,465)	55.5 (69,171)	54.8 (95,409)	54.3 (101,036)	53.8 (101,379)	52.7 (102,496)	51.7 (102,871)	50.2 (103,067)	48.2 (105,505)	46.1 (108,619)
MINO	16	47.8 (61,549)	47.7 (69,421)	47.7 (74,880)	52.1 (81,925)	49.7 (115,648)	48.9 (123,860)	50.3 (125,728)	50.9 (128,160)	47.2 (130,729)	48.1 (133,174)	50.8 (135,820)	51.9 (139,723)
VCM	32	<0.05 (61,747)	<0.05 (69,719)	<0.05 (75,162)	<0.05 (81,867)	<0.05 (115,100)	<0.05 (124,305)	<0.05 (126,510)	<0.05 (129,545)	<0.05 (132,526)	<0.05 (135,184)	<0.05 (137,887)	<0.05 (142,316)
TEIC	32	<0.05 (56,591)	<0.05 (63,747)	<0.05 (69,500)	<0.05 (76,160)	<0.05 (105,403)	<0.05 (112,636)	<0.05 (113,501)	<0.05 (115,397)	<0.05 (117,097)	<0.05 (118,367)	<0.05 (120,564)	<0.05 (124,347)
LVFX	8	19.3 (58,877)	18.0 (65,934)	15.5 (70,895)	13.7 (77,563)	12.5 (109,160)	11.9 (117,297)	11.2 (120,136)	10.4 (122,551)	10.1 (125,836)	9.5 (128,449)	9.0 (131,088)	8.3 (134,507)

The unit of BP is μg/mL.

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

Table 12. Resistance rates (%) of *Enterococcus faecium*

	BP	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
PCG	16	86.9 (17,642)	87.4 (21,139)	87.7 (23,466)	86.9 (24,534)	87.6 (34,752)	88.2 (38,060)	87.8 (39,478)	87.5 (42,178)	87.4 (46,021)	86.9 (49,002)	87.1 (50,976)	87.1 (53,508)
ABPC	16	86.0 (19,780)	86.2 (23,885)	86.9 (26,199)	86.9 (28,564)	87.6 (41,459)	88.0 (45,069)	87.9 (47,046)	87.6 (49,207)	88.0 (52,929)	87.6 (54,632)	87.9 (56,395)	87.7 (59,105)
EM	8	87.2 (17,668)	88.1 (21,498)	85.9 (23,594)	84.5 (25,922)	84.5 (37,536)	84.0 (40,509)	83.1 (42,259)	83.0 (43,555)	83.1 (45,992)	83.1 (47,133)	80.0 (49,083)	79.5 (51,391)
MINO	16	26.9 (21,877)	28.8 (25,961)	29.3 (28,387)	32.2 (31,550)	35.1 (46,351)	34.7 (50,325)	36.2 (52,494)	38.3 (54,540)	33.0 (58,314)	31.7 (60,040)	30.2 (62,137)	31.5 (64,243)
VCM	32	1.0 (21,782)	0.4 (25,787)	0.7 (28,334)	0.7 (30,996)	0.7 (45,514)	0.9 (49,618)	0.8 (52,127)	0.9 (54,279)	1.5 (58,377)	1.4 (60,412)	2.6 (62,811)	2.6 (65,363)
TEIC	32	0.4 (20,163)	0.3 (23,855)	0.2 (26,282)	0.2 (29,151)	0.3 (41,905)	0.6 (45,388)	0.4 (47,321)	0.6 (48,991)	1.0 (52,502)	0.8 (54,125)	1.4 (55,948)	1.5 (58,342)
LVFX	8	82.9 (19,417)	83.4 (23,032)	84.5 (25,629)	84.7 (28,448)	85.8 (42,068)	86.6 (45,834)	86.5 (48.995)	86.7 (51,003)	87.6 (55,293)	86.9 (57,199)	87.2 (59,808)	86.9 (62,209)
LZD	8	0.0 (12,877)	0.1 (16,296)	<0.05 (18,561)	0.1 (22,044)	0.1 (33,382)	0.1 (37,099)	<0.05 (39,584)	0.1 (41.596)	0.1 (44,887)	0.1 (46,611)	0.1 (47,809)	0.1 (49,958)

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. Resistance rates (%) of *Streptococcus pneumoniae* (spinal fluid specimens)

	BP	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
PCG	0.125	38.6 (101)	47.4 (97)	47.0 (83)	40.5 (126)	36.4 (140)	29.1 (117)	38.3 (94)	32.0 (100)	33.3 (57)	59.5 (42)	50.9 (57)
CTX	2	3.7 (82)	1.2 (84)	2.9 (69)	2.0 (100)	1.0 (105)	2.1 (97)	4.5 (88)	1.2 (85)	4.3 (47)	5.6 (36)	4.1 (49)
MEPM	1	4.2 (95)	2.2 (92)	1.2 (83)	4.2 (119)	0.7 (134)	5.0 (120)	2.1 (95)	1.0 (99)	6.0 (50)	6.8 (44)	8.9 (56)
EM	1	82.5 (80)	82.7 (81)	92.5 (67)	84.9 (86)	75.5 (98)	82.4 (91)	75.0 (76)	84.8 (79)	76.7 (43)	86.5 (37)	77.8 (45)
CLDM	1	53.8 (65)	68.7 (67)	65.1 (63)	62.7 83)	61.2 (98)	49.5 (91)	43.7 (71)	64.0 (75)	57.1 (42)	52.8 (36)	57.8 (45)
LVFX	8	0.0 (88)	0.0 (91)	1.3 (76)	0.0 (105)	0.0 (123)	0.9 (111)	2.3 (88)	0.0 (93)	0.0 (50)	0.0 (40)	1.9 (52)
VCM	2	0.0 (91)	0.0 (90)	0.0 (82)	0.0 (119)	0.0 (134)	0.0 (116)	0.0 (98)	0.0 (96)	0.0 (56)	0.0 (42)	0.0 (56)

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. Resistance rates (other than spinal fluid specimens) (%) of *Streptococcus pneumoniae*

	BP	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
PCG*	4	3.2 (24,980)	2.7 (26,932)	2.5 (27,206)	2.7 (36,475)	2.1 (35,960)	2.1 (34,415)	2.2 (33,483)	2.2 (31,506)	3.5 (16,056)	3.4 (16,526)	3.8 (14,510)
CTX	4	2.4 (21,654)	2.0 (23,096)	1.8 (23,002)	1.6 (30,734)	1.4 (29,405)	1.6 (27,773)	1.4 (27,004)	1.4 (26,040)	2.1 (13,140)	2.1 (13,878)	2.4 (12,372)
MEPM	1	6.9 (22,989)	5.1 (24,986)	5.4 (25,760)	5.0 (34,461)	5.7 (34,885)	6.0 (34,011)	6.3 (33,115)	6.4 (31,489)	8.9 (16,152)	8.9 (16,479)	8.8 (14,452)
EM	1	87.0 (21,979)	86.2 (22,435)	86.7 (22,215)	85.5 (30,501)	84.4 (30,144)	82.4 (28,097)	81.3 (27,154)	81.5 (26,270)	80.4 (13,529)	80.5 (14,352)	82.0 (12,750)
CLDM	1	56.4 (17,513)	56.1 (19,719)	57.1 (20,296)	56.1 (27,555)	54.1 (28,541)	50.5 (27,536)	49.9 (26,459)	50.9 (25,404)	49.5 (13,651)	49.5 (14,047)	50.3 (12,386)
LVFX	8	3.0 (24,105)	3.1 (25,764)	3.3 (26,236)	3.5 (35,457)	4.1 (35,431)	4.3 (34,241)	4.4 (33,551)	4.7 (32,057)	6.4 (16,499)	6.0 (16,818)	6.4 (14,805)
VCM	2	0.0 (24,085)	0.0 (25,425)	0.0 (25,775)	0.0 (33,530)	0.0 (33,670)	0.0 (32,681)	0.0 (31,741)	0.0 (30,250)	0.0 (15,625)	0.0 (16,176)	0.0 (14,140)

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 2021 were publicized as confirmed reported data. Cases reported since 2013 are listed below. The scope of reporting was limited to cases where the isolated bacteria was regarded as the cause of an infectious disease or cases where it was detected from specimens that normally should be aseptic. Colonization was 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 *Enterococcus* spp. (VRE) infection per year since 2017, representing a slight rise from the trend of 50 to 60 reports per year between 2013 and 2016. Since 2017, the number of cases has been increasing and in 2021, 124 cases were reported. No case of vancomycin-resistant *Staphylococcus aureus* (VRSA) infection has been reported since November 5, 2003, when this disease became notifiable. Carbapenem-resistant *Enterobacteriales* (CRE) infection became a notifiable disease on September 19, 2014, with 2,066 cases reported in 2021 and generally ranging from 2,000 to 2,300 cases since 2018. Surveillance for multidrug-resistant *Acinetobacter* spp. (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 6 cases reported in 2021.

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 have been using the PCR method to test strains isolated from notified cases of CRE infection for carbapenemase-producing genes and other information. In 2021 results for 1,441 strains were reported. The major carbapenemase-producing gene was detected in 217 (15.1%) isolates, with the IMP-type of the domestic carbapenemase-producing gene accounting for the majority, 189 (87.1%). Bacterial species detected with IMP-type carbapenemase-producing genes and IMP genotypes showed similar regional characteristics since 2017.

Looking at antimicrobial-resistant infections notified by Japan's designated sentinel sites (in principle medical institutions that have 300 or more beds, 500 institutions nationwide), both the number of reports of MRSA infections and the number of reports per sentinel site had decreased since 2011, with 14,516 cases reported in 2021. Multidrug-resistant *Pseudomonas aeruginosa* (MDRP) infections have generally declined since 2013, with 118 cases reported in 2021. Penicillin-resistant *Streptococcus pneumoniae* (PRSP) infections continued to decline in both the number of reports and the number of reports per sentinel.

i. Diseases subject to notifiable disease surveillance

Table 15. Number of cases reported for diseases subject to notifiable disease surveillance (2013-2021)

	2013	2014	2015	2016	2017	2018	2019	2020	2021
VRE	55	56	66	61	83	80	80	136	124
VRSA	0	0	0	0	0	0	0	0	0
CRE	-	314*	1,673	1,573	1,660	2,289	2,333	1,956	2,066
MDRA	-	15*	38	33	28	24	24	10	6

* 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 (2013-2021)

		2013	2014	2015	2016	2017	2018	2019	2020	2021
PRSP	Total	3,161	2,292	2,057	2,017	2,001	1,895	1,754	879	846
	Per site	6.65	4.79	4.29	4.21	4.18	3.94	3.65	1.84	1.77
MRSA	Total	20,155	18,082	17,057	16,338	16,551	16,311	16,241	14,940	14,516
	Per site	42.43	37.83	35.61	34.11	34.55	33.91	33.84	31.19	30.30
MDRA*	Total	8	4	-	-	-	-	-	-	-
	Per site	0.02	0.01	-	-	-	-	-	-	-
MDRP	Total	319	268	217	157	128	121	127	116	118
	Per site	0.67	0.56	0.45	0.33	0.27	0.25	0.26	0.24	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 104 outbreaks of food-borne illness that occurred in Tokyo in 2022, 19 outbreaks (18.3%) were caused by *Campylobacter* spp., being the largest cause of bacterial food-borne illness since 2005.[1] The strains provided for antimicrobial susceptibility tests were *Campylobacter jejuni* and *Campylobacter coli* isolated from sporadic diarrhea patients in Tokyo. Resistance rates for 2011-2021 are shown in the tables. In 2021, the number of strains tested was very low due to the impact of the epidemic of novel coronavirus infection. The resistance rate of *C. jejuni* to CPFX was 34.1%, lower than in 2019. The resistance rate of EM was 2.4%, and the resistance rate of *C. coli* to CPFX was 100%, which was higher than the previous year. In both cases, the resistance rate has remained largely unchanged, although it has increased or decreased from year to year. 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. Resistance rates (%) of *Campylobacter jejuni* * from sporadic diarrhea

(Number of samples)	2011 (108)	2012 (83)	2013 (85)	2014 (125)	2015 (116)	2016 (113)	2017 (115)	2018 (110)	2019 (132)	2020 (86)	2021 (42)
EM	3.7	2.4	1.2	0.8	0.9	0.9	1.7	1.8	3.0	0.0	2.4
NA	53.7	62.7	50.6	50.4	37.1	53.1	46.1	51.7	54.5	31.4	31.0
CPFX	53.7	62.7	50.6	50.4	37.1	52.2	43.5	51.8	54.5	31.4	31.0

* Strains isolated from diarrhea cases in Tokyo.

Prepared from [5] with partial modification.

Table 18. Resistance rates (%) of *Campylobacter coli* * from sporadic diarrhea

(Number of samples)	2011 (8)	2012 (9)	2013 (12)	2014 (7)	2015 (8)	2016 (14)	2017 (8)	2018 (8)	2019 (16)	2020 (7)	2021 (3)
EM	12.5	22.2	16.7	28.6	0.0	14.3	25.0	62.5	25.0	28.6	33.3
NA	87.5	66.7	75.0	57.1	50.0	50.0	62.5	50	68.8	57.1	100.0
CPFX	87.5	66.7	75.0	57.1	50.0	35.7	62.5	37.5	68.8	57.1	100.0

* Strains isolated from diarrhea cases in Tokyo.

Prepared from [5] with partial modification.

ii. Non-typhoidal *Salmonella* spp.

Source: Public Health Institutes

The 21-23 Public Health Institutes across Japan conducted research on the multidrug-resistant status of the 3,303 *Salmonella* spp. that were isolated between 2015 and 2022, using a standardized methodology.[2] Table 19 lists the key serotypes of human-derived strains and food-derived strains.

In total, 38.3% of the 2,316 human-derived strains (from symptomatic humans) and 90.4% of the 987 food-derived strains indicated resistance to one or more of the 17 antimicrobials used in the study (Tables 20 and 21). Although this investigation was not conducted as a routine national surveillance operation, this was nationwide surveillance and the resistance rates of the strains isolated between 2015 and 2022 are considered to reflect the current status in Japan. In this reporting period (2022), 73 (30.5%) of 239 human-derived strains and 120 (90.9%) of 132 food-derived strains were resistant to one or more agents, which did not differ significantly from the resistance rates of 2,077 human-derived strains (39.2%) and 855 food-derived strains (90.3%), which were isolated between 2015-2021. As for multidrug resistance, the proportion of three-agent resistance was large both among human-derived strains and among food-derived strains. Forty-two (1.8%) among 2,316 human-derived strains, and 64 (6.5%) among 987 food-derived strains, indicated multidrug resistance to as many as 6 to 11 agents. In addition, resistant strains to MEPM were detected for the first time in human-derived isolates in 2020 (Table 20). This isolated strain was *S.* Heidelberg, a multidrug-resistant strain resistant to eight agents, including MEPM. On the other hand, no MEPM-resistant strains have been detected in food-derived strains to date.

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, *S.* Schwarzengrund in particular accounted for a higher proportion of isolates in the recent period (2020-2022) than in 2015-2019, but the resistance trends were not significantly different. In human-derived strains, on the other hand, as resistance trends were observed characteristic to each serotype, the resistance rates were compared by serotype over time and shown.

Three serotypes (*S.* Schwarzengrund, *S.* Infantis, and *S.* Manhattan) were found commonly in both the top 10 human-derived and top 5 food-derived serotypes, and the antimicrobial resistance rates of these three serotypes were compared between human- and food-derived strains (Table 29). Clear similarities were observed in overall

resistance trends to various antimicrobials, suggesting a strong association between human-derived resistant strains (approximately 40% of S. Infantis and the majority of *S.* Schwarzengrund and *S.* Manhattan) and food-derived resistant strains.

In addition to antimicrobial susceptibility tests, strains isolated between 2015 and 2021 (2,077 human-derived strains, 855 food-derived strains) that were resistant to one or more of the agents, for CTX, CAZ, and CFX (44 human-derived strains, and 49 food-derived strains) underwent testing to detect ESBL and AmpC β-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-type. CIT-type was the most common genotype among the AmpC-producing genes in human-derived and food-derived strains alike, followed by TEM-type. These results showed similarities in trends toward the detection of ESBL and AmpC-producing genes in both human-derived and food-derived strains, while the CTX-M-9 group (ESBL-producing genes) was detected only in human-derived strains, and the EBC-type (AmpC genes) was detected only in food-derived strains. Strain characteristic detections were also observed.

Table 19. Serotypes of human- and food-derived non-typhoidal *Salmonella* spp. (2015-2022)

Human-derived strains (n= 2,316)	%	Food-derived strains (n= 987)	%
Enteritidis	13.3	Schwarzengrund	55.0
4: i:-	10.8	Infantis	20.9
Infantis	8.6	Manhattan	8.0
Thompson	8.1	Agona	1.8
Typhimurium	6.3	Heidelberg	1.8
Saintpaul	5.8	Others	12.5
Schwarzengrund	5.4	Total	100.0
Stanley	3.5		
Newport	2.9		
Manhatten	2.2		
Others	33.1		
Total	100.0		

Table 20. Resistance rates of human-derived non-typhoidal *Salmonella* spp. (2015-2022)

	2015 (n=387)	2016 (n=360)	2017 (n=393)	2018 (n=315)	2019 (n=265)	2020 (n=211)	2021 (n=146)	2022 (n=239)	SUM (n=2316)
ABPC	17.3	18.1	16.0	19.4	14.7	14.7	12.3	14.2	16.3
GM	0.3	0.6	0.8	0.6	1.5	0.5	0.7	0.4	0.6
KM	5.9	11.7	7.4	8.3	6.4	6.2	7.5	4.6	7.4
SM	27.4	30.0	26.2	29.2	23.8	25.6	21.9	19.2	26.1
TC	32.6	29.2	27.5	25.4	22.6	26.1	21.9	18.4	26.3
ST	4.4	6.7	8.1	6.3	3.4	9.0	4.8	2.9	5.8
CP	2.3	6.4	5.3	6.0	5.3	5.2	5.5	4.2	5.0
CTX	0.3	2.5	3.3	3.2	1.5	0.9	2.1	1.3	1.9
CAZ	0.3	2.2	1.8	1.9	0.8	0.9	1.4	0.8	1.3
CFX	0.0	1.4	0.5	0.6	0.0	0.9	1.4	0.8	0.6
FOM	0.0	0.3	0.3	0.3	0.4	0.5	0.0	0.0	0.2
NA	7.0	8.1	8.9	5.7	4.2	5.2	5.5	13.4	7.4
CPFX	0.3	0.8	1.8	0.3	0.4	0.0	1.4	0.8	0.7
NFLX	0.3	0.8	0.5	0.0	0.8	0.0	0.0	0.8	0.4
AMK	0.0	0.0	0.0	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	0.0	0.0	0.0
MEPM	0.0	0.0	0.0	0.0	0.0	0.5	0.0	0.0	0.0
Number resistant to one or more antimicrobials	164	161	147	125	89	83	46	73	888
Proportion resistant to one or more antimicrobials	42.4	44.7	37.4	39.7	33.6	39.3	31.5	30.5	38.3

Table 21. Resistance rates of food-derived non-typhoidal *Salmonella* spp.* (2015-2022) (%)

	2015 (n=156)	2016 (n=110)	2017 (n=86)	2018 (n=108)	2019 (n=126)	2020 (n=129)	2021 (n=140)	2022 (n=132)	SUM (n=987)
ABPC	17.9	13.6	11.6	12.0	11.1	12.4	5.0	2.3	10.7
GM	0.0	0.9	1.2	0.0	0.0	0.0	0.7	0.0	0.3
KM	48.1	47.3	45.3	50.0	57.1	65.9	62.9	59.1	55.0
SM	82.7	70.9	69.8	77.8	64.3	70.5	71.4	81.1	74.0
TC	85.9	76.4	73.3	78.7	70.6	82.9	80.7	81.8	79.3
ST	19.9	16.4	12.8	38.0	25.4	24.8	14.3	22.0	21.7
CP	7.1	10.0	2.3	8.3	4.0	7.0	4.3	4.5	6.0
CTX	5.1	5.5	8.1	6.5	6.3	4.7	1.4	0.0	4.5
CAZ	4.5	6.4	8.1	6.5	4.8	3.9	0.0	0.0	4.0
CFX	2.6	3.6	8.1	4.6	5.6	5.4	1.4	0.0	3.6
FOM	0.0	0.9	1.2	0.0	0.0	0.0	0.0	0.0	0.2
NA	18.6	18.2	14.0	16.7	27.0	23.3	20.0	22.0	20.3
CPFX	0.0	0.9	1.2	0.0	0.0	0.0	0.0	0.0	0.2
NFLX	0.0	0.0	0.0	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	0.0	0.0	0.0
IPM	0.0	0.0	0.0	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	0.0	0.0	0.0
Number resistant to one or more antimicrobials	143	96	77	98	113	124	121	120	892
Proportion resistant to one or more antimicrobials	91.7	87.3	89.5	90.7	89.7	96.1	86.4	90.9	90.4

Table 22. Resistance rates of food-derived *S.* Infantis (2015-2022) (%)

	2015 (n=65)	2016 (n=33)	2017 (n=19)	2018 (n=27)	2019 (n=24)	2020 (n=8)	2021 (n=20)	2022 (n=10)	SUM (n=206)
ABPC	10.8	12.1	5.3	14.8	8.3	37.5	10.0	0.0	11.2
GM	0.0	3.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5
KM	46.2	42.4	15.8	33.3	37.5	62.5	35.0	60.0	40.3
SM	81.5	72.7	68.4	85.2	58.3	50.0	60.0	100.0	74.3
TC	89.2	81.8	68.4	85.2	58.3	37.5	70.0	100.0	78.6
ST	18.5	30.3	0.0	44.4	12.5	0.0	30.0	30.0	22.3
CP	3.1	3.0	0.0	0.0	0.0	12.5	5.0	0.0	2.4
CTX	4.6	6.1	5.3	11.1	8.3	12.5	0.0	0.0	5.8
CAZ	3.1	9.1	5.3	11.1	0.0	12.5	0.0	0.0	4.9
CFX	4.6	9.1	5.3	14.8	8.3	25.0	5.0	0.0	7.8
FOM	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
NA	3.1	9.1	0.0	3.7	16.7	0.0	15.0	0.0	6.3
CPFX	0.0	0.0	0.0	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	0.0	0.0	0.0
AMK	0.0	0.0	0.0	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	0.0	0.0	0.0
MEPM	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Table 23. Resistance rates of food-derived *S.* Schwarzengrund (2015-2022) (%

	2015 (n=47)	2016 (n=38)	2017 (n=45)	2018 (n=51)	2019 (n=66)	2020 (n=95)	2021 (n=107)	2022 (n=94)	SUM (n=543)
ABPC	17.0	5.3	0.0	7.8	3.0	5.3	1.9	0.0	4.2
GM	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
KM	85.1	86.8	77.8	80.4	92.4	73.7	72.0	71.3	78.1
SM	93.6	78.9	82.2	76.5	74.2	80.0	73.8	80.9	79.2
TC	95.7	84.2	80.0	86.3	81.8	93.7	83.2	85.1	86.4
ST	36.2	18.4	24.4	56.9	43.9	30.5	12.1	21.3	28.5
CP	19.1	13.2	4.4	9.8	6.1	5.3	4.7	6.4	7.6
CTX	0.0	0.0	2.2	0.0	0.0	1.1	0.9	0.0	0.6
CAZ	0.0	0.0	2.2	0.0	0.0	0.0	0.0	0.0	0.2
CFX	0.0	0.0	2.2	0.0	0.0	1.1	0.0	0.0	0.4
FOM	0.0	2.6	2.2	0.0	0.0	0.0	0.0	0.0	0.4
NA	25.5	21.1	6.7	23.5	27.3	20.0	18.7	22.3	20.8
CPFX	0.0	2.6	0.0	0.0	0.0	0.0	0.0	0.0	0.2
NFLX	0.0	0.0	0.0	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	0.0	0.0	0.0
IPM	0.0	0.0	0.0	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	0.0	0.0	0.0

Table 24. Resistance rates of human-derived *S.* Infantis (2015-2022) (%)

	2015 (n=34)	2016 (n=48)	2017 (n=47)	2018 (n=22)	2019 (n=16)	2020 (n=19)	2021 (n=9)	2022 (n=5)	SUM (n=200)
ABPC	0.0	2.1	0.0	9.1	6.3	5.3	0.0	0.0	2.5
GM	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
KM	20.6	14.6	6.4	22.7	12.5	5.3	11.1	0.0	13.0
SM	29.4	33.3	19.1	50.0	31.3	26.3	22.2	0.0	29.0
TC	47.1	33.3	21.3	54.5	37.5	47.4	22.2	20.0	36.0
ST	14.7	14.6	2.1	18.2	0.0	21.1	0.0	0.0	10.5
CP	0.0	0.0	0.0	9.1	6.3	5.3	0.0	0.0	2.0
CTX	0.0	0.0	0.0	4.5	6.3	5.3	0.0	0.0	1.5
CAZ	0.0	0.0	0.0	0.0	0.0	5.3	0.0	0.0	0.5
CFX	0.0	2.1	0.0	0.0	0.0	5.3	0.0	0.0	1.0
FOM	0.0	0.0	0.0	0.0	6.3	0.0	0.0	0.0	0.5
NA	8.8	4.2	8.5	0.0	12.5	5.3	11.1	0.0	6.5
CPFX	0.0	0.0	0.0	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	0.0	0.0	0.0
AMK	0.0	0.0	0.0	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	0.0	0.0	0.0
MEPM	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Table 25. Resistance rates of human-derived *S.* Enteritidis (2015-2022) (%)

	2015 (n=39)	2016 (n=41)	2017 (n=47)	2018 (n=43)	2019 (n=37)	2020 (n=35)	2021 (n=20)	2022 (n=47)	SUM (n=309)
ABPC	5.1	19.5	4.3	7.0	5.4	0.0	0.0	23.4	9.1
GM	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
KM	2.6	2.4	0.0	0.0	0.0	0.0	0.0	0.0	0.6
SM	12.8	12.2	10.6	14.0	5.4	2.9	0.0	23.4	11.3
TC	10.3	2.4	4.3	9.3	5.4	2.9	0.0	6.4	5.5
ST	5.1	0.0	0.0	0.0	0.0	5.7	0.0	0.0	1.3
CP	2.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3
CTX	0.0	2.4	0.0	0.0	0.0	0.0	5.0	0.0	0.6
CAZ	0.0	2.4	0.0	0.0	0.0	0.0	0.0	0.0	0.3
CFX	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
FOM	0.0	0.0	0.0	2.3	0.0	0.0	0.0	0.0	0.3
NA	10.3	26.8	12.8	25.6	10.8	14.3	15.0	44.7	21.0
CPFX	0.0	0.0	0.0	0.0	0.0	0.0	5.0	0.0	0.3
NFLX	0.0	0.0	0.0	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	0.0	0.0	0.0
IPM	0.0	0.0	0.0	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	0.0	0.0	0.0

Table 26. Resistance rates of human-derived *S.* Saintpaul (2015-2022) (%)

	2015 (n=27)	2016 (n=26)	2017 (n=41)	2018 (n=10)	2019 (n=8)	2020 (n=12)	2021 (n=7)	2022 (n=4)	SUM (n=135)
ABPC	7.4	7.7	14.6	10.0	0.0	8.3	0.0	0.0	8.9
GM	0.0	0.0	2.4	0.0	0.0	0.0	0.0	0.0	0.7
KM	0.0	3.8	4.9	0.0	0.0	0.0	0.0	0.0	2.2
SM	3.7	3.8	12.2	0.0	0.0	8.3	0.0	0.0	5.9
TC	40.7	15.4	22.0	10.0	12.5	25.0	14.3	25.0	23.0
ST	0.0	11.5	17.1	10.0	12.5	8.3	0.0	0.0	9.6
CP	3.7	0.0	14.6	0.0	12.5	0.0	0.0	0.0	5.9
CTX	0.0	0.0	12.2	0.0	0.0	0.0	0.0	0.0	3.7
CAZ	0.0	0.0	2.4	0.0	0.0	0.0	0.0	0.0	0.7
CFX	0.0	3.8	0.0	0.0	0.0	0.0	0.0	0.0	0.7
FOM	0.0	0.0	2.4	0.0	0.0	0.0	0.0	0.0	0.7
NA	7.4	3.8	19.5	0.0	0.0	0.0	0.0	25.0	8.9
CPFX	3.7	0.0	9.8	0.0	0.0	0.0	0.0	0.0	3.7
NFLX	3.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.7
AMK	0.0	0.0	0.0	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	0.0	0.0	0.0
MEPM	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Table 27. Resistance rates of human-derived *S.* 4: i:- (2015-2022) (%)

	2015 (n=60)	2016 (n=37)	2017 (n=36)	2018 (n=36)	2019 (n=23)	2020 (n=24)	2021 (n=17)	2022 (n=16)	SUM (n=249)
ABPC	71.7	64.9	77.8	86.1	82.6	79.2	76.5	75.0	75.9
GM	1.7	0.0	2.8	0.0	0.0	0.0	0.0	0.0	0.8
KM	3.3	5.4	2.8	8.3	4.3	4.2	11.8	0.0	4.8
SM	73.3	70.3	80.6	91.7	82.6	70.8	70.6	68.8	76.7
TC	85.0	62.2	77.8	80.6	65.2	50.0	76.5	75.0	73.5
ST	5.0	10.8	5.6	8.3	8.7	0.0	5.9	6.3	6.4
CP	3.3	10.8	8.3	13.9	8.7	4.2	11.8	6.3	8.0
CTX	0.0	2.7	2.8	2.8	0.0	0.0	0.0	0.0	1.2
CAZ	0.0	2.7	2.8	0.0	0.0	0.0	0.0	0.0	0.8
CFX	0.0	0.0	2.8	0.0	0.0	0.0	0.0	0.0	0.4
FOM	0.0	2.7	0.0	0.0	0.0	0.0	0.0	0.0	0.4
NA	1.7	2.7	5.6	0.0	0.0	0.0	0.0	0.0	1.6
CPFX	0.0	0.0	0.0	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	0.0	0.0	0.0
AMK	0.0	0.0	0.0	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	0.0	0.0	0.0
MEPM	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Table 28. Resistance rates of human-derived *S.* Thompson (2015-2022) (%)

	2015 (n=28)	2016 (n=28)	2017 (n=29)	2018 (n=29)	2019 (n=27)	2020 (n=11)	2021 (n=14)	2022 (n=21)	SUM (n=187)
ABPC	0.0	10.7	0.0	0.0	7.4	0.0	0.0	0.0	2.7
GM	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
KM	7.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.1
SM	7.1	7.1	3.4	6.9	0.0	0.0	7.1	0.0	4.3
TC	3.6	7.1	6.9	0.0	0.0	0.0	0.0	0.0	2.7
ST	0.0	7.1	0.0	0.0	0.0	0.0	0.0	0.0	1.1
CP	0.0	7.1	0.0	0.0	0.0	0.0	0.0	0.0	1.1
CTX	0.0	10.7	0.0	0.0	0.0	0.0	0.0	0.0	1.6
CAZ	0.0	7.1	0.0	0.0	0.0	0.0	0.0	0.0	1.1
CFX	0.0	7.1	0.0	0.0	0.0	0.0	0.0	0.0	1.1
FOM	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
NA	0.0	0.0	0.0	3.4	0.0	0.0	0.0	0.0	0.5
CPFX	0.0	7.1	0.0	0.0	0.0	0.0	0.0	0.0	1.1
NFLX	0.0	7.1	0.0	0.0	0.0	0.0	0.0	0.0	1.1
AMK	0.0	0.0	0.0	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	0.0	0.0	0.0
MEPM	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Table 29. Resistance rates of *S.* Infantis, *S.* Schwarzengrund, and *S.* Manhattan detected in humans and food (2015-2022) (%)

	Infantis		Schwarzengrund		Manhattan	
	Human (n=200)	Food (n=206)	Human (n=125)	Food (n=543)	Human (n=52)	Food (n=79)
ABPC	2.5	11.2	2.4	4.2	1.9	12.7
GM	0.0	0.5	0.0	0.0	0.0	0.0
KM	13.0	40.3	63.2	78.1	0.0	0.0
SM	29.0	74.3	65.6	79.2	90.4	96.2
TC	36.0	78.6	65.6	86.4	88.5	79.7
ST	10.5	22.3	24.0	28.5	0.0	5.1
CP	2.0	2.4	2.4	7.6	0.0	0.0
CTX	1.5	5.8	2.4	0.6	0.0	8.9
CAZ	0.5	4.9	1.6	0.2	0.0	8.9
CFX	1.0	7.8	0.0	0.4	0.0	1.3
FOM	0.5	0.0	0.0	0.4	0.0	0.0
NA	6.5	6.3	14.4	20.8	7.7	15.2
CPFX	0.0	0.0	0.0	0.2	0.0	1.3
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	0.0	0.0

iii. Neisseria gonorrhoeae

Source: National Institute of Infectious Diseases

The 618, 675, 982, 1,167, and 1,023, 825, 698, and 950 *Neisseria gonorrhoeae* strains that were respectively isolated between 2015 and 2021 were tested for antimicrobial susceptibility (based on EUCAST breakpoints; Table 30). CTRX-resistant strains respectively accounted for 6.2%, 4.3%, 4.3%, 3.5%, 5.4%, 2.7%, 0.7 and 1.9% since 2015. Strains assessed as resistant based on the CLSI Criteria (MIC ≥ 0.5 μg/mL) accounted for 0.6%, 0.4%, 0.5%, 0.3%, 0.4%, 0%, 0% and 0.1% since 2015. No SPCM-resistant strains were present. On the other hand, the resistance rate of AZM was 13.0% in 2015 and shifted between 33% and 43.9% from 2016 to 2020, with 11.6% and 18.4% in 2021 and 2022, respectively.

The CLSI Criteria do not provide a resistance breakpoint for AZM, but, using the 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 2022, 3.2%, 4.0%, 4.0%, 6.3%, 7.5%, 7.0%, 6.7 and 9.8% 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 AZM MIC of 1 μg/mL or higher can reasonably be regarded as resistant. Under this criterion (R ≥ 1 μg/mL), AZM-resistant strains accounted for 11.0%, 9.3%, 11.2%, 15.9%, 14.9%, 14,3%, 11.5% and 18.2% of strains respectively between 2015 and 2022. Among the other three antimicrobials, the proportion of CFIX-resistant strains accounted for approximately 20-40%, and that of CPFX-resistant strains accounted for approximately 60-80%. PCG would not have a therapeutic effect on more than 80% of strains.

Table 30. Resistance rates of *Neisseria gonorrhoeae* (%)

	2015 (618 strains)	2016 (675 strains)	2017 (982 strains)	2018 (1167 strains)	2019 (1023 strains)	2020 (825 strains)	2021 (698 strains)	2022 (950 strains)
CTRX	6.2	4.3	4.3	3.5	5.4	2.7	0.7	1.9
SPCM	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
AZM	13.0	33.5	42.6	43.9	40.1	40.2	11.6	18.4
PCG*	38.4(96.6)	36.3(96.9)	37.8(99.0)	31.7(82.5)	35.8(88.5)	37.1(98.9)	23.5 (92.7)	22.3 (98.7)
CFIX	36.2	43.2	31.0	28.4	33.4	33.1	21.9	25.9
CPFX	79.5	78.0	75.8	66.9	64.6	71.2	75.6	83.4

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 14-46 *Salmonella* Typhi strains that were isolated between 2015 and 2022 were tested for antimicrobial susceptibility (Excluding the year 2021, which is estimated to have been significantly affected by the novel coronavirus pandemic. The same applies to *Salmonella* Paratyphi A and *Shigella* spp.). CPFX-non-susceptible strains accounted for 60.7-83.9%, while strains with advanced resistance (MIC ≥ 4 μg/mL) to CPFX accounted for 5.9-42.9%. During this period, 17 strains of multidrug-resistant *Salmonella* Typhi that indicated resistance to ABPC, CP, and ST were isolated, along with five strains of CTX-resistant *Salmonella* Typhi.

The 5-30 *S.* Paratyphi A strains isolated between 2015 and 2022 were tested for antimicrobial susceptibility. CPFX non-susceptible strains accounted for 76.9-100%. No strains with advanced CPFX or CTX-resistance were isolated among the *Salmonella* Paratyphi A.

The 14-156 *Shigella* spp. strains that were isolated between 2015 and 2022 were tested for antimicrobial susceptibility. ST-resistant strains accounted for 71.4-91.9%; CPFX-resistant strains for 7.1-45.7%; and CTX-resistant strains for 0.0-27.0%.

Table 31. Resistance rates of *Salmonella* Typhi (%)

	2015 (32 strains)	2016 (46 strains)	2017 (31 strains)	2018 (34 strains)	2019 (28 strains)	2020 (20 strains)	2021 (3 strains)	2022 (14 strains)
ABPC	5.7	2.2	12.9	2.9	10.7	20.0	0.0	14.3
CP	5.7	2.2	12.9	5.9	10.7	25.0	0.0	14.3
ST	5.7	2.2	12.9	5.9	10.7	25.0	0.0	21.4
NA	68.8	63.0	83.9	61.7	57.1	55.0	66.7	57.1
CPFX	68.8(12.5*)	63.0(23.9*)	83.9(16.1*)	61.7(5.9*)	60.7(10.7*)	65.0(25.0*)	100.0(0.0*)	64.3 (42.9)
CTX	0.0	0.0	0.0	2.9	3.6	15.0	0.0	0.0

*Advanced resistance to fluoroquinolone

Table 32. Resistance rates of *Salmonella* Paratyphi A (%)

	2015 (30 strains)	2016 (20 strains)	2017 (13 strains)	2018 (21 strains)	2019 (16 strains)	2020 (5 strains)	2021 (0 strains)	2022 (10 strains)
ABPC	0.0	0.0	0.0	0.0	0.0	0.0	-	10.0
CP	0.0	0.0	0.0	0.0	0.0	0.0	-	0.0
ST	0.0	0.0	0.0	0.0	0.0	0.0	-	0.0
NA	80.0	80.0	76.9	100.0	87.5	100.0	-	70.0
CPFX	83.3	83.3	76.9	100.0	87.5	100.0	-	100.0
CTX	0.0	0.0	0.0	0.0	0.0	0.0	-	0.0

Table 33. Resistance rates of *Shigella* spp. (%)

	2015 (105 strains)	2016 (73 strains)	2017 (91 strains)	2018 (156 strains)	2019 (91 strains)	2020 (74 strains)	2021 (2 strains)	2022 (14 strains)
ABPC	21.9	42.5	31.9	19.2	14.3	41.9	50.0	14.3
CP	11.4	24.7	26.4	9.0	6.6	4.1	50.0	7.1
ST	81.0	80.8	73.6	76.9	76.9	91.9	50.0	71.4
NA	63.8	52.1	52.8	45.5	33.0	83.8	50.0	7.1
CPFX	45.7	35.6	35.2	21.2	14.3	35.1	0.0	7.1
CTX	5.7	16.4	13.2	5.1	3.3	27.0	0.0	0.0

5) Mycobacterium tuberculosis

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

Looking at major anti-tuberculosis antibiotics, INH, RFP, and EB, among patients with culture-positive pulmonary tuberculosis who were newly notified between 2012 and 2022, 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 SM resistance in 2017, it has mostly remained at the same level since 2018. The number of newly reported cases of multidrug-resistant *M. tuberculosis* that are resistant at least to both INH and RFP remained in the range of approximately 40 to 60 (0.4- 0.9%) per year, decreasing to 26 by 2022.

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

	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Culture-positive patients, N	10,915	11,261	10,523	10,259	10,035	9,878	9,580	9,016	8,110	6,645	5,902	5,231
INH-resistant, n (%)*	386 (4.8)	380 (4.6)	369 (4.8)	349 (4.6)	372 (4.9)	369 (4.8)	383 (4.9)	377 (5.0)	359 (5.4)	297 (5.7)	221 (4.9)	200 (4.9)
RFP-resistant, n (%)*	86 (1.1)	73 (0.9)	64 (0.8)	76 (1.0)	77 (1.0)	74 (1.0)	80 (1.0)	87 (1.1)	65 (1.0)	60 (1.2)	56 (1.2)	41 (1.0)
INH & RFP-resistant†, n (%)*	60 (0.7)	60 (0.7)	47 (0.4)	56 (0.5)	48 (0.5)	49 (0.6)	52 (0.7)	55 (0.6)	44 (0.7)	46 (0.9)	41 (0.9)	26 (0.6)
SM-resistant, n (%)§	-	509 (6.1)	475 (6.2)	469 (6.2)	476 (6.3)	461 (6.0)	557 (7.1)	471 (6.3)	428 (6.5)	356 (6.9)	287 (6.4)	272 (6.7)
EB-resistant, n (%)¶	-	151 (1.8)	106 (1.4)	130 (1.7)	129 (1.7)	100 (1.3)	106 (1.3)	130 (1.7)	126 (1.9)	78 (1.5)	79 (1.9)	59 (1.4)

* 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, 6,658 (82.1%) patients in 2019, 5,209 (78.4%) patients in 2020, and 4,551 patients in 2021.

-: Not under surveillance

† INH- and RFP- resistant tuberculosis 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, 41 patients in 2019, 38 patients in 2020, 36 patients in 2021 and 23 patients in 2022.

¶ 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, 8 in 2019, 14 in 2020, and 9 patients in 2021).

6) *Clostridioides difficile* infection

Clostridioides difficile infection (CDI) 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]

Existing 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 (TC) 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] Comparison of prevalence rates among hospitals and with other countries should take into account the influence of specimen collection wards, testing methods, definition of relapse, differences in average length of hospital stay, and other factors.

Since 2019, the AMR Clinical Reference Centre (AMRCRC) has been operating the J-SIPHE, preparing annual reports, and investigating CDI trends. The number of CDI outbreaks per 10,000 patient hospital days (n in the table is the number of facilities, and the distribution of occurrences per facility (number of occurrences/total number of patients in hospital x 10,000) is shown) showed a decreasing trend: in 2019, 1.38 (IQR: 0.56-2.43) in 276 facilities; in 2020, 1.20 (IQR: 0.45-2.13) in 347 facilities; in 2021, 0.96 (IQR: 0.32-1.97) in 470 facilities; in 2022, 0.82 (IQR: 0.14-1.66) in 1,241 facilities. The impact of changes in population characteristics with the increase in the number of participating facilities should be considered.

Table 35. Distribution of *Clostridioides difficile* outbreaks in hospitals (outbreaks per 10,000 patient hospital days)

	2019 (n=276)*	2020 (n=347)**	2021 (n=470)	2022 (n=1,241）**
Clostridioides difficile (IQR)	1.38 (0.56-2.43)	1.20 (0.45-2.13)	0.96 (0.32-1.97)	0.82 (0.14-1.66)

n in the table indicates the number of facilities and the distribution of the number of occurrences per facility (number of occurrences/total number of patients in hospital x 10,000)

*2019 included 253 facilities for toxin testing using immunochromatography, 3 facilities for testing using NAAT, and 20 other facilities.

**2020: Only toxin is confirmed by immunochromatography and judged as CDI when positive, and the test is terminated when negative. 81 facilities in 2020, 65 facilities in 2021, and 194 facilities in 2022. If the test is negative, the test is terminated. 8 facilities in 2020, 2 facilities in 2021, and 5 facilities in 2022. Immunochromatography to confirm both GDH and toxin and determine CDI if GDH-positive and toxin-positive; if GDH-positive and toxin-negative, the test is completed without determining CDI. 115 facilities in 2020, 203 facilities in 2021, and 500 facilities in 2022. If both GDH and toxin are confirmed by immunochromatography and both GDH-positive and toxin-positive, the test is determined as CDI; if GDH-positive and toxin-negative, the test is determined for toxin using culture colonies and if both are negative, the test is terminated. 226 facilities. Immunochromatography confirms both GDH and toxin and determines CDI if GDH positive and toxin positive; if GDH positive and toxin negative, determines toxin by toxin gene test in faces; if negative, test terminated. 36 facilities in 2020, 59 in 2021, 177 in 2022 36 facilities in 2020, 59 facilities in 2021, and 177 facilities in 2022. If the test is negative, the test is terminated. 3 facilities in 2020, 1 facility in 2021, and 29 facilities in 2022. Others (other than above): 38 facilities in 2020, 45 facilities in 2021, and 136 facilities in 2022.

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 10 years. In 2022 among 313,110 surgical operations undertaken at 814 institutions, SSIs were reported in 12,227 cases (4.2%). The number of reported SSIs had been on a downward trend since 2011 but remained flat in 2022.

In the intensive care unit (ICU) division of JANIS, the incidence of ventilator-associated pneumonia has been 1.2-1.8 per 1,000 days of ICU stay over the past 10 years, with a rate of 1.4 per 1,000 days of ICU stay recorded in 2022. While the incidence of urinary tract infection was around 0.5-0.8 per 1,000 days of ICU stay, the incidence of catheter-related bloodstream infection was around 0.6-0.8 per 1,000 days of ICU stay. Both of these rates have been fluctuating slightly. JANIS monitors cases of infections that occurred between 48 hours after admission to ICU and discharge from ICU.

i. Surgical site infection

Table 36. The trend (%) of reported SSI cases

	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Total SSI cases per total surgical operations (%)*	**6.0**	**6.8**	**6.5**	**6.0**	**5.8**	**5.7**	**5.4**	**5.1**	**4.6**	**4.4**	**4.2**	**4.2**
Participated medical institutions	333	363	442	552	671	730	772	802	785	786	768	814
Total surgical operations	127,731	129,825	161,077	207,244	251,832	274,132	292,031	305,960	307,052	290,795	291,958	313,110
Total SSI cases	7,719	8,771	10,445	12,508	14,701	15,674	15,889	15,566	14,226	12,696	12,227	12,998

*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) x100

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

ii. Infections at Intensive Care Unit (ICU)

Table 37. Incidence rates of infection at ICU

		2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Ventilator-associated pneumonia	**Total infection incidence rate***	**1.7**	**1.4**	**1.3**	**1.4**	**1.5**	**1.5**	**1.3**	**1.3**	**1.3**	**1.2**	**1.8**	**1.4**
	Total infections at monitored medical institutions	382	327	324	395	522	499	405	409	387	333	508	421
Urinary tract infection	**Total infection incidence rate***	**0.5**	**0.5**	**0.6**	**0.5**	**0.5**	**0.6**	**0.7**	**0.8**	**0.6**	**0.7**	**0.5**	**0.6**
	Total infections at monitored medical institutions	111	124	143	148	190	219	213	244	174	183	157	184
Catheter-related bloodstream infection	**Total infection incidence rate***	**0.7**	**0.7**	**0.8**	**0.7**	**0.7**	**0.8**	**0.7**	**0.6**	**0.6**	**0.7**	**0.7**	**0.8**
	Total infections at monitored medical institutions	168	162	204	205	240	263	213	190	177	193	214	229

*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) x1,000

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 2022 Annual Report covers a total of 1,876 participating medical institutions (868 institutions calculating Infection Prevention and Control Premium 1, 493 calculating Premium 2, 487 calculating Premium 3, and 28 calculating no premium). Registration information was optional for each participating facility. The median number of blood cultures submitted at hospitals (n=1,049) was 23.2/1,000 patient days (IQR: 0-131.8), while the median rate of multiple sets (n=960, counting facilities submitting 20 or more) for adults was 90.3%. The median positive rate (n=960, counting facilities submitting 20 or more) was 17.9% (IRQ: 1.3-85.8).

The number of outbreak of bacteria detected in blood samples per 10,000 patient days was the highest for *Escherichia coli* with a median of 2.4 (IQR: 1.8-3.5), followed by *Staphylococcus aureus* with 1.9 (IQR: 1.3-2.6), *Klebsiella pneumoniae* at 1.0 (IQR: 0.5-1.5), showing a slight increase compared to the previous year. On the other hand, the incidences of drug-resistant *S. aureus*, *E. coli* and *K. pneumoniae* have remained unchanged.

The overall hand hygiene compliance rate (n=110) was 67.0%, while the breakdown of the figures by ward function showed that critical care wards (n=110) had a higher rate of compliance, at 72.2% compared to general wards. The total amount of hand sanitizer consumed (n=988) was 10.4 L/1,000 patient days (IQR: 6.5-15.6), while the breakdown of the figures by ward function showed that critical care wards (n=364) used the most with 45.3 L/1,000 patient days (IQR: 28.85-86.57) compared to general wards. The use of hand hygiene products has been on an increasing trend since 2019, indicating an increased awareness of hand hygiene associated with countermeasures against COVID-19, while 2022 was flat compared to the previous year.

The estimated number of deaths in patients with bloodstream infections was also 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 shown declining or unchanged trends, while the number of deaths due to fluoroquinolone-resistant *E. coli* has remained 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). This time, *Streptococcus pneumoniae*, *K. pneumoniae*, and *Pseudomonas aeruginosa* were added to the list.

DALYs, an indicator of the burden of disease that includes losses due to factors other than death (e.g. sequelae), were published. Some of the parameters used in the estimation were borrowed from previous studies overseas.

Table 38. Basic information on medical institutions participating in J-SIPHE for annual report

	2019	2020	2021	2022
Number of participating facilities	581	778	818	1,876
(Premium 1)	(449)	(539)	(547)	(868)
(Premium 2)	(127)	(232)	(263)	(493)
(Premium 3)	-	-	-	(487)
(without Premium)	(5)	(7)	(8)	(28)
Number of beds, median (IQR)	340.5(221.3-525.3)	308.1(196.0-498.3)	301 (184-480)	214 (129.8-382.2)
Average hospital days, median (IQR)	13.6(11.7-17.1)	14.4(12.0-19.0)	14.0 (11.8-19.7)	16.9 (12.3-34.7)

IQR (Interquartile range)

*Premium 3 was newly established in April 2022.

Table 39. Distribution of multiplesets of blood culture at hospitals (%)

	2019	2020	2021	2022
All patients, median (IQR)	90.6 (83.6-95.4) (n=276)	92.8 (87.9-96.1) (n=326)	93.1 (88.0-96.7) (n=401)	93.1 (87.1-96.4) (n=960)
Patients aged 15 years and older, median (IQR)	95.0 (90.8-97.2) (n=276)	95.7 (92.3-97.5) (n=326)	96.0 (92.8-97.7) (n=401)	95.6 (91.2-97.6) (n=960)
Patients aged under 15 years, median (IQR)	4.9 (0.9-16.8) (n=178)	5.2 (0.0-21.7) (n=211)	7.9 (1.4-26.7) (n=261)	7.6 (0.7-22.5) (n=510)

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

2020: Data from facilities with 20 or more blood culture submissions during the period of interest.

(n in the table indicates the number of facilities, the distribution of blood culture set rates per facility)

Table 40. Distribution of occurrencesof bloodstream infectionsat hospitals (total number per 10,000 patient days)

	2019（n=253）	2020（n=329）	2021（n=329）	2022 (n=1.030）
S. aureus, median（IQR）*	1.61（0.86-2.17）	1.38（0.75-2.21）	1.53 (0.80-2.27)	1.50（0.63-2.27）
Enterococcus faecalis（IQR）*	0.37（0.12-0.65）	0.38（0.07-0.65）	0.39 (0.12-0.67)	0.31（0.00-0.59）
Escherichia coli, median（IQR）*	2.20（1.40-3.37）	2.13（1.23-3.26）	2.21 (1.42-3.25)	2.07（1.01-3.14）
Klebsiella pneumoniae, median（IQR）*	0.83（0.43-1.29）	0.77（0.32-1.26）	0.83 (0.36-1.29)	0.72（0.22-1.27）
Klebsiella aerogenes（IQR）†	-	-	-	0.00（0.00-0.20）
Enterobacter spp., median（IQR）*	0.32（0.08-0.61）	0.31（0.00-0.67）	0.34 (0.03-0.67)	-
Enterobacter cloacae complex（IQR）†	-	-	-	0.15（0.00-0.40）
Streptococcus pneumoniae, median（IQR）	0.00（0.00-0.15）	0.00（0.00-0.08）	0.00（0.00-0.07）	0.00（0.00-0.00）
MRSA, median（IQR）*	0.59（0.26-0.94）	0.56（0.24-0.89）	0.56 (0.26-0.96)	0.56（0.15-0.97）
3CREC, median（IQR）	0.42（0.16-0.84）	0.50（0.14-0.83）	0.49 (0.21-0.85)	0.46（0.00-0.81）
FQREC, medina（IQR）	0.64（0.27-1.18）	0.66（0.28-1.11）	0.69 (0.35-1.13)	0.64（0.18-1.07）
3CRKP, median（IQR）	0.00（0.00-0.09）	0.00（0.00-0.12）	0.00 (0.00-0.11)	0.00（0.00-0.12）
PRSP, median（IQR）	0.00（0.00-0.00）	0.00（0.00-0.00）	0.00（0.00-0.00）	0.00（0.00-0.00）

MRSA; methicillin-resistant S. aureus, 3CREC; 3rd generation Cephalosporine resistant *E. coli*, FQREC; fluoroquinolone resistant *E coli*, 3CRKP; 3rd generation Cephalosporine resistant *K. pneumoniae*, PRSP; penicillin resistant *S. pneumoniae*

* The tabulation includes MRSA for *S. aureus*, FQREC or 3CREC for *E. coli*, 3CRKP for *K. pneumoniae*, and PRSP for *S. pneumoniae*.

† Enterobacter spp. are counted by dividing them into *Enterobacter cloacae* complex and *Klebsiella aerogenes* starting in January 2022.

(n in the table indicates the number of facilities, the distribution of bloodstream infections per facility)

Table 41. Distribution of handhygiene compliance rate at hospitals (%)

	2019	2020	2021	2022
Overall, median (IQR)	57.5 (45.0-68.3) (n=45)	62.6 (50.3-75.1) (n=47)	68.4 (50.9-78.0) (n=50)	67.0 (49.0-78.9) (n=110)
Critical Care Area, median (IQR)	67.0 (55.8-75.2) (n=22)	68.9 (52.9-78.3) (n=22)	75.6 (51.6-83.4) (n=26)	72.2 (57.8-81.6) (n=45)
General wards, median (IQR)	56.9 (42.6-68.0) (n=44)	62.8 (48.4-75.1) (n=41)	67.9 (48.4-78.6) (n=48)	67.6 (47.2-77.2) (n=93)
Other wards, median (IQR)	59.1 (39.0-75.2) (n=22)	68.3 (42.6-82.6) (n=26)	64.0 (52.0-75.4) (n=26)	65.0 (49.8-79.7) (n=55)

(n in the table indicates the number of facilities, the distribution of hygiene compliance rate per facility)

Table 42. Distribution of total amount of hand sanitizer consumed at hospitals (L/1,000 patient days)

	2019	2020	2021	2022
Overall, median (IQR)	7.41(4.21-11.42) (n=198)	9.63(5.69-14.48) (n=245)	10.39 (6.66-16.50) (n=321)	10.39 (6.49-15.64) (n=988)
Critical Care Area, median (IQR)	33.61(18.51-58.52) (n=111)	41.15(28.67-76.19) (n=120)	52.43 (28.85-86.57) (n=159)	45.34 (26.70-69.83) (n=364)
General wards, median (IQR)	7.35(4.71-12.16) (n=184)	9.12 (6.36-14.83) (n=219)	9.85 (6.70-15.58) (n=290)	10.28 (6.96-15.16) (n=829)
Other wards, median (IQR)	6.31(3.98-12.84) (n=125)	8.95 (4.91-15.57) (n=168)	10.12 (5.71-17.53) (n=227)	9.86 (5.64-16.23) (n=731)

(n in the table indicates the number of facilities, the distribution of hand sanitizer consumed per facility)

Table 43. Estimated number of deaths from bloodstream infection (patients)

	2015	2016	2017	2018	2019	2020	2021	2022
Staphylococcus. aureus (95% CI) *	7,372 (5,721-9,047)	7,935 (6,172-9,725)	8,070 (6,271-9,885)	8,187 (6,361-10,034)	8,732 (6,793-10,693)	7,510 (5,399-9,624)	8,039 (5,776-10,316)	9,528 (7,387-11,620)
MRSA (95% CI)	3,608 (2,357-4,873)	3,758 (2,453-5,078)	3,716 (2,428-5,029)	3,690 (2,411-4,979)	3,966 (2,590-5,363)	3,633 (2,516-4,901)	3,917 (2,715-5,288)	3,938 (2,602-5,386)
Staphylococcus pneumoniae (95% CI) *	480 (160-879)	430 (144-787)	447 (149-818)	463 (154-846)	410 (137-750)	247 (82-453)	204 (68-374)	198 (66-363)
PRSP (95% CI)	126 (42-231)	108 (36-198)	94 (31-173)	113 (38-206)	106 (35-194)	77 (26-141)	74 (25-136)	60 (20-101]
Escherichia coli (95% CI) *	7,130 (5,701-8,643)	7,636 (6,111-9,251)	8,001 (6,404-9,688)	8,154 (6,523-9,890)	8,666 (6,921-10,506)	8,527 (6,829-10,240)	8,713 (6,983-10,481)	8,542 (6,843-10,311)
FQREC (95% CI)	2,889 (2,715-3,071)	3,310 (3,113-3,528)	3,376 (3,173-3,591)	3,753 (3,534-3,994)	4,201 (3,955-4,467)	4,118 (3,876-4,394)	4,170 (3,920-4,445)	4,172 (3,930-4,434)
3CREC (95% CI)	2,146 (1,155-3,300)	2,252 (1,212-3,462)	2,377 (1,280-3,660)	2,647 (1,425-4,074)	3,009 (1,620-4,625)	2,890 (1,559-4245)	3,028 (1,635-4,445)	2,970 (1,601-4,565)
Klebsiella pneumoniae (95% CI) *	4,167 (3,171-5,276)	4,218 (3,207-5,318)	4,311 (3,275-5,437)	4,561 (3,466-5,755)	4,506 (3,424-5,704)	4,484 (3,405-5,668)	4,529 (3,444-5,727)	4,659 (3,453-5,840)
3CRKP (95% CI)	474 (344-608)	492 (359-633)	461 (334-592)	533 (386-685)	530 (385-680)	597 (432-761)	682 (495-870)	762 (572-974)
Pseudomonas aeruginosa (95% CI) *	2,036 (1,320-2,855)	2,109 (1,369-2,957)	2,074 (1,345-2,909)	2,188 (1,418-3,069)	2,243 (1,455-3,148)	2,139 (1,385-2,996)	2,344 (1,516-3,282)	2,282 (1,373-3,197)
CRPA (95% CI)	343 (296-388)	369 (318-418)	303 (263-343)	318 (275-360)	324 (280-367)	344 (297-388)	399 (345-448)	3233 (281-366)

MRSA; methicillin-resistant S. *aureus*, PRSP; penicillin-resistant *S. pneumoniae*, FQREC; fluoroquinolone-resistant *E. coli*, 3CREC; 3rd generation cephalosporine resistant *E. coli*, 3CRKP; 3rd generation cephalosporine resistant *K. pneumoniae*, CRPA; Carbapenem resistant *P. aeruginosa*,

†The method for calculating the estimated number of deaths followed that reported by Tsuzuki et al (Tsuzuki S et al. IJID 2021. DOI: 10.1016/j.ijid.2021.05.018). The total number of bacteremia cases was estimated from the number of beds at participating facilities and the actual number of beds each year based on JANIS data. The estimated number of deaths was then multiplied by the mortality rate per microorganism obtained from previous studies. Mortality rates due to bacteremia per microorganism are in the appendix to the above literature (https://www.ijidonline.com/article/S1201-9712(21)00419-7/fulltext#supplementaryMaterial).

**S. aureus* includes MRSA, *S. pneumoniae* includes PRSP, *E. coli* includes FQREC or 3CREC (FQREC and 3CREC are calculated independently for bacteria that are resistant to each drug), *K. pneumoniae* includes 3CRKP, and *P. aeruginosa* includes CRPA. Figures in parentheses represent 95% confidence intervals.

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 Medical long-term care wards/hospitals

A Point Prevalence Survey (PPS) was conducted by randomly selecting 1,175 facilities with medical long-term care wards from members of the Japan Association of Medical and Care Facilities (January 2020 survey). Eighty facilities (7.8% response rate) responded. The median patient age was 84.0 years (78, 90). The median age of male patients was 82.0 years (75, 87.8) and that of female patients was 87.0 years (80.8, 92). The top infectious foci were ”pneumonia” in 199 patients (39.5%), ”urinary tract infection” in 135 patients (26.8%), and ”bronchitis” in 19 patients (3.8%). The main antimicrobial agents used were injectable third-generation cephalosporins, oral quinolones, carbapenems, and penicillins.

ii Long-term care facilities for the elderly

The center randomly selected facilities from among the members of the Japan Association of Geriatric Health Services Facilities and conducted a PPS. In the 1st PPS (conducted in February 2019, 1,500 facilities), responses were received from 134 facilities (a response rate of 8.9%), in the 2nd PPS (conducted in February 2022, 1,000 facilities), responses were received from 100 facilities (a response rate of 10.0%)

The antimicrobial use rate in the 1st PPS was 1.7% (172 antimicrobial users, total 10,148 residents). 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 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.

The antimicrobial use rate in the 2nd PPS was 1.3% (110 antimicrobial users, total of 8,291 residents). The median age of the patients was 89.0 years (IQR: 84-93), while the median age of male patients was 85.0 years (IQR: 80.5-89.5) and that of female patients was 89.0 years (IQR: 86.5-94.0). The top focus of infection was urinary tract infections, affecting 47 people (51.6%); pneumonia, affecting 14 people (15.4%); and cellulitis, affecting 7 people (7.7%). The main antimicrobials used to treat urinary tract infections and pneumonia were oral fluoroquinolones and injectable third-generation cephalosporins.

iii 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 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 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.

Table 44. Use of antimicrobial agents in long-term care wards/hospitals and elderly care facilities

facility ［Number of facilities responding］	Antimicrobial use rate (Antimicrobial users/residents on survey date)	Major infections for which antimicrobial agents were used	Major antimicrobial classes (All infectious diseases)
Medical long-term care (Medical institutions) [82]	9.4% (630/6,729)	Pneumonia (39.5%) Urinary tract infections (26.8%) Bronchitis (3.8%)	Injectable 3rd gen cephalosporins Oral fluoroquinolones Carbapenems Penicillins
Medical and rehabilitation facilities (Geriatric health care) 1st PPS [126]	1.7% (172/10,148)	Urinary tract infection (51.3%) Pneumonia (24.3%) Upper respiratory tract infections (9.9%)	Third-generation cephalosporins Fluoroquinolonespenicillins
2nd PPS [98]	1.3% (110/8,291)	Urinary tract infection (51.6%) Pneumonia (15.4%) Cellulitis (7.7%)	Injectable 3rd gen cephalosporins Oral fluoroquinolones Penicillins
Nursing care and welfare (Special nursing homes) [137]	1.0% (94/9,044)	Urinary tract infection (31.1%) Pneumonia (14.9%) Upper respiratory tract infection (12.2%)	Injectable 3rd generation cephalosporins Oral fluoroquinolones Oral penicillins

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(2) Animals

1) Bacteria derived from food-producing animals

Source: Japanese Veterinary Antimicrobial Resistance Monitoring System (JVARM)

Under the JVARM, antimicrobial susceptibility tests were performed using the broth microdilution method according to the CLSI guidelines to determine the MICs of antimicrobial agents for various strains collected. For agents with a breakpoint (BP) established by the CLSI, antimicrobial 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). Agents for which BPs could not be established using these methods were not listed in the table as it was not possible to calculate the resistance rate.

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. With regard to the site of bacterial isolation, *Salmonella* spp. were mainly isolated from feces, gastrointestinal tract, and liver, *Staphylococcus* spp. mainly from milk and udder, and *Escherichia coli* mainly from feces, gastrointestinal tract, and lungs.

i. *Salmonella* spp.

Monitoring of antimicrobial resistance was carried out on 11 agents between 2011 and 2018, and from 2019 onward, 12 agents were surveyed with MEPM added. For resistance rates in cattle- and swine-derived strains collected in 2021, more than 40% were resistant to TC. In contrast, the resistance rates of CTX and CPFX, important antimicrobial agents in human medicine, were less than 5% in swine-derived strains, 26.5% for CTX and 2% for CPFX in cattle-derived strains, and 0.0% for MEPM in both cattle, swine, and chicken. It must be noted that the BPs of 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 from 2014 to 2020 were *S.* Typhimurium and its monophasic variant *S.* 4: i:- among cattle; *S.* Typhimurium, *S.* Choleraesuis and *S.* 4: i:- among swine; and *S.* Schwarzengrund, *S.* Infantis, and *S.* Enteritidis among chickens. In the strains collected in 2021, the isolation rate of *S.* Dublin increased in cattle, all of which were CTX and CL-resistant. Regarding resistance rates by serotype, more than 50% of *S.* Choleraesuis from swine were resistant to ABPC and TC. Resistance greater than 70% was observed for ABPC and TC in cattle- and swine-derived *S.* 4: i:-, for TC in chicken-derived *S.* Infantis, and for KM and TC in chicken-derived *S.* Schwarzengrund.

On the other hand, the resistance rates to CTX and CPFX, important antimicrobial agents in human medicine, were less than 10% for both serotypes.

Table 45. The resistance rates (%) of *Salmonella* spp. isolated from diseased animals

Agent	BP	Animal species	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
ABPC	32*	Cattle	28.0	32.9	60.7	61.9	56.6	50.0	40.7	36.8	56.1	39.2	42.9
		Swine	25.4	25.3	45.0	41.4	46.9	41.1	40.9	50.0	50.7	38.5	25.8
		Chickens	12.0	9.4	4.0	3.9	14.3	-	-	4.5	18.8	0.0	0.0
CEZ	32 (8* since 2016)	Cattle	10.0	1.2	8.9	7.9	7.9	22.9	5.1	3.5	19.3	19.6	30.6
		Swine	0.0	0.0	0.0	0.0	6.1	23.2	6.8	9.4	18.8	13.5	0.0
		Chickens	0.0	3.1	4.0	0.0	0.0	-	-	0.0	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	1.8	0.0	26.5
		Swine	0.0	0.0	0.0	0.0	4.1	0.0	0.0	0.0	0.0	1.9	0.0
		Chickens	0.0	0.0	4.0	0.0	0.0	-	-	0.0	0.0	0.0	0.0
MEPM	4*	Cattle	-	-	-	-	-	-	-	-	0.0	0.0	0.0
		Swine	-	-	-	-	-	-	-	-	0.0	0.0	0.0
		Chickens	-	-	-	-	-	-	-	-	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	1.8	17.6	14.3
		Swine	6.3	3.6	15.0	15.5	8.2	17.9	15.9	4.7	7.2	15.4	0.0
		Chickens	0.0	0.0	2.0	0.0	0.0	-	-	0.0	18.8	0.0	0.0
KM	64*	Cattle	12.0	3.7	25.0	14.3	21.1	25.7	5.1	0.0	8.8	3.9	4.1
		Swine	9.5	12.0	6.7	8.6	6.1	10.7	13.6	4.7	18.8	13.5	3.2
		Chickens	24.0	15.6	22.0	29.4	42.9	-	-	63.6	62.5	37.5	57.1
TC	16*	Cattle	30.0	32.9	66.1	50.8	55.3	42.9	39.0	33.3	56.1	43.1	44.9
		Swine	61.9	53.0	66.7	60.3	61.2	58.9	50.0	50.0	44.9	44.2	48.4
		Chickens	36.0	34.4	30.0	39.2	42.9	-	-	77.3	68.8	81.3	71.4
NA	32*	Cattle	2.0	7.3	1.8	3.2	11.8	5.7	5.1	1.8	1.8	25.5	38.8
		Swine	15.9	21.7	5.0	15.5	6.1	7.1	9.1	20.3	24.6	19.2	16.1
		Chickens	8.0	6.3	8.0	3.9	28.6	-	-	0.0	43.8	37.5	42.9
CPFX	4 (1* since 2016)	Cattle	0.0	0.0	0.0	0.0	0.0	0.0	1.7	1.8	1.8	0.0	2.0
		Swine	0.0	0.0	0.0	0.0	0.0	3.6	4.5	4.7	1.4	0.0	3.2
		Chickens	0.0	0.0	0.0	0.0	0.0	-	-	0.0	18.8	0.0	0.0
CL	16 (4* since 2016)	Cattle	0.0	0.0	0.0	0.0	0.0	1.4	5.1	0.0	1.8	0.0	26.5
		Swine	0.0	0.0	1.7	0.0	0.0	3.6	4.5	6.3	8.7	3.8	3.2
		Chickens	0.0	3.1	2.0	0.0	0.0	-	-	18.2	18.8	6.3	28.6
CP	32*	Cattle	14.0	12.2	10.7	17.5	22.4	12.9	3.4	3.5	28.1	2.0	26.5
		Swine	12.7	13.3	11.7	25.9	12.2	8.9	18.2	21.9	10.1	17.3	9.7
		Chickens	0.0	6.3	6.0	3.9	14.3	-	-	0.0	0.0	0.0	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	24.6	3.9	2.7
		Swine	25.4	21.7	36.7	32.8	22.4	21.4	25.0	12.5	24.6	21.2	3.2
		Chickens	20.0	15.6	14.0	29.4	42.9	-	-	59.1	50.0	37.5	14.3
Number of isolates tested (n)		Cattle	50	82	56	63	76	70	59	57	57	51	49
		Swine	63	83	60	58	49	56	44	64	69	52	31
		Chickens	25	32	50	51	7	-	-	22	16	16	7

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 (2011-2021)

Serotypes	Cattle	Swine	Chickens	Total	(%)
Typhimurium	200	264	4	468	29.1
4: i:-	221	116	0	337	20.9
Choleraesuis	3	117	2	122	7.6
Schwarzengrund	9	3	65	77	4.8
Derby	2	31	0	33	2.0
Infantis	21	12	42	75	4.7
Braenderup	7	2	10	19	1.2
Newport	19	7	5	31	1.9
Mbandaka	11	1	12	24	1.5
Thompson	25	2	7	34	2.1
Enteritidis	2	1	16	19	1.2
Dublin	38	0	0	38	2.4
Rissen	21	15	0	36	2.2
Stanley	27	3	0	30	1.9
Tennessee	0	0	8	8	0.5
Others	142	60	58	260	16.1
Total	748	634	229	1611	100.0

Table 47. Resistance rates (%) of *Salmonella enterica* from diseased animals by serotype (2011-2021)

		Typhimurium		4: i:-		Choleraesuis	Infantis	Schwarzengrund
Agents	BP	Cattle (n=200)	Swine (n=264)	Cattle (n=230)	Swine (n=120)	Swine (n=137)	Chickens (n=41)	Chickens (n=61)
ABPC	32*	48.0	26.5	87.4	68.3	43.8	4.9	4.9
CEZ	8*	12.5	5.7	18.7	14.2	5.1	0.0	0.0
CTX	4*	7.0	0.0	3.0	0.0	1.5	0.0	0.0
GM	16*	1.0	4.2	10.4	10.8	23.4	0.0	0.0
KM	64*	27.0	4.9	6.5	6.7	26.3	46.3	78.7
TC	16*	41.5	41.3	86.5	80.8	62.8	80.5	96.7
NA	32*	9.5	10.6	10.9	13.3	29.9	12.2	23.0
CPFX	1*	0.0	3.0	0.9	1.7	0.0	0.0	0.0
CL	4*	0.5	3.8	1.3	5.0	0.0	4.9	3.3
CP	32*	19.5	20.8	14.8	12.5	10.9	2.4	3.3
ST （TMP） **	76/4* （TMP is 16）	4.5	19.7	11.7	7.5	23.4	43.9	67.2

The unit of BP is μg/mL.* BP follows CLSI Criteria. ** TMP from 2012 to 2016.

ii. Staphylococcus aureus

Monitoring of antimicrobial resistance was carried out on 7 agents between 2011 and 2018. Starting from 2019, an additional 8 agents were surveyed, including MPIPC. Resistance rates of ABPC and TC in swine-derived strains were observed to exceed 50% in 2021. Resistance rates to all antimicrobials were observed to be higher in strains isolated from swine than in those derived from cattle and chickens. Resistance to CPFX, which is a critically important antimicrobial for human medicine was less than 1% in strains isolated from cattle and chickens, while in strains from swine was 13.6%.

Table 48. Resistance rates (%) of *Staphylococcus aureus* isolated from disease appraisal samples

Agents*.	BP	Animal species	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
ABPC (PCG since 2019)	0.5	Cattle	5.5	13.6	11.0	11.1	21.3	7.8	7.4	9.3	6.4	7.0	2.0
		Swine	-	-	-	-	-	75.6	71.4	82.4	87.5	81.0	81.8
		Chickens	0.0	25.0	0.0	15.4	50.0	3.7	22.6	8.0	0.0	12.5	0.0
MPIPC	4†	Cattle	-	-	-	-	-	-	-	-	2.4	0.8	0.0
		Swine	-	-	-	-	-	-	-	-	15.0	4.8	0.0
		Chickens	-	-	-	-	-	-	-	-	0.0	0.0	0.0
SM	64	Cattle	6.4	2.3	2.8	1.1	2.7	1.4	3.4	5.8	8.0	4.7	5.9
		Swine	-	-	-	-	-	33.3	20.4	39.2	17.5	19.0	31.8
		Chickens	0.0	10.0	0.0	7.7	16.7	3.7	0.0	0.0	0.0	0.0	15.0
GM	16†	Cattle	0.9	2.3	1.8	0.0	1.3	0.0	0.6	0.0	0.0	0.8	0.0
		Swine	-	-	-	-	-	2.2	14.3	11.8	7.5	4.8	4.5
		Chickens	0.0	15.0	0.0	0.0	0.0	3.7	9.7	4.0	0.0	0.0	0.0
EM	8†	Cattle	1.8	3.4	5.5	0.0	6.7	2.8	1.7	5.8	4.8	3.9	1.0
		Swine	-	-	-	-	-	37.8	38.8	52.9	52.5	33.3	18.2
		Chickens	50.0	55.0	0.0	15.4	16.7	22.2	6.5	4.0	17.6	4.2	5.0
TC	16†	Cattle	0.0	2.3	8.3	5.5	6.7	0.0	0.0	0.6	2.4	0.8	2.0
		Swine	-	-	-	-	-	57.8	53.1	60.8	77.5	57.1	54.5
		Chickens	37.5	5.0	0.0	16.7	16.7	33.3	19.4	20.0	17.6	20.8	5.0
CP	32†	Cattle	0.0	0.0	0.9	0.0	1.3	0.0	0.6	0.6	1.6	0.0	5.9
		Swine	-	-	-	-	-	22.2	30.6	43.1	37.5	28.6	22.7
		Chickens	0.0	0.0	0.0	15.4	33.3	3.7	3.2	8.0	0.0	12.5	5.0
CPFX	4†	Cattle	0.0	0.0	0.9	0.0	1.3	0.7	0.6	0.0	1.6	1.6	1.0
		Swine	-	-	-	-	-	11.1	8.2	23.5	5.0	23.8	13.6
		Chickens	25.0	0.0	4.2	15.4	33.3	3.7	3.2	2.8	0.0	16.7	0.0
Number of isolates tested (n)		Cattle	109	88	109	91	75	141	175	172	125	128	101
		Swine	-	-	-	-	-	45	49	51	40	21	22
		Chickens	8	20	24	12	6	27	31	25	17	24	20

Units of BP are in μg/ml. -: Swine-derived strains up to 2015 are not shown because the number of isolates was less than 5 in each year.

* NA is also included in the survey, but its resistance rates are not listed as BPs cannot be set. † BP follows CLSI Criteria.

iii. *Escherichia coli*

Monitoring of antimicrobial resistance was carried out on 12 agents between 2012 and 2018 and on 13 agents from 2019 to 2021. In 2021, an antimicrobial resistance rate exceeding 50% was observed for ABPC, SM, and TC in cattle, swine, and chickens, in CP and ST in swine, and in NA among chickens. Resistance rates to 7 out of 13 antimicrobials were observed to be higher in strains isolated from swine 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 8.0 to 13.9%, 21.6 to 31.7%, and 0.0 to 23.9%, respectively, while the resistance rate to MEPM was 0.0%. It must be noted that the BPs of CEZ and CL since 2016 and CPFX since 2019 were the CLSI's revised figures. For CL, in 2018 its designation as a feed additive was revoked and its use was prohibited, and it was positioned as a second-line agent for veterinary use and its use is restricted. The resistance rate to CL showed more than 50% for swine-derived strains in 2017, but it decreased to 23.9% in 2021, and it will be necessary to continue to monitor future trends in the resistance rate due to the strengthening of these risk management measures.

Table 49. Resistance rates (%) of *Escherichia coli* isolated from disease appraisal material

Agent	BP	Animal species	2012†	2013†	2014†	2015	2016	2017	2018	2019	2020	2021
ABPC	32*	Cattle	-	61.4	57.8	63.8	37.7	50.0	51.7	62.8	63.8	52.8
		Swine	-	65.2	50.4	57.4	74.5	70.7	62.8	68.3	61.2	63.6
		Chickens	75.6	54.2	-	60.4	43.5	33.3	52.9	47.5	56.8	55.0
CEZ	8*(~2015: BP 32)	Cattle	-	21.1	6.7	14.9	15.6	15.6	17.2	28.7	27.7	18.5
		Swine	-	10.1	6.1	9.3	34.3	35.0	21.5	23.8	17.6	21.6
		Chickens	40.2	16.7	-	14.6	15.2	11.1	17.6	20.0	13.5	13.3
CTX	4*	Cattle	-	10.5	6.7	8.5	7.8	8.9	9.2	14.9	22.3	13.9
		Swine	-	2.5	0.0	3.7	2.9	3.3	3.3	5.0	2.4	8.0
		Chickens	37.8	14.6	-	10.4	6.5	5.6	11.8	7.5	8.1	11.7
SM	32	Cattle	-	-	68.9	78.7	49.4	61.1	57.5	63.8	63.8	61.1
		Swine	-	-	64.3	66.7	74.5	72.4	54.5	65.3	61.2	62.5
		Chickens	-	-	-	60.4	56.5	38.9	51.0	65.0	67.6	61.7
GM	16*	Cattle	-	17.5	6.7	12.8	10.4	8.9	10.3	8.5	11.7	7.4
		Swine	-	24.1	8.7	19.4	21.6	22.8	13.2	12.9	14.1	22.7
		Chickens	6.1	3.1	-	2.1	10.9	5.6	2.0	5.0	10.8	0.0
KM	64*	Cattle	-	38.6	26.7	29.8	16.9	26.7	28.7	31.9	29.8	22.2
		Swine	-	34.2	33.9	31.5	46.1	39.0	32.2	27.7	24.7	25.0
		Chickens	51.2	35.4	-	39.6	50.0	36.1	27.5	25.0	37.8	33.3
TC	16*	Cattle	-	50.9	66.7	66.0	54.5	62.2	58.6	66.0	66.0	63.0
		Swine	-	79.1	75.7	75.9	87.3	78.9	70.2	69.3	69.4	80.7
		Chickens	74.4	61.5	-	70.8	78.3	55.6	72.5	60.0	70.3	63.3
MEPM	4*	Cattle	-	-	-	-	-	-	-	0.0	0.0	0.0
		Swine	-	-	-	-	-	-	-	0.0	0.0	0.0
		Chickens	-	-	-	-	-	-	-	0.0	0.0	0.0
NA	32*	Cattle	-	29.8	33.3	36.2	18.2	33.3	33.3	36.2	34.0	28.7
		Swine	-	60.1	52.2	50.0	48.0	50.4	33.1	27.7	32.9	38.6
		Chickens	73.2	59.4	-	52.1	56.5	55.6	35.3	60.0	32.4	61.7
CPFX	1*(~2018: BP 4*)	Cattle	-	19.3	24.4	34.0	11.7	17.8	21.8	28.7	28.7	25.0
		Swine	-	36.1	23.5	32.4	24.5	28.5	22.3	15.8	20.0	21.6
		Chickens	22.0	25.0	-	8.3	8.7	11.1	11.8	35.0§1	18.9	31.7
CL	4*(~2015: BP16*)	Cattle	-	5.3	6.7	0.0	10.4	20.0	11.5	11.7	1.1	0.9
		Swine	-	3.2§2	0.0§2	2.8§2	56.9	52.0	35.5	27.7	27.1	23.9
		Chickens	2.4	1.0	-	0.0	8.7	0.0	2.0	10.0	0.0	0.0
CP	32*	Cattle	-	21.1	28.9	46.8	19.5	28.9	31.0	38.3	40.4	35.2
		Swine	-	64.6	64.3	61.1	69.6	59.3	57.0	55.4	57.6	61.4
		Chickens	22.0	25.0	-	16.7	21.7	11.1	21.6	15.0	32.4	18.3
ST (TMP from 2012 to 2017)	76/4* (TMP: 16*)	Cattle	-	22.8	33.3	44.7	23.4	35.6	42.5	41.5	40.4	33.3
		Swine	-	49.4	59.1	64.8	62.7	56.9	52.9	57.4	51.8	53.4
		Chickens	31.7	33.3	-	33.3	23.9	13.9	19.6	35.0	24.3	31.7
Strains tested (n)		Cattle	-	57	45	47	77	90	87	94	94	108
		Swine	-	158	115	108	102	123	121	101	85	88
		Chickens	82	96	-	48	46	36	51	40	37	60

The unit of BP is μg/mL. * BP follows CLSI Criteria. Resistance rates for years prior to the change are based on BP before the change.

-: Not under surveillance.

§1 The resistance rate to CPFX in chicken-derived strains for 2019 was 22.5% when adopting the pre-2018 BP:4.

§2 The resistance rates to CL in swine-derived strains for 2013, 2014, and 2015 were 42.4%, 44.3%, and 62.0%, respectively, when adopting the post-2016 BP:4 μg/mL.

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 parallelly launched 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 since 2018 was carried out. In 2021, resistance to TC in swine- and chicken-derived strains, ABPC, SM, and KM in chicken-derived strains was observed to exceed 40%. The rates of resistance to critically important antimicrobials for human medicine CTX, CPFX, and CL were less than 5%, less than 15%, and 5%, less than 5%, respectively, while the resistance rate to MEPM was 0.0%.

Table 50. Resistance rates (%) of *Escherichia coli* from animal slaughterhouses and poultry slaughterhouses

Agent	BP	Animal species	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
ABPC	32*	Cattle	2.4	6.5	3.0	5.5	7.4	4.8	11.6	6.3	5.1	5.0
		Swine	32.3	26.0	43.0	34.4	36.7	33.7	34.9	32.5	44.1	33.3
		Chickens	30.8	35.5	40.1	43.5	35.4	39.3	36.1	36.7	30.6	40.7
CEZ	8* (32 before 2015)	Cattle	0.4	0.3	0.0	0.0	1.9	0.8	0.5	1.0	0.4	1.1
		Swine	1.0	0.8	1.1	1.0	6.7	1.2	2.4	3.8	1.1	2.0
		Chickens	3.0	7.8	5.8	3.8	10.1[§1]	6.7[§1]	7.7[§1]	4.7[§1]	6.6	3.4
CTX	4*	Cattle	0.0	0.0	0.4	0.0	0.4	0.4	0.0	0.7	0.0	0.0
		Swine	0.0	0.0	1.1	0.0	1.1	1.2	0.0	2.5	0.0	2.0
		Chickens	1.5	4.8	4.1	2.2	5.1	4.7	3.2	3.1	4.1	2.1
MEPM	4*	Cattle	—	—	—	—	—	—	0.0	0.0	0.0	0.0
		Swine	—	—	—	—	—	—	0.0	0.0	0.0	0.0
		Chickens	—	—	—	—	—	—	0.0	0.0	0.0	0.0
SM	32	Cattle	14.9	12.3	17.1	12.4	22.1	19.0	18.5	19.7	14.6	18.0
		Swine	44.1	44.9	52.7	39.6	50.0	41.0	49.4	41.3	45.2	24.5
		Chickens	39.1	38.6	44.8	41.8	51.3	41.3	48.4	40.6	47.1	48.3
GM	16*	Cattle	0.0	0.3	0.0	0.0	0.8	0.0	0.0	0.0	0.4	0.4
		Swine	0.5	2.4	6.5	2.1	3.3	3.6	3.6	2.5	1.1	1.0
		Chickens	1.5	1.8	2.9	2.2	5.1	6.0	5.2	6.3	3.3	1.4
KM	64*	Cattle	1.2	1.5	0.4	0.7	4.3	1.2	0.0	0.7	0.4	0.8
		Swine	9.7	7.9	9.7	8.3	10.0	10.8	8.4	10.0	5.4	8.8
		Chickens	24.1	24.1	33.1	37.5	43.0	36.7	43.9	37.5	31.4	44.8
TC	16*	Cattle	19.0	16.4	19.8	18.6	29.8	21.0	26.5	22.9	19.8	23.8
		Swine	58.5	62.2	59.1	45.8	56.7	55.4	55.4	47.5	62.4	52.0
		Chickens	49.6	44.0	43.6	54.9	56.3	46.0	49.0	62.5	52.9	46.2
NA	32*	Cattle	2.4	1.8	2.3	2.6	2.3	2.0	2.1	1.4	3.2	1.9
		Swine	4.1	11.0	9.7	5.2	15.6	12.0	12.0	11.3	8.6	9.8
		Chickens	39.8	36.1	45.3	35.9	35.4	39.3	40.6	36.7	48.8	37.2
CPFX	1* (-2019: BP4*)	Cattle	0.0	0.6	0.8	0.0	0.4	0.0	0.5	0.3	0.4	0.0
		Swine	1.5	0.8	2.2	3.1	4.4	0.0	1.2	2.5	2.2	2.0
		Chickens	6.0	5.4	9.9	4.9	9.5	12.0	12.3	12.5	18.2	14.5
CL	4* (16 before 2015)	Cattle	0.0	0.0	0.8	0.0	0.4	1.2	0.0	0.3	0.0	0.0
		Swine	0.0	0.0	0.0	0.0	4.4[§2]	2.4[§2]	6.0[§2]	2.5[§2]	4.3	2.0
		Chickens	0.8	0.6	0.0	0.5	1.9	3.3	0.0	0.0	0.8	0.0
CP	32*	Cattle	5.2	2.3	3.8	2.9	2.3	2.8	4.8	4.2	5.9	6.5
		Swine	23.6	23.6	34.4	25.0	25.6	21.7	25.3	22.5	30.1	26.5
		Chickens	11.3	11.4	15.1	9.8	19.6	11.3	17.4	15.6	20.7	9.7
ST	76/4*	Cattle	2.0	2.9	5.3	2.9	0.4	2.0	5.3	2.8	2.8	3.4
		Swine	23.6	26.8	34.4	30.2	4.4	26.5	32.5	23.8	25.8	30.4
		Chickens	24.8	31.9	30.2	28.3	27.8	34.7	33.5	30.5	22.3	23.4
Number of isolates tested (n)		Cattle	248	341	263	274	258	252	189	288	253	261
		Swine	195	127	93	96	90	83	83	80	93	102
		Chickens	133	166	172	184	158	150	155	128	121	145

The unit of BP is μg/mL.

* BP follows CLSI Criteria. Resistance rates for years prior to the change are based on BP before the change.

[§1] If the BP of 32 μg/mL used until 2015 is applied, CEZ resistance rate in chicken-derived strains was 7.0% in 2016, 4.7% in 2017, 3.2% in 2018, and 3.5% in 2019.

[§2] If the BP of 16 μg/mL used until 2015 is applied, CL resistance rate in swine-derived strains was 1.1% in 2016, 0.0% in 2017, 0.0% in 2018, and 0.0% in 2019.

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 2021, resistance to TC, NA, and CPFX in cattle- and chicken-derived strains and TC in cattle-derived strains exceeded 30%. On the other hand, resistance to SM and EM was less than 5% in each case. Resistance to CPFX and AZM, which are critically important antimicrobials for human medicine, was 60.5% and 0.9% in cattle-derived strains, respectively, and 33.9% and 0.0% in chicken-derived strains, respectively.

Table 51. Resistance rates (%) of *Campylobacter jejuni* from animal and poultry slaughterhouses

Agents*	BP	Animal species	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
ABPC	32	Cattle	0.0	9.1	12.9	8.9	7.4	8.2	8.6	11.4	8.2	10.5
		Chickens	19.7	19.8	17.5	19.1	16.2	28.4	14.9	14.3	22.4	15.3
SM	32	Cattle	2.4	3.5	3.8	3.2	6.2	4.1	8.6	1.8	3.6	4.4
		Chickens	1.4	0.0	3.5	2.1	8.8	1.5	0.0	0.0	2.0	0.0
EM	32†	Cattle	0.0	0.7	0.0	1.3	0.0	0.0	5.7	0.0	2.7	0.9
		Chickens	0.0	0.0	0.0	0.0	0.0	1.5	0.0	0.0	4.1	0.0
AZM	4	Cattle	—	—	—	—	—	0.0	5.7	0.0	2.7	0.9
		Chickens	—	—	—	—	—	1.5	0.0	0.0	4.1	0.0
TC	16†	Cattle	45.1	52.4	49.2	52.2	63.0	72.2	65.7	67.5	70.9	62.3
		Chickens	38.0	44.4	38.6	28.7	33.8	46.3	23.4	34.3	22.4	28.8
CP	16	Cattle	0.0	6.3	0.0	1.3	1.2	6.2	2.9	6.1	0.9	6.1
		Chickens	0.0	0.0	1.8	0.0	2.9	0.0	2.1	0.0	0.0	0.0
NA	32	Cattle	34.1	33.6	50.8	42.7	44.4	48.5	31.4	60.5	62.7	64.9
		Chickens	39.4	48.1	29.8	27.7	57.4	46.3	31.9	37.1	32.7	44.1
CPFX	4†	Cattle	34.1	29.4	49.2	40.8	44.4	50.5	31.4	59.6	62.7	60.5
		Chickens	39.4	39.5	29.8	26.6	51.5	44.8	29.8	34.3	32.7	33.9
Strains tested (n)		Cattle	82	143	132	157	81	97	35	114	110	114
		Chickens	71	81	57	94	68	67	47	35	49	59

The unit of BP is μg/mL.

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

† BP follows CLSI Criteria. Resistance rates for years prior to the change are based on BP before the change.

iii. *Campylobacter coli*

Monitoring of antimicrobial resistance to 7 agents between 2012 and 2016 was carried out, and AZM was added in 2017, taking the total number to 8. In swine-derived strains in 2021, resistance to SM and TC exceeding 60%, and resistance to NA and CPFX exceeding 50% was observed. On the other hand, CP resistance was less than 3%. Resistance to CPFX, which is a critically important antimicrobial for human medicine, was 54.9%, while the AZM resistance rate was 33.8%.

Table 52. Resistance rates (%) of slaughterhouse-derived *Campylobacter coli*

Agent*	BP	Animal species	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
ABPC	32	Swine	23.3	25.5	36.6	24.6	15.4	29.5	17.2	26.7	21.4	23.9
SM	32	Swine	67.4	78.3	69.9	72.3	64.1	68.9	69.0	68.3	71.4	64.8
EM	32†	Swine	32.6	44.3	43.0	26.2	38.5	31.1	20.7	33.3	21.4	33.8
AZM	4	Swine	—	—	—	—	—	31.1	20.7	31.7	21.4	33.8
TC	16†	Swine	84.5	93.4	80.6	87.7	89.7	83.6	86.2	78.3	73.8	76.1
CP	16	Swine	10.9	3.8	7.5	9.2	15.4	1.6	3.4	3.3	2.4	2.8
NA	32	Swine	46.5	53.8	52.7	47.7	61.5	50.8	58.6	45.0	52.4	54.9
CPFX	4†	Swine	46.5	46.2	50.5	47.7	59.0	54.1	58.6	40.0	50.0	54.9
Strains tested (n)		Swine	129	106	93	65	39	61	29	60	42	71

The unit of BP is μg/mL.

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

† BP follows CLSI Criteria.

iv. *Enterococcus* spp.

Monitoring of antimicrobial resistance was carried out on 10 agents between 2012 and 2014, and 11 agents since 2015, VCM added. From 2018, DSM, OTC, and ERFX were changed to SM, TC, and CPFX, respectively, of which resistance rates were investigated for 10 agents except SM as no BPs were established for it. In 2021, resistance rates exceeding 40% were observed to KM in chicken-derived strains and to TC in swine- and chicken-derived strains. In contrast, resistance rates to ABPC were less than 1% in all cattle-, swine-, and chicken-derived strains. Resistance rates to CPFX, which belongs to the fluoroquinolone class of antibiotics important in human medicine, ranged from 1.3 to 8.8%. The resistance rate to VCM, which is important in human medicine, was 0.0%.

In 2021, among *Enterococcus* spp., *E. faecalis* ranged from 2.2% (5 out of 231) of cattle-derived strains to 37.3% (81 out of 217) of chicken-derived strains, and *E. faecium* ranged from 1.3% (3 out of 231) of cattle-derived strains to 11.1% (13 out of 117) of swine-derived strains. Resistance to CPFX-in *E. faecalis* was 0.0% (cattle-derived) to 8.3% (swine-derived), and in *E. faecium* was 33.3%, 23.1% and 34.8% in cattle-, swine- and chicken-derived strains, respectively, with higher rates among *E. faecium* from cattle and chicken.

Table 53. Resistance rates (%) of *Enterococcus* spp. from animal and poultry slaughterhouses

Agent*	BP	Animal species	2012	2014 †	2015	2016	2017	2018	2019	2020	2021
ABPC	16 §	Cattle	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		Swine	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		Chickens	0.0	0.6	0.0	0.0	0.0	0.0	0.8	0.5	0.5
DSM	128	Cattle	85.6	31.2	14.9	2.9	0.8	-	-	-	-
		Swine	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	13.5	3.1	8.6	2.2
		Swine	43.3	3.4	3.1	4.4	1.2	19.0	10.0	6.5	2.6
		Chickens	29.3	5.5	9.4	4.5	3.4	12.6	9.5	6.2	3.2
KM	128	Cattle	55.2	5.0	4.1	1.3	0.8	15.9	6.3	15.7	13.9
		Swine	56.2	20.5	31.3	17.6	22.0	35.4	21.3	33.1	19.7
		Chickens	68.4	37.0	47.0	41.4	41.9	61.6	49.2	48.2	40.6
OTC	16	Cattle	24.4	21.2	27.1	27.6	26.4	-	-	-	-
		Swine	61.9	54.5	59.4	64.8	58.5	-	-	-	-
		Chickens	72.2	58.0	63.0	66.2	52.0	-	-	-	-
TC	16 §	Cattle	-	-	-	-	-	24.7	24.3	20.6	25.1
		Swine	-	-	-	-	-	58.2	55.0	59.7	48.7
		Chickens	-	-	-	-	-	64.2	54.8	59.6	41.9
CP	32 §	Cattle	1.5	0.0	0.0	0.4	0.4	0.6	0.4	0.4	0.4
		Swine	17.5	17.0	10.4	15.4	14.6	15.2	11.3	16.1	10.3
		Chickens	13.5	8.8	7.2	10.2	8.8	9.3	12.7	9.8	6.9
EM	8 §	Cattle	5.0	3.8	1.5	2.5	2.1	1.8	2.4	3.7	4.3
		Swine	41.8	28.4	30.2	34.1	26.8	27.8	23.8	31.5	22.2
		Chickens	50.4	43.1	42.5	45.2	41.2	36.4	34.9	36.8	26.3
LCM	128	Cattle	27.9	3.1	0.7	2.5	2.1	1.8	2.0	2.2	3.9
		Swine	59.8	50.0	34.4	37.4	35.4	36.7	41.3	39.5	29.1
		Chickens	52.6	34.3	43.1	47.1	40.5	37.7	41.3	40.9	34.6
ERFX	4	Cattle	6.0	1.2	0.4	0.8	0.0	-	-	-	-
		Swine	22.7	9.1	2.1	1.1	3.7	-	-	-	-
		Chickens	9.8	3.9	13.3	3.8	2.7	-	-	-	-
CPFX	4 §	Cattle	-	-	-	-	-	2.4	1.6	0.4	1.3
		Swine	-	-	-	-	-	17.7	7.5	4.8	5.1
		Chickens	-	-	-	-	-	6.6	11.1	7.3	8.8
TS.	64	Cattle	2.0	2.3	0.7	2.1	2.5	1.8	2.4	2.2	4.3
		Swine	33.0	21.6	19.8	28.6	24.4	26.6	23.8	29.8	17.9
		Chickens	49.6	42.0	35.9	42.7	41.2	34.4	34.1	30.6	24.0
VCM	32	Cattle	-	-	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		Swine	-	-	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		Chickens	-	-	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Number of isolates tested (n)		Cattle	201	260	269	289	242	170	255	267	231
		Swine	194	88	96	91	82	79	80	124	117
		Chickens	133	181	181	157	148	151	126	193	217

The unit of BP is μg/mL.

* While AZM, SM, NA, BC and SNM were also included in the scope of the survey, the resistance rates were not listed because BP could not be established.

† The monitoring was not conducted on *Enterococcus* spp. derived from animal slaughterhouses in 2013.

§ BP follows CLSI Criteria.

-: Not under surveillance.

Table 54. Resistance rates (%) of *Enterococcus faecalis* from animal and poultry slaughterhouses

Agent*	BP	Animal species	2012	2014†	2015	2016	2017	2018	2019	2020	2021
ABPC	16§	Cattle	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		Swine	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		Chickens	0.0	0.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DSM	128	Cattle	90.6	36.4	35.7	12.5	0.0	-	-	-	-
		Swine	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	40.0	0.0	16.7	20.0
		Swine	76.5	12.5	15.4	8.7	7.7	31.0	35.7	17.9	4.2
		Chickens	35.6	9.9	14.3	6.3	3.5	15.1	15.0	7.0	4.9
KM	128	Cattle	71.9	9.1	14.3	0.0	0.0	46.7	0.0	25.0	40.0
		Swine	72.9	12.5	69.2	30.4	30.8	51.7	42.9	53.8	20.8
		Chickens	71.2	57.1	66.3	55.2	58.8	66.0	51.7	47.7	51.9
OTC	16	Cattle	31.3	27.3	28.6	37.5	10.0	-	-	-	-
		Swine	64.7	87.5	92.3	73.9	84.6	-	-	-	-
		Chickens	75.0	67.0	70.4	83.3	65.9	-	-	-	-
TC	16§	Cattle	-	-	-	-	-	26.7	25.0	12.5	100.0
		Swine	-	-	-	-	-	65.5	57.1	66.7	54.2
		Chickens	-	-	-	-	-	70.8	66.7	77.9	59.3
CP	32§	Cattle	9.4	0.0	0.0	12.5	10.0	6.7	25.0	4.2	20.0
		Swine	30.6	62.5	53.8	39.1	38.5	27.6	35.7	41.0	20.8
		Chickens	17.3	13.2	9.2	15.6	12.9	11.3	20.0	14.0	12.3
EM	8§	Cattle	21.9	9.1	0.0	0.0	10.0	0.0	25.0	8.3	60.0
		Swine	51.8	62.5	69.2	52.2	61.5	44.8	50.0	56.4	37.5
		Chickens	58.7	64.8	60.2	59.4	58.8	43.4	53.3	44.2	40.7
LCM	128	Cattle	34.4	9.1	0.0	0.0	10.0	0.0	25.0	4.2	60.0
		Swine	76.5	75.0	92.3	56.5	61.5	51.7	50.0	59.0	37.5
		Chickens	57.7	45.1	54.1	59.4	55.3	43.4	55.0	43.0	40.7
ERFX	4	Cattle	3.1	0.0	0.0	0.0	0.0	-	-	-	-
		Swine	5.9	0.0	7.7	0.0	0.0	-	-	-	-
		Chickens	2.9	1.1	0.0	2.1	0.0	-	-	-	-
CPFX	4§	Cattle	-	-	-	-	-	0.0	0.0	0.0	0.0
		Swine	-	-	-	-	-	3.4	7.1	5.1	8.3
		Chickens	-	-	-	-	-	2.8	3.3	0.0	4.9
TS.	64	Cattle	6.3	0.0	0.0	0.0	10.0	0.0	25.0	4.2	60.0
		Swine	50.6	62.4	69.2	52.2	61.5	44.8	50.0	56.4	37.5
		Chickens	57.7	65.9	53.1	59.4	60.0	43.4	55.0	44.2	40.7
VCM	32	Cattle	-	-	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		Swine	-	-	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		Chickens	-	-	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Strains tested (n)		Cattle	32	11	14	8	10	15	4	24	5
		Swine	85	8	13	23	13	29	14	39	24
		Chickens	104	91	98	96	85	106	60	86	81

The unit of BP is μg/mL.

* While AZM, SM, NA, BC and SNM were also included in the scope of the survey, the resistance rates were not listed because BP could not be established.

† The monitoring was not conducted on *Enterococcus* spp. derived from animal slaughterhouses in 2013.

§ BP follows CLSI Criteria.

-: Not under surveillance.

Table 55. Resistance rates (%) of *Enterococcus faecium* from animal and poultry slaughterhouses

Agent*	BP	Animal species	2012	2014 †	2015	2016	2017	2018	2019	2020	2021
ABPC	16 §	Cattle	0.0	0.0	0.0	0.0	0.0	-	0.0	0.0	0.0
		Swine	0.0	0.0	0.0	0.0	0.0	0.0	-	0.0	0.0
		Chickens	2.4	0.0	0.0	0.0	0.0	0.0	0.0	4.5	0.0
DSM	128	Cattle	22.7	33.3	0.0	25.0	0.0	-	-	-	-
		Swine	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	-	0.0	0.0	0.0
		Swine	0.0	0.0	0.0	0.0	0.0	50.0	-	0.0	7.7
		Chickens	3.6	2.8	3.2	10.0	9.1	0.0	0.0	4.5	0.0
KM	128	Cattle	34.1	33.3	16.7	0.0	50.0	-	0.0	16.7	100.0
		Swine	30.3	25.0	72.7	28.6	72.7	100.0	-	57.1	76.9
		Chickens	34.5	33.3	35.5	40.0	45.5	90.0	85.7	100.0	87.0
OTC	16	Cattle	9.1	0.0	16.7	0.0	0.0	-	-	-	-
		Swine	42.4	41.7	9.1	42.9	54.5	-	-	-	-
		Chickens	63.1	58.3	64.5	60.0	31.8	-	-	-	-
TC	16 §	Cattle	-	-	-	-	-	-	0.0	0.0	0.0
		Swine	-	-	-	-	-	50.0	-	28.6	46.2
		Chickens	-	-	-	-	-	60.0	57.1	72.7	26.1
CP	32 §	Cattle	0.0	0.0	0.0	0.0	0.0	-	0.0	0.0	0.0
		Swine	0.0	25.0	0.0	0.0	9.1	0.0	-	0.0	23.1
		Chickens	4.8	8.3	6.5	0.0	9.1	10.0	28.6	4.5	4.3
EM	8 §	Cattle	11.4	0.0	33.3	25.0	0.0	-	0.0	33.3	0.0
		Swine	15.2	58.3	54.5	57.1	45.5	0.0	-	14.3	46.2
		Chickens	32.1	30.6	35.5	20.0	27.3	40.0	28.6	50.0	30.4
LCM	128	Cattle	9.1	0.0	0.0	0.0	0.0	-	0.0	0.0	0.0
		Swine	39.4	50.0	9.1	28.6	27.3	0.0	-	14.3	30.8
		Chickens	31.0	19.4	29.0	20.0	27.3	20.0	28.6	40.9	30.4
ERFX	4	Cattle	36.4	0.0	16.7	25.0	0.0	-	-	-	-
		Swine	45.5	25.0	0.0	0.0	27.3	-	-	-	-
		Chickens	65.5	13.9	71.0	30.0	18.2	-	-	-	-
CPFX	4 §	Cattle	-	-	-	-	-	-	0.0	0.0	33.3
		Swine	-	-	-	-	-	0.0	-	28.6	23.1
		Chickens	-	-	-	-	-	20.0	42.9	36.4	34.8
TS.	64	Cattle	9.1	0.0	0.0	0.0	0.0	-	0.0	0.0	0.0
		Swine	12.1	16.7	0.0	28.6	18.2	0.0	-	0.0	15.4
		Chickens	26.2	19.4	22.6	20.0	27.3	20.0	28.6	18.2	21.7
VCM	32	Cattle	-	-	0.0	0.0	0.0	-	0.0	0.0	0.0
		Swine	-	-	0.0	0.0	0.0	0.0	-	0.0	0.0
		Chickens	-	-	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Strains tested (n)		Cattle	44	6	6	4	4	0	1	6	3
		Swine	84	12	11	7	11	2	0	7	13
		Chickens	64	36	31	10	22	10	7	22	23

The unit of BP is μg/mL.

* While AZM, SM, NA, BC and SNM were also included in the scope of the survey, the resistance rates were not listed because BP could not be established.

† The monitoring was not conducted on *Enterococcus* spp. derived from animal slaughterhouses in 2013.

§ 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, and MEPM was added in 2018, bringing the number monitored to 13 agents. Among chicken-derived strains in 2021 resistance to TC exceeding 70%, resistance to KM and SM exceeding 60%, and resistance to ST exceeding 40% were observed. On the other hand, resistance to CEZ was less than 5% and no resistance to GM was observed. In the realm of critically important antimicrobials for human medicine, the rate of resistance to CTX and CPFX was less than 3.0% and resistance to CL or MEPM was 0.0%.

The *Salmonella* serotypes most isolated from poultry slaughterhouses from 2015 to 2020 were *S.* Schwarzengrund, *S.* Infantis and *S.* Typhimurium. In a comparison of *Salmonella* serotypes isolated from poultry slaughterhouses with those isolated from food and from humans (source: Nippon AMR One Health Report 2022: Table 19) (Table 58, Figure 1), the same trends were observed in *Salmonella* serotypes isolated from poultry slaughterhouses as in those isolated from food. The top two serotypes isolated from poultry slaughterhouses were the same as those isolated from food, respectively accounting for 88.8% and 75.4% 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 two serotypes isolated from poultry slaughterhouses accounting for 23.8% of human-derived strains, which suggested the possibility that there isa variety of origin other than poultry or their food products. Comparison of the resistance rates of the top two serotypes *S.* Schwarzengrund and *S.* Infantis, which account for most of the poultry slaughterhouse-derived strains, between poultry slaughterhouse-derived and food-derived strains and human strains (Table 59, Fig. 2) (source: Nippon AMR One Health Report 2022: Table 29) showed that KM, SM, and TC resistance rates were similar between food- and poultry slaughterhouse-derived strains.

In *S.* Schwarzengrund, similarities were observed in the resistance rates of human-derived strains as well as those of poultry slaughterhouse- and food-derived strains. On the other hand, the human-derived *S.* Infantis strains showed different resistance rates compared to the strains of other isolates, suggesting that the human-derived *S.* Infantis may have originated from sources other than chickens and foods.

Table 56. Resistance rates (%) of *Salmonella* spp. from poultry slaughterhouses

Agent	BP	Animal species	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
ABPC	32*	Chickens	31.9	22.9	17.2	13.0	13.5	8.0	6.8	5.6	1.8	11.9
CEZ	32 (8* from 2016)	Chickens	7.4	5.9	3.1	1.6	7.7	3.6	3.4	3.7	1.8	3.8
CTX	4*	Chickens	7.4	5.1	2.3	1.6	1.9	1.8	2.6	1.9	0.9	2.5
MEPM	4*	Chickens	—	—	—	—	—	—	0.0	0.0	0.0	0.0
SM	32	Chickens	77.7	84.7	85.9	76.4	77.9	60.7	77.8	33.6	48.6	69.9
GM	16*	Chickens	0.0	0.0	0.0	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	75.7	68.8	63.2
TC	16*	Chickens	74.5	82.2	85.2	83.7	82.7	77.7	77.8	69.2	73.4	78.3
CP	32*	Chickens	0.0	0.8	1.6	1.6	0.0	0.9	1.7	0.9	0.0	0.9
CL	16 (4* from 2016)	Chickens	0.0	0.0	0.0	0.0	0.0	0.0	0.9	1.9	0.0	0.4
NA	32*	Chickens	29.8	19.5	17.2	15.4	12.5	17.0	18.8	8.4	11.9	17.0
CPFX	4 (1* from 2016)	Chickens	0.0	0.0	0.0	0.0	0.0	0.0	0.9	0.9	0.9	0.4
ST	76/4*	Chickens	31.9	48.3	51.6	57.7	56.7	55.4	53.0	52.3	45.9	49.5
Strains tested (n)		Chickens	94	118	128	123	104	112	117	107	109	129

The unit of BP is μg/mL.

* BP follows CLSI Criteria.

Table 57. Serotypes of *Salmonella enterica* derived from poultry slaughterhouses (2015-2021)

Serotypes	Number of strains isolated	(%)
Schwarzengrund	550	68.7
Infantis	161	20.1
Typhimurium	35	4.4
Agona	12	1.5
Manhattan	25	3.1
Others	18	2.2
Total	801	100.0

Table 58. Serotypes of *Salmonella enterica* derived from poultry slaughterhouses, food, and humans (2015-2021)

From poultry slaughterhouses (n=801)	%
Schwarzengrund	68.7
Infantis	20.1
Typhimurium	4.4
Manhattan	3.1
Agona	1.5
Others	2.2
Total	100.0

From food (n=855)*	%
Schwarzengrund	52.5
Infantis	22.9
Manhattan	7.6
Heidelberg	2.1
Enteritidis	2.1
Others	12.8
Total	100.0

From humans (n=2,093)*	%
Enteritidis	12.7
4:i:-	11.1
Infantis	9.4
Thompson	8.0
Saintpaul	6.3
Typhimurium	6.3
Schwarzengrund	5.3
Newport	2.9
Stanley	2.9
Agona	2.3
Others	32.9
Total	100.0

*Source: Nippon AMR One Health Report 2022: Table 19

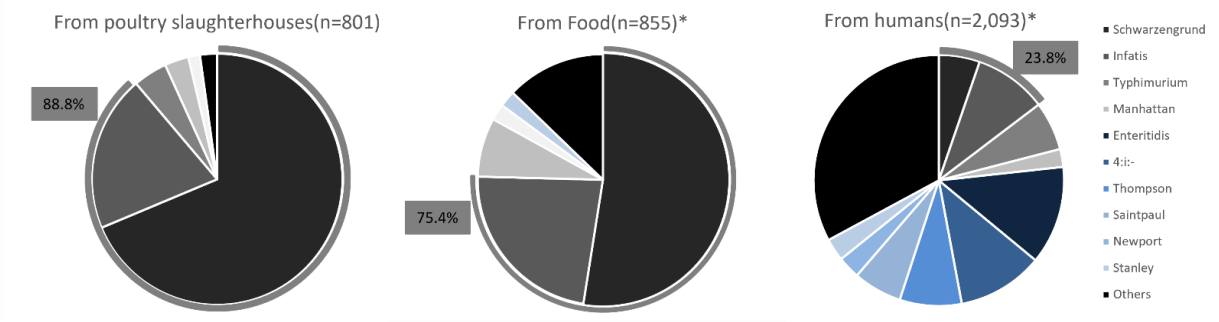

Figure 1. Proportions of the top 2 serotypes of *Salmonella* enterica derived from poultry slaughterhouses isolated in food and humans (2015-2021)
(figures for proportions in human-derived and food-derived strains are quoted from Nippon AMR One Health Report 2022: Table 19)

Table 59. Resistance rates (%) of *S*. Infantis and *S*. Schwarzengrund strains isolated from poultry slaughterhouses (chickens), food, and humans (2015-2021)

	Infantis			Schwarzengrund		
	Chicken (n=161)	Food (n=196)*	Humans (n=196)*	Chicken (n=550)	Food (n=449)*	Humans (n=110)*
ABPC	8.2	11.7	2.6	2.2	5.1	2.7
GM	0.0	0.5	0.0	0.0	0.0	0.0
KM	41.8	39.3	13.3	84.0	79.5	63.6
SM	73.3	73.0	30.1	67.3	78.8	68.2
TC	78.8	77.6	36.7	81.3	86.6	68.2
CP	0.7	2.6	2.0	1.1	7.8	1.8
CTX	6.5	6.1	1.5	0.6	0.7	1.8
NA	6.2	6.6	6.6	11.1	20.5	12.7
CPFX	0.0	0.0	0.0	0.8	0.2	0.0

*Source: Nippon AMR One Health Report 2022: Table 29

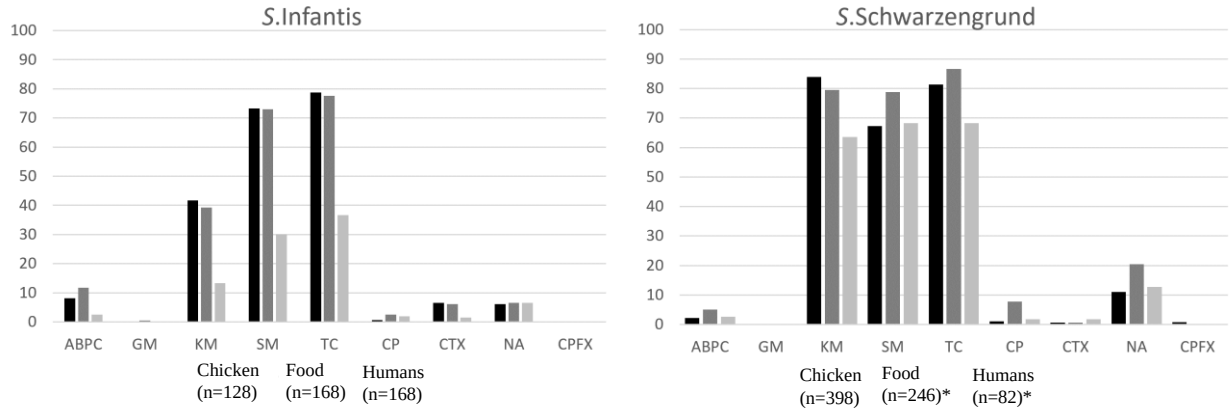

Figure 2. Resistance rates of *S*. Infantis and *S*. Schwarzengrund strains derived from humans, food, and poultry slaughterhouses (2015-2021)
(Figures for resistance rates in human-derived and food-derived strains are quoted from Nippon AMR One Health Report 2022: Table 29)

2) Aquatic animal farming

Source: Japanese Veterinary Antimicrobial Resistance Monitoring System (JVARM)

For the monitoring and surveillance of antimicrobial resistance in the marine aquaculture sector under the JVARM, antimicrobial susceptibility monitoring was conducted focusing on *Lactococcus garvieae*, *Photobacterium damselae* subsp. *piscicida* and *Vibrio* spp. that were derived from diseased fish, and on *Vibrio parahaemolyticus* that was 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 4 to 6 prefectures per year, increasing to 8 in 2017, 12 in 2018, and 11 prefectures provided strains each year from 2019 to 2021.

To further enhance surveillance of trends in antimicrobial resistance in the marine aquaculture sector, the scope of surveillance was expanded to all farmed fishes in 2017, and antimicrobial susceptibility monitoring of *Lactococcus garvieae* and *Vibrio* spp. is now being carried out.

In antimicrobial susceptibility tests, MIC was measured using a broth microdilution method or an agar plate dilution method compliant with the CLSI Guidelines. For antimicrobial agents with a BP established by the CLSI, antimicrobial susceptibility was interpreted using the CLSI Criteria. The BPs of the other antimicrobial agents were determined microbiologically (midpoint of a bimodal MIC distribution).

Diseased fish-derived bacteria

i. *Lactococcus garvieae* derived from diseased fish

The monitoring of antimicrobial resistance was conducted on four agents that had been approved as fisheries medicine from 2011 to 2021. In 2021, resistance to LCM was 66.2%. Resistance rates remained low at 14.5% for EM in 2021. As the MIC distribution of FF was not bimodal, the BP could not be established, and the resistance rate could therefore not be calculated. However, all strains had low MICs (≤4 μg/mL) (Table 60).

Table 60. Resistance rates (%) of *Lactococcus garvieae*

Agent*1	BP (-2019)	BP (2020-)	2011	2012	2013	2014	2015	2016	2017*2*3	2018	2019	2020	2021
EM	8	16	0.0	10.3	0.0	0.0	2.2	1.7	1.9	0.0	3.1	0.6	14.5
LCM	8	16	92.6	76.9	68.2	40.0	53.3	58.3	61.0	31.5	54.6	53.8	66.2
OTC	8	16	0.0	12.8	0.0	0.0	2.2	1.7	0.0	0.0	2.6	0.6	1.0
Strains tested (n)			27	39	22	25	45	60	105	149	194	158	207

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 (Amberjacks)

The monitoring of antimicrobial resistance from 2011 to 2016 was conducted on five agents that had been approved as a fisheries medicine against pseudotuberculosis. 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 OA. However, the resistance rate remained at 7.1% or lower both for BCM and for FOM. Although the proportion of FF-resistant strains was not calculated given that no bimodal MIC distribution was observed, MICs were low (MIC ≤ 1 μg/mL) in all strains, suggesting that susceptibility was maintained. The strains tested in 2015 showed low MICs for all the tested agents (Table 61).

Table 61. Resistance rates (%) of 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 four agents that had been approved as a fisheries medicine against vibriosis has been carried out since 2017 with respect of strains derived from diseased fish. In 2021, resistance to OTC was 4.2%. FF was not bimodal and almost all bacterial strains showed low MICs (MIC ≤ 4 μg/ml). Although the MIC distribution of OA was not bimodal, all strains showed low MICs (MIC ≤ 0.5 μg/ml), which suggested that susceptibility to these agents was maintained. SMMX, however, did not show a clear bimodal MIC distribution, so the resistance rate could not be calculated (Table 62).

Table 62. Trends in resistance rates among *Vibrio* spp. (%)

Agent*	BP (-2019)	BP (2020-)	2017	2018	2019	2020	2021
OTC	8	16	12.8	15.7	0.0	11.9	4.2
Strains tested (n)			39	51	40	42	71

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 fisheries medicine (EM, LCM, OTC, OA, and FF) was carried out using 53 and 50 strains derived from aquaculture environments in 2011 and 2012, respectively.

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, however, were low (EM: MIC ≤ 2 μg/mL、OTC and FF: MIC ≤ 1 μg/mL, OA: MIC ≤ 0.5 μg/mL) in all strains, excluding lincomycin (32 ≤ MIC ≤ 256 μg/mL for LCM), which suggested that the antimicrobial susceptibility was maintained to these agents.

Healthy fish-derived bacteria

Monitoring of healthy fish-derived bacteria (*Lactococcus garvieae* and *Vibrio spp*.) was initiated in 2021 on a trial basis. The number of fish farms sampled was 10, and each farm sampled 10 fish.

i. *Lactococcus garvieae*, the causative agent of streptococci from healthy cultured yellowtail

The investigation of the healthy cultured yellowtail-derived strains caught in 2021 were piloted. Although this organism is pathogenic and its life cycle in seawater is unknown, based on the results of this year's survey, the organism was not isolated in 6 of the 10 facilities. Although *L. garvieae* was sampled due to the lack of suitable Gram-positive indicator bacteria, further discussion is needed on the sampling method, species selection, or isolation method.

ii. *Vibrio* spp. from healthy cultured yellowtail

The investigation of the strains derived from healthy cultured yellowtail caught in 2021 was piloted for four agents approved for use in fisheries against Vibrio disease.

The BPs adopted the values established in the 2020 survey of diseased fish origin (Table 62). *Vibrio* spp. was isolated from all aquaculture farms, as some species of *Vibrio* spp. are pathogenic to fish and other organisms, while others are non-pathogenic and endemic in seawater. Of the 169 isolates, 10.7% were resistant to OTC, and all strains had low MICs (≤8 μg/mL for FF and ≤2 μg/mL for OA), although BPs could not be determined for FF and OA because the MIC distributions were not bimodal. On the other hand, SMMX also did not show distinct bimodality in MIC distribution and BP could not be determined.

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 2017, as part of efforts to strengthen monitoring under the AMR Action Plan. Monitoring of antimicrobial resistance in bacteria derived from diseased animals, unlikely from healthy animals, has the potential to be affected using 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 were performed using a broth microdilution method according to the CLSI criteria with respect of the bacterial strains collected. For agents with a BP indicated by the CLSI, antimicrobial 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).

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 based on the number of notifications of veterinary clinics (small animal and other animals) establishment received.

Samples of *E. 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*

In 2022, as in the years before, the rates of resistance to ABPC and NA were high, ranging from 47.9 to 55.1% among the surveyed agents. On the other hand, the rates of resistance to GM, KM, and CP, and to SM and ST in strains isolated from cats were less than 20%. The rates of resistance to critically important antimicrobials for human medicine in dog- and cat-derived strains respectively were as follows: 25.9% and 24.3% to CTX, 37.3% and 29.6% to CPFX, and both 0.0% to CL and MEPM.

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

Agent	BP	Animal species	2017	2018	2019	2020	2021	2022
ABPC	32*	Dog	55.3	63.0	51.1	50.3	54.4	53.5
		Cat	64.0	65.6	60.2	56.5	59.4	47.9
CEZ	32*	Dog	31.2	47.4	30.3	31.1	32.8	30.3
		Cat	37.5	49.5	32.0	29.8	33.5	32.0
CEX	32†	Dog	31.7	42.9	31.5	32.8	32.8	32.4
		Cat	41.9	47.3	31.3	31.7	37.1	32.5
CTX	4*	Dog	26.1	41.6	26.4	27.1	27.8	25.9
		Cat	33.8	39.8	26.6	26.1	29.4	24.3
MEPM	4*	Dog	0.0	0.0	0.0	0.0	0.0	0.0
		Cat	0.0	0.0	0.0	0.0	0.0	0.0
SM	32†	Dog	29.6	29.9	20.2	27.1	25.6	20.5
		Cat	32.4	34.4	28.9	19.3	23.5	17.8
GM	16*	Dog	14.1	18.8	12.9	13.0	12.2	11.9
		Cat	12.5	15.1	9.4	9.9	17.1	10.7
KM	64*	Dog	6.5	7.8	5.1	5.6	5.6	7.6
		Cat	8.1	12.9	7.0	3.7	6.5	4.1
TC	16*	Dog	28.1	27.3	21.3	23.2	20.6	20.0
		Cat	24.3	28.0	26.6	16.8	24.1	23.1
CP	32*	Dog	12.6	16.9	11.8	7.9	12.8	5.4
		Cat	13.2	15.1	7.8	5.0	8.2	8.3
CL	4*	Dog	1.0	0.0	0.0	0.0	0.0	0.0
		Cat	0.0	1.1	0.0	0.6	0.6	0.0
NA	32*	Dog	61.8	72.7	56.2	58.8	56.1	55.1
		Cat	58.8	68.8	46.9	55.9	54.7	53.3
CPFX	4* (1*since 2018)	Dog	43.2	55.2	38.8	42.4	40.6	37.3
		Cat	39.0	50.5	37.5	38.5	41.2	29.6
ST	76/4*	Dog	24.6	27.9	17.4	19.2	18.3	24.3
		Cat	22.1	34.4	22.7	14.3	21.8	16.0
Strains tested (n)		Dog	199	154	178	177	180	185
		Cat	136	93	128	161	170	169

The unit of BP is μg/mL.

* BP follows CLSI Criteria.

† BP follows EUCAST Criteria.

ii. *Klebsiella* spp.

Of the *Klebsiella* spp., *K. pneumoniae* was the most collected, and *K. oxytoca* was also collected. In 2022, resistance exceeding 40% was observed to NA and CPFX in dog- and cat-derived strains, and to CEZ, CEX, 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 in dog- and cat-derived strains to critically important antimicrobials for human medicine, resistance to CTX was 33.7% and 60.9%, respectively, resistance to CPFX was 42.7% and 68.1%, respectively, and resistance to CL was 0.0%, 2.9%, respectively. Resistance to MEPM was both 0.0%.

Table 64. Trends in resistance rates (%) of *Klebsiella* spp. derived from diseased dogs and cats

Agent	BP	Animal species	2017	2018	2019	2020	2021	2022
CEZ	32*	Dog	47.2	51.0	42.0	45.8	44.0	37.1
		Cat	84.6	90.0	67.6	61.3	69.3	63.8
CEX	32†	Dog	44.4	46.9	42.0	45.8	44.0	33.7
		Cat	84.6	80.0	62.2	58.1	64.0	63.8
CTX	4*	Dog	41.7	36.7	34.6	34.9	37.4	33.7
		Cat	80.8	75.0	56.8	48.4	56.0	60.9
MEPM	4*	Dog	0.0	0.0	0.0	0.0	0.0	0.0
		Cat	0.0	0.0	0.0	0.0	0.0	0.0
SM	32†	Dog	26.4	34.7	29.6	31.3	30.8	32.6
		Cat	57.7	55.0	59.5	41.9	52.0	46.4
GM	16*	Dog	26.4	28.6	21.0	28.9	24.2	30.3
		Cat	61.5	55.0	40.5	33.9	44.0	49.3
KM	64*	Dog	8.3	12.2	6.2	10.8	9.9	9.0
		Cat	23.1	20.0	13.5	12.9	9.3	18.8
TC	16*	Dog	33.3	42.9	30.9	33.7	26.4	29.2
		Cat	57.7	65.0	48.6	40.3	56.0	50.7
CP	32*	Dog	25.0	32.7	19.8	25.3	20.9	21.3
		Cat	26.9	45.0	16.2	25.8	26.7	27.5
CL	4*	Dog	1.4	0.0	0.0	0.0	0.0	0.0
		Cat	3.8	0.0	0.0	1.6	4.0	2.9
NA	32*	Dog	51.4	61.2	46.9	48.2	54.9	46.1
		Cat	84.6	95.0	81.1	54.8	77.3	75.4
CPFX	4* (1 since 2018)	Dog	44.4	57.1	46.9	44.6	49.5	42.7
		Cat	84.6	90.0	75.7	56.5	73.3	68.1
ST	76/4*	Dog	41.7	46.9	37.0	39.8	38.5	34.8
		Cat	76.9	70.0	56.8	43.5	54.7	56.5
Strains tested (n)		Dog	72	49	81	83	91	89
		Cat	26	20	37	62	75	69

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* was also collected.

For *S. pseudintermedius*, dog- and cat-derived strains have shown resistance rates exceeding 50% to all agents except GM and CP since the start of the surveillance in 2017 and 2022 with resistance rates exceeding 50%, except for the GM resistance rate for dog-derived strains. 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 PCG, MPIPC, CEX, CFX, EM, AZM, and CPFX was observed to exceed 50% in 2022. On the other hand, the resistance rate to SM was low (4.8%). Rates of resistance to CTX, AZM, and CPFX, which are critically important antimicrobials for human medicine, were observed to be more than 40%.

Table 65. Resistance rates (%) of *Staphylococcus pseudintermedius* derived from diseased dogs and cats

Agent*	BP	Animal species	2017	2018	2019	2020	2021	2022
PCG	0.25†	dog	-	-	97.4	95.9	97.4	98.9
		cat	-	-	97.6	98.0	98.4	95.7
MPIPC	0.5†	dog	58.2	56.6	62.8	51.4	56.6	60.2
		cat	68.6	81.8	81.0	77.6	78.7	76.1
GM	16†	dog	26.2	54.2	64.1	25.7	40.8	44.3
		cat	13.7	63.6	52.4	44.9	50.8	63.0
TC	16†	dog	62.3	67.5	66.7	73.0	71.1	65.9
		cat	52.9	81.8	85.7	71.4	85.2	73.9
CP	32†	dog	43.4	49.4	60.3	58.1	55.3	59.1
		cat	64.7	72.7	83.3	67.3	82.0	65.2
EM	8†	dog	67.2	74.7	79.5	77.0	71.1	77.3
		cat	70.6	86.4	95.2	79.6	91.8	89.1
AZM	8†	dog	67.2	74.7	79.5	77.0	71.1	77.3
		cat	66.7	86.4	95.2	79.6	91.8	91.3
CPFX	4†	dog	64.8	75.9	75.6	74.3	73.7	79.5
		cat	88.2	100.0	97.6	93.9	91.8	97.8
Strains tested (n)		dog	122	83	78	74	76	88
		cat	51	22	42	49	61	46

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

Agent	BP	Animal species	2017	2018	2019	2020	2021	2022
PCG	0.25	cat	-	-	90.0	84.6	96.3	81.0
MPIPC	4 †	cat	61.9	70.6	70.0	65.4	51.9	50.0
CEZ	4 $	cat	61.9	64.7	66.7	57.7	44.4	47.6
CEX	16 $	cat	61.9	70.6	70.0	61.5	59.3	52.4
CFX	8 $	cat	61.9	64.7	70.0	61.5	51.9	50.0
CTX	8 $	cat	61.9	64.7	70.0	61.5	55.6	47.6
SM	32 $	cat	4.8	5.9	0.0	3.8	3.7	4.8
GM	16 †	cat	47.6	58.8	36.7	57.7	22.2	31.0
TC	16 †	cat	14.3	41.2	43.3	38.5	14.8	21.4
CP	32 †	cat	0.0	0.0	0.0	0.0	3.7	0.0
EM	8 †	cat	66.7	76.5	70.0	61.5	70.4	52.4
AZM	8 †	cat	66.7	76.5	70.0	61.5	70.4	52.4
CPFX	4 †	cat	61.9	76.5	83.3	73.1	63.0	59.5
Strains tested (n)		cat	21	17	30	26	27	42

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 2022, rates of resistance to TC were the highest in both dog- and cat-derived strains (65.9% in dogs and 66.9% in cats), followed by EM (43.4% in dogs and 38.0% in cats), and the resistance rate to ABPC in dog-derived strains and to CP in dog- and cat-derived strains were less than 20%. For CPFX, an important antimicrobial agent in human medicine, 34.1% and 40.5% of dog- and cat-derived strains were found to be resistant, respectively. Measurement of VCM as a test agent began in 2019, and the resistance rates of both dog- and cat-derived strains were 0.0%.

Table 67. Resistance rates (%) of *Enterococcus* spp. derived from diseased dogs and cats

Agent*	BP	Animal species	2017	2018	2019	2020	2021	2022
ABPC	16†	dog	26.7	20.5	20.0	14.6	13.3	14.8
		cat	17.3	31.6	33.0	26.4	24.1	24.5
GM	32§	dog	16.8	15.4	25.2	25.7	27.8	33.0
		cat	14.3	24.6	25.2	25.7	27.1	20.9
TC	16†	dog	65.6	67.9	68.9	64.9	63.9	65.9
		cat	70.4	73.7	64.1	68.2	65.9	66.9
CP	32†	dog	20.6	14.1	18.5	14.6	13.3	14.8
		cat	20.4	15.8	8.7	18.2	15.3	12.3
EM	8†	dog	61.8	39.7	43.0	45.0	46.1	43.4
		cat	41.8	54.4	39.8	48.0	45.9	38.0
CPFX	4†	dog	42.7	28.2	31.1	25.1	27.8	34.1
		cat	34.7	49.1	43.7	40.5	40.6	40.5
VCM	32†	dog	-	-	0.0	0.0	0.0	0.0
		cat	-	-	0.0	0.0	0.0	0.0
Strain tested (n)		dog	131	78	135	171	180	182
		cat	98	57	103	148	170	163

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 2002) was used.

Bacterial strains from healthy dogs and cats

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 based on the number of notifications of veterinary clinics (small animals 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. *E. coli* and *Enterococcus* spp. were then isolated from the samples, identified, and performed antimicrobial susceptibility tests.

i. *Escherichia coli*

In 2022, healthy dog- and cat-derived strains, as in previous surveys, showed a trend toward higher resistance rates to ABPC and NA among the agents surveyed than to the other agents, while resistance rates to the other agents (see Table 68) were all less than 20%. The rates of resistance to critically important antimicrobials for human medicine in dog- and cat-derived strains were as follows: 8.8% and 7.7% to CTX, and 10.5% and 7.1% to CPFX, 0.0% and 0.6% to CL, while the resistance rates to MEPM were both 0.0%. In all agents in which resistant strains had been found, resistance rates of *E. coli* derived from healthy dogs and cats were lower than that from diseased dogs and cats collected in the same year.

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

Agent	BP	Animal species	2018	2019	2020	2021	2022
ABPC	32*	dog	33.8	23.3	29.5	17.5	28.1
		cat	28.5	27.1	18.5	21.7	25.4
CEZ	32*	dog	17.2	11.4	17.8	10.4	14.6
		cat	17.1	13.3	7.5	9.9	13.6
CEX	32†	dog	17.9	11.4	17.1	9.7	14.0
		cat	18.4	13.3	8.9	10.6	14.8
CTX	4*	dog	13.2	8.8	13.0	7.8	8.8
		cat	10.8	6.4	2.7	7.5	7.1
MEPM	4*	dog	0.0	0.0	0.0	0.0	0.0
		cat	0.0	0.0	0.0	0.0	0.0
SM	32†	dog	19.2	13.0	14.4	8.4	13.5
		cat	11.4	11.7	8.9	11.2	7.7
GM	16*	dog	3.3	2.6	8.2	1.9	3.5
		cat	2.5	4.3	3.4	4.3	2.4
KM	64*	dog	5.3	3.6	4.1	2.6	2.9
		cat	1.9	3.2	3.4	3.1	2.4
TC	16*	dog	16.6	13.0	12.3	8.4	11.1
		cat	10.8	10.1	8.2	8.1	3.6
CP	32*	dog	4.6	5.7	5.5	3.2	4.7
		cat	1.3	3.7	1.4	2.5	1.2
CL	4*	dog	0.0	0.0	0.0	0.0	0.0
		cat	0.0	0.0	0.0	0.0	0.6
NA	32*	dog	27.8	20.7	22.6	10.4	19.3
		cat	24.7	28.7	17.8	17.4	20.1
CPFX	1*	dog	18.5	8.8	12.3	7.1	10.5
		cat	12.0	13.3	4.8	7.5	7.1
ST	76/4*	dog	13.2	7.8	11.6	5.8	11.1
		cat	12.0	9.6	5.5	7.5	6.5
Strains tested (n)		dog	151	193	146	154	171
		cat	158	188	146	161	169

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*, and *E. casseliflavus* were also collected. In strains isolated from dogs and cats in 2022, the highest rate of resistance was to TC, followed by EM, while rates of resistance to the other antimicrobials were all less than 20%. The rates of resistance to critically important antimicrobials for human medicine CPFX in dog- and cat-derived strains were 15.8 and 8.6%, and both 0.0% to VCM.

Table 69. Resistance rates (%) of *Enterococcus* spp. derived from healthy dogs and cats

Agent*	BP	Animal species	2018	2019	2020	2021	2022
ABPC	16 †	dog	6.9	1.9	5.4	0.0	2.9
		cat	2.2	3.4	1.3	1.2	3.4
GM	32 §	dog	12.4	7.0	14.0	10.2	9.9
		cat	11.1	15.7	22.1	11.9	6.9
TC	16 †	dog	55.9	41.8	43.4	47.7	45.6
		cat	48.9	61.8	44.2	58.3	47.4
CP	32 †	dog	15.9	10.1	10.1	11.7	11.1
		cat	11.1	14.6	14.3	15.5	6.0
EM	8 †	dog	32.4	23.4	27.9	23.4	28.1
		cat	34.4	34.8	32.5	38.1	29.3
CPFX	4 †	dog	13.8	5.7	10.1	5.5	15.8
		cat	14.4	13.5	10.4	4.8	8.6
VCM	32 †	dog	0.0	0.0	0.0	0.0	0.0
		cat	0.0	0.0	0.0	0.0	0.0
Strains tested (n)		dog	145	158	129	128	171
		cat	90	89	77	84	116

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 *E. 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 *Tokara-Ushi*); and 2 strains from 2 Amami rabbits) within Japan between 2013 and 2017 (Table 70). Strains isolated from deer and wild boar demonstrated resistance to eight agents, while those isolated from small mammals showed resistance to 10 agents. Resistant *E. coli* was observed in 5.9% of strains isolated from deer, with resistance to TC (4.4%) highest, followed by CL (1.5%), ABPC, and 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 the case of small mammals, most of antimicrobial-resistant strains were observed in strains from facilities related to food-producing animals, with resistance to ABPC, ST, TC, and NA observed to be more than 10%. However, resistance to only two 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. ESBL-producing bacteria 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. 848 *E. coli* isolates from wild deer from 2016 to 2019 also showed a low rate of agent resistance (9 isolates, 1.1%), although the antimicrobials tested varied (Table 71). Thus, 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.

In addition, 135 strains of *E. coli* from the Amami rabbit inhabiting a remote island (Amami Oshima) from 2017 to 2020 were susceptible to the antimicrobials tested. Future research is expected to determine whether the Amami rabbit, which mainly feeds on grasses and trees, has less opportunity to receive resistant bacteria from humans, domestic animals, and even other wildlife.

Among 144 *E. coli* strains isolated from common cormorants caught in Gunma, Gifu, Shiga, and Oita prefectures from 2018 to 2019, 5.6% were resistant, and resistance was observed to ABPC (3.5%), TC (2.8%), NA (1.4%), CPFX (0.7%), CL (0.7%), CP (1.4%), and ST (1.4%) (Table 71). In 110 *E. coli* isolates from white-fronted goose feces collected in Miyajima-numa (Hokkaido, Japan) in 2019, one (0.9%) was resistant (ABPC-CEZ resistant) and carried a plasmid-mediated AmpC β-lactamase gene (bla_{ACC}) (Table 71). Although it must be taken into account that the fact that the common cormorant is a resident bird and the white-fronted goose is a migratory bird affects the distribution of resistant strains, attention must be paid to the spread of resistant bacteria and contamination of the aquatic environment through wild waterfowl, as fluoroquinolone-resistant and transmissible *β*-lactamase-producing strains were isolated from wild waterfowl.

Seven-hundred fifty *E. coli* strains isolated from the feces of 274 (75%) of 366 wild animals in Japan between 2018 and 2021 (517 isolates from 189 of 243 deer, 33 isolates from 12 of 43 nutria, 61 isolates from 22 of 22 masked palm civets, 54 isolates from 18 of 18 wild boars, 24 isolates from 8 of 8 raccoon dogs, 9 isolates from 5 of 5 badgers, 11 isolates from 4 of 4 weasels, 11 isolates from 4 of 4 foxes, 7 isolates from 4 of 4 small Japanese field mouse, 9 isolates from 3 of 3 Japanese macaques, 2 isolates from of 1 of 2 raccoons, 6 isolates from 2 of 2 wild cats, 3 isolates from 1 of 1 bear, 3 isolates from 1 of 1 marten) were tested for antimicrobial susceptibility.

Antimicrobial resistance was found in *E. coli* from deer (5.4%, 28/517), masked palm civet (1.6%, 1/61), wild boar (7.4%, 4/54), badger (11%, 1/9), fox (9.1%, 1/11), Japanese monkey (11.1%, 1/9) and raccoon (50%, 1/2). Resistance was observed in five agents in the fox-derived strain, four drugs in the deer-derived strain, and one drug in the masked palm civet, wild boar, Japanese macaque and common raccoon-derived strains (Table 72). Overall, tetracycline (TC, 5.4%) resistance was the highest, and resistance to six other drugs was observed. The CIP-resistant strains found in foxes were multidrug-resistant strains to ABPC, TC, and CP.

CTX-resistant and quinolone-resistant *E. coli* were isolated on the DHL agar medium containing antimicrobials (Table 73). CTX-resistant *E. coli* isolated on cephalosporin (CEZ, CEX, or CTX)-containing media were isolated from 5 of 366 (1.4%, 14 strains). Isolates were from 2 of 243 deer (0.8%, 6 strains), 1 of 6 badgers (16.7%, 2 strains), 1 of 4 foxes (25%, 3 strains) and 1 of 2 raccoons (50%, 2 strains). One strain from foxes was an AmpC *β*-lactamase-producing strain (CMY-2), while the others were ESBL-producing strains (CTX-M-27, CTX-M-55, and CTX-M-1). Thirty-five strains of quinolone-resistant *E. coli* were isolated from 17 of 366 (4.6%) specimens on NA-containing media and the animals were deer (10, 4.1%), masked palm civet (1, 13.6%), raccoon dog (1, 12.5%), fox (2, 50%) and raccoon (1, 50%). Quinolone-resistant strains showed mutations in the quinolone resistance-determining region (QRDR) of DNA gyrase or topoisomerase IV, and some strains (1 deer, 2 foxes) carried a plasmid-mediated quinolone resistance gene (*qnrB19*).

Recently, a study using an antimicrobial-containing isolation medium for wildlife in urban areas was reported (Table 73): 20 strains of CTX-resistant *E. coli* were isolated on CTX-containing medium from 20 of 80 (25%) raccoon dogs captured in Kanagawa Prefecture in 2016-2017. The breakdown of *β*-lactamases produced was 18

isolates had CMY-2 (n=7), CTX-M-14 (n=5), CTX-M-2 (n=2), CTX-M-1 (n=1), CTX-M-55 (n=1), DHA-1 (n=1), 1 isolate had CMY-2 and CTX-M-14, and 1 was unknown. In 2018, quinolone-resistant *E. coli* were isolated using NA-containing media from deer faecal samples in urban areas, mainly in Nara Park. NA-resistant *E. coli* were isolated from 41 of 59 (69.5%) deer, and NA-resistant *E. coli* isolated from 22 of them were also resistant to fluoroquinolones. In this area, antimicrobial-resistant *E. coli* with similar genotypes were observed in several deer species, suggesting a high distribution rate of resistant bacteria through deer-deer transmission (intra-species transmission). Resistant *E. coli* was also isolated from deer feces collected in urban areas, primarily Nara Park in 2019-2020, rural areas neighboring Nara Park around urban areas in 2018-2021, and mountainous areas in the prefecture in 2019, using cephalexin-containing and NA-containing media. CTX-resistant *E. coli* was isolated from deer in urban areas (24.3%, 35/ 144) and deer in rural areas (4.3%, 1/23), but not from deer in mountainous areas (0/30). Regarding quinolone-resistant *E. coli*, CPFX-resistant *E. coli* was isolated from deer in urban areas (11.1%, 16/144) and rural areas (4.3%, 1/23), but not from deer in mountain areas (0/30). The genotypes of resistant *E. coli* carried by multiple deer in urban areas and deer in rural areas were different, and no dissemination of resistant *E. coli* from deer in urban area to those in rural area was observed.

Table 70. Resistance rates (%) of *Escherichia coli* derived from wild animals from 2013 to 2017

Agent (BP)	Deer				Wild boar	Small mammals				Other		
	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 of 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	0.0	18.1	40.0	66.7	50.0
ABPC (32)	0.6	2.0	0.0	0.8	3.6	23.6	0.0	0.0	12.6	10.0	0.0	0.0
CEZ (32)	0.0	0.0	0.0	0.0	0.0	2.8	0.0	0.0	1.5	0.0	0.0	0.0
CTX (4)	0.0	0.0	0.0	0.0	0.0	1.9	0.0	0.0	1.0	0.0	0.0	0.0
MEPM (2)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
GM (16)	0.3	0.0	0.0	0.2	0.4	2.8	0.0	0.0	1.5	0.0	0.0	0.0
KM (64)	0.9	0.0	0.0	0.6	1.3	5.7	0.0	0.0	3.0	20.0	0.0	0.0
TC (16)	3.1	2.0	11.5	4.4	4.0	17.9	12.8	0.0	12.6	20.0	33.3	0.0
NA (32)	0.9	0.0	0.0	0.6	0.9	11.3	0.0	0.0	6.0	0.0	0.0	0.0
CPFX (2)	0.3	0.0	0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
CL (4)	1.2	2.9	1.0	1.5	1.3	3.8	0.0	0.0	2.0	10.0	33.3	50
CP (32)	0.0	0.0	0.0	0.0	1.8	1.9	0.0	0.0	1.0	0.0	0.0	0.0
ST (76/4)	0.6	2.0	0.0	0.8	0.9	18.9	6.4	0.0	11.6	0.0	0.0	0.0

BP units are in μg/mL.* Number of strains resistant to at least one agent.

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.

Table 71. Resistance rates (%) of *Escherichia coli* from wild animals

Agent (BP)	Deer (2016-2019)	Amami rabbit (2017~2020)	Common cormorant (2018~2019)	White-fronted goose (2019)
		Amami Oshima	Gunma, Gifu, Shiga, Oita	Miyajima swamp, Hokkaido
Number of strains	848	135	144	110
Number of resistant	9	0	8	1
Resistance rate (%)	1.1	0.0	5.6	0.9
ABPC (32)	0.1	0.0	3.5	0.9
CEZ (32)	0.1	0.0	0.0	0.9
CTX (4)	0.0	0.0	0.0	0.0
MEPM (2)	Not implemented	0.0	0.0	0.0
GM (16)	0.0	0.0	0.0	0.0
KM (64)	0.0	0.0	0.0	0.0
TC (16)	0.0	0.0	2.8	0.0
NA (16)	0.0	0.0	1.4	0.0
CPFX (2)	0.0	0.0	0.7	0.0
CL (4)	Not implemented	0.0	0.7	0.0
CP (32)	0.1	0.0	1.4	0.0
ST (76/4)	0.6	0.0	1.4	0.0

BP units are in μg/mL.* Number of strains resistant to at least one agent.

Source:

Deer: Tamamura-Andoh Y, Tanaka N, Sato K, Mizuno Y, Arai N, Watanabe-Yanai A, Akiba M, Kusumoto M. A survey of antimicrobial resistance in Escherichia coli J Vet Med Sci. 83(5):754-758, 2021.

Amami rabbit: Matsunaga N, Suzuki M, Andoh M, Ijiri M, Ishikawa K, Obi T, Chuma T, Fujimoto Y. Analysis of fecal samples from Amami rabbits (*Pentalagus furnessi*) indicates low levels of antimicrobial resistance in *Escherichia coli*. Eur J Wildl Res 66: 84, 2020.

Great cormorant: Odoi JO, Sugiyama M, Kitamura Y, Sudo A, Omatsu T, Asai T. Prevalence of antimicrobial resistance in bacteria isolated from Great Cormorants（*Phalacrocorax carbo hanedae*）in Japan. J Vet Med Sci. 83(8):1191-1195, 2021.

White-fronted goose: Fukuda A, Usui M, Ushiyama K, Shrestha D, Hashimoto N, Sakata MK, Minamoto T, Yoshida O, Murakami K, Tamura Y, Asai T. Prevalence of antimicrobial-resistant *Escherichia coli* in migratory Greater White-fronted Goose (*Anser albifrons*) and their habitat in Miyajimanuma, Japan. Wildl Dis. 57(4): 954-958, 2021.

Table72 Resistance rates of *Escherichia coli* isolated from wild animals from 2018 to 2021 (%)

s	Deer	Masked palm civet	Wild boar	Nutria	Racoon dog	Fox	Weasel	Badger	Monkey	Small Japanese field mouse	Wild cat	Bear	Marten	Racoon
Number of strains	517	61	54	33	24	11	11	9	9	7	6	3	3	2
Number of resistant*	28	1	4	0	0	1	0	1	1	0	0	0	0	1
Resistance rate (%)	5.4	1.6	7.4	0.0	0.0	9.1	0.0	11.1	11.1	0.0	0.0	0.0	0.0	50.0
ABPC (32)	0.4	1.6	0.0	0.0	0.0	9.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
CEZ (32)	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
CTX (4)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
MEPM (2)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
GM (16)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
KM (64)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
TC (16)	4.1	0.0	7.4	0.0	0.0	9.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
NA (16)	0.0	0.0	0.0	0.0	0.0	9.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
CPFX (2)	0.0	0.0	0.0	0.0	0.0	9.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
CL (4)	1.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	11.1	0.0	0.0	0.0	0.0	50.0
CP (32)	0.0	0.0	0.0	0.0	0.0	9.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
ST (76/4)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

BP units are in μg/mL.* Number of strains resistant to at least one agent.

Source: Asai T, Usui M, Sugiyama M, Andoh M. A survey of antimicrobial-resistant Escherichia coli prevalence in wild mammals in Japan using antimicrobial-containing media. J Vet Med Sci. 84(12):1645-1652, 2022.

Table 73 Survey of distribution of drug-resistant bacteria in wild animals using antimicrobial-containing media

Surveyed area	Surveyed year	Animal species	CTX-resistant *E. coli*	CPFX-resistant *E. coli*	Author
Gifu, Wakayama, Kagoshima	2018-2021	Deer	2/243 (0.8%)	2/243 (0.8%)	Asai et al., 2022
Gifu	2018-2021	Masked palm civet	0/22 (0%)	1/22 (4.5%)	
Gifu, Yamaguchi	2018-2021	Badger	1/6 (16.7)	0/6 (0%)	
Gifu	2018-2021	Fox	1/4 (25%)	2/4 (50%)	
Gifu	2018-2021	Racoon	1/2 (50%)	1/2 (50%)	
Kanagawa - Urban area	2016-2017	Racoon dog	20/80 (25%)	Not implemented	Shimizu et al., 2023
Nara - Urban area	2018	Deer	Not implemented	22/59（37.3%）	Ikushima et al., 2021
Nara - Urban area	2019-2020	Deer	35/144 (24.3%)	16/144 (11.1%)	Ikushima et al., 2023
Naara – rural area	2018-2021	Deer	1/23 (4.3%)	1/23 (4.3%)	
Nara - Mountain area	2019	Deer	0/30 (0%)	0/30 (0%)	

Asai T, Usui M, Sugiyama M, Andoh M. A survey of antimicrobial-resistant *Escherichia coli* prevalence in wild mammals in Japan using antimicrobial-containing media. J Vet Med Sci. 84(12): 1645-1652, 2022.

Shimizu T, Kido N, Miyashita N, Tanaka S, Omiya T, Morikaku K, Kawahara M, Harada K. Antimicrobial resistance in *Escherichia coli* isolates from Japanese raccoon dogs (*Nyctereutes viverrinus*) in Kanagawa Prefecture, Japan: Emergence of extended-spectrum cephalosporin-resistant human-related clones. J Med Microbiol. 71(12) 001631, 2022.

companion.

Ikushima S, Torii H, Asano M, Suzuki M, Asai T. Clonal Spread of Quinolone-Resistant *Escherichia coli* among Sika Deer (*Cervus nippon*) Inhabiting an Urban City Park in Japan. J Wildl Dis. 57(1): 172-177, 2021.

Ikushima S, Torii H, Sugiyama M, Asai T. Characterization of quinolone-resistant and extended-spectrum β-lactamase-producing *Escherichia coli* derived from sika deer populations of the Nara Prefecture, Japan. J Vet Med Sci. 85(9): 937-941, 2023.

(3) Food

The status of foodborne resistant bacteria is based on the results of a research project (2022 Health and Labour Sciences Research Grant General Report on the Research Project to Promote Food Safety: "Research to strengthen the surveillance system for food-borne antimicrobial-resistant bacteria based on One Health" Principal Investigator Motoyuki Sugai). After each local public health institute (CHIKEN, 22 CHIKEN participating voluntarily) purchased commercial meat from the relevant region, *Salmonella* spp., *Campylobacter* spp., *E. coli*, and other bacteria contaminating the meat were cultured and isolated using selective media according to the protocols established thus far. Antimicrobial susceptibility tests of the isolated strains were tested for 12 agents by the CLSI disk diffusion method. The results for *Salmonella* spp. were summarized in section (iv) ii, Non-typhoidal *Salmonella* spp., (local public health institutes) (see p. 34-40). In summary, for serotypes *S*. Infantis, *S*. Schwarzengrund, and *S*. Manhattan, food-derived isolates showed a high similarity to the antimicrobial resistance rates and resistance patterns of human patient feces-derived isolates, suggesting a strong association between food-derived and human-derived resistant bacteria.

The emergence of antimicrobial-resistant strains of *Campylobacter* spp.: *C. jejuni* and *C. coli* showed high rates of resistance to fluoroquinolones (52.7% and 91.7%, respectively). The resistance to EM, the first-line treatment for Campylobacter enteritis, was not observed.

Emergence of antimicrobial-resistant *E. coli* from commercial chicken meat: *E. coli* isolated from domestic chicken meat showed high resistance rates to four agents, KM, SM, TC, and CP. On the other hand, high resistance rates of *E. coli* isolated from foreign chicken meat were observed against five agents, ABPC, CTX, CAZ, GM, and NA, and ST, CPFX, and NFLX had similar resistance rates. The trends of antimicrobial resistance were different between domestic- and foreign-derived strains. The CTX-resistance rate of domestic-derived strains has remained at 1.0-2.4% since 2019. In contrast, foreign-derived strains increased from 3.5% (2020) to 6.6% (2021) and 12.2% (2022).

For ESBL-producing genes, in *Salmonella* spp., the CTX-M-1 group, and the TEM-type were detected in both human- and food-derived strains, while the CTX-M-9 group was detected only in human-derived strains. For the AmpC *β*-lactamase-producing genes, CIT-type was detected in both. In *E. coli*, on the other hand, AmpC genes possession were rarely observed and ESBL genes were mainly detected; in EHEC, CTX-M-1 group, and TEM type were detected, but CTX-M-9 group, and CTX-M-2 group were rarely detected. On the other hand, CTX-M-9 group, CTX-M-2 group, and TEM-type were frequently detected in other *E. coli*. The possession of CL-resistant genes (*mcr*-1~*mcr*-10) was examined in *E. coli* and *Salmonella* spp. isolated from slaughterhouses and poultry slaughterhouses in 2020 with MIC of CL greater than 2 μg/mL. *mcr*-1, *mcr*-5, and *mcr*-3 genes were detected in *E. coli*, but at low rates (< 5% for each year and for each animal species).

Antimicrobial-resistant *E. coli* from feces of healthy subjects: the highest resistance rate was observed against ABPC (31.1%), followed by NA (25.8%), TC (22.7%), and ST (17.8%). Fluoroquinolone-resistance was 9.1% for CPFX and 8.7% for NFLX, and cephalosporin-resistance was 4.2%, both trends similar to previous years. CL-resistant *mcr*-bearing strains accounted for 1.1%.

(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. In general, sewage from human activities is treated to effluent standards at sewage treatment plants and other domestic wastewater treatment facilities and discharged into the environment (rivers and oceans) when the effluent 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.

1) Results of the Ministry of Health, Labor and Welfare Scientific Research Grant Project

Survey Methods and Continuation of Fact-Finding Surveys in Japan

Currently, there are only a few quantitative reports on how many antimicrobial-resistant bacteria (AMR bacteria: ARB) and derived antimicrobial-resistant genes (AMR genes: ARGs) are released into the environment, and how much they continue to burden the environment. With only a few quantitative reports available at present concerning how many ARBs and the ARGs that stem from them is being released into the environment and continuing to impose a burden on the environment, a systematic nationwide survey is regarded as important. Accordingly, the Ministry of Health, Labour and Welfare research "Research for the establishment of survey method of antimicrobial-resistant bacteria and antimicrobial agents in the environment. Principal Investigator: Hajime Kanamori H30-R02, R03-R05" has been formed for the purpose of conducting ongoing environmental AMR surveillance. Led by Hajime Kanamori, the research group (hereinafter referred to as “Kanamori’s group”) is conducting a study entitled “Research to Establish Methods of Surveying ARB and Antimicrobials in the Environment” for three years from 2018 to 2020. In FY 2008 - FY 2020, this research group prepared a procedure manual contributing to environmental AMR monitoring and conducted research to establish a method for investigating ARB and residual antimicrobial agents in environmental water. A system was established by this research to develop a nationwide environmental AMR monitoring survey of discharged treated water, and the actual environmental burden of local governments was elucidated at the genetic level. In addition, a domestic and international literature review was conducted to clarify the current status and issues related to agent resistance in the environment.

From 2018 to 2022, 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 discharged treated water samples from sewage treatment plants provided by 44 local governments (515 samples in total, collected in summer (August) and winter (February) from August 2018 to August 2022). As a result of the 5-year (9 times) continuous survey, an increase or decrease in ARGs, presumably due to the impact of the new coronavirus outbreak, was confirmed from the winter of 2020 onwards. Fluctuation in ARGs, presumably due to the impact of the COVID-19 pandemic, was observed from winter 2020 onwards. Although sulfate (sulfonamide)-resistance genes had been showing an increasing trend until winter 2020, they showed a marked decrease in summer 2020 and remained low for two years until winter 2022. Macrolide-resistance genes once showed a decreasing trend in winter 2020, but in winter 2022 they were found to have increased to the levels prior to the COVID-19 pandemic. 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 regarding the isolation of quinolone-resistant *E. coli*. As Kanamori’s 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 quinolone-resistance genes acquired through lateral gene transfer may be decreasing and approaching a desirable situation, it is important to further continue surveillance. As the research group’s metagenomic analysis technique conforms to metagenomic analysis techniques used globally and is important when comparing reports from different countries. The group plans to continue conducting nationwide surveillance twice a year (in summer and winter) with the cooperation of local governments and put in place Japanese environmental AMR (Resistome) infrastructure.

In addition to ARGs in discharged treated water, it is vital to identify the presence of ARB that could potentially exist and proliferate in the environment. Kanamori’s group has reported that at a water reclamation center in Tokyo Bay, a KPC-2 carbapenemase-producing *Klebsiella pneumoniae* (Sequence type 11: ST11) rarely found in clinical isolates, had been isolated from the environmental water, that ST11 was the same type as clinical isolates widely isolated in East Asia [1], that KPC-2 was found in *Aeromonas* spp. rarely isolated in wound infections,[2] and that *E. coli* with NDM-5 carbapenemase, which has acquired broader-spectrum activity than NDM-1, had been isolated[3], and information on the situation within Japan is gradually becoming increasingly clear. A report has also been published on a comprehensive AMR study carried out on hospital wastewater, inlet and treated 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 was isolated from non-ozone-treated outlet water from sewage treatment plants and that hospital wastewater imposes an environmental AMR burden. [4] The reality is that, as in the case of the situation overseas, no small number of ARBs are isolated in environmental water in Japan.

As establishing surveillance techniques for monitoring environmental AMR and residual antimicrobials, and conducting fact-finding studies are important, a procedure for metagenomic analysis of treated effluent from sewage treatment plants was developed as a method for investigating antimicrobial resistance in environmental water. In addition to metagenomic analysis, conventional culture methods were also important, and not only the detection of ARGs but also the analysis of the characteristics of live ARB in sewage was conducted. It is hoped that conducting both the metagenomic analysis and the culture method approaches will lead to a better understanding of the overall picture of antimicrobial resistance in environmental waters.

In addition to a nationwide environmental water AMR survey, Kanamori's group also conducted a survey of the status of environmental AMR of local hospital effluent and the sewage from a local pig farm and a measurement of antimicrobial residue in local sewage treatment water in Japan. Risk assessment should be based on the findings from these studies and the results of the literature review on environmental AMR. To set out the evidence concerning the environmental AMR from overseas, the research group published a translation of Initiatives for Addressing Antimicrobial Resistance in the Environment: Current Situation and Challenges. 2018 [5].

Important issues for environmental AMR control include: 1) the environment can be contaminated with antimicrobial agents and resistant bacteria if wastes are not appropriately treated; 2) the impact of environmental contamination of antimicrobial agents and resistant bacteria in wastes on human health is not fully understood; 3) to understand the risk of ARB to human health, it is important to assess where and how many ARB are present in environmental water; and 4) to evaluate sampling and testing methods and standardize practices to measure ARB in environmental water.

A Japanese literature review reported that a considerable amount of ARB and ARGs remain in effluent water after treatment and in the river water that receives it, placing a concern for environmental contamination; ARB (such as KPC-2 and NDM-5-producing bacteria), which are rarely isolated clinically in Japan, have been detected in sewage, and suggesting sewage is useful for monitoring in the city. Although the existence of antimicrobial resistance in the environment has been proven in this way in Japan and overseas, the reality is that there is insufficient evidence of the risks to humans and animals due to the lack of established survey methods and assessment criteria for environmental AMR.

A literature review was conducted on sewage AMR in Japan.[6] As a result, of 37 eligible papers from 1991-2021, 26 reported on AMR, 10 on antimicrobial agents, and one on both AMR and antimicrobial agents. The presence of clinically important ARB, ARGs, and residual antimicrobials such as ESBL-producing *Enterobacterales*, CRE, MDRP, MDRA, MRSA, and VRE in Japanese sewage was observed. Hospital drainage may be a reservoir of clinically important ARB, but the direct risk to humans of ARB in hospital drainage is not clear. In addition, antimicrobials commonly used in Japan may create an environment conducive to the growth of AMR in sewage and may further contribute to the dissemination of AMR through proliferation. While the promotion of AMR control in humans, animals, and the environment is necessary, knowledge o AMR in the environment is still limited compared to humans and animals. Progress in surveys and research on environmental AMR in Japan is anticipated.

Although efforts have been made to assess the risk of infection transmission and the health effects in cases of nosocomial infection based on the results of field epidemiology and molecular epidemiological analysis of isolates, as described above, research findings indicating that ARB 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 [7] and assessments of the risk of exposure to AMR through water-based recreation [8] are starting to be reported, albeit only little by little, a certain degree of a risk cycle is being calculated. 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. A multidisciplinary One Health approach at the human-animal-environment interface to infectious diseases is essential to assess the risk to humans and animals of agent resistance in the environment [9].

2) Results of the Environment Research and Technology Development Fund (FY2020-2022) [10]

It has been pointed out that the aquatic environment, where wastewater containing various antimicrobial agents and resistant bacteria ultimately flows into, may be a reservoir for the dissemination of ARB. To control the dissemination of ARB, it is important to clarify the mechanism of ARG dissemination in the aquatic environment. Therefore, the "Elucidation of Transmission Potential and Transmission Mechanism of Drug Resistance Genes in the Environment" project funded by the Environment Research and Technology Development Fund (FY2020-2022), a survey of the distribution of resistant bacteria in major rivers in Japan and an evaluation experiment of the transmission potential of ARGs using an *in vitro* transmission experiment were conducted.

In the distribution survey of ARB, eight rivers in the Tohoku region (Aka, Mogami, Omono, Iwaki, Mabuchi, Kita, Natori, and Abukuma Rivers) were surveyed. In all rivers, the concentration of *E. coli* in river water was determined to be low in terms of *E. coli* contamination, meeting the environmental standard for Type A on the day of water sampling. The detected *E. coli* was isolated and identified, and their antimicrobial susceptibilities to 18 antimicrobial agents were evaluated. As a result, 26.8% of *E. coli* were detected to be resistant to one or more of the tested antimicrobial agents, and the largest number of 178 isolates (24.2%) were resistant to ampicillin. [11] Of the strains resistant to ABPC, 23 (3.5%) and 1 (0.2%) strains were detected to be resistant to CTX and CEZ, respectively. Of all *E. coli* isolates, 10% were multidrug-resistant (ABPC, CVA/AMPC, TC, quinolones (CPFX, LVFX). ESBL-producing *E. coli*, which are positioned as having increased concerns by WHO, were also detected. Since a one-year river monitoring of the Akagawa and Mogami Rivers enabled the isolation of ESBL-producing *E. coli*, the ESBL-producing genes (*bla*) of the isolates were characterized. Of the 21 types of *bla* tested, 17 types were detected, with $bla_{\text{CTX-M-1-group}}$ being the most abundant. It is noteworthy that not only bla_{IMP}, a domestic-type carbapenemase, but bla_{KPC}, $bla_{\text{OXA-48}}$, bla_{VIM}, and bla_{NDM}, which are considered foreign types because there are few cases detected in Japan, were also detected. Comparing the number of *bla* detected at each location, the highest number of 15 types of *bla* was detected in the strains isolated directly under the sewage treatment plant. The results indicate that healthy people living in the city as well as in clinical care settings are also a source of ARB in rivers. In an experimental evaluation of the transmission potential of ARGs using in vitro transmission experiments, in vitro transmission experiments were conducted using *Enterococcus* spp. and *E. coli* as model bacteria to simulate the environment. As a result, only *vanA* was confirmed to be transmitted in *Enterococcus* spp., and the transmission potential was confirmed to be in the range of 10^{-3} to 10^{-7} depending on the combination of donor and recipient bacteria. In addition, no transmission was observed in the liquid phase of river water, and transmission was observed in activated sludge, an environment in which bacteria accumulate, although at a low probability (10^{-7}). On the other hand, when *Enterobacteriales* harboring $bla_{\text{CTX-M}}$ were used, transmission was confirmed (10^{-4} to 10^{-8}) under conditions simulating any of the environments. Furthermore, Gram-negative bacteria showed higher potential for a field (transmission field) to transmit ARGs compared to Gram-positive bacteria. It was suggested that the dissemination of ARGs in the environment is highly possible, and that intensive treatment is necessary, especially in areas where bacterial density is assumed to be high. It was highlighted that antimicrobial-resistant and ESBL-producing *E. coli* are already dispersed in the river water in Japan. On the other hand, the origin of these environmental AMRs and the extent of their impact on humans and animals are unknown. There is no doubt that antimicrobial-resistant bacteria are released into the environment from their human and animal origins; however, the active accumulation of information in the environmental field is needed to clarify the effects of these bacteria from the environment on humans and animals.

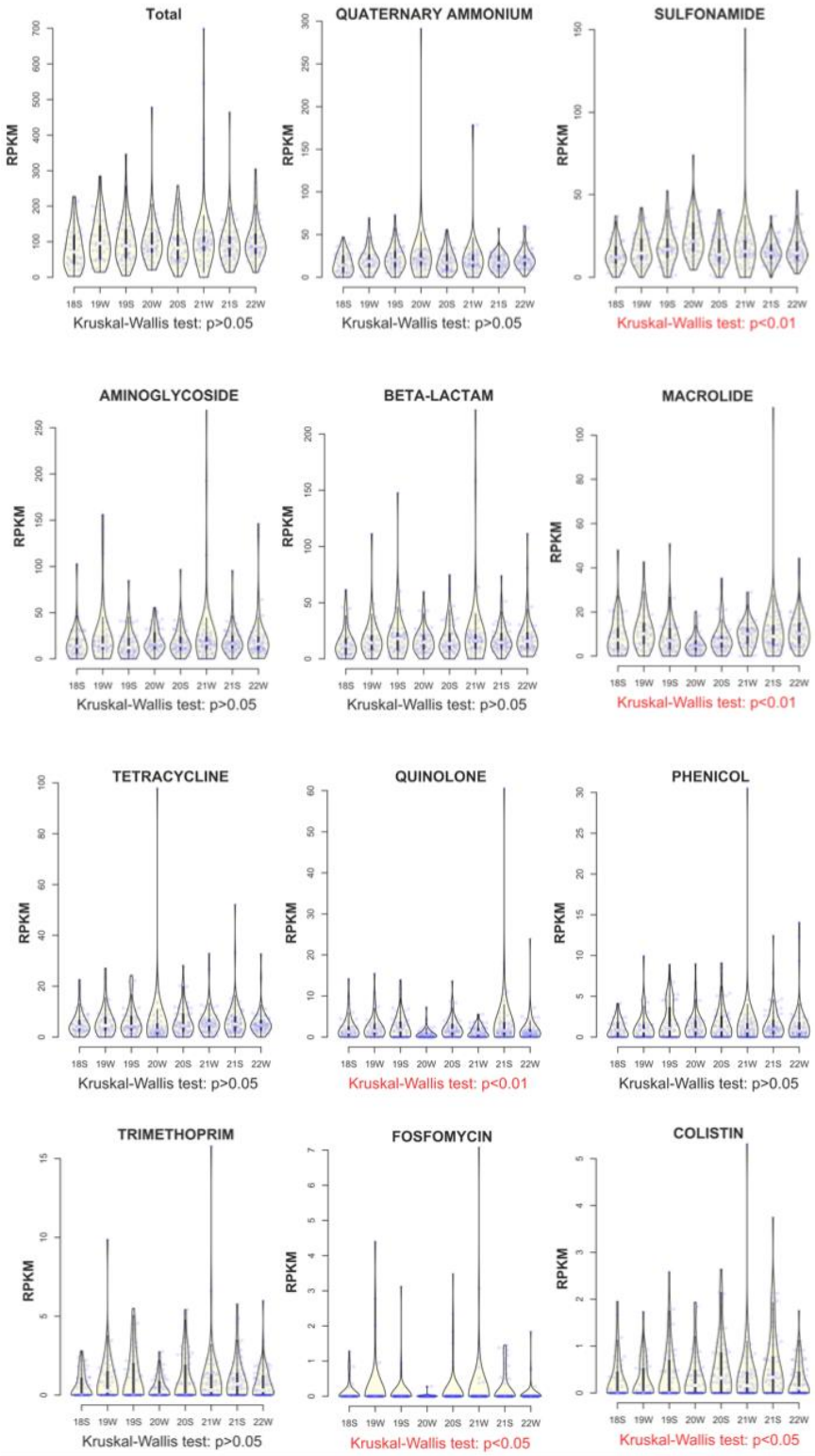

Figure 3. Metagenomic analysis (Metagenomic DNA-Seq) of wastewater discharged from Japanese sewage treatment plants (water reclamation centers) The quantity of antimicrobial-resistant genes (ARGs) in each category detected in treated effluent water provided by local governments were standardized using Reads Per Kilobase of gene per Million mapped reads (RPKM) for a total of 9 time periods from summer 2018 (18S) to summer 2022 (22S) in biannual surveys. Because of frequent updates of the ARGs database since 2018, metagenomic data from all samples were again used to calculate RPKMs for ARGs using ARGs_OAP v3.2.212.

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7. Current Volume of Use of Antimicrobials in Japan

(1) Antimicrobials for humans

1) Usage of antimicrobials in Japan

Source: Japan Surveillance of Antimicrobial Consumption (JSAC)

Antimicrobial use based on sales volume in Japan from 2013 to 2022 is shown in Table 72 (oral agents), Table 73 (injectable agents), and Table 74 (total of oral and injectable antimicrobial agents). Overall use of antimicrobials in Japan in 2021 amounted to 9.77 DID. A comparison with DID in major countries in 2020 shows that this was lower than France (21.5 DID), Italy (17.5 DID), and Sweden (10.1 DID), but higher than the Netherlands (8.5 DID) and Austria (8.8 DID) [1]. Looking at changes over time, no significant changes in antimicrobial use were observed from 2013 to 2016, but the decline began in 2017, with the decrease becoming smaller. In the midst of such a trend, there was an epidemic of COVID-19, and overall antimicrobial use in 2020 declined more sharply compared to the previous years. Compared to 2020, there was a 3.9% decrease in 2022. The use of oral agents in 2022 (Table 72) as a percentage of total antimicrobial use is 8.84 DID (90.4%), of which oral third-generation cephalosporins (1.63 DID) which are targeted to be reduced by 40% in the National Action Plan on Antimicrobial Resistance (AMR), oral fluoroquinolones (1.52 DID), which are targeted for a 25% reduction, and oral macrolides (2.66 DID), which are targeted for a 25% reduction, together accounted for 65.7% of all oral antimicrobial agents. While this trend has not changed since 2013, when comparing each use to 2020, use of oral cephalosporins, oral fluoroquinolones, and oral macrolides in 2022 fell by 11.9%, 8.4%, 9.2%, respectively. The use of parenteral carbapenems increased by 2.9% between 2020 and 2022 (Table 73). It was thought that 2019 may have seen a decrease in first-generation cephalosporins and an increase in narrow-range penicillins, penicillin with β-lactamase inhibitors, second- and third-generation cephalosporins, and carbapenems, especially due to cephazolin supply shortage issues [2]. Overall antimicrobial use decreased scince 2020, which may be due not only to the promotion of appropriate antimicrobial use, but also to the impact of COVID-19 (e.g., fewer patients seen with infections other than COVID-19). A similar trend was seen to continue after 2022 also due to the continuing pandemic.

Table 75 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-line 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 ABPC and CEX), 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 VCM, MEPM, LVFX, and CTRX), Reserve (antimicrobials that should be used as the last resort when no other alternatives can be used. Examples include TGC, CL, and DAP), 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, SBT/CPZ). The WHO has set a target of at least 60% of antimicrobial consumption being from medicines classified as the Access Group. While consumption of antimicrobials classified as the Access Group as a proportion of total use tends to be lower in Japan than other countries,[3] the figure has risen gradually over the years since 2013 from 11.0% to 23.8% in 2022, with the percentage of antimicrobials classified as the Watch Group falling from 87.6% to 74.9%, which can mean that Japan is on its way towards the actions recommended in the National Action Plan on AMR (2023-2027).

However, various factors, such as the problem of antimicrobial supply shortages and the impact of new coronavirus infections, are also of concern and require continued close monitoring.

A survey of oral and parenteral antimicrobial use in terms of potency by weight from a One Health perspective (Table 76) also confirmed a decrease in overall use as well. The decrease in the use of oral third-generation cephalosporins, fluoroquinolones, and macrolides accounted for half of the total, and it is necessary to clarify the factors from the viewpoint of proper use, including the impact of COVID-19 infection. Since there may be a temporary decline, it is important to carefully monitor future trends in antimicrobial use on an ongoing basis.

The establishment of a surveillance system, which was one of the goals of the National Action Plan on AMR, made it possible to assess the use of antimicrobial agents in Japan over time. Although the impact of AMR control was recognized in the gradual decline of oral agents through 2019, parenteral antimicrobial agents remained flat to increased, which was thought to be due to factors such as an increase in the elderly population. In 2020, however, oral agents declined further, and parenteral antimicrobial agents also began to decline. One reason for the decrease may be the various effects associated with the new coronavirus infections, and although there has not been another increase at this time, it is necessary to understand future trends. Furthermore, the purpose of antimicrobial use will be clarified, and appropriateness will be evaluated by continuing surveillance of antimicrobial use based not only on sales volume data but also on National Database for Prescription and National Health Checkups (NDB).

Table 74. Trends in oral antimicrobial use in Japan based on the volume of sales

	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Tetracyclines	0.76	0.75	0.77	0.80	0.81	0.88	0.96	1.10	1.18	1.18
Amphenicols	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	＜0.01
Penicillins with extended spectrum	0.60	0.61	0.68	0.66	0.65	0.69	0.77	0.61	0.59	0.60
β-lactamase-sensitive penicillins	0.01	0.01	0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	＜0.01
Combinations of penicillins, including *β*-lactamase inhibitors	0.15	0.16	0.17	0.18	0.19	0.20	0.23	0.18	0.19	0.19
First-generation cephalosporins	0.07	0.07	0.07	0.07	0.07	0.08	0.09	0.09	0.10	0.11
Second-generation cephalosporins	0.30	0.30	0.29	0.29	0.28	0.28	0.30	0.29	0.31	0.32
Third-generation cephalosporins	3.54	3.41	3.46	3.32	3.08	2.83	2.63	1.85	1.70	1.63
Carbapenems	0.01	0.02	0.02	0.02	0.01	0.01	0.01	0.01	0.01	＜0.01
Other cephalosporins and penems	0.14	0.14	0.13	0.12	0.12	0.11	0.10	0.09	0.09	0.08
Combinations of sulfonamides and trimethoprim, including derivatives	0.25	0.27	0.29	0.31	0.33	0.36	0.38	0.41	0.44	0.46
Macrolides	4.83	4.50	4.59	4.56	4.18	3.96	3.84	2.93	2.72	2.66
Lincosamides	0.01	0.01	0.02	0.01	0.02	0.02	0.02	0.02	0.02	0.02
Fluoroquinolones	2.83	2.83	2.71	2.75	2.57	2.42	2.32	1.66	1.48	1.52
Other quinolones	0.01	<0.01	<0.01	<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	0.06	0.06	0.06
Total	13.62	13.18	13.30	13.19	12.38	11.92	11.74	9.31	8.88	8.84

* As a unit, DIDs (DDDs/1,000 inhabitants/day) is used.

* Figures for DDD (defined daily dose) are those for January 1, 2023.

Table 75. Trends in parenteral antimicrobial use in Japan based on the volume of sales

	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Tetracyclines	0.02	0.02	0.02	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	＜0.01	＜0.01	＜0.01
Penicillins with extended spectrum	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
β-lactamase sensitive penicillins	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	0.01	＜0.01	＜0.01	＜0.01
Combinations of penicillins, incl. *β*-lactamase inhibitors	0.13	0.15	0.16	0.18	0.19	0.21	0.22	0.18	0.20	0.23
First-generation cephalosporins	0.13	0.13	0.14	0.14	0.15	0.15	0.12	0.13	0.14	0.15
Second-generation cephalosporins	0.11	0.11	0.10	0.10	0.10	0.09	0.10	0.08	0.08	0.09
Third-generation cephalosporins	0.18	0.19	0.21	0.22	0.23	0.24	0.27	0.22	0.21	0.22
Fourth-generation cephalosporins	0.04	0.03	0.03	0.03	0.03	0.03	0.02	0.02	0.02	0.02
Monobactams	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01
Carbapenems	0.09	0.08	0.08	0.08	0.08	0.08	0.08	0.07	0.07	0.07
Other cephalosporins and penems	-	-	-	-	-	-	＜0.01	＜0.01	＜0.01	＜0.01
Combinations of sulfonamides and trimethoprim, incl. derivatives	＜0.01	＜0.01	＜0.01	＜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	＜0.01	＜0.01	＜0.01
Lincosamides	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.01	0.01	0.01
Streptogramins	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	-	-	-
Streptomycins	＜0.01	＜0.01	＜0.01	＜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	0.03	0.03	0.03	0.02	0.02
Fluoroquinolones	0.03	0.03	0.03	0.04	0.03	0.03	0.03	0.03	0.03	0.03
Glycopeptide antibacterials	0.03	0.03	0.03	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	＜0.01	＜0.01	＜0.01
Metronidazole	＜0.01	＜0.01	＜0.01	＜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	0.01	0.01	0.01
Total	0.90	0.90	0.94	0.96	0.98	0.99	1.01	0.87	0.89	0.94

* As a unit, DID (DDDs/1,000 inhabitants/day) is used.

* Figures for DDD (defined daily dose) are those for January 1, 2023.

Table 76. Trends in oral and parenteral antimicrobial use in Japan based on the volume of sales

	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Tetracyclines	0.79	0.77	0.79	0.82	0.83	0.90	0.98	1.12	1.19	1.19
Amphenicols	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01
Penicillins with extended spectrum	0.63	0.64	0.70	0.68	0.67	0.71	0.79	0.63	0.61	0.62
β-lactamase sensitive penicillins	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	＜0.01	＜0.01
Combinations of penicillins, incl. *β*-lactamase inhibitors	0.29	0.31	0.34	0.36	0.38	0.41	0.45	0.36	0.38	0.42
First-generation cephalosporins	0.20	0.20	0.20	0.21	0.22	0.23	0.21	0.22	0.24	0.26
Second-generation cephalosporins	0.41	0.40	0.39	0.39	0.37	0.38	0.41	0.38	0.39	0.41
Third-generation cephalosporins	3.72	3.60	3.67	3.54	3.31	3.07	2.90	2.07	1.91	1.85
Fourth-generation cephalosporins	0.04	0.03	0.03	0.03	0.03	0.03	0.02	0.02	0.02	0.02
Monobactams	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01
Carbapenems	0.10	0.10	0.10	0.10	0.09	0.09	0.09	0.07	0.08	0.07
Other cephalosporins and penems	0.14	0.14	0.13	0.12	0.12	0.11	0.10	0.09	0.09	0.08
Combinations of sulfonamides and trimethoprim, incl. derivatives	0.25	0.27	0.29	0.32	0.34	0.36	0.39	0.41	0.44	0.46
Macrolides	4.84	4.51	4.59	4.56	4.18	3.96	3.84	2.93	2.73	2.66
Lincosamides	0.04	0.04	0.04	0.04	0.03	0.03	0.04	0.03	0.03	0.03
Streptogramins	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	-	-	-
Streptomycins	＜0.01	＜0.01	＜0.01	＜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	0.03	0.03	0.03	0.02	0.02
Fluoroquinolones	2.86	2.86	2.74	2.78	2.60	2.45	2.35	1.69	1.51	1.55
Other quinolones	0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01
Glycopeptide antibacterials	0.03	0.03	0.03	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	＜0.01	＜0.01	＜0.01
Metronidazole	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01
Other antibacterials	0.12	0.12	0.12	0.12	0.10	0.10	0.10	0.08	0.07	0.07
Total	14.52	14.08	14.23	14.15	13.36	12.91	12.75	10.18	9.77	9.78

* As a unit, DID (DDDs/1,000 inhabitants/day) is used.

* Figures for DDD (defined daily dose) are those for January 1, 2023.

Table 77. Trends in antimicrobial use in Japan by AWaRe classification

AWaRe Classification	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Access (%)	1.62	1.67	1.79	1.84	1.90	2.06	2.25	2.17	2.29	2.39
	(10.96)	(11.62)	(12.31)	(12.72)	(13.94)	(15.65)	(17.29)	(20.89)	(22.83)	(23.78)
Watch (%)	12.94	12.47	12.51	12.39	11.54	10.93	10.59	8.08	7.59	7.52
	(87.57)	(86.92)	(86.27)	(85.91)	(84.71)	(83.03)	(81.40)	(77.68)	(75.78)	(74.90)
Reserve (%)	0.19	0.18	0.18	0.17	0.16	0.15	0.15	0.13	0.12	0.12
	(1.288)	(1.289)	(1.252)	(1.204)	(1.186)	(1.156)	(1.141)	(1.252)	(1.216)	(1.151)
Non-recommended (%)	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
	(0.155)	(0.155)	(0.152)	(0.149)	(0.154)	(0.153)	(0.158)	(0.167)	(0.163)	(0.157)
Unclassified (%)	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	＜0.01	-	-	-	-
	(0.011)	(0.010)	(0.008)	(0.007)	(0.006)	(＜0.01)	(＜0.01)	(＜0.01)	(＜0.01)	(＜0.01)
Total	14.78	14.34	14.50	14.43	13.63	13.17	13.00	10.40	10.01	10.04

* As a unit, DID (DDDs/1,000 inhabitants/day) is used.

* Figures for DDD (defined daily dose) are those for January 1, 2023. AWaRe classification 2021 edition was used.

* The above values are based on WHO's AWaRe classification, which includes some non-ATC code J01, so there are slight changes from previous values.

Table 78. Antimicrobial consumption by weight based on sales volume in Japan, converted to potency (t)

	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Tetracyclines	7.1	6.9	7.1	7.2	7.0	7.3	7.7	8.4	8.7	8.5
Amphenicols	0.2	0.1	0.1	0.1	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	49.3	47.9	48.5
β-lactamase-sensitive penicillins	1.7	1.8	1.7	1.5	1.4	1.3	1.8	1.3	1.1	1.1
Combinations of penicillins, including *β*-lactamase inhibitors	88.4	95.7	106.1	114.9	124.4	132.2	146.0	118.0	129.2	146.4
First-generation cephalosporins	25.0	24.9	25.2	26.3	27.2	28.4	24.9	26.5	28.9	30.2
Second-generation cephalosporins	28.5	27.4	27.0	26.7	25.9	26.0	28.6	25.5	26.5	27.7
Third-generation cephalosporins	97.7	95.1	97.8	95.9	91.2	86.6	85.3	64.0	59.8	58.8
Fourth-generation cephalosporins	6.6	6.1	6.0	5.7	5.5	4.8	4.5	4.3	4.2	4.4
Monobactams	0.1	0.1	0.1	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	8.8	9.1	9.1
Other cephalosporins and penems	4.8	4.7	4.6	4.3	4.0	3.8	3.6	3.3	3.0	2.9
Combinations of sulfonamides and trimethoprim including derivatives	45.8	49.9	53.7	58.6	62.1	65.7	71.0	75.7	81.3	84.6
Macrolides	108.0	101.4	103.4	102.9	94.5	89.7	87.2	67.8	63.4	61.9
Lincosamides	2.8	2.7	2.6	2.5	2.4	2.4	2.7	2.1	2.1	2.2
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	0.1	0.1	0.1
Other aminoglycosides	1.0	0.9	0.9	0.8	0.8	0.7	0.7	0.5	0.5	0.5
Fluoroquinolones	61.3	60.2	56.6	57.4	53.2	50.1	47.7	33.0	29.2	29.1
Other quinolones	0.5	0.4	0.3	0.3	0.2	0.1	0.1	0.1	<0.1	<0.1
Glycopeptides	2.2	2.1	2.3	2.4	2.5	2.4	2.6	2.7	2.4	2.6
Polymyxins	<0.1	<0.1	<0.1	<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	0.2	0.2	0.2
Other antibacterials	17.5	16.5	16.6	16.7	14.3	13.8	13.1	10.3	9.3	8.9
Total	563.0	560.6	580.1	591.4	581.6	582.9	600.2	501.9	507.0	527.8

Table 79. Trends in the use of total oral and parenteral antimicrobial agents in Japan based on NDB

	2013	2014	2015	2016	2017	2018	2019	2020	2021
Tetracyclines	0.75	0.74	0.75	0.78	0.79	0.85	0.93	1.06	1.13
Amphenicols	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01
Penicillins with extended spectrum	0.53	0.56	0.64	0.64	0.63	0.67	0.76	0.61	0.61
β-lactamase sensitive penicillins	0.01	0.01	0.01	0.01	< 0.01	< 0.01	0.01	0.01	< 0.01
Combinations of penicillins, incl. *β*-lactamase inhibitors	0.25	0.27	0.29	0.31	0.33	0.35	0.38	0.31	0.33
First-generation cephalosporins	0.14	0.15	0.16	0.16	0.17	0.18	0.17	0.19	0.22
Second-generation cephalosporins	0.34	0.35	0.36	0.35	0.34	0.34	0.37	0.35	0.36
Third-generation cephalosporins	3.47	3.54	3.69	3.57	3.34	3.11	2.94	2.10	1.91
Fourth-generation cephalosporins	0.03	0.03	0.03	0.03	0.02	0.02	0.02	0.02	0.02
Monobactams	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01
Carbapenems	0.08	0.08	0.08	0.08	0.08	0.07	0.07	0.06	0.06
Other cephalosporins and penems	0.12	0.12	0.12	0.11	0.11	0.10	0.10	0.09	0.08
Combinations of sulfonamides and trimethoprim, incl. derivatives	0.23	0.25	0.27	0.29	0.31	0.33	0.36	0.38	0.42
Macrolides	4.97	4.93	5.07	5.03	4.64	4.44	4.37	3.30	3.04
Lincosamides	0.04	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
Streptogramins	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
Streptomycins	< 0.01	< 0.01	< 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	0.03	0.03	0.02	0.02
Fluoroquinolones	2.78	2.74	2.93	2.93	2.74	2.61	2.51	1.78	1.63
Other quinolones	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01
Glycopeptide antibacterials	0.02	0.02	0.02	0.02	0.02	0.02	0.03	0.03	0.03
Polymyxins	< 0.01	< 0.01	< 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	< 0.01	< 0.01
Other antibacterial agents	0.11	0.11	0.11	0.11	0.09	0.09	0.09	0.07	0.06
Total	13.93	13.99	14.63	14.51	13.70	13.28	13.15	10.41	9.96

* As a unit, DID (DDDs/1,000 inhabitants/day) is used.

* Figures for DDD (defined daily dose) are those for January 1, 2023.

2) Usage of parenteral antimicrobials in hospitals

Source: J-SIPHE

J-SIPHE, operated by AMRCRC, uses an integrated inpatient EF file* to survey antimicrobial use in participating facilities and publishes annual reports.[5] In 2021, overall, in-hospital use of intravenous antimicrobial agents followed a similar trend to the previous year. Penicillins (AUD 3.92, DOT 5.77) were the most used, followed by 3rd generation cephalosporins (AUD 2.91, DOT 4.02), 1st generation cephalosporins (AUD 2.52, DOT 3.40), and carbapenems (AUD 1.12, DOT 2.04). It is necessary to continuously monitor the trend in the future.

Table 80. Use of parenteral antimicrobials at medical institutions (AUD, DOT)

	2019		2020		2021		2022	
	AUD (IQR) (DDDs/100 patient-days)	DOT (IQR) (DOTs/100 patient-days)	AUD (IQR) (DDDs/100 patient-days)	DOT (IQR) (DOTs/100 patient-days)	AUD (IQR) (DDDs/100 patient-days)	DOT (IQR) (DOTs/100 patient-days)	AUD （IQR）	DOT (IQR）
Penicillin	3.90(2.71-5.10)	5.94(4.15-7.82)	3.48(2.15-4.82)	5.19(3.53-7.01)	3.92 (2.32-5.32)	5.77 (3.7-7.35)	3.86 (1.85-5.75)	5.64 (3.20-7.99)
1st generation cephalosporins	1.71(0.83-2.86)	2.23(1.21-3.94)	2.28(1.15-3.27)	3.11(1.58-4.36)	2.52 (1.22-3.62)	3.40 (1.72-4.73)	2.21 (0.79-3.62)	3.02 (1.08-4.75)
2nd generation cephalosporins	0.18(0.09-0.41)	0.37(0.19-0.83)	0.15(0.06-0.35)	0.29(0.13-0.69)	0.14 (0.06-0.29)	0.27 (0.12-0.60)	0.15 (0.07-0.32)	0.31 (0.14-0.66)
3rd generation cephalosporins	3.33(2.18-4.74)	4.58(3.05-6.30)	3.00(1.95-4.32)	4.04(2.87-5.60)	2.91 (1.90-4.32)	4.02 (2.68-5.42)	2.84 (1.74-4.17)	3.91 (2.52-5.36)
4th generation cephalosporins	0.34(0.14-0.70)	0.53(0.25-1.01)	0.31(0.14-0.76)	0.49(0.26-1.05)	0.32 (0.16-0.74)	0.55 (0.28-1.02)	0.27 (0.14-0.62)	0.46 (0.25-0.97)
Oxacefemmes	0.30(0.11-0.70)	0.31(0.12-0.76)	0.25(0.11-0.61)	0.27(0.11-0.64)	0.20 (0.09-0.54)	0.20 (0.10-0.55)	0.22 (0.10-0.46)	0.22 (0.10-0.48)
Cephamycins	0.89(0.52-1.41)	1.70(0.99-2.62)	0.91(0.47-1.42)	1.67(0.93-2.62)	1.01 (0.53-1.52)	1.87 (1.04-2.76)	0.94 (0.43-1.55)	1.76 (0.84-2.78)
Cephalosporins with β-lactamase inhibitors	0.06(0.03-0.10)	0.07(0.03-0.11)	0.09(0.06-0.14)	0.09(0.06-0.13)	0.00(0.00-0.00)	0.00(0.00-0.00)	0.10 (0.06-0.18)	0.10 (0.06-0.14)
Carbapenems	1.23(0.63-1.79)	2.05(1.15-3.00)	1.09(0.55-1.87)	1.95(1.04-2.90)	1.12 (0.56-1.91)	2.04 (1.09-3.05)	0.88 (0.43-1.71)	1.71 (0.89-2.83)
Monobactams	0.04(0.02-0.09)	0.07(0.03-0.11)	0.04(0.02-0.09)	0.07(0.04-0.10)	0.05 (0.03-0.07)	0.07 (0.05-0.11)	0.06 (0.03-0.11)	0.07 (0.05-0.14)
Glycopeptides	0.56(0.27-0.94)	0.81(0.46-1.32)	0.48(0.25-0.92)	0.77(0.40-1.30)	0.50 (0.26-0.95)	0.77 (0.43-1.32)	0.42 (0.22-0.79)	0.70 (0.38-1.20)
Oxazolidinones	0.11(0.07-0.16)	0.11(0.07-0.17)	0.11(0.07-0.18)	0.12(0.08-0.20)	0.12 (0.07-0.19)	0.13 (0.08-0.21)	0.12 (0.07-0.20)	0.13 (0.08-0.22)
Arbekacine	0.07(0.04-0.13)	0.07(0.04-0.12)	0.08(0.04-0.14)	0.08(0.04-0.15)	0.08 (0.04-0.16)	0.08 (0.04-0.16)	-	-
Lipopeptides	0.25(0.14-0.38)	0.17(0.11-0.28)	0.24(0.14-0.39)	0.16(0.11-0.26)	0.26 (0.15-0.44)	0.18 (0.11-0.30)	0.26 (0.15-0.43)	0.18 (0.11-0.29)
Quinolones	0.39(0.21-0.61)	0.41(0.23-0.64)	0.37(0.22-0.59)	0.40(0.25-0.63)	0.35 (0.22-0.59)	0.38 (0.24-0.63)	0.35 (0.21-0.59)	0.38 (0.23-0.62)
Aminoglycosides	0.10(0.06-0.18)	0.23(0.14-0.45)	0.10(0.05-0.17)	0.24(0.14-0.43)	0.10 (0.05-0.20)	0.25 (0.15-0.49)	0.11 (0.06-0.21)	0.27 (0.15-0.49)
Streptomycins							0.05 (0.03-0.09)	0.06 (0.03-0.10)
Tetracyclines	0.14(0.09-0.26)	0.17(0.10-0.29)	0.15(0.09-0.27)	0.17(0.10-0.33)	0.15 (0.09-0.30)	0.17 (0.10-0.32)	0.18 (0.11-0.34)	0.21 (0.12-0.39)
Lincosamides	0.22(0.13-0.39)	0.32(0.19-0.55)	0.20(0.13-0.33)	0.28(0.18-0.46)	0.19 (0.12-0.32)	0.27 (0.18-0.43)	0.20 (0.12-0.32)	0.28 (0.18-0.43)
Macrolides	0.07(0.04-0.10)	0.07(0.04-0.10)	0.07(0.05-0.11)	0.07(0.05-0.12)	0.07 (0.04-0.11)	0.07 (0.05-0.11)	0.08 (0.05-0.13)	0.08 (0.05-0.13)
ST	0.07(0.03-0.11)	0.06(0.03-0.09)	0.07(0.03-0.14)	0.06(0.03-0.11)	0.08 (0.04-0.14)	0.07 (0.04-0.11)	0.08 (0.05-0.15)	0.07 (0.04-0.12)
Metronidazole	0.10(0.07-0.17)	0.11(0.07-0.18)	0.11(0.06-0.17)	0.12(0.07-0.19)	0.12 (0.08-0.18)	0.14 (0.09-0.21)	0.14 (0.09-0.22)	0.15 (0.10-0.24)

*E-file: Medical billing data; F-file: “Receipt” file for inpatients with procedure statement information integrated

AUD: Antimicrobial Use Density, DOT: Days of Therapy, tabulated by DDDs/100 patient-days

DOT: Days of Therapy, tabulated by DOTs/100 patient-days

*Note: Cephalosporin/β-lactamase inhibitor combination has not been using in 2021 due to supply disruptions.

*Note: Benzylpenicillin benzathine has been counting as penicillin agent starting in September 2022.

* Note: Imipenem/cilastatin/relebactam has been counting as carbapenems from September 2022.

* Tabulation definitions have changed since 2022.

- Arbekacin and spectinomycin are counted as aminoglycosides.

- Streptomycin is counted as streptomycin instead of aminoglycoside.

- Change of class names: Ceftolozane/tazobactam is changed to cephalosporin with β-lactamase inhibitor, daptomycin to lipopeptide, lincomycin to lincosamide, sulfamethoxazole/trimethoprim to ST.

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(2) Veterinary agents

Source: Japanese Veterinary Antimicrobial Resistance Monitoring System (JVARM)

Based on the same volumes of sales of antibiotics and synthesized antimicrobials, as reported under the Veterinary Agent Control Regulations, the amounts of veterinary antimicrobials were calculated in terms of active ingredients (metric tons (t)). In the period from 2013 to 2021, the volume of sales of veterinary antimicrobials ranged between 748.44 to 858.09 t. The total volume of sales in 2021 decreased by approx. 42 t since 2020. Antimicrobials reduced their sales included sulfonamides (approx. 17 t) and macrolides (approx. 16 t), with a particularly significant impact by the decrease in chickens for sulfonamides and by that in aquatic animals (saltwater fish) for macrolides. Tetracyclines represented the largest share of antimicrobial sales over the period monitored, accounting for between 36.1% and 43.7%, which, however, have fallen below 40% in recent years.

On the other hand, third-generation cephalosporins and fluoroquinolones, which are important antimicrobials for human medicine, accounted for approximately 0.1% and 1.0% of the overall volume of sales, respectively.

Table 81. Amounts of veterinary antimicrobials in terms of active ingredients by class (t)

	2013	2014	2015	2016	2017	2018	2019	2020	2021
Penicillins	78.17	77.96	83.73	90.01	88.08	88.99	92.41	96.97	89.02
Cephalosporins(total)	5.58	5.50	5.89	6.45	6.65	7.06	8.02	7.72	8.03
1st generation cephalosporins	(4.71)	(4.58)	(4.98)	(5.41)	(5.50)	(5.67)	(6.62)	(6.40)	(6.61)
2nd generation cephalosporins	(0.19)	(0.20)	(0.12)	(0.16)	(0.18)	(0.22)	(0.14)	(0.15)	(0.13)
3rd generation cephalosporins	(0.68)	(0.71)	(0.79)	(0.88)	(0.96)	(1.18)	(1.26)	(1.16)	(1.28)
Aminoglycosides	39.52	40.64	35.47	47.86	44.76	35.61	35.17	36.89	29.84
Macrolides	77.70	70.43	98.41	134.12	140.83	154.72	180.71	173.72	157.72
Lincosamides	38.99	43.26	28.66	21.87	25.26	22.76	21.29	21.45	22.45
Tetracyclines	340.52	324.85	333.86	331.55	347.05	311.18	313.03	304.38	305.75
Peptides	11.78	9.98	14.54	14.02	19.99	12.34	19.56	19.06	18.40
Other antibioitics	25.98	28.85	32.39	31.96	36.19	37.50	35.96	36.34	37.45
Sulfonamides	103.90	97.57	96.67	95.85	99.06	88.77	84.69	98.53	81.96
Quinolones	1.01	1.91	1.71	1.74	1.84	1.48	2.57	2.34	1.72
Fluoroquinolones	5.53	5.63	7.35	6.08	6.83	6.65	7.53	7.06	8.39
Amphenicols	21.53	26.15	29.73	26.49	27.11	24.82	27.38	25.55	27.02
Furan and derivatives	14.46	1.76	1.24	1.57	1.36	1.34	1.35	1.23	1.55
Other synthetic antibacterials	15.02	13.97	13.35	12.12	13.09	11.98	11.71	11.68	11.57
Total	779.70	748.44	782.98	821.70	858.09	805.19	841.37	842.92	800.87

* 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, swine accounted for the largest amount, followed by seawater fish. Since 2020, sales have decreased in swine and saltwater fish, with the effect of vaccines on saltwater fish and the decrease in livestock possibly due to increased awareness of the need for prudent use and improved rearing hygiene management due to outbreaks of classical swine fever and highly pathogenic avian influenza.

To conduct comparisons of usage by animal species, the number of heads and weight per head of the animal should be considered. Accordingly, there is a comparison method that 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. The WOAH (OIE) has recently set out a method for calculating biomass weight as part of its data collection of veterinary antimicrobial usage data and published data on use per biomass weight (sales volume) by region, but this is a summary of all livestock and is not comparable by species. Therefore, it is necessary to consider the calculation of the amount used by livestock species in Japan based on the WOAH calculation method.

Table 82. Estimated amounts of veterinary antimicrobials in terms of active ingredients by animal species (t)

	2013	2014	2015	2016	2017	2018	2019	2020	2021
Beef cattle	23.02	20.35	23.77	25.00	25.92	33.17	33.40	58.33	59.27
Dairy cow	31.73	30.45	32.48	35.10	34.55	41.01	36.79	48.71	47.97
Horse	2.18	2.01	2.10	2.31	2.17	3.90	3.49	3.84	1.84
Swine	502.64	490.42	503.13	513.86	541.61	471.36	450.24	421.27	410.52
Broiler	65.90	70.14	62.36	63.81	61.74	62.79	69.81	77.53	69.14
Layer	23.29	23.67	19.36	19.78	15.32	15.86	17.56	17.13	9.32
Fish (saltwater)	112.36	93.41	123.02	143.03	159.07	164.00	217.66	204.15	190.56
Fish (freshwater)	6.84	5.61	7.28	10.10	9.07	2.91	2.74	2.27	2.03
Ornamental fish	0.72	1.07	1.60	1.95	1.74	1.63	1.64	1.56	2.14
Dog/Cat	8.49	8.10	7.78	6.67	6.90	8.56	8.03	8.11	8.08
Other	2.54	3.22	0.09	0.10	0.00	0.00	0.00	0.00	0.00
Total	779.70	748.44	782.96	821.70	858.09	805.19	841.37	842.92	800.87

1) Food-producing animals

The estimated volumes of veterinary antimicrobials sold for food-producing animals (cattle, swine, horses, chickens, and others) in terms of active ingredients are listed in Table83. In the period from 2013 to 2021, the estimated volume of sales ranged between 598.07 t and 681.31 t, with sales in 2021 being the lowest volume since 2013. All livestock species had similar amounts to or decreased from 2020. The most common antimicrobials were tetracyclines (236.49 t to 286.74 t), which accounted for 38.3% to 44.0% of the antimicrobials for livestock animals, but in 2021 they were at their lowest volume (236.49 t) since 2013. This is largely due to the decreased use of swine. In contrast, third-generation cephalosporins and fluoroquinolones, which are critically important antimicrobials for human medicine, each accounted for 0.1% and 1% of the antimicrobial agents for livestock animals, respectively.

Table 83. The estimated volumes of sales of veterinary antimicrobials for food-producing animals (cattle, swine, horses, chickens, and others) in terms of active ingredients (t)

	2013	2014	2015	2016	2017	2018	2019	2020	2021
Penicillins	59.50	61.96	67.25	73.82	71.75	74.48	73.76	76.22	72.44
Cephalosporins (total)	3.12	3.06	3.22	3.34	3.44	3.91	4.11	3.79	4.05
First-generation cephalosporins	(2.45)	(2.34)	(2.52)	(2.52)	(2.51)	(2.73)	(2.93)	(2.68)	(2.85)
Second-generation cephalosporins	(0.19)	(0.20)	(0.12)	(0.16)	(0.18)	(0.22)	(0.14)	(0.15)	(0.13)
Third-generation cephalosporins	(0.49)	(0.51)	(0.58)	(0.65)	(0.74)	(0.96)	(1.04)	(0.95)	(1.07)
Aminoglycosides	37.40	38.66	34.07	47.46	44.37	34.69	34.77	36.52	29.75
Macrolides	56.00	53.30	60.36	72.68	71.96	72.09	73.29	72.71	73.03
Lincosamides	35.88	36.61	23.65	15.62	19.39	16.72	16.26	17.48	19.11
Tetracyclines	286.74	275.83	276.24	280.66	286.01	257.36	242.93	240.12	236.49
Peptides	11.77	9.97	14.54	14.01	19.98	12.34	19.56	19.05	18.39
Other antibiotics	25.71	28.43	32.23	31.55	35.72	36.87	35.64	35.54	37.30
Sulfonamides	95.62	88.43	84.40	78.57	84.10	78.59	68.64	84.38	64.16
Quinolones	0.22	0.20	0.20	0.16	0.31	0.01	0.11	0.18	0.16
Fluoroquinolones	4.64	4.73	6.41	5.19	5.93	5.80	6.66	6.18	7.54
Amphenicols	19.66	25.14	27.39	24.82	25.34	23.28	23.89	23.11	24.23
Furan and derivatives	0.00	0.00	0.00	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	11.68	11.53	11.41
Total	651.24	640.25	643.28	659.95	681.31	628.09	611.29	626.83	598.07

* 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 84. In the period from 2013 to 2021, the estimated volume of sales ranged between 119.91 t to 222.05 t, accounting for between 13.4% and 26.4% of the total volume of veterinary antimicrobial sales. Tetracyclines took up the largest share in the overall volume of sales until 2015 but it has changed to a macrolide (EM) since 2016. The approximately 75 t increase in the volume of sales between 2013 and 2021 was due to a rise in sales of a macrolide (EM), which was presumably attributed to an outbreak and treatment of infections caused by *Lactococcus garvieae* (type II α-hemolytic streptococcal disease and others) different to the conventional serotypes. The macrolides (EM) in 2021 amounted to 84.69 t, a decrease of 16.32 t from 101.01 t in the previous year.

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

Table 84. The estimated volumes of sales of veterinary antimicrobials for aquatic animals (seawater fish, freshwater fish, and ornamental fish) in terms of active ingredients (t)

	2013	2014	2015	2016	2017	2018	2019	2020	2021
Penicillins	16.31	13.87	14.38	14.62	14.66	12.85	17.01	19.21	14.29
Cephalosporins (total)	0.00	0.00	0.00	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	0.00	0.00	0.00
2nd generation cephalosporins	0.00	0.00	0.00	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	0.00	0.00	0.00
Aminoglycosides	0.00	0.00	0.00	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	107.40	101.01	84.69
Lincosamides	3.02	6.56	4.90	6.12	5.73	5.91	4.88	3.82	3.19
Tetracyclines	53.78	49.01	57.62	50.89	61.05	52.55	69.57	63.84	68.84
Peptides	0.00	0.00	0.00	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	0.32	0.80	0.16
Sulfonamides	7.68	8.59	11.71	16.74	14.39	9.64	15.56	13.36	17.53
Quinolones	0.79	1.71	1.51	1.58	1.53	1.47	2.45	2.15	1.56
Fluoroquinolones	0.00	0.00	0.00	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	3.48	2.43	2.78
Furan and derivatives	14.46	1.76	1.24	1.57	1.36	1.34	1.35	1.23	1.55
Other synthetic antibacterials	0.02	0.04	0.02	0.04	0.06	0.02	0.02	0.12	0.13
Total	119.91	100.09	131.91	155.08	169.88	168.54	222.05	207.98	194.72

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 85. In the period from 2013 to 2021, the estimated volume of sales ranged between 6.67 to 8.56 t, with 8.08 t in 2021, about the same amount as in 2020. The sales volume 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 Agents & 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. The results of its surveillance revealed that the volume of human antimicrobials sold for use in companion animals is slightly less than the volume of veterinary antimicrobials sold for that purpose. Including those for human antimicrobials, the most sold antimicrobials were first-generation cephalosporins and penicillins.

Table 85. The estimated volumes of sales of veterinary and human antimicrobials for companion animals (dogs and cats) in terms of active ingredients (t)

	2013	2014	2015	2016		2017		2018	
	Animal	Animal	Animal	Animal	Human	Animal	Human	Animal	Human
Penicillins	2.36	2.13	2.08	1.57	1.93	1.68	1.75	1.66	2.14
Cephalosporins(total)	2.45	2.44	2.67	3.12	3.23	3.21	2.39	3.16	1.98
First-generation cephalosporins	(2.26)	(2.23)	(2.46)	(2.89)	(3.08)	(2.99)	(2.27)	(2.93)	(1.86)
Second-generation cephalosporins	(0.00)	(0.00)	(0.00)	(0.00)	(0.04)	(0.00)	(0.03)	(0.00)	(0.03)
Third-generation cephalosporins	(0.20)	(0.20)	(0.21)	(0.23)	(0.11)	(0.22)	(0.09)	(0.22)	(0.09)
Aminoglycosides	2.07	1.97	1.40	0.41	0.02	0.39	0.01	0.91	0.01
Macrolides	0.00	0.00	0.00	0.00	0.17	0.00	0.16	0.02	0.17
Lincosamides	0.09	0.09	0.11	0.13	0.10	0.13	0.10	0.14	0.10
Tetracyclines	0.00	0.00	0.00	0.00	0.28	0.00	0.31	1.27	0.33
Peptides	0.01	0.01	0.01	0.01	0.00	0.01	0.00	0.01	0.00
Other antibiotics**	0.00	0.00	0.00	0.00	0.22	0.00	0.21	0.00	0.22
Sulfonamides	0.60	0.55	0.56	0.53	0.19	0.57	0.19	0.53	0.22
Quinolones	0.00	0.00	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	0.11	0.84	0.12
Amphenicols	0.00	0.00	0.00	0.00	0.12	0.01	0.10	0.01	0.11
Furan and derivatives	0.00	0.00	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	0.10	0.01	0.10
Total	8.49	8.10	7.78	6.67	6.48	6.90	5.43	8.56	5.51

	2019		2020		2021	
	Animal	Human	Animal	Human	Animal	Human
Penicillins	1.64	1.98	1.54	1.56	2.29	1.88
Cephalosporins (total)	3.91	2.04	3.93	1.62	3.97	1.50
First-generation cephalosporins	(3.69)	(1.90)	(3.72)	(1.49)	(3.76)	(1.39)
Second-generation cephalosporins	(0.00)	(0.03)	(0.00)	(0.03)	(0.00)	(0.03)
Third-generation cephalosporins	(0.22)	(0.11)	(0.21)	(0.10)	(0.21)	(0.08)
Aminoglycosides	0.40	0.02	0.37	0.02	0.09	0.01
Macrolides	0.02	0.18	0.00	0.18	0.00	0.15
Lincosamides	0.15	0.09	0.15	0.08	0.15	0.07
Tetracyclines	0.53	0.35	0.42	0.34	0.42	0.31
Peptides	0.01	0.00	0.01	0.00	0.01	0.00
Other antibio tics**	0.00	0.22	0.00	0.23	0.00	0.18
Sulfonamides	0.50	0.25	0.78	0.25	0.26	0.25
Quinolones	0.00	0.00	0.00	0.00	0.00	0.00
Fluoroquinolones	0.87	0.16	0.88	0.11	0.85	0.08
Amphenicols	0.01	0.12	0.01	0.11	0.01	0.09
Furan and derivatives	0.00	0.00	0.00	0.00	0.00	0.00
Other synthetic antibacterials***	0.00	0.13	0.02	0.11	0.02	0.09
Total	8.03	5.53	8.11	4.60	8.08	4.61

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

** Includes fosfomycin and rifamycin, etc. (vancomycin for human was 0.0006 t in 2016, 0.0005 t in 2017, 0.0006 t in 2018, 0.0006 t in 2019, 0.0006 t in 2020, 0.0004 t in 2021)

*** Includes trimethoprim, penems, carbapenems, etc. (carbapenems for human was 0.0066 t in 2016, 0.0057 t in 2017, 0.0062 t in 2018, 0.0083 t in 2020, 0.0070 t in 2021)

References

1. Gochez D., Raicek M., Ferreira J. P., Jeannin M., Moulin G., Erlacher-Vindel E. OIE annual report on antimicrobial agents intended for use in animals: methods used. Frontiers in Vet. Sci. 2019. 6. doi: 10.3389/fvets.2019.00317

(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 86. The volume of such additives distributed showed a slight decrease in the period 2020 to 2021, ranging between 234.9 t and 211.1 t, with a major decrease of approximately 23 t in polyethers (not used in humans). 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 86. Volume of distribution of antibiotic feed additives in terms of effective value (t)

	2013	2014	2015	2016	2017	2018	2019	2020	2021
Aminoglycosides	0.0	0.0	0.0	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	6.4	7.1	10.4
Tetracyclines	1.6	2.2	2.6	2.0	0.0	0.0	0.0	0.0	0.0
Macrolides	5.6	5.3	5.5	1.4	3.5	0.0	0.0	0.0	0.0
Polysaccharides	0.2	0.0	0.1	0.1	0.1	0.0	2.3	3.4	1.4
Polyethers	136.0	142.5	141.7	159.9	165.5	161.0	174.1	192.5	169.7
Other antimicrobials	20.8	18.3	12.5	14.6	19.8	26.2	17.6	11.9	12.5
Synthetic antimicrobials	35.9	29.3	24.4	18.1	17.1	20.1	25.1	20.0	17.1
Total	235.1	225.9	216.4	228.2	221.2	216.7	225.5	234.9	211.1

(4) Agrochemicals

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

The volume of shipment in Japan of antimicrobials that are used as agrochemicals is shown in the table, in terms of active ingredients (unit: tons). In the period from 2013 to 2021, the volume of shipments of antimicrobials used as agrochemicals remained at around the 150 t mark, ranging from 133.24 to 181.43 t.

Table 87. The volume of shipment in Japan of antimicrobials that are used as agrochemicals, in terms of active ingredients (t)

	2013	2014	2015	2016	2017	2018	2019	2020	2021
Streptomycin	45.19	45.30	44.41	49.80	56.04	36.19	35.90	37.52	36.78
Oxytetracycline	19.49	22.23	23.25	19.46	17.81	0.13	0.16	0.35	0.91
Kasugamycin	23.43	23.92	23.69	23.68	23.90	21.22	19.79	18.41	18.35
Validamycin	23.11	25.50	24.97	24.80	24.71	23.35	23.85	24.78	23.67
Oxolinic acid	40.08	40.79	41.16	42.17	44.38	44.53	43.29	41.33	41.85
Polyoxins	16.24	15.49	15.25	15.80	14.59	13.65	13.23	13.52	11.67
Total	167.54	173.24	172.73	175.71	181.43	139.07	136.22	135.90	133.24

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

Table 88 shows the total use (or sales) of antimicrobials in humans, food-producing animals, aquatic animals, companion animals, antimicrobial feed additives, and agrochemicals. Antimicrobial selective pressure in Japan from a One Health perspective has decreased by approximately 4% compared to 2013. The highest frequency was observed among tetracyclines at 18-21%, followed by penicillins at 13-17%, and macrolides at 11-15%. The use of 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 88. Current volume of antimicrobial use (or sales) in Japan (t)

	2013	2014	2015	2016	2017	2018	2019	2020	2021
Penicillins	222.0	229.1	249.2	262.8	268.5	279.9	302.8	265.5	267.3
Cephalosporins	168.2	163.7	166.5	165.3	160.4	156.7	154.9	131.2	130.4
Monobactams	0.1	0.1	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	8.8	9.1
Aminoglycosides	97.2	98.8	93.1	109.1	104.1	93.7	91.6	93.3	85.5
Macrolides	191.3	177.1	207.4	238.4	238.9	244.4	267.9	241.5	221.1
Lincosamides	41.8	46.0	31.3	24.3	27.6	25.1	24.1	23.6	24.6
Tetracyclines	359.7	345.9	356.0	351.3	363.7	318.7	320.9	313.1	315.3
Peptides and glycopeptides	49.0	40.4	46.4	48.5	37.7	24.1	28.6	28.7	31.2
Sulfonamides*.	149.7	147.5	150.4	154.4	161.2	154.4	155.7	174.3	163.2
Fluoroquinolones	66.8	65.8	63.9	63.5	60.0	56.7	55.3	40.1	37.6
Other quinolones	41.6	43.1	43.2	44.3	46.0	46.1	46.0	43.8	43.7
Amphenicols, thiamphenicols and derivatives	21.8	26.2	29.8	26.6	27.2	24.9	27.5	25.6	27.1
Furan and derivatives	14.5	1.8	1.2	1.6	1.4	1.3	1.4	1.2	1.6
Polysaccharides	0.2	0.0	0.1	0.1	0.1	0.0	2.3	3.4	1.4
Polyethers	136.0	142.5	141.7	159.9	165.5	161.0	174.1	192.5	169.7
Polyoxins	16.2	15.5	15.3	15.8	8.6	13.7	13.2	13.5	11.7
Others*.	138.4	132.6	124.6	118.6	122.8	133.3	127.4	115.2	111.9
Total	1724.3	1685.9	1730.2	1795.0	1803.7	1743.9	1803.4	1715.5	1652.5

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

Table 89. Changes in the volume of antimicrobial use (or sales) in Japan by year (unit: metric tons) (cont.)

	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	143.8	59.5	16.3	2.4	0.0	0.0	151.1	62.0	13.9	2.1	0.0	0.0	165.3	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*	17.6	40.7	0.3	0.0	56.7	23.1	16.6	42.4	0.5	0.0	47.6	25.5	16.9	45.6	0.2	0.0	36.9	25.0
Total	563.0	651.2	119.9	8.5	235.1	146.6	560.6	640.2	100.1	8.1	225.9	151.0	580.1	643.3	131.9	7.8	216.4	150.7
Total for year						1,724.5						1,686.0						1,730.2

Table 89. Changes in the volume of antimicrobial use (or sales) in Japan by year (unit: metric tons) (cont.)

	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	172.8	73.8	14.6	1.6	0.0	0.0	180.2	71.7	14.7	1.7	0.0	0.0	190.9	74.5	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	149.5	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	50.1	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*	17.0	43.6	0.5	0.0	32.7	24.8	14.6	48.7	0.5	0.0	36.9	22.1	14.1	48.8	0.7	0.0	46.3	23.4
Total	591.4	659.9	155.1	6.7	228.2	153.6	581.6	681.3	169.9	6.9	221.2	142.7	582.9	628.1	168.5	8.6	216.7	139.1
Total for year						1795.0						1803.7						1743.9

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

Table 89. Changes in the volume of antimicrobial use in Japan by year (unit: metric tons) (cont.)

	2019						2020						2021					
	Humans	Food-producing animals	Aquatic animals	Companin 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	210.4	73.8	17.0	1.6	0.0	0.0	168.6	76.2	19.2	1.5	0.0	0.0	178.3	72.4	14.3	2.3	0.0	0.0
Cephalosporins	146.9	4.1	0.0	3.9	0.0	0.0	123.5	3.8	0.0	3.9	0.0	0.0	122.3	4.1	0.0	4.0	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	10.0	0.0	0.0	0.0	0.0	0.0	8.8	0.0	0.0	0.0	0.0	0.0	9.1	0.0	0.0	0.0	0.0	0.0
Aminoglycosides	0.7	34.8	0.0	0.4	0.0	55.7	0.5	36.5	0.0	0.4	0.0	55.9	0.5	29.8	0.0	0.1	0.0	55.1
Macrolides	87.2	73.3	107.4	0.0	0.0	0.0	67.8	72.7	101.0	0.0	0.0	0.0	63.4	73.0	84.7	0.0	0.0	0.0
Lincosamides	2.7	16.3	4.9	0.2	0.0	0.0	2.1	17.5	3.8	0.2	0.0	0.0	2.1	19.1	3.2	0.2	0.0	0.0
Tetracyclines	7.7	242.9	69.6	0.5	0.0	0.2	8.4	240.1	63.8	0.4	0.0	0.4	8.7	236.5	68.8	0.4	0.0	0.9
Peptides and glycopeptides	2.6	19.6	0.0	0.0	6.4	0.0	2.7	19.0	0.0	0.0	7.0	0.0	2.4	18.4	0.0	0.0	10.4	0.0
Sulfonamides	71.0	68.6	15.6	0.5	0.0	0.0	75.7	84.4	13.4	0.8	0.0	0.0	81.2	64.2	17.5	0.3	0.0	0.0
Fluoroquinolones	47.7	6.7	0.0	0.9	0.0	0.0	33.0	6.2	0.0	0.9	0.0	0.0	29.2	7.5	0.0	0.9	0.0	0.0
Other quinolones	0.1	0.1	2.5	0.0	0.0	43.3	0.1	0.2	2.2	0.0	0.0	41.3	0.0	0.2	1.6	0.0	0.0	41.9
Amphenicols, thiamphenicols and derivatives	0.1	23.9	3.5	0.0	0.0	0.0	0.1	23.1	2.4	0.0	0.0	0.0	0.1	24.2	2.8	0.0	0.0	0.0
Furan and derivatives	0.0	0.0	1.4	0.0	0.0	0.0	0.0	0.0	1.2	0.0	0.0	0.0	0.0	0.0	1.6	0.0	0.0	0.0
Polysaccharides	0.0	0.0	0.0	0.0	2.3	0.0	0.0	0.0	0.0	0.0	3.4	0.0	0.0	0.0	0.0	0.0	1.4	0.0
Polyethers	0.0	0.0	0.0	0.0	174.1	0.0	0.0	0.0	0.0	0.0	192.5	0.0	0.0	0.0	0.0	0.0	169.7	0.0
Polyoxins	0.0	0.0	0.0	0.0	0.0	13.2	0.0	0.0	0.0	0.0	0.0	13.5	0.0	0.0	0.0	0.0	0.0	11.7
Others*	13.3	47.3	0.3	0.0	42.7	23.8	10.5	47.1	0.9	0.0	31.9	24.8	9.6	48.7	0.3	0.0	29.6	23.7
Total	600.2	611.4	222.1	8.0	225.5	136.2	501.9	626.8	208.0	8.1	234.8	135.9	507.0	598.1	194.7	8.1	211.1	133.2
Total for year						1,803.8						1715.4						1652.2

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

(6) Research into antimicrobial stewardship

The following provides a summary of past reports on studies related to the appropriate use of antimicrobial agents in Japan and those published since this report last year (from the latter half of 2022). 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] 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, 5-7], IQVIA Inc.'s IQVIA Claims[8], and MDV's MDV analyzer[11]). Unless otherwise indicated, figures in square brackets ([]) in the text show the 95% confidence interval.

1. Past reports on antimicrobial stewardship

Studies have been reported on the appropriate use of antimicrobial agents for acute respiratory tract infections and acute diarrhea, which are addressed in the Manual of Antimicrobial Stewardship[1-7]. It was suggested that although antimicrobial use has been gradually decreasing, there is still room for intervention to support appropriate use, as there are still many prescribed for acute respiratory tract infections and acute diarrhea. In this context, in 2018, the appropriate use of pediatric antimicrobial agents was introduced as a premium national health insurance (NHI) item for children under 3 years of age, and the eligible age was further raised to under 6 years of age in the 2020 revision. Muraki et al. examined the effect of this premium item in 2018 for children under 15 years of age using the IQVIA's database, revealing that the percentage of antimicrobial prescriptions was lower at facilities that had claimed this premium item compared to those that had not.[8] In addition to these results, the eligible age range for the item is being expanded, and expansion of the study period and age, and a more detailed investigation of the effect on appropriate use of antimicrobials with and without age-specific introduction are also to be considered for the promotion of appropriate use of antimicrobial agents in the future. As for children, a new study investigating the effects of Action Plans targeting pediatric clinics has been reported and is described in the next section.[9] With regard to acute diarrhea, Okubo et al. previously showed antimicrobial use from April 2012 to December 2015 for children (<18 years old) using the JMDC's database7. Insurance claims on 4,493 outpatients with acute diarrhea were studied, of which 29.6% of the patients were prescribed some type of antimicrobial agent, with FOM being the most common antimicrobial agent (20.3%). For adults, Ohno et al. used the JMDC database to investigate antimicrobial use for acute diarrhea among 0–65-year-olds from January 2013 to December 2018.10 Over the 6-year study period, 94.6% of all subjects had non-bacterial diarrhea, but the antimicrobial prescription rate (number of prescriptions/visits) was 46.5% in adult males and 40.8% in adult females. The antimicrobial prescription rate for children (0-17 years) was 30.5% for boys and 30.4% for girls, which was not significantly different from a previous survey by Okubo et al [7]. Sugiyama et al. also investigated the status of oral antimicrobial prescriptions for acute diarrhea using a practice database-based analysis tool (MDV analyzer: Medical Data Vision Inc., Tokyo, Japan) [11]. The investigation was conducted between January 2013 and December 2019 with hospitals participating in the Diagnosis Procedure Combination / Per-Diem Payment System and registered on the MDV analyzer nationwide, which showed that the number of patients prescribed has decreased over time, similarly to the results of Ohno et al.'s study.

[Study on the impact of the introduction of the premium for appropriate use of pediatric antimicrobials].

Using the JMDC database, Jindai investigated the impact of the premium, introduced in April 2018, that offers incentives for not prescribing antimicrobials for respiratory tract infections and diarrhea (0-2 years) and the healthcare provider education (6 years and older) based on the information from April 2013 to February 2020. The effect was assessed using interrupted time series analysis.[12] The results showed that antimicrobial prescribing decreased significantly after the introduction of the premium in the 0-2 years group (-47.5 prescriptions [77.3 to -17.6] per 1,000 monthly clinic visits). Education for healthcare providers reduced antimicrobial prescribing for all ages. These showed an immediate effect after introduction, but no long-term effect.

Okubo et al. used NDB to similarly assess the effect of the premium using a difference-in-differences analysis and found a reduction in antimicrobial prescribing (DID estimate, -228.6 DOT per 1,000 cases [95% confidence interval -272.4 to -184.9]) [13].

There was also no increase in out-of-hour consultations with the treatment of respiratory symptoms (DID estimate, -256.9 DOT [-379.3 to -134.5] per 1,000 cases) or antihistamines (DID estimate, -198.5 DOT [-282.1 to -114.9] per 1,000 cases) [DID estimate, -4.43 per 1,000 cases [-12.8 to -3.97]. There was also no increase in hospital admissions [DID estimate, -0.08 per 1,000 cases [-0.48 to 0.31]. The study showed that it led to a reduction in unnecessary antimicrobial prescribing without any negative impact on healthcare.

[Research on prescribing status]

Using JMDC, Sato et al. analyzed the prescribing of prophylactic antimicrobials after tooth extractions for people aged 18 years and older between September 2015 and August 2018 to investigate the impact of the AMR

Action Plan [14]. The results showed that of the 662,435 eligible patients, those who were prescribed prophylactic antimicrobials accounted for 83% of the overall patients and 82% of those defined as being at low risk of post-operative infection. Although this proportion did not change within the study period, the breakdown by class showed a decrease in the prescriptions for third-generation cephalosporins from 58% to 34% (hospitals) and from 57% to 56% (clinics).

There was an increase in AMPC from 16% to 37% (hospitals) and from 6% to 10% (clinics).

Araki et al. also used JMDC to survey 18,659 working-age population members who had undergone medical examinations for at least five years and had been diagnosed with the common cold at least twice between January 2005 and February 2016 [15]. The results showed 49.2% (9,180 patients) were prescribed antimicrobials, and it was revealed that its factors included lack of chronic disease, male patients, and clinics or hospitals with less than 20 beds. In addition, 40-45% were prescribed cephalosporins. In interpretation, it should be noted that the study subjects were from the working-age population.

The situation of inappropriate prescribing was revealed, with cephalosporins being the most commonly used, indicating the need to promote ASP.

2. New research reports on antimicrobial stewardship

Tsuzuki et al. noted that although antimicrobial use continued to decrease over time from 2015 to 2021, there was no evident decrease in the disease burden of bacteremia caused by resistant bacteria over the same period. There are multiple hypotheses as to why this phenomenon was observed, but it suggests that simply decreasing antimicrobial use may not be an adequate measure to effectively combat AMR.[16]

Using NDB, Muro et al. examined the utility of blood cultures and the impact of blood cultures on mortality, length of hospital stays, and antimicrobial use in patients with community-acquired pneumonia admitted between April 2016 and March 2017. Propensity score matching was used to compare the blood culture implementation group with the control group, and the results showed that the blood culture implementation group had significantly lower mortality and length of hospital stay and predominantly higher antimicrobial use than the control group, indicating that blood culture implementation in community-acquired pneumonia is associated with appropriate use [17].

Ide et al. used JMDC to study the prescribing of oral macrolide antimicrobials from 2013 to 2018. Macrolides accounted for 30% of oral antimicrobial prescriptions, of which clarithromycin accounted for 60%. Most prescriptions were for the common cold, with some prescriptions for chronic conditions such as allergic diseases and skin conditions. The study suggests a need to review the use of macrolides for the common cold and to properly evaluate their long-term use for skin and allergic diseases.[18]

Goto et al. used MDV to investigate factors affecting efficacy and safety in patients treated with vancomycin from 2010 to 2019 in the TDM implementation group and the target group. While drug administration fees contributed to a reduction in 30-day mortality, infection team placement had no effect, suggesting the need for individualized pharmacological management of patients.[19]

3. New data collection and analysis methods for appropriate use of antimicrobial agents

A system is being developed to tabulate the percentage of antimicrobial use for respiratory tract infections using NDB information. We are examining the ratio of antimicrobial prescriptions for specific illnesses and injuries. Monitoring by region, age group, and type of antimicrobial agent is planned.

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(7) Research on the prudent use of antimicrobial agents for veterinary use

A new Action Plan has been published, setting targets for the reduction of antimicrobial agents in the animal (livestock) sector. While building up information on diseases for which veterinary antimicrobial agents are used, it is necessary to develop prevention and treatment guidelines for major diseases. In addition, since pet animals share living space with their family members in the home, it has been pointed out that antimicrobial-resistant bacteria may be cross-transmitted within the home, so it is extremely important to understand the actual status of antimicrobial agents uses. The following is a survey on the prudent use of antimicrobial agents for veterinary antimicrobial settings although the study area is limited.

1. Utilization of digital medical record data of Agricultural Mutual Ais Associations

Terashi et al. used digital medical record data maintained by NOSAI Gifu to tabulate the therapeutic purposes and net-end equivalents of antimicrobial agents used to treat cattle.[1] Antimicrobial agents were used predominantly (85%) for gastrointestinal (50.4%) and respiratory (34.4%) diseases, with sulfonamides (49.2%) for coccidiosis and phenicol agents (21.7%), mainly florfenicol, for respiratory disease, being the main components. National data from the Ministry of Agriculture, Forestry, and Fisheries (MAFF) indicate that tetracycline antibiotics are also commonly used in cattle, suggesting that there are regional differences in antimicrobial use.

2. Use of second-line drugs in companion animals

Murakami et al. in cooperation with the Gifu Veterinary Medical Association surveyed 35 pet hospitals where cases receiving fluoroquinolones (FQs), third-generation cephalosporins, carbapenems, and/or vancomycin products were investigated.[2] They were used in 1,209 cases during the study period, including 734 cases of FQs, 467 cases of third-generation cephalosporins, and 8 cases of carbapenems, and no vancomycin products were used; for both FQs and third-generation cephalosporins, the percentage of injectable formulations used was significantly higher in cats than in dogs. These two agents tended to be used more frequently for skin/ear diseases regardless of animal species, but their use for other diseases differed between dogs and cats.

3. New data collection and analysis methodologies

In the Japan Racing Association livestock promotion Project, a pilot test of an electronic instruction system is being conducted with several swine farmers. Once this system is in operation, it will allow real-time monitoring of diseases that are problematic in the swine farming industry and facilitate understanding of the actual usage of antimicrobial agents, including their components and administration methods.

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(8) Environment

Pharmaceutical products including antimicrobials, agents, and daily necessities, are collectively referred to as "Pharmaceuticals and Personal Care Products (PPCPs)." PPCPs may have physiological activity even at low concentrations, causing concerns about the effect on aquatic ecosystems.[10] Regarding antimicrobials as a type of PPCP, 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 OFLX and NFLX, 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 CAM indicated certain similarities 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 CAM were contained in sewage at the respective concentrations of 51 to 442 ng/L and 886 to 1,866 ng/L. In addition, in the environmental survey of chemical substances conducted by the Ministry of the Environment, a maximum of 130 ng/L of AZM, 2.3 ng/L of AMPC, 3.1 ng/L of thiamulin, 540 ng/L of LVFX, and 240 ng/L of CAM were detected and up to 1.4 ng/L of ABPC and up to 2.3 ng/L of SM have been detected in river water and other water.[14, 15, 16]

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8. Public Awareness regarding Antimicrobial Resistance in Japan

(1) Surveys of the general public

1) Surveys of attitudes among the public

Public awareness surveys concerning antimicrobial resistance funded by a Ministry of Health, Labour and Welfare research grant were conducted in March 2017, February 2018, September 2019, and September 2020, and the fifth survey in October 2022. [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 survey was initiated with a target number of 3,000 respondents, and the 2017 survey had 3,390 valid responses, the 2018 survey 3,192, the 2019 survey 3,218, the 2020 survey 3,200, and the 2022 survey 3,193. Women comprised 48.8% of respondents in 2017, 49.7% in 2018, 52.2% in 2019, 50.4% in 2020, and 50.4% in 2022. Until 2019, more than 40% of all respondents experienced taking antibiotics because of cold, which decreased to 29.8% in 2020 and to 19.6% in 2022. 15.5% of respondents reported taking oral antibiotics for a new coronavirus infection, and 35.1% when combined with a cold. The percentage of respondents taking antimicrobials against a cold had decreased. However, the percentage remained largely unchanged, with approximately 40% of respondents saying that antibiotics are effective against colds 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 results of this survey were similar to the trends of responses in the previous four surveys, so ongoing efforts to raise public awareness using a variety of measures, including behavioral economics methodology, are required in order to change attitudes among the public.

Table 90. Reasons for taking oral antibiotics (%)

(select all that applied)	2017 (%) (n=3,390)	2018 (%) (n=3,192)	2019 (%) (n=3,218)	2020 (%) (n=3,200)	2022 (%) (n=3,193)
Cold	45.5	44.7	41.2	29.8	19.6
Others/unknown	24.3	21.2	23.2	30.4	32.5
Influenza	11.6	12.4	12.0	5.8	2.6
Fever	10.7	11.3	8.5	7.8	9.9
Nasopharyngitis	9.5	10.8	10.5	9.9	8.3
Cough	9.0	10.8	6.9	4.5	5.0
Sore throat	7.7	7.8	8.2	7.1	8.1
Skin or wound infection	6.5	7.0	9.0	14.5	11.8
Bronchitis	5.4	6.6	5.1	5.9	5.8
Headache	4.3	5.0	4.1	5.0	7.0
Diarrhea	3.1	3.2	2.6	3.1	2.3
Urinary tract infection	2.3	2.5	2.7	4.7	3.5
Pneumonia	1.4	1.7	1.3	1.2	1.2
Novel coronavirus infection	-	-	-	-	15.5

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)	2020 (n=3,200)	2022 (n=3,193)
Antibiotics beat viruses	Correct	46.8	46.6	52.4	42.6	46.3
	Incorrect	21.9	20.3	17.7	23.5	19.5
	Do not know	31.3	33.0	29.9	33.9	34.2
Antibiotics have effect on cold and influenza	Correct	40.6	43.8	43.9	40.4	43.1
	Incorrect	24.6	22.1	22.7	23.1	20.7
	Do not know	34.8	34.1	33.4	36.4	36.2
Unnecessary use of antibiotics may result in the loss of their effect	Correct	67.5	68.8	66.4	64.9	60.8
	Incorrect	3.1	3.7	3.4	3.3	4.3
	Do not know	29.4	27.5	30.2	31.8	34.9
Adverse effects are involved in the use of antibiotics	Correct	38.8	41.5	45.7	45.6	42.6
	Incorrect	12.7	13.4	10.5	9.9	11.2
	Do not know	48.6	45.0	43.8	44.5	46.2

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

		2017 (n=3,390)	2018 (n=3,192)	2019 (n=3,218)	2020 (n=3,200)	2022 (n=3,193)
I have discontinued taking antibiotics, or adjusted a dose or frequency based on my own judgment	Yes	23.6	24.0	24.6	23.3	22.2
	No	76.4	76.0	75.4	76.7	77.8
I keep antibiotics in my house	Yes	11.7	11.9	9.8	9.3	10.2
	No	88.3	88.1	90.2	90.7	89.8

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

		2017 (n=396*)	2018 (n=426*)	2019 (n=3,218)	2020 (n=298)	2022 (n=326)
I have used antibiotics that I kept at home for myself	Yes	75.8	77.5	75.6	76.2	81.3
	No	24.2	22.5	24.4	23.8	18.7
I have given antibiotics that I kept at home to my family or friend	Yes	26.5	27.2	28.5	25.5	35.6
	No	73.5	72.8	71.5	74.5	64.4

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

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2) Surveys of perception of antimicrobial agents and treatment-seeking behavior among 20-30-year-olds

Surveillance based on the National Database for Prescription and National Health Checkups (NDB) shows that the use of antimicrobial agents (DID) is higher among women than among men in all age groups, especially among women aged 20-39. To find out the reason for this, an Internet survey was conducted in February 2021 on how antimicrobial agents are perceived and how they seek treatment, targeting 1,000 respondents each for males, females, aged 20-29, and aged 30-39, for a total of 4,000 respondents. 22.6% of men and 36.1% of women reported having visited a hospital or clinic (including dentistry) at least 6 times during the past year, with women having more frequent visits. 38.6% of men and 38.4% of women reported that antimicrobial agents were prescribed during their visits. 40.2% of men and 24.3% of women reported that the reason they were prescribed antimicrobials was a cold. 22.2% of men and 18.3% of women had requested antimicrobial agents at a hospital or clinic. 11.6% of men and 8.4% of women went to see a doctor immediately when they caught a cold, and 31.2% of men and 39.8% of women thought it was better to take medicine instead of trying to be stoic when feeling sick. The survey results showed no difference between men and women in the percentage of those who are prescribed antimicrobial agents per visit, suggesting that the difference in the number of visits is the cause of the difference in the use of antimicrobial agents between men and women. To effectively promote the proper use of antimicrobial agents, it is necessary to consider specific messages that also take into account awareness and attitudes toward infectious diseases and antimicrobial agents, as well as treatment-seeking behavior.

(2) Surveys of healthcare providers

1) Awareness survey of clinic physicians

The Joint Survey Committee on Appropriate Use of Antimicrobial Agents in Outpatients of the Japanese Society of Chemotherapy and the Japanese Association of Infectious Diseases conducted the second survey of awareness among physicians working in clinics in February 2018 and from September to October 2020. The survey questionnaire was distributed to 3,000 randomly selected clinics nationwide, and the forms were filled and returned. Compared to the survey in 2018, awareness of the National Action Plan on AMR increased, and the number of respondents who answered that they had "never heard of it" decreased from 44.9% to 34.8% (Table 93). The percentage of antimicrobial prescriptions for common cold decreased from 62.0% to 71.1% with "0-20%" as the percentage of prescriptions (Table 95). Responding to requests for antimicrobial prescriptions, 35.5% of the respondents said they would "explain and not prescribe," while 10.8% and 49.1% said they would "prescribe as requested" and "prescribe if not satisfied after explanation," respectively, hardly different from the results of the previous survey (Table 96). These results suggest that the intention to be actively involved in patient education and communication is not necessarily high. 44.7% "never," 28.7% "not very often," 24.1% "sometimes," and 2.5% "always" take antimicrobial agents when they themselves have a common cold, and 39.1% "never," 31.5% "not very often," and 27.4% "sometimes," and 2.1% "always" recommend antimicrobial agents when their family member has a common cold. These results suggest that physicians who prescribe more antimicrobial agents for the common cold may be expecting a therapeutic effect when prescribing them. As in the previous survey, the percentage of prescribing antimicrobial agents for acute bronchitis was also high (Table 97).

The development of simpler pathogen diagnostic tests may be effective in promoting the appropriate use of antimicrobial agents. Doctors aged 60 years or older were more aware of the appropriate use of antimicrobial agents than physicians younger than 60 years (69.6% vs. 58.5%). However, the percentage of respondents who prescribed antimicrobial agents to "20% or less" of those diagnosed with common cold was less than those under 60 (79.5% vs. 65.3%), suggesting that although they understood the importance of agent resistance control, this did not necessarily lead to prescribing behavior (Tables 98 and 99). The majority of respondents cited the campaign to the public as necessary to achieve the National Action Plan on AMR, which was unchanged from the previous survey.

Table 94 Awareness of National Action Plan on AMR (%)

	2018 (n=267)	2020 (n=627)
I can explain it to people.	1.9	3.5
I understand it.	21.0	27.8
I only know the name.	32.2	33.1
I have no idea.	44.9	34.8

Table 95 Percentage of antimicrobials prescribed when diagnosing with a common cold (%)

	2018 (n=242)	2020 (n=543)
0-20%	62.0	71.1
21-40%	17.8	16.6
41-60%	7.4	6.8
61-80%	8.3	3.5
81% or more	4.5	2.0

Table 96 Response when patients or family members diagnosed with a common cold request for antimicrobial agent (%)

	2018 (n=252)	2020 (n=609)
Prescribe it if they are not convinced by explanation	50.4	49.1
Explain and not prescribe	32.9	35.5
Prescribe as requested	12.7	10.8
Other	3.7	4.6

Table 97 Frequency of antimicrobial prescription when diagnosing an acute bronchitis (in the past year) (%)

	2018 (n=232)	2020 (n=522)
0-20%	31.0	35.4
21-40%	23.7	24.9
41-60%	14.2	15.7
61-80%	9.5	9.0
81% or more	21.6	14.9

Table 98 How much aware of the appropriate use of antimicrobial agents in the past year (%)

How much aware of the appropriate use of antimicrobial agents in the past year (%)	Always/quite aware	Somewhat/not at all consciously
Under 60 years old	58.5	41.5
60 years old and over	69.6	30.4

Table 99 Frequency of antimicrobial prescription when diagnosing a common cold (in the past year) (%)

	20% or less	20% or more
Under 60 years old	79.5	20.5
60 years old and over	65.3	34.7

2) Research on infectious diseases and antimicrobials in pharmacy education

Pharmacists are important members of the healthcare team responsible for in-hospital and community infection control and prevention (ICP) and antimicrobial stewardship program (ASP) activities, and the need for education on AMR and clinical infectious diseases among pharmacists is increasing. However, the current state of education on clinical infectious diseases in the faculty of pharmacy of Japanese universities was not clear, so a nationwide survey of pharmacy schools in Japan was conducted from February to March 2022. Questionnaires were sent to pharmacy schools across Japan and 44 out of 74 universities responded.

The median number of teaching staff members in charge of infectious disease education was 7 [4-12], of which practitioners were 3 [1-6]. At 62.8% of the universities, teaching staff members possessed clinical experience in infectious diseases. Regarding the contents of education, the most frequently reported as “inadequate” or “not implemented” were: the concept of prophylactic antimicrobials in the perioperative period (74.5% inadequate or not implemented in total), how to explain to patients when antimicrobial is not necessary (76.8% total), patient education on prudent antimicrobial (79% in total), team approach to infectious disease care and infection control (53.5% in tot), and education on antimicrobial research and development (76.8%in total). Insufficient time for lectures and a lack of specialists were the top issues in clinical infectious disease education. The survey also revealed that educational status and resources for clinical infectious diseases and AMR varied widely. It was suggested that resources, including the overall curriculum and the number of teachers, need to be examined and improved.

(3) Survey of veterinary medicine students

The Ministry of Agriculture, Forestry and Fisheries has been conducting lectures and awareness surveys on antimicrobial resistance measures for veterinary students nationwide since the fiscal year 2019. Until the fiscal year 2020, awareness surveys were conducted after lectures, but since the fiscal year 2021, surveys have also been conducted before lectures to assess the effectiveness of the lectures. The fiscal year 2022 survey was conducted in the form of a questionnaire survey via the Internet; 530 students from 12 universities (2nd and 3rd- year students: 269, 4th-year students: 176, 5th-year students: 85) responded to the fiscal year 2022 survey.

In the awareness survey conducted prior to the lecture, 93.6% of the students answered "effective against bacterial infections" in the question about antimicrobial agents (Table 100), indicating a slight increase in the number of students with correct knowledge, and inferring that they have acquired a certain level of knowledge about antimicrobial agents in their veterinary education. However, a certain number of students chose "effective against a common cold" or " effective against viral infection," suggesting that continued efforts should be made to ensure the dissemination of the correct knowledge.

As for what they know about antimicrobial resistance control in the veterinary field (Table 101), a high percentage of students chose " Japanese Veterinary Antimicrobial Resistance Monitoring System (JVARM) is being conducted." and "Partnership between the veterinary and human medicine fields," but the results showed that more than half of the total students are still unaware of them. In addition, only approximately 30% of the students were aware of the important knowledge for practicing drug resistance countermeasures in the field, such as Reduction of infection opportunities through vaccination contributes to antimicrobial resistance control" and "The existence of antimicrobial agents called second-line agents". In particular, the trend in the percentage of students who know that "Reduction of infection opportunities through vaccination contributes to antimicrobial resistance control" has not changed over the past three years.

Because veterinarians play a key role in antimicrobial resistance control in the veterinary field, it is important to continue to educate veterinary students on the correct knowledge and prudent use of antimicrobial agents.

Table 100. Please give your perceptions about antimicrobials (%)

	2nd and 3rd year (n=269)	4th year (n=176)	5th year (n=85)	Whole (2020) (n=394)	Whole (2021) (n=404)	Whole (2022) (n=530)
Effective against a common cold	32.0	38.1	22.4	26.6	32.2	32.5
Effective against bacterial infections	94.1	90.3	98.8	92.4	91.0	93.6
Effective against viral infections	26.8	24.4	7.1	4.8	10.4	22.8
Effective to prevent complications after surgery	39.4	47.7	78.8	58.6	64.9	48.5
Used as a feed additive to be mixed with feed	31.6	44.9	34.1	53.8	41.6	36.4
Used in pesticides for vegetables and other produce	16.7	17.6	12.9	8.4	13.6	16.4

**This had been phrased as "effective against an influenza" until the fiscal year 2021.

**The fiscal year 2020 awareness survey was conducted only after the lecture, which may have biased the numbers (The faiscal years 2021 and 2022 show the results of surveys conducted prior to the lecture).

Table 101. Please select what you know about antimicrobial resistance control in the veterinary sector (%)

	2nd and 3rd year student (n=269)	4th year student (n=176)	5th year (n=85)	Whole (2020) (n=394)	Whole (2021) (n=404)	Whole (2022) (n=530)
An Action Plan on Antimicrobial Resistance (AMR) has been developed and is being implemented	17.1	46.6	42.4	43.9	18.8	30.9
The existence of antimicrobial agents called second-line agents	21.6	30.7	82.4	32.7	33.4	34.3
Japanese Veterinary Antimicrobial Resistance Monitoring System (JVARM) is being conducted	42.4	48.3	51.8	21.6	18.6	45.8
Reduction of infection opportunities through vaccination contributes to antimicrobial resistance control.	29.0	29.0	29.4	28.9	29.0	29.1
Partnership between the veterinary and human medicine fields	39.8	47.2	64.7	45.9	44.6	46.2
Determination of risk management measures based on risk assessment	31.2	45.5	40	31.7	21.3	37.4
I don't know	17.8	6.3	5.9	9.9	18.1	12.1

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9. Way Forward

The National Action Plan on AMR (2016-2020), published in 2016, aimed to conduct an integrated One Health trend survey on the current status of antimicrobial-resistant bacteria and antimicrobial usage in the human, animal, agricultural, food, and environmental sectors. This report consolidates the results and contributes to the further promotion of AMR countermeasures. It has allowed for a detailed understanding of the challenge of antimicrobial resistance in Japan and the development of measures based on this understanding. The National Action Plan on AMR (2023-2027) proposes updated goals and strategies based on the achievements to date and presents a new path forward in the fight against AMR. The importance of a One Health approach to the AMR problem has been reemphasized, and it is expected that information on AMR trends and countermeasures be analyzed and evaluated regularly by linking information from human, animal, agricultural, food, and environmental trends studies and by making international comparisons. It also emphasizes the importance of updating methodologies for collecting and analyzing data on trends in antimicrobial resistance and antimicrobial use in Japan and abroad, as well as international cooperation and collaboration for AMR countermeasures. Continued efforts to conduct advanced research are considered important for leading the global effort to combat AMR.

In the human field, with reference to the "Manual of Antimicrobial Stewardship" and other guidelines, unnecessary antimicrobial prescriptions should be reduced, particularly for acute respiratory tract infections, and when antimicrobial agents are prescribed, appropriateness is expected. Advancement of appropriate use of antimicrobial agents is dependent on the availability of appropriate antimicrobial agents when they are needed. Given the current status where some antimicrobial agents have become difficult to obtain in clinical settings, it is important to ensure a stable supply of essential antimicrobial agents. Considering that it has become possible to obtain information on antimicrobial resistance and antimicrobial use on a regional basis using various surveillance systems related to AMR, it is advisable to use this information to select antimicrobial agents and promote appropriate infection control measures according to local conditions. Furthermore, in promoting the appropriate use of antimicrobial agents, it is necessary to continue and develop educational and awareness-raising activities for the public and healthcare professionals using various methods, including behavioral economic methodologies.

In the animal field, resistance rate to third-generation cephalosporins and fluoroquinolones in *Escherichia coli* isolated from diseased companion animals, surveillance of which began in 2017, weas found to be higher than in *E. coli* isolated from food-producing animals. Therefore, in addition to the measures against antimicrobial resistance in the food-producing animals that have been implemented, it is necessary to continue and strengthen measures against antimicrobial resistance through the dissemination of the “Guide for Prudent Use in Companion Animals” which was published in 2020. In addition, the resistance rates of *E. coli* from healthy livestock animals to third-generation cephalosporins and fluoroquinolones, which are the outcome indicators of the National Action Plan on AMR (2016-2020), have remained low and are on target.

In food-producing animal field, although the volume of tetracycline sales fell in 2018 and 2020, the resistance rate to tetracycline in *E. coli* isolated from healthy food-producing animals—an outcome index—has not changed. Therefore, it is necessary to continuously reduce opportunities to use all antimicrobials through the development, commercialization, and promotion of the use of vaccines and the improvement of raising hygiene management standards, to promote appropriate and prudent use of these antimicrobials and to monitor trends in resistance rates to various antimicrobials.

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 class of antimicrobial, the reporting of antimicrobial resistance rates in healthy companion animals to accompany existing reporting on rates in diseased companion animals, following that of diseased companion animals and the enhancement of data on trends in antimicrobial-resistant bacteria in food and the environment. We expect to see further progress in the surveillance in each field which will continue next year and beyond.

Furthermore, in the National Action Plan on AMR (2016-2020), the annual Nippon AMR One Health Report (NAOR) has been playing an important role as a one-stop hub to confirm antimicrobial susceptibility data of antimicrobial-resistant bacteria in humans, animals, and foods. In the future, the analysis of antimicrobial-resistant genes and antimicrobial-resistant bacteria genome data will be extremely crucial in understanding whether and to what extent specific antimicrobial-resistant bacteria and antimicrobial-resistant genes increase or decrease and migrate between different sectors within the One Health framework, and in applying this information to risk assessment and risk management. It is also vital to steadily implement this point based on the National Action Plan on AMR (2023-2027). Industry, government, and academia will work closely together to promote collaboration among organizations in charge of different fields, while conducting cross-sectional assessments of risks to humans, animals, and the environment. These efforts will facilitate effective responses to the AMR challenge both domestically and internationally and will also play an important role in Japan's leading role in the global AMR control effort. In addition, the collection and analysis of data on antimicrobial resistance is an indispensable foundation for AMR countermeasures, and progress is expected to be made in these efforts in the future. These efforts are anticipated to make a significant contribution to AMR countermeasures in Japan and to improve the

people's health and public health.

Appendix

(1) Japan Nosocomial Infections Surveillance (JANIS)

1) Overview

JANIS is conducted to have an overview of nosocomial infections in Japan, by surveying the status of healthcare-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 healthcare-associated infections in medical settings. The aggregated data of information from all medical institutions patriated are published on the website of JANIS (https://janis.mhlw.go.jp/english/index.asp). The result of the analysis is reported back to each institution so that such feedback can be utilized for the formulation and evaluation of infection control measures at each institution. JANIS participation is voluntary with approximately 3,200 participating medical institutions as of December 2023.

Clinical Laboratory Division of JANIS collects the laboratory data of bacteria that are isolated at hospitals across Japan and publishes aggregated data regarding the proportion of clinically important bacterial species that are resistant to major antimicrobials. As of December 2023, 3,074 hospitals participated in the laboratory section. Bacteria that are isolated from specimens from inpatients as well as outpatients at participating hospitals are included in aggregated data. Since 2014, figures have also been compiled based on hospital scale, divided into hospitals with 200 or more beds and those with fewer than 200 beds. 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 (However, some of them are under Japan's Act on the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases).

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 require 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 by the operation council comprised of experts in infectious diseases, antimicrobial resistance, and other relevant professional fields. Antimicrobial Resistance Research Center (AMR-RC), 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 bacteria 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 2022 have already been submitted. 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 animals and other areas is 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, the Clinical Laboratory Division handles surveillance regarding the status of isolates of antimicrobial-resistant bacteria. 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 being 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 bias based on this sampling policy in JANIS should be addressed. With regard to clinics that were not previously covered by JANIS, clinics that perform at least one bacterial culture test per month will be able to participate in the JANIS laboratory section beginning in 2022, and discussions are in progress to compile and publish this data.

(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 *Enterobacteriales* 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 101 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 102. Reporting criteria

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

3) System

Hospitals directly input and register the information into NESID, or Public Health Centers input and register the information into NESID after confirming the details notified by hospitals. 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 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 are 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

In 2017, the governance of the Regional Infection Control Support System (RICSS) was transferred to the AMR Clinical Reference Centre to utilize the system for AMR control as a surveillance platform for infection control at regional as well as national levels. The system was renamed to Japan Surveillance for Infection Prevention and Healthcare Epidemiology: J-SIPHE.

The system has been launched as a system that can be utilized for AMR measures in hospitals as well as for the promotion of regional cooperation, and a large amount of data has been accumulated and an annual report is published annually to return the data to the facilities using the system. The J-SIPHE 2022 Annual Report covers a total of 1,876 participating medical institutions. The system is designed to collect information on the status of infectious disease treatment, infection control measures and the appropriate use of antimicrobials, the occurrence of healthcare-associated infections, the occurrence of major bacteria and antimicrobial-resistant bacteria, the occurrence of bloodstream infections caused by them, and the use of antimicrobials at participating facilities, and to make use of this information at the facilities themselves and in regional networks. With these as its purpose, the system also establishes indicators as an indicator for AMR control.

2) System

This system is based on participation in a regional cooperation network within the framework of the medical fee premium for infection prevention measures. To support AMR measures by utilizing the regional cooperation network, etc., information can be shared within the group based on unified standards, and the system visualizes data that are necessary and adequate for AMR measures by making secondary use of existing information such as returned JANIS laboratory section data and integrated inpatients EF files, while reducing the burden on participating facilities.

3) Prospects

The system needs to be further renovated so that it can be utilized for activities such as regional collaborative conferences, and to make it more accessible and meaningful for facilities that lack human resources for infection control. The system aims to make the system more effectively used in building infection control networks at the regional level and in decision-making on infection control.

(4) Trend surveillance of antimicrobial-resistant *Mycobacterium tuberculosis*

1) Overview

The 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 cases and incidence rates, the number of patients with tuberoses, treatment status, the number of deaths from tuberculosis, and so on. Information regarding to patients infected with *Mycobacterium tuberculosis* is limited to the smear-positive ratio, the number of culture-positive, data on antimicrobial susceptibility tests, and so on. Though limited, this report exclusively provides routine national information regarding antimicrobial-resistant tuberculosis bacillus.

2) System

When physicians diagnose and report a tuberculosis case to the Public Health Center, corresponding public health nurses collect detailed information from patients and physicians. The results of antimicrobial susceptibility tests are collected mostly from hospital and commercial laboratories. Those individual data are entered by Public Health Centers across Japan into NESID.

3) Survey methods

Based on the registered tuberculosis patient information, the results of antimicrobial susceptibility tests 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 agent-susceptibility testing" under "Conditions of disease" in Item 4, Paragraph 1, Article 27-8.

4) Prospects

The surveillance based on the registered tuberculosis patient information system contains the antimicrobial susceptibility results of newly registered patients with culture-positive pulmonary tuberculosis, as reported by all medical institutions. Therefore, data are considered nationally representative. Improvement in the entry rate of antimicrobial susceptibility testing results (approximately 80% at present); the establishment of a system for nationwide quality assurance for antimicrobial 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, considering its influence on human healthcare (Figure 4). 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. In FY2021, a discussion on the methodologies for antimicrobial resistance monitoring in the livestock environment started.

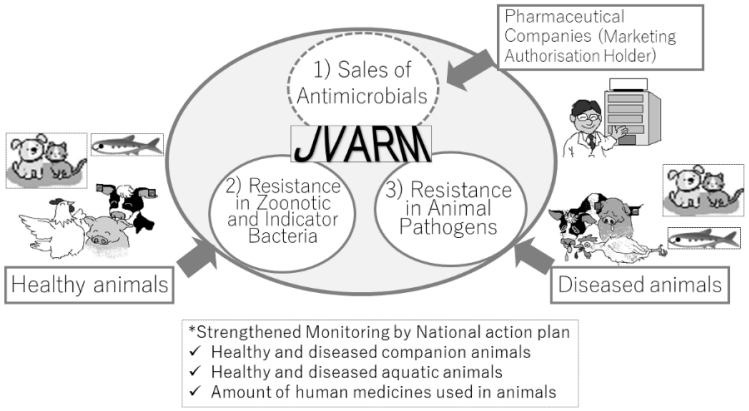


Figure 4. Overview of veterinary antimicrobial resistance monitoring

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 2012, as this facilitated more intensive sampling at a stage closer to the final food product. In 2016, 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 5). Bacteria were isolated from fecal samples collected from slaughterhouses (five sites nationwide) and poultry slaughterhouses (13 sites nationwide), 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 monitoring. The MIC for these strains is measured by the National Veterinary Assay Laboratory using a broth microdilution method based on the CLSI Criteria (Figure 5). 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 WOAH Terrestrial Animal Health Code.[3]

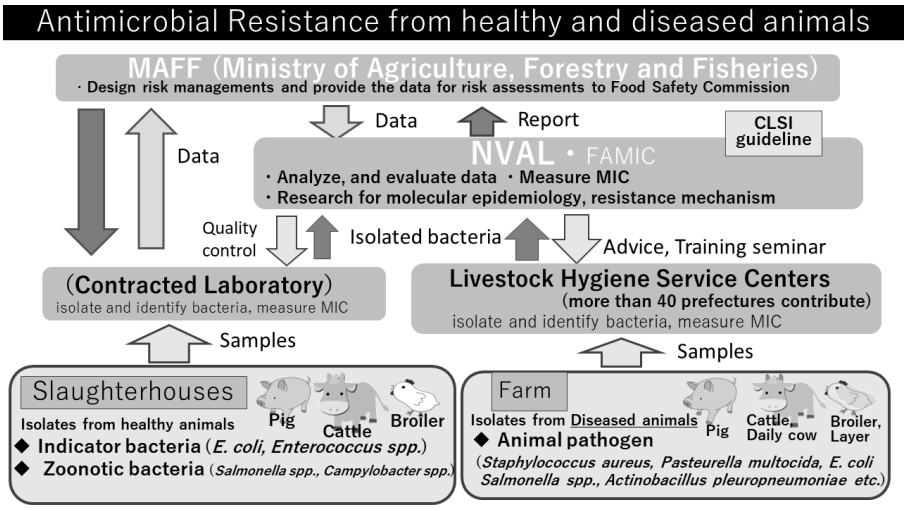


Figure 5. Monitoring system for antimicrobial-resistant bacteria from healthy livestock (slaughterhouses and poultry slaughterhouses) and from diseased livestock (farms).

For the companion animal survey, the survey method was determined based on the results of the discussion at the Working Group on Companion Animal AMR Surveillance, and from 2017, strains derived from diseased dogs and cats were collected from clinical laboratories. Also, in 2018, healthy dogs and cats were targeted, and specimens were collected from veterinary hospitals nationwide with the cooperation of the Japan Veterinary Medical Association (Fig. 6).

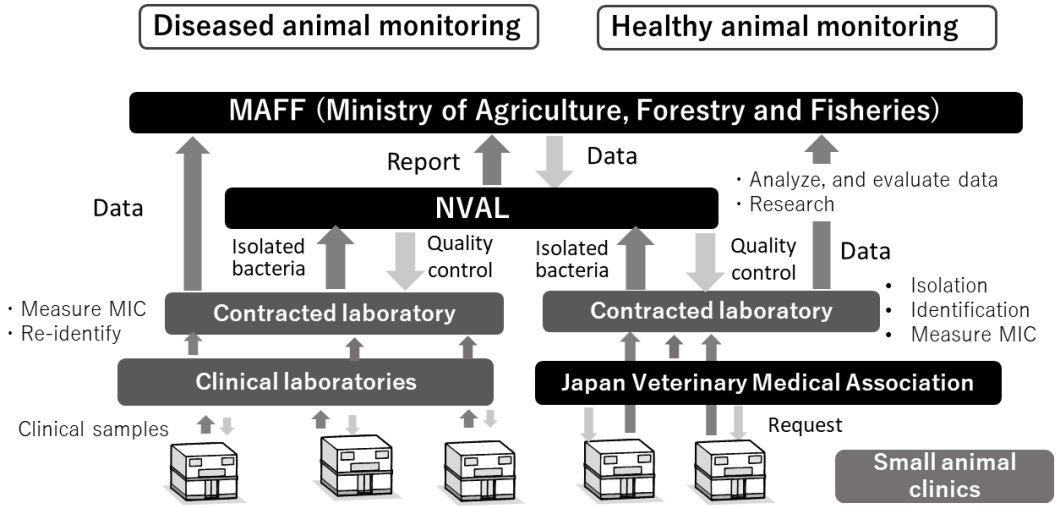


Figure 6. System for antimicrobial resistance monitoring in healthy and diseased dogs and cats

Isolation of bacteria from specimens was carried out using selective media in all cases, with one strain of one species per hospital. The MICs of the collected strains were determined at the contract laboratory using the broth microdilution method according to CLSI. Antimicrobial substances to the survey were selected for each species of bacteria, considering the drugs used in clinical settings for companion animals in addition to those targeted in the livestock survey.

Efforts are made to achieve standardization in the isolation and identification of strains and antimicrobial susceptibility tests, 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, for the molecular epidemiological survey of antimicrobial-resistant strains. Antimicrobial feed additives are analyzed by the FAMIC. Data collected through JVARM is 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.

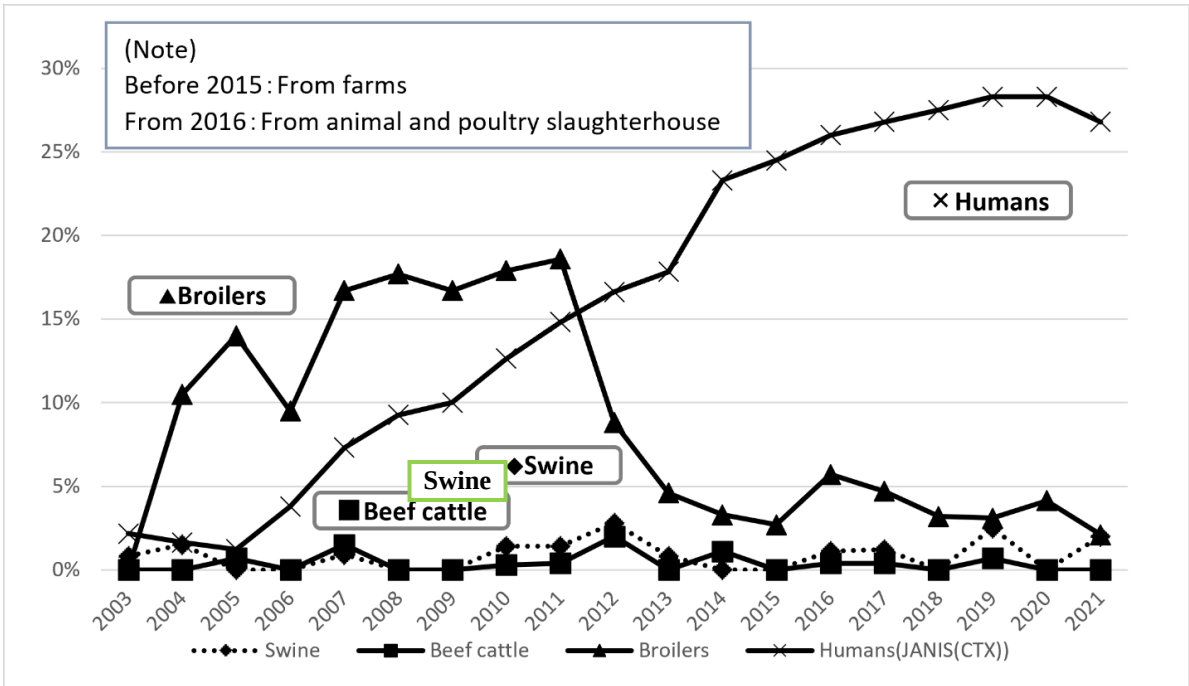


Figure 7. Comparison of the proportion of third-generation cephalosporin-resistant *Escherichia coli* derived from humans and food-producing animal

Comparing data from JVARM and JANIS, which monitors resistant bacteria in human medical settings, the resistance rate to third-generation cephalosporins had increased until 2011 in both human-derived and broiler-derived *E. coli*, but then has decreased drastically in broiler since 2012. This may be due to the discontinuation of the off-label use of third-generation, which had been practiced cephalosporins in some egg hatcheries, in response to the guidance given to the relevant organizations advising to stop it by presenting the JVARM results.[6] In humans, on the other hand, the rate has continued to increase showing different trends in broiler (Figure 7).

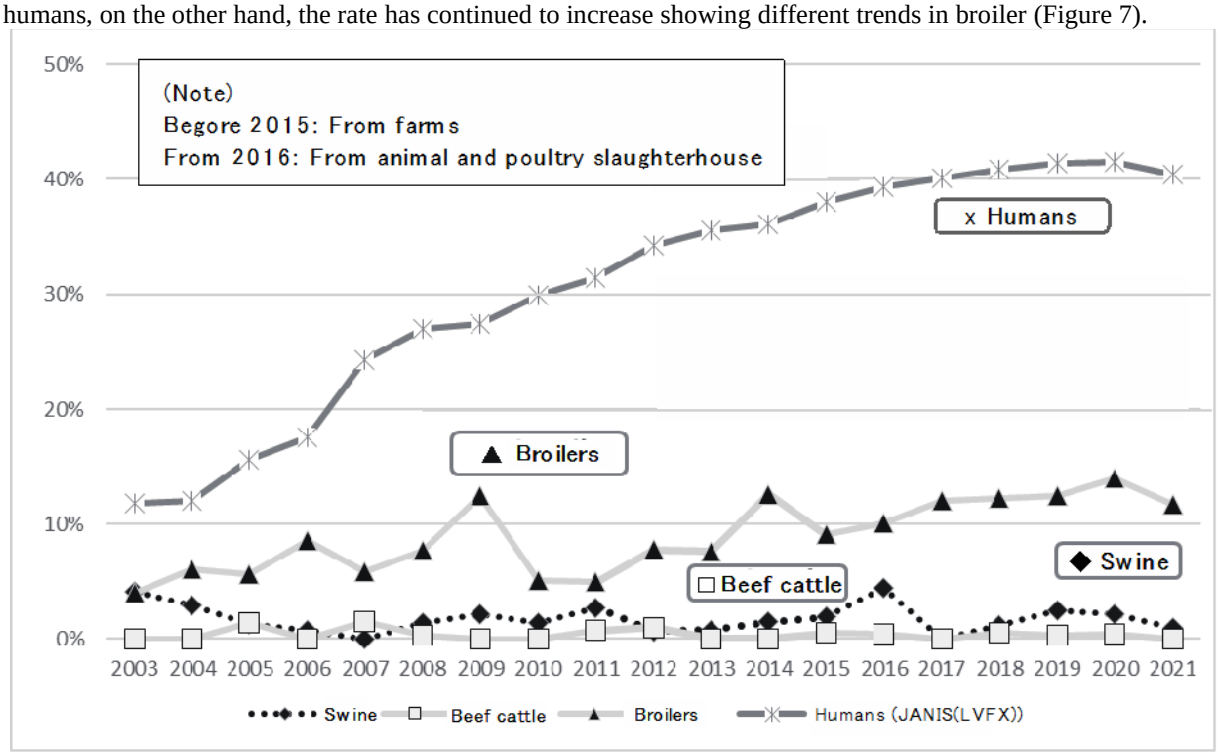


Figure 8. Comparison of the proportion of fluoroquinolone resistant *Escherichia coli* derived from humans and food-producing animal

While an increasing trend in the fluoroquinolone resistance rate of human *E. coli* has been observed since 2003, the fluoroquinolone resistance rate of *E. coli* from livestock has remained below 5% for swine and beef cattle-derived strains and below 15% for broiler-derived strains, showing different trends between human and livestock

(Figure 8).

3) Monitoring of the sales volumes of veterinary antimicrobials

An annual monitoring is conducted on the volumes of sales of veterinary antimicrobials, based on the reported quantities of veterinary agents handled by marketing authorization holders, under Article 71-2 of the Veterinary Agent Control Regulations (MAFF Ordinance No. 107 of 2004) (Figure 9). Starting in 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 sales volumes 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 agents, Quasi-agents and Medical Devices." Under the WOAH Terrestrial Animal Health Code's section on antimicrobial usage (Chapter 6.8), [4] these data are submitted to the WOAH for the activity to understand and compare usage in each country of the world.

Figure 9. Monitoring of the sales volumes of veterinary antimicrobials

4) Future prospects

The main issues to be addressed by JVARM in the future are 1) further promotion of more advanced investigation and analysis of antimicrobial resistance genes and others through whole-genome analysis of bacteria from livestock and companion animals, and consideration of their use in trend surveys and comparison with the human field; 2) evaluation of the amount of veterinary antimicrobial use concerning the biomass weight calculated by the unified method proposed by WOAH; 3) establishing and implementing methodology to investigate the distribution of antimicrobial-resistant bacteria in the environment around livestock production sites. While continuing to carry out the monitoring already implemented in the JVARM will begin efforts to address these issues. Furthermore, to promote the One Health surveillance and monitoring, we will continue to enhance our collaboration with JANIS, for example by comparing whole-genome analysis data. The data accumulated will lay the ground for risk assessment and risk management by clarifying the transmission of the process of antimicrobial resistance bacteria through collaborating with other fields.

(6) Trend Surveillance of Antimicrobial Agents in Japan (JSAC, J-SIPHE)

1) Overview

The governance of Japan Antimicrobial Consumption Surveillance (JACS), an antimicrobial use surveillance system established in 2015 through the Ministry of Health, Labour and Welfare (MHLW) Science Research, was transferred to the AMRCRC and it was renamed to Japan Surveillance of Antimicrobial Consumption (JSAC) (Antimicrobial Use Surveillance) in 2022 to conduct a monitoring of antimicrobial use in humans in Japan on an annual and continuous basis at national level and utilize it for in AMR measures. Currently, JSAC (http://amrcrc.ncgm.go.jp/surveillance/index.html) investigates antimicrobial use (AMU) in Japan and by prefecture using sales volume information and NDB. In addition, AUDs and DOTs of each participating facility are compiled and published as an annual report in J-SIPHE (https://j-siphe.ncgm.go.jp/).

2) Monitoring methods

The sales volume data is used to calculate the potency for each agent for overall use and by dosage form (oral and parenteral) and by prefecture, 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 (DDDs/1,000 inhabitants/day). 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.

* ATC Classification: Anatomical Therapeutic Chemical Classification System, a classification system for pharmaceutical products proposed by WHO.
* AWaRe classification: an indicator of appropriate antimicrobial use recommended by WHO (see p. 86)

3) Prospects

The establishment of Japan's first AMU surveillance programs in the form of JSAC and J-SIPHE put in place a system that enables trends in AMU over time to be fed back to the public. Sources of AMU information include both data on the volume of sales and insurance billing data. The sources of information used and how 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 of 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] 42 *C. jejuni* and 3 *C. coli* strains isolated from the feces of diarrhea patients at hospitals in Tokyo in 2021 were tested using five antimicrobials such as ABPC, TC, NA, CPFX, and EM. The number of samples for the 2021 isolates was very small due to the COVID-19 pandemic. Results were determined by measuring the diameter of the inhibition zone and following the criteria of antimicrobial susceptibility in the protocol[9].

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 by standards unified as part of a Ministry of Health, Labour and Welfare-funded research project concerning the promotion of food safety, concerning 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, to know the emergence of antimicrobial-resistant bacteria nationwide.

(8) Monitoring of the antimicrobial-resistant non-typhoidal *Salmonella* spp. isolated from humans and 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, antimicrobial resistance monitoring was conducted using the common protocol, antimicrobials, instruments, etc., concerning bacteria, particularly *Salmonella* spp., derived from human patients and food, as collected by these Public Health Institutes.[10] The monitoring was targeted at *Salmonella* spp. strains that were isolated from human patients and food in 2015 and 2021. 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, by the Public Health Institute Group Protocol for Antimicrobial Susceptibility Tests, using strains that were assessed as *Salmonella* spp. The 17 agents of ABPC, GM, KM, SM, TC, ST, CP, CTX, CAZ, CFX, FOM, NA, CPFX, NFLX, AMK, IPM, and MEPM disks were used in the CLSI disk diffusion method. 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 the inhibition zone would not be coalesced. The diameters of the inhibition zone were measured, and the measurements were assessed based on the criteria of the antimicrobial susceptibility in the protocol.

3) Prospects

The clear similarity was observed in the proportion of antimicrobial-resistant bacteria 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 of the antimicrobial-resistant *Neisseria gonorrhoeae*

1) Overview

In the diagnosis of gonococcal infection, the utilization of nucleic acid amplification 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 *N. gonorrhoeae* has been undertaken as research activity 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 SPCM as recommended agents; for AZM, which was used as part of the two-agent 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 antimicrobial susceptibility tests (Table 102). For reference, the proportion of resistant strain based on CLSI Guidelines (M100-S25) (Table 104) is indicated in Table 104. 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 a potential success rate of 95% or higher. At present, CTRX and SPCM are the only recommendable agents in Japan. Because *N. gonorrhoeae* that are present in the pharynx are an important source of infection, *N. gonorrhoeae* in the pharynx should be treated. Due to its *in vivo* pharmacokinetics, SPCM does not influence *N. gonorrhoeae* present in the pharynx. Therefore, CTRX is the only practically recommendable agent.

In sporadic cases, strains isolated in Japan indicate the CTRX MIC of 0.5 μg/mL in antimicrobial susceptibility tests. CTRX is administered by intramuscular injection overseas, and therefore subject to dose limitation. Therefore, if strains that indicate the CTRX MIC of 0.5 μg/mL are transmitted overseas, it is likely that CTRX loses its effect. Hence, it is required to continue with the careful monitoring of strains in the 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 103. Antimicrobial susceptibility assessment criteria based on EUCAST (μg/mL) for *N. 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 104. Antimicrobial susceptibility assessment criteria based on CLSI (μg/mL) for *N. 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 105. The proportion (%) of antimicrobial-resistant *N. 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 of the antimicrobial-resistant *Salmonella* Typhi, *Salmonella* Paratyphi A, and *Shigella* spp.

1) Overview

For typhoid and paratyphoid fever, and shigellosis, a 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., antimicrobial 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, the assessment was performed byCLSI standards, using a broth microdilution method for *Salmonella* Typhi, *Salmonella* Paratyphi A, and *Shigella* spp. in 2022 and after, and using a disk diffusion method for *Shigella* spp. in 2021 and before.

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 is high in *Shigella* spp., and therefore recurrence is also possible even after administering antimicrobials. Careful monitoring is required to prevent the possible spread of infection in Japan.

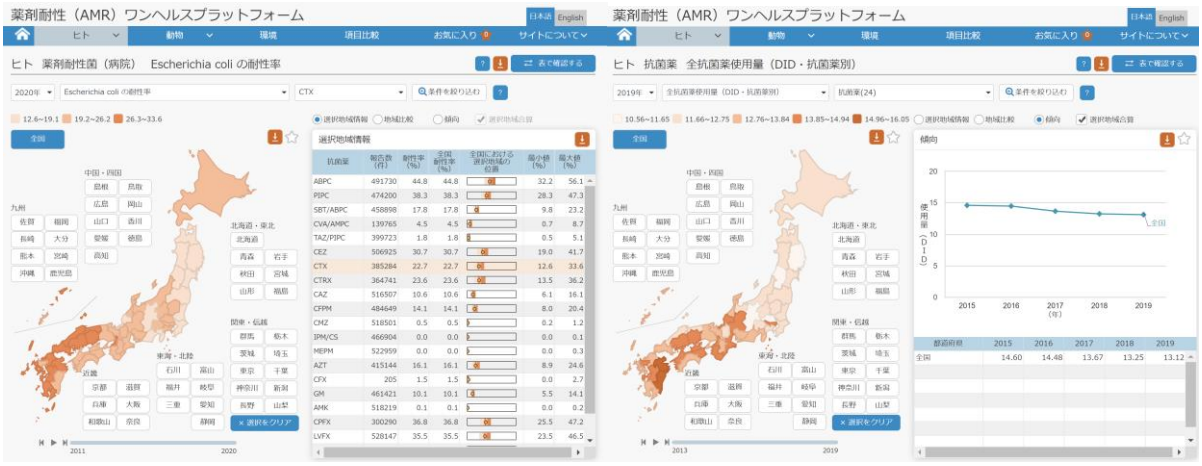
(11) Antimicrobial Resistance (AMR) One Health Platform

1) Overview

In October 2019, the AMRCRC published the “Antimicrobial Resistance (AMR) One Health Platform" (https://amr-onehealth-platform.ncgm.go.jp/home), a website that provides easy-to-understand information related to infectious diseases in the human, animal and environmental fields.

This system allows users to freely view trends in agent resistance rates, antimicrobial use, and other AMR-related indicators by field, prefecture, and year. The information handled is mainly secondary use from outputs of this report, AMED research, and other deliverables.

In November 2021, the prefectural homepage was newly established, which allows users to view various indicators in one place from the homepage of each prefecture. We hope that this platform will be utilized to further promote AMR measures in each region.



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Websites of Key Trend Surveys

AMR Clinical Reference Center

http://amrcrc.ncgm.go.jp/

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

https://j-siphe.ncgm.go.jp/

Nippon AMR One Health Report

https://amr-onehealth.ncgm.go.jp/

Antimicrobial Resistance (AMR) One Health Platform

https://amr-onehealth-platform.ncgm.go.jp/home

Japan Surveillance of Antimicrobial Consumption (JSAC)

http://amrcrc.ncgm.go.jp/surveillance/index.html

Japan Nosocomial Infections Surveillance (JANIS), Ministry of Health, Labour and Welfare

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/

The Antimicrobial Resistance One Health Surveillance Committee: Terms of References

January 16, 2017
Partially amended on October 4, 2023

1. Objective

As sentiment is being elevated to promote Antimicrobial Resistance (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 Antimicrobial Resistance (AMR) (2023-2027), enacted on April 7, 2023, also requires promoting 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 Department of Infectious Disease Prevention and Control, Public Health Bureau, Ministry of Health, Labour and Welfare (MHLW), in order to review necessary technical matters that pertain to One Health AMR surveillance and prepare annual reports.

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 of the Department of Infectious Disease Prevention and Control, Public Health Bureau may request non-member experts to participate in 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 Department of Infectious Disease Prevention and Control, Public Health Bureau, HLW.
(2) Clerical affairs for the Committee should be handled by the Division of Infectious Disease Prevention and Control, Department of Infectious Disease Prevention and Control, Public Health 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, 9th meeting on 1/17/2022, 10th meeting on 11/21/2022, and 11th meeting on 12/13/2023.

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Cooperating governmental agencies

Food Safety Commission Secretariat	Ministry of Land, Infrastructure, Transport and Tourism
Ministry of Agriculture, Forestry and Fisheries	
Ministry of the Environment	

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