2025

Nippon AMR One Health Report（NAOR）Highlight

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Preface

The AMR Countermeasure Action Plan (2023-2027), formulated in April 2023, promotes the continued publication and enhancement of the Nippon AMR One Health Report (NAOR). It emphasizes the implementation of measures considering the interconnection of human, animal, food, and environmental health.

The NAOR is structured to provide an understanding of the status and trends of antimicrobial-resistant bacteria and antimicrobial usage (or sales) across the human, animal, food, and environmental sectors in Japan. It serves as a key resource for the selection and evaluation of various AMR mitigation measures.

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The summary version of the NAOR extracts key data accumulated since 2011, presenting it primarily through clear illustrations and figures. It facilitates easy comprehension of trends, including comparisons with the targets for 2020 and 2027, the progression of resistance rates by antimicrobial agents and antimicrobial-resistant bacteria, and the status of various surveillance efforts.

The NAOR summary aims to disseminate information on Japan's AMR situation to a broad audience, from beginners to government officials and researchers involved in AMR.

*For the original data (sources, etc.) of the NAOR highlights, please refer to the latest edition of the " Nippon AMR One Health Report (NAOR)" available at the following link: (https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/0000120172.html）

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Explanation of Abbreviations

Class			Nonproprietary name	Abbreviation*
Beta-lactam antibiotics	Penicillins		Benzylpenicillin (penicillin G)	PCG
			ampicillin	ABPC
	Cephalosporins	2nd generation	cefoxitin	CFX
		3rd generation	cefotaxime	CTX
			ceftazidime	CAZ
		4th generation	cefepime	CFPM
		Cephalosporins combined with beta-lactamase inhibitor	tazobactam/ceftolozane	TAZ/CTLZ
	Carbapenems		meropenem	MEPM
			imipenem	IPM
ST			sulfamethoxazole-trimethoprim	ST
Macrolides			erythromycin	EM
Lincomycins			lincomycin	LCM
Tetracyclines			tetracycline	TC
			oxytetracycline	OTC
Aminoglycosides			streptomycin	SM
			gentamicin	GM
			amikacin	AMK
			kanamycin	KM
Quinolones (◎fluoroquinolones)			◎ ciprofloxacin	CPFX
			◎ levofloxacin	LVFX
			◎ norfloxacin	NFLX
			nalidixic acid	NA
Glycopeptides			vancomycin	VCM
Glycopeptides			colistin	CL
Amphenicols			chloramphenicol	CP
Other antibacterial agents			fosfomycin	FOM

* Quoted from the Glossary of Antimicrobial Chemotherapy, the Annual Report of the Japanese Society of antibiotics 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 fields 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, antimicrobials: Antimicrobial agents are a collective term for drugs that possess antimicrobial activity against microorganisms—generally classified as bacteria, fungi, viruses, and parasites—and are used for the treatment and prevention of infectious diseases. Antimicrobial agents used in humans include antibacterial agents (those with activity against bacteria), antifungal agents, antiviral agents, and antiparasitic agents.

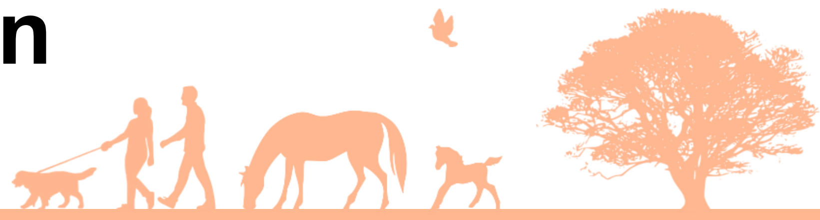
antibacterial agents: Antimicrobial substances that specifically act against bacteria.

antibiotics: A substance that inhibits or suppresses the functions of microorganisms or other cells (referred to as antibacterial activity), and strictly speaking, denotes chemical compounds produced by microorganisms.

antibiotic agents: A commonly used term referring to drugs that utilize the antibacterial activity of antibiotics.

Reference: Guidance on the Appropriate Use of Antimicrobial Agents, Fourth Edition — Outpatient Section / Inpatient Section

Outcome Indices for the Action Plan



Proportion of specified antimicrobial-resistant bacteria			
	Indices	2020	2027 (target value)
Human-related	Number of vancomycin-resistant enterococci infections	136 patients	80 patients or less (maintained 2019 level)
Human-related	Proportion of methicillin resistant *Staphylococcus aureus*	35.9%	20% or less
Human-related	Proportion of fluoroquinolone resistant in *Escherichia coli*	35.4%	30% or less (maintained)
Human-related	Proportion of carbapenem resistant Pseudomonas aeruginosa	7.1%	3% or less
Human-related	Proportion of carbapenem (meropenem) resistant *Escherichia coli* and Klebsiella pneumoniae	0.1-0.4%	0.2% or less (maintained)
Animal-related	Proportion of tetracycline-resistant *Escherichia coli*	Cattle 19.8%, Swine 62.4%, Chicken 52.9%	Cattle 20% or less, Swine 50% or less, Chicken 45% or less
Animal-related	Proportion of third generation cephalosporin-resistant *Escherichia coli*	Cattle 0.0%, Swine 0.0%, Chicken 4.1%	Cattle 1% or less, Swine 1% or less, Chicken 5% or less
Animal-related	Proportion of fluoroquinolone-resistant *Escherichia coli*	Cattle 0.4%, Swine 1.1%, Chicken 18.2%	Cattle 1% or less, Swine 2% or less, Chicken 15% or less

*The 2027 target values for humans, from the perspective of excluding the impact of colonization, will be based on the following: the methicillin resistance rate of *Staphylococcus aureus* and the carbapenem resistance rate of *Pseudomonas aeruginosa* will be determined using blood samples, while the fluoroquinolone resistance rate of *E. coli* will be based on urine samples.

Use of antimicrobials			
	Indices	2020	2027 (target value) (Change from 2020)
Human-related	All antimicrobials (DID)	10.18	15% reduction
Human-related	Oral third generation cephalosporins (DID)	1.85	40% reduction
Human-related	Oral fluoroquinolones (DID)	1.66	30% reduction
Human-related	Oral macrolides (DID)	2.93	25% reduction
Human-related	Intravenous carbapenems (DID)	0.07	20% reduction
Animal-related	Total use of veterinary antimicrobials in the livestock sector	626.8t	15% reduction
Animal-related	Total use of second-line veterinary antimicrobials in the livestock sector* *Third generation cephalosporins, 15-membered ring macrolides (tulathromycin, gamithromycin), fluoroquinolones, colistin	26.7t	Maintain below 27t

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

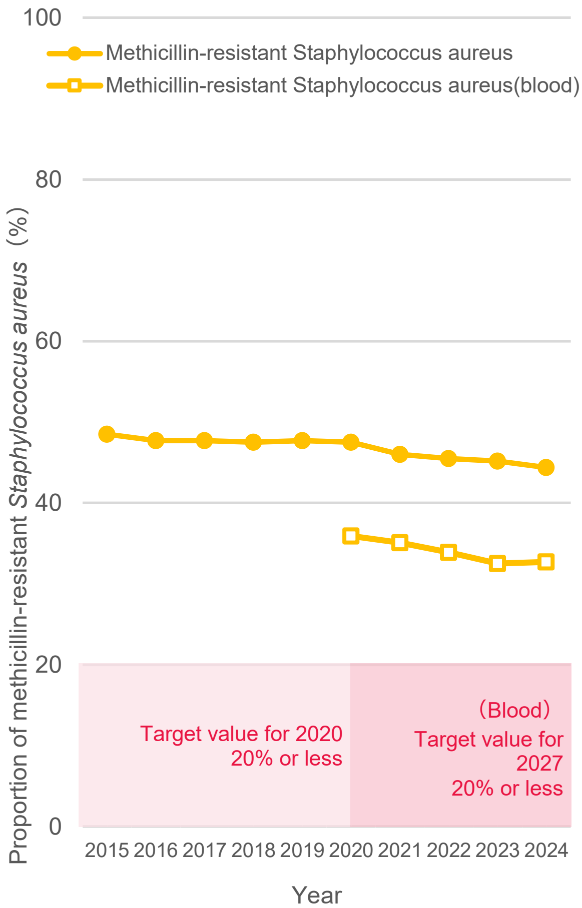
Outcome Indices for the Action Plan's Outcomes

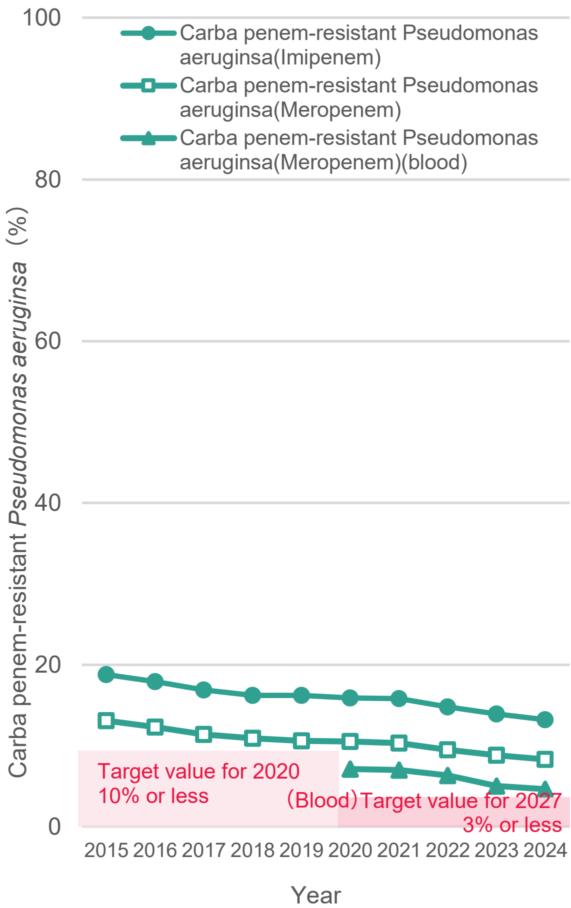
Changes in the proportion of human-related antimicrobial-resistant bacteria

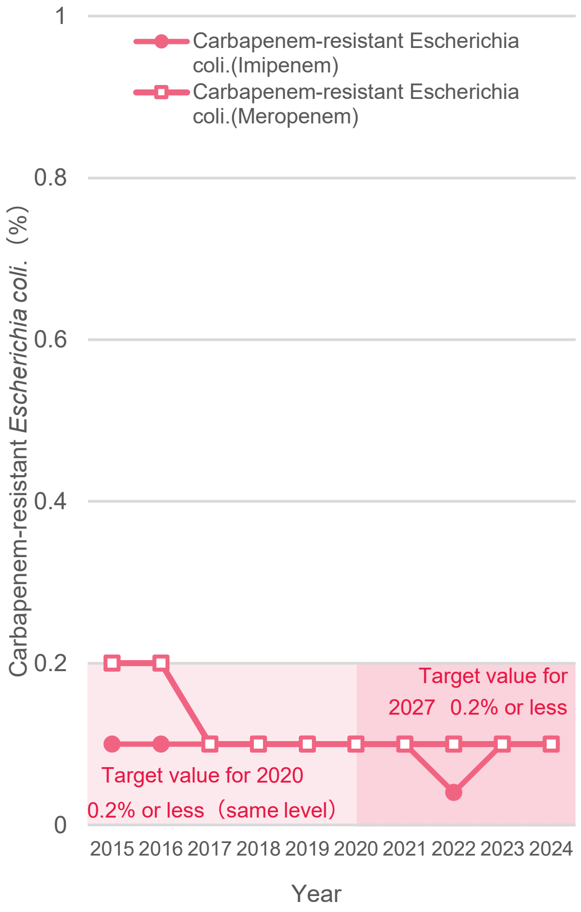
- The number of reported cases of vancomycin-resistant enterococci infections was 115 in 2023.
- While the proportion of methicillin-resistant *Staphylococcus aureus* (MRSA) is decreasing, it remained at a higher level compared to the target value of 2020 (below 20%).
- The carbapenem resistance rate in Pseudomonas aeruginosa is on a decreasing trend, with meropenem reaching 9.5% in 2022, achieving the 2020 target value below 10% for the first time. Imipenem, on the other hand, was 13.2% in 2024.
- The resistance rate of fluoroquinolone-resistant *Escherichia coli* has been on an uptrend but decreased for the first time in 2021. However, it remains at a higher level than the target value of 2020 (below 25%).
- The proportion of carbapenem-resistant *Escherichia coli* and Klebsiella pneumoniae have remained below 1%.

2021	2022	2023	2027 target value
124 Infections	133 Infections	115 Infections	80 Infections or less

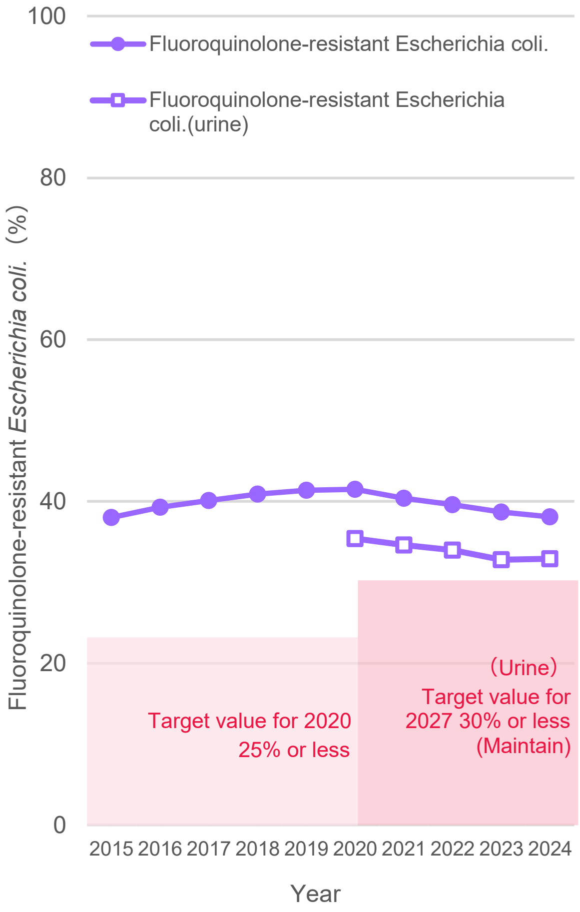
The number of reported cases of vancomycin-resistant enterococci infections



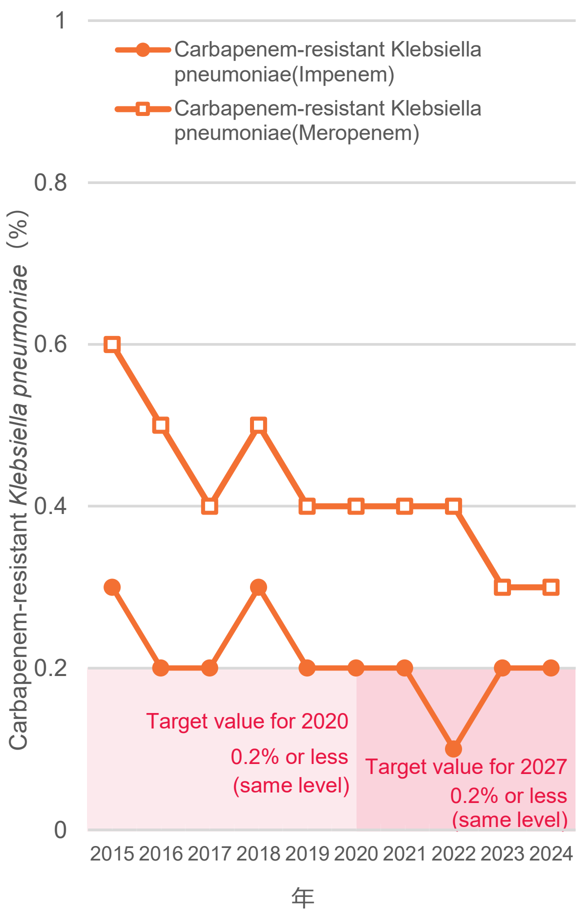




Carbapenem-resistant Escherichia coli.(Imipenem)
Carbapenem-resistant Escherichia coli.(Meropenem)
Carbapenem-resistant Escherichia coli.（%）
Target value for 2027 0.2% or less
Target value for 2020
0.2% or less（same level）
1
0.8
0.6
0.4
0.2
0
2015 2016 2017 2018 2019 2020 2021 2022 2023 2024
Year



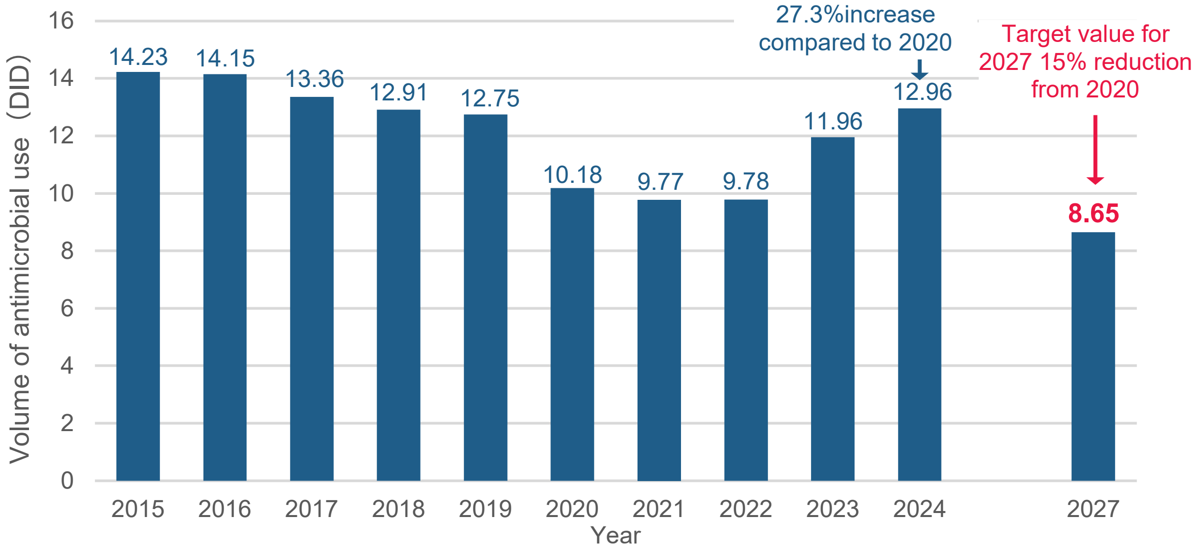
Fluoroquinolone-resistant Escherichia coli.
Fluoroquinolone-resistant Escherichia coli.(urine)
Fluoroquinolone-resistant Escherichia coli.（%）
Target value for 2020
25% or less
（Urine）
Target value for 2027 30% or less
(Maintain)
100
80
60
40
20
0
2015 2016 2017 2018 2019 2020 2021 2022 2023 2024
Year



Carbapenem-resistant Klebsiella pneumoniae(Impenem)
Carbapenem-resistant Klebsiella pneumoniae(Meropenem)
Carbapenem-resistant Klebsiella pneumoniae（%）
Target value for 2020
0.2% or less
(same level)
Target value for 2027
0.2% or less
(same level)
1
0.8
0.6
0.4
0.2
0
2015 2016 2017 2018 2019 2020 2021 2022 2023 2024
年

Trends in the usage of antimicrobial agents for humans in Japan

Antimicrobial usage in humans based on their sales volume in Japan (DID*) was 12.96 DID in 2024, representing a 27.3% increase compared to 2020, but a 9.0% decrease compared to 2015.

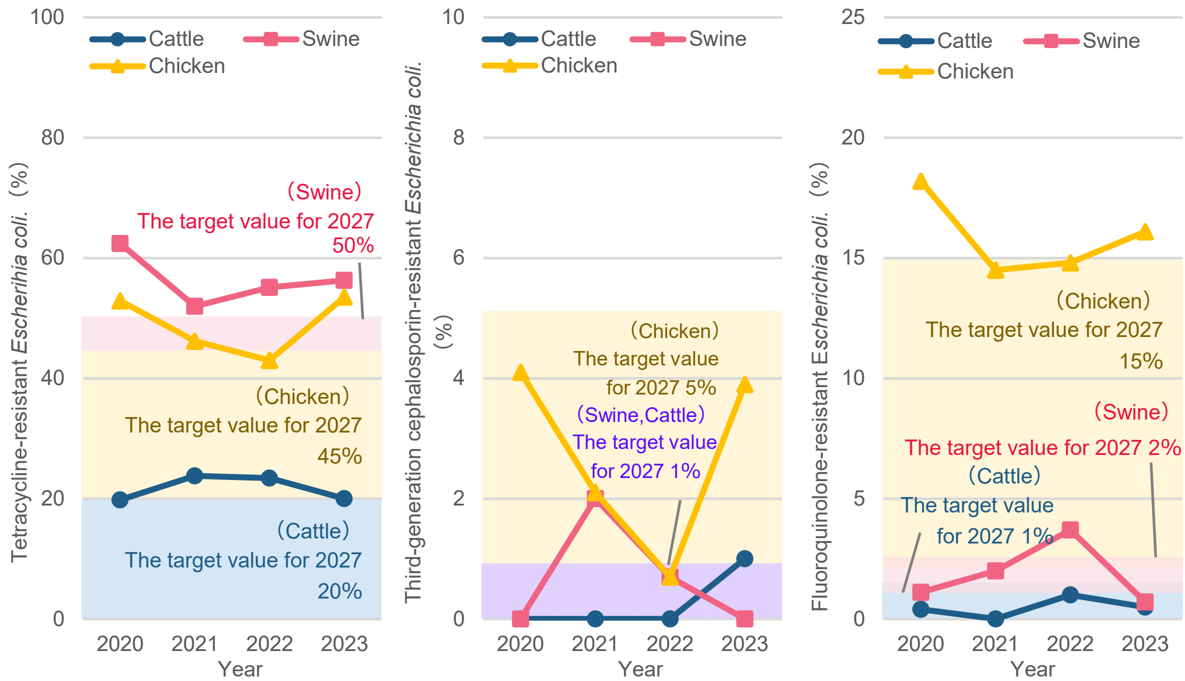


*DID: Defined daily dose/1,000 inhabitants/day

Animal-related indices

As the outcome indicators for the Action Plan (2023-2027), target resistance rates of *Escherichia coli* by livestock animal species have been established for the same antimicrobial agents as in the Action Plan (2016-2020), allowing for the assessment of the results of more refined efforts addressing species specific issues. Additionally, the total usage of veterinary antimicrobials in the livestock sector and the total usage of second-line veterinary antimicrobials have been set as new outcome indicators.

Of the antimicrobials for animals, the sales volume veterinary antimicrobials in the livestock sector (t) were 559.4 t in 2023, decreasing by 8.6 t from 568.0 t in 2022. The 2027 target value is set at 532.8 t, which is a 15% decrease from the 2020 level. Additionally, the outcome indicator for the sales volume of second-line veterinary antimicrobials in the livestock sector is set to be kept below 27.0 t, which was 23.5 t in 2023.



Section A
Antimicrobial Resistant Bacteria

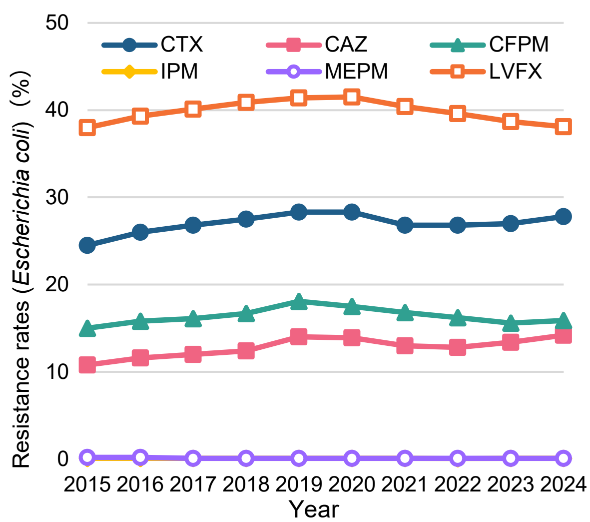
Section A:
Antimicrobial-Resistant Bacteria

A1: Antimicrobial resistance for humans

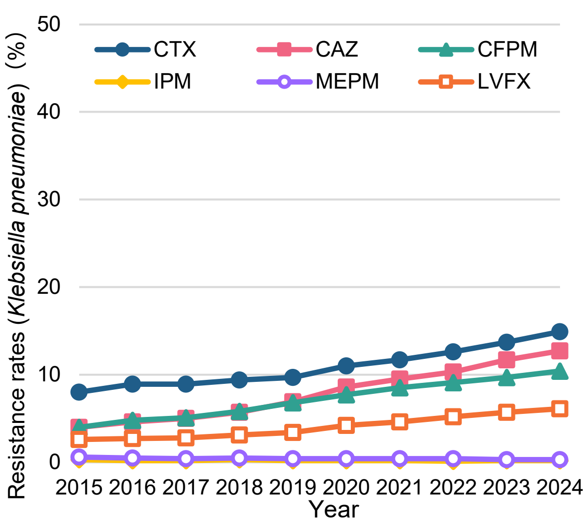
A1.1 Gram-negative bacteria

- The resistance rates of *Escherichia coli* to third-generation cephalosporins (cefotaxime: CTX, ceftazidime: CAZ) and fluoroquinolones (levofloxacin: LVFX) had been increasing until 2020, but for the first time, they turned to decrease in 2021.
- The resistance rates of *Klebsiella pneumoniae* to third-generation cephalosporins (cefotaxime: CTX, ceftazidime: CAZ) and fluoroquinolones (levofloxacin: LVFX) are showing an increasing trend.
- The resistance rates of *Pseudomonas aeruginosa* to carbapenems (imipenem: IPM, meropenem: MEPM) and fluoroquinolones (levofloxacin: LVFX) have been showing a decreasing trend since 2015.
- The resistance rates of *Acinetobacter* spp., to various antibiotics remain at low levels. In particular, the resistance rates to carbapenems (imipenem: IPM, meropenem: MEPM) are low, ranging from 1% to 3%.

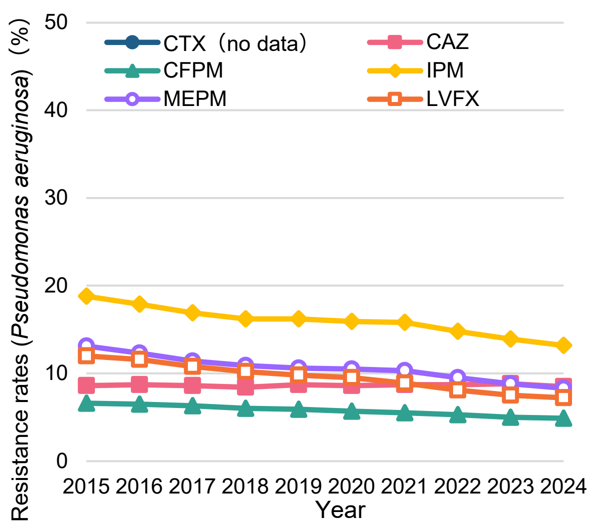
Escherichia coli



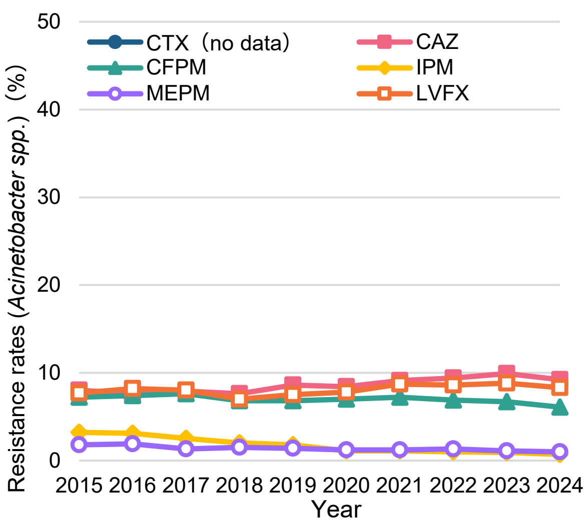
Klebsiella pneumoniae



Pseudomonas aeruginosa

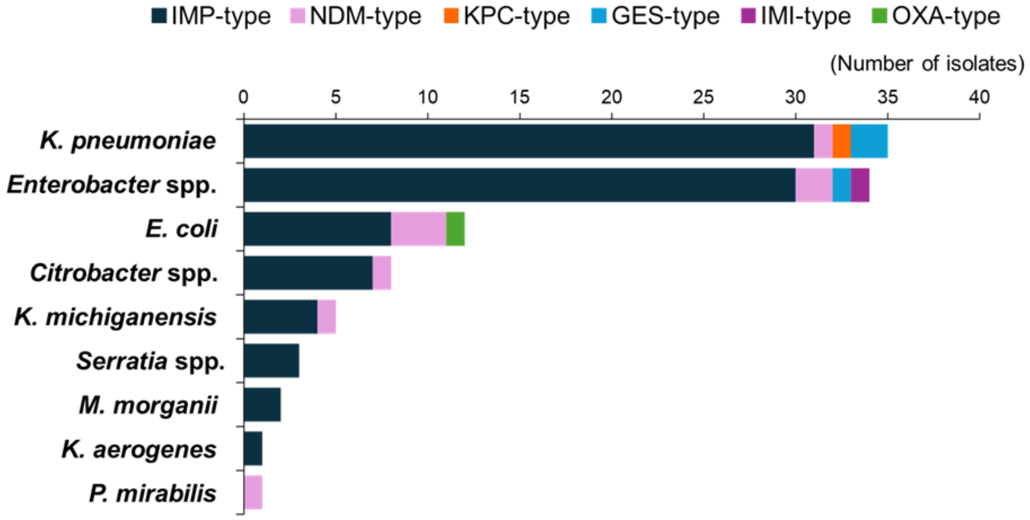


***Acinetobacter* spp.**



Enterobacterales harboring carbapenemase genes

Among the 101 isolates collected nationwide in 2023, the major bacterial species were *Klebsiella pneumoniae* (35%, 35/101 isolates), *Enterobacter* spp. (34%, 34/101 isolates), *Escherichia coli* (12%, 12/101 isolates), and *Citrobacter* spp. (8%, 8/101 isolates). The predominant carbapenemase genes detected were of the IMP type (85%, 86/101 isolates), followed by NDM (9%, 9/101 isolates) and GES (3%, 3/101 isolates).



Breakdown of carbapenemase genes by bacterial taxon among the 101 isolates

Evaluation of the seven new antimicrobial agents and meropenem (MEPM) against these isolates revealed that four agents—CFDC, CFPM/NAC, AZT/NAC, and AZT/AVI—were effective regardless of the carbapenemase gene type. Notably, even among isolates harboring the IMP-type carbapenemase gene, which is predominant in Japan, susceptibility rates exceeded 98%, indicating the efficacy of these four agents against clinical Enterobacterales isolates carrying carbapenemase genes in Japan.

Ambler's class	β-lactamase family	Number of isolates	CFDC ≦4	CFPM/ NAC ≦8	AZT/ NAC ≦4	AZT/ AVI ≦4	CAZ/ AVI ≦8	CFPM/ EMT ≦4	IPM/ REL ≦1	MEPM ≦1
B	IMP	86	98%	98%	100%	100%	8%	29%	29%	13%
	NDM	9	78%	89%	100%	100%	0%	0%	11%	11%
A	GES	3	100%	100%	100%	100%	100%	67%	33%	0%
	KPC	1	100%	100%	100%	100%	100%	0%	100%	0%
	IMI	1	100%	100%	100%	100%	100%	100%	0%	0%
D	OXA	1	100%	100%	100%	100%	100%	100%	100%	100%

Susceptibility rates to the new antimicrobial agents and meropenem, classified by the type of carbapenemase gene carried by the isolates

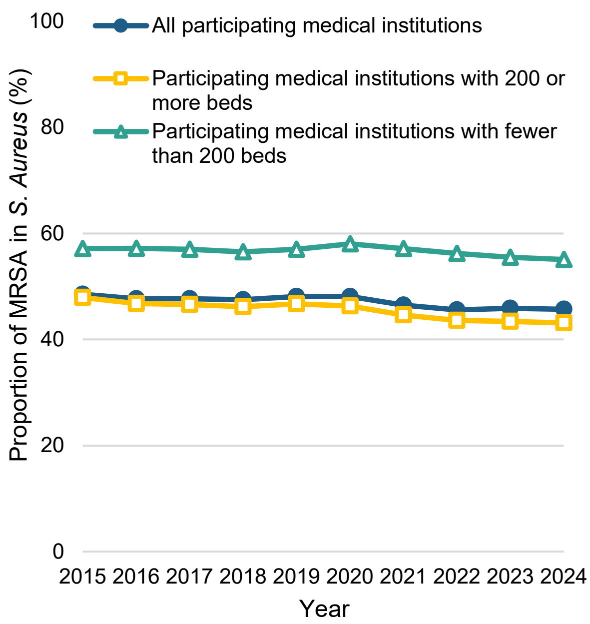
Notably, 13% of the isolates (13/101) were identified as “stealth strains,” which, despite harboring resistance genes, exhibited susceptibility to MEPM and therefore may not be detected by routine clinical laboratory testing.

A1.2

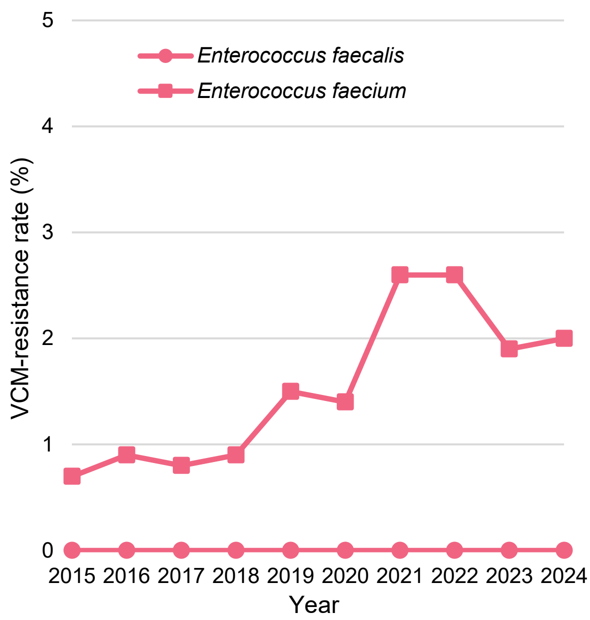
A1.2 Gram-positive bacteria

- In *Staphylococcus aureus,* the proportion of methicillin-resistant strains (MRSA) is approximately 50%, with a decreasing trend in recent years.
- In *Enterococcus*, the vancomycin (VCM) resistance rate in 2024 was at low levels, being below 0.05% for *Enterococcus faecalis* and 2.0% for *Enterococcus faecium*. However, in *E. faecium*, the vancomycin (VCM) resistance rate significantly increased in 2021, and widespread hospital outbreaks associated with VCM-resistant *E. faecium* were observed in some regions. It is necessary to carefully monitor changes in resistance rates at the regional level moving forward.
- The resistance rate to penicillin (PCG) in *Streptococcus pneumoniae* varies due to the small number of cerebrospinal fluid samples tested, with approximately 100 samples per year, resulting in fluctuations in the data. However, it generally remains around 50%. In samples other than cerebrospinal fluid, the resistance rate is below 1%, and even when including intermediate resistance, it remains below 5%, indicating a low level of resistance.

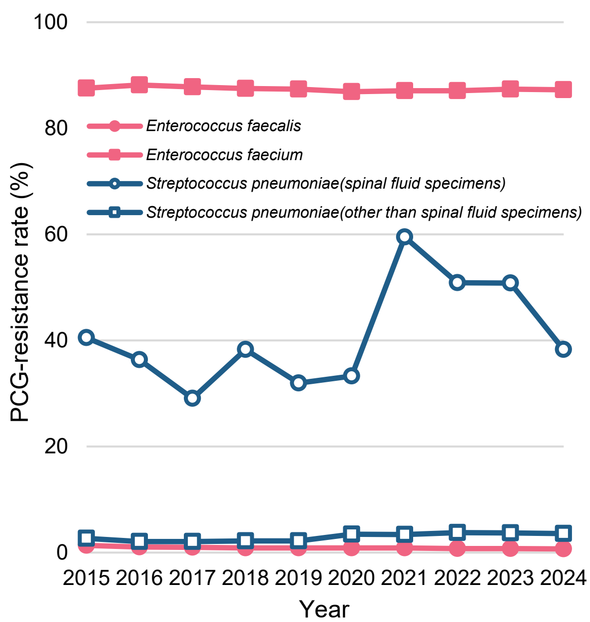
Staphylococcus aureus



***Enterococcus* spp.**



Streptococcus pneumoniae

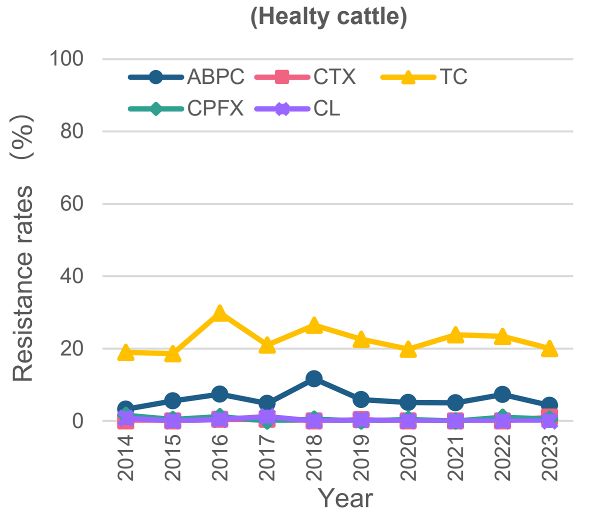


A2: Antimicrobial resistance bacteria in animal

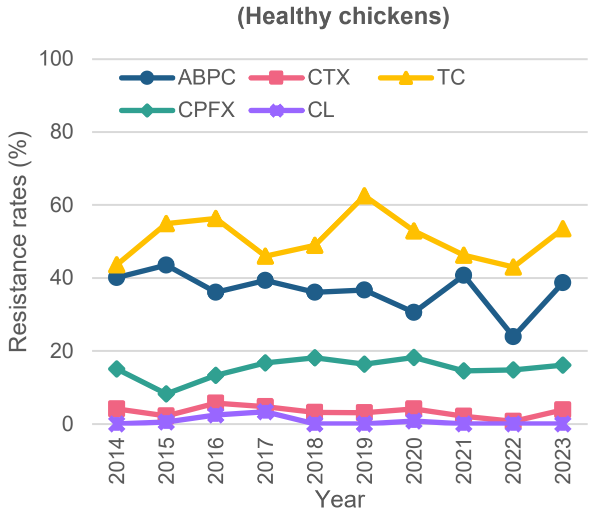
A2.1 Bacteria derived from livestock animals

Escherichia coli

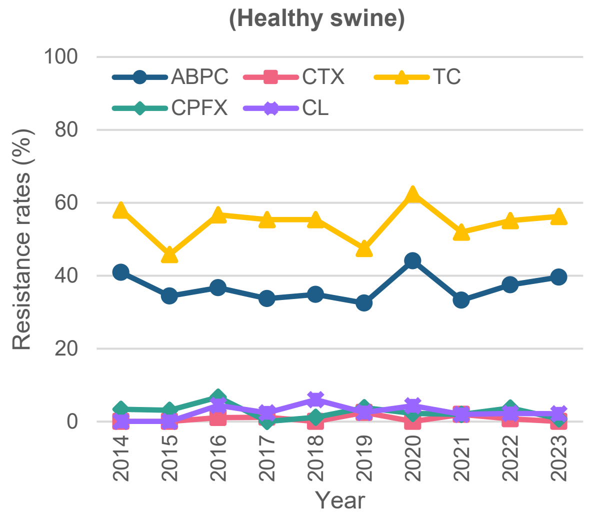
Escherichia coli derived from healthy livestock animals collected at slaughterhouses and poultry processing plants, which is an important indicator bacterium in the surveillance, exhibited resistance rates exceeding 40% to tetracycline (TC) in pigs and chickens. However, there were no significant fluctuations in the resistance rates to cefotaxime (CTX), ciprofloxacin (CPFX), and colistin (CL), which are critically important antimicrobials in human medicine, and the resistance rates remained low across all livestock species.



	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Number of tests (strains)	252	274	258	252	189	288	253	261	286	210



	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Number of tests (strains)	172	184	158	150	155	128	121	145	142	155



	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Number of tests (strains)	88	96	90	83	83	80	93	102	136	144

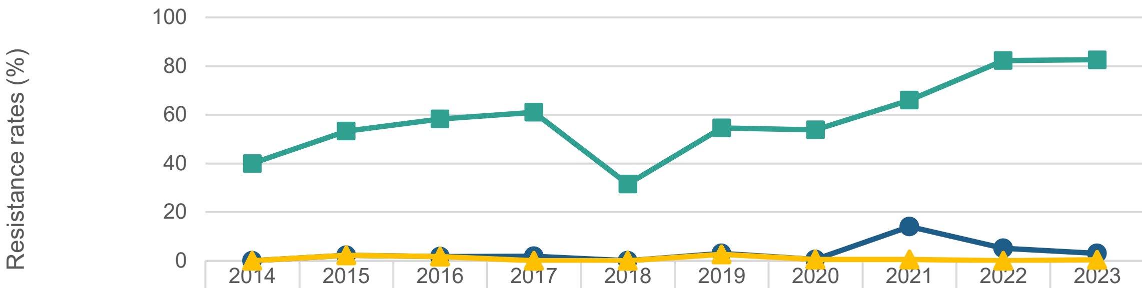
A2.2 Farm-raised aquatic animals

As part of strengthening monitoring outlined in the National Action Plan on AMR, the target species monitored for antimicrobial resistance in diseased fish was expanded to all farmed fish species in 2017, and a survey targeting healthy fish was initiated in 2018.

The pathogenic bacteria of α-hemolytic lactococcosis derived from diseased fish

The resistance rates to lincomycin (LCM) have shown a high tendency, reaching 82.6 % in 2023, suggesting the influence of serotypes II and III. The resistance rate to erythromycin (EM) was 3.0 % in 2023.

*All the pathogenic bacteria of α-hemolytic lactococcosis were originally considered to be *Lactococcus garvieae*. However, due to the emergence of a strain different from the conventional serotype from about 2013, the new type was distinguished as type II, separate from the conventional type (serotype I). In 2023, this strain was reclassified as *Lactococcus formosensis*. Additionally, since 2021, another serotype (type III) of α-hemolytic lactococcosis has also emerged.



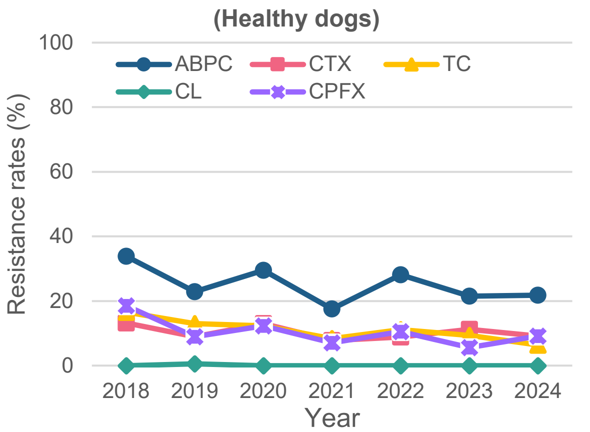
	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
EM	0	2.2	1.7	1.9	0	3.1	0.6	14.1	5.2	3
LCM	40	53.3	58.3	61	31.5	54.6	53.8	66	82.3	82.6
OTC	0	2.2	1.7	0	0	2.6	0.6	0.5	0	0.4
Number of tests (strains)	25	45	60	105	149	194	158	206	271	235

A2.3 Companion animals

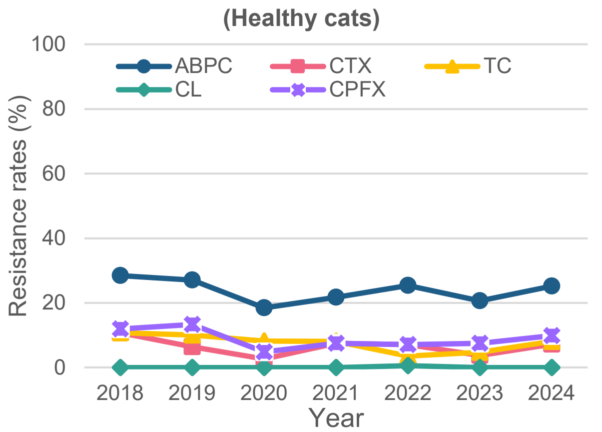
As part of strengthening monitoring set out in the National Action Plan on AMR, antimicrobial resistance monitoring in diseased dogs and cats was initiated in fiscal year (FY)2017, and that in healthy dogs and cats was initiated in FY2018.

Escherichia coli

The resistance rates of *Escherichia coli* derived from healthy companion animals, which is an important indicator bacterium in the surveillance, remained below 20% for all except ABPC, with susceptibility generally being maintained.



	2018	2019	2020	2021	2022	2023	2024
Number of tests (strains)	151	192	146	154	171	107	110



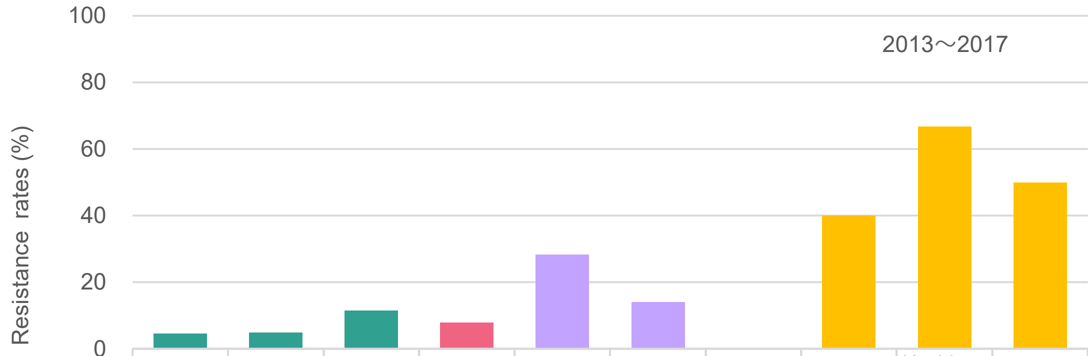
	2018	2019	2020	2021	2022	2023	2024
Number of tests (strains)	158	188	146	161	169	107	111

A2.4 Wild Animals

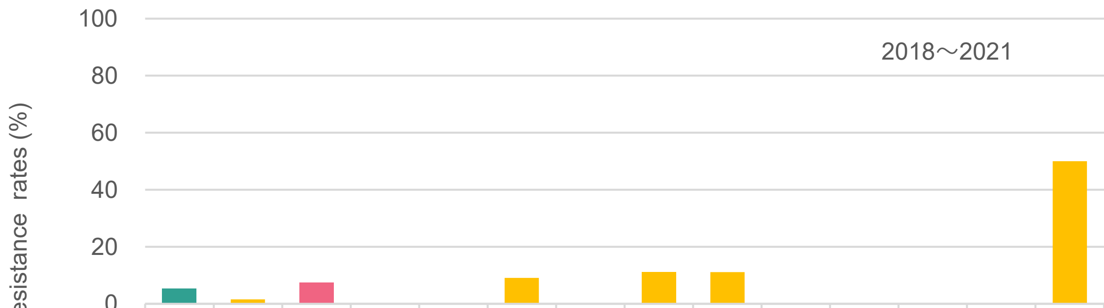
Antimicrobial susceptibility testing was conducted on *Escherichia coli* isolated from wild animals in two periods: from 2013 to 2017 and from 2018 to 2021.

In the 2013 to 2017 survey, 5.9% of deer-derived strains, 8.0% of wild boar-derived strains and 18.1% of small mammal-derived strains exhibited resistance. In particular, resistance to tetracycline (TC) and ampicillin (ABPC) was observed. In small mammals, multidrug resistance was detected in strains from livestock-associated facilities, while those from urban fields and mountainous fields showed less resistance. ESBL-producing bacteria were detected in one strain from small mammals. Although antimicrobial-resistant bacteria in wild animals depends on the habitats, the overall resistance rates were low compared to livestock and companion animals.

In the 2018-2021 survey, antimicrobial-resistant bacteria continued to show low prevalence. However, in investigations using antimicrobial-containing media, cefotaxime (CTX)-resistant bacteria were isolated from foxes and raccoons, and quinolone-resistant bacteria were isolated from masked palm civets, Japanese raccoon dogs, foxes and raccoons, some of which carried plasmid-mediated quinolone resistance genes. This study revealed that wild animals harbor resistant bacteria to medically important antimicrobial agents.



	Deer			Wild boar	Small mammals			Other		
	Mountains	Shrines	Parks	Mountains	Livestock facilities	Urban areas	Mountains	Badgers	Kuchinoshima cattle	Amami rabbits
Resistance rates (%)	4.6	4.9	11.5	8.0	28.3	14.0	0.0	40.0	66.7	50.0
Number of strains (n)	327	102	96	224	106	47	46	10	3	2

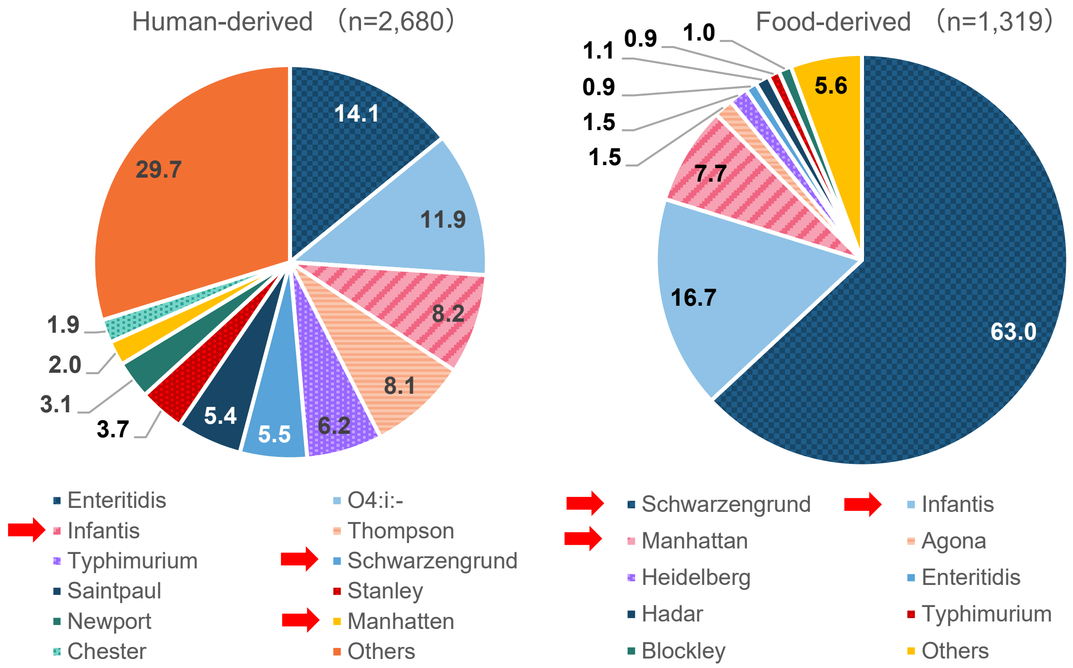


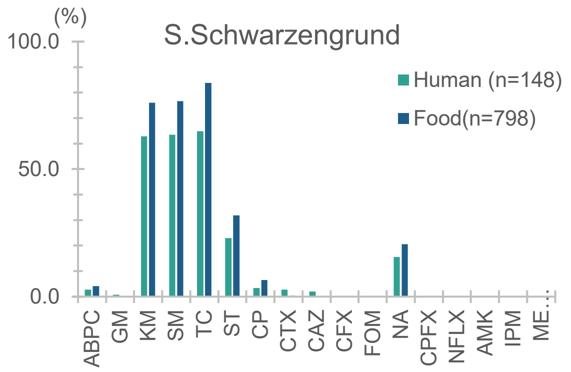
	Deer	Masked palm civet	Wild boar	Nutria	Japanese raccoon dog	Fox	Weasel	Badger	Japanese macaque	Small Japanese field mouse	Wild cat	Bear	Marten	Raccoon
Resistance rates (%)	5.4	1.6	7.4	0.0	0.0	9.1	0.0	11.1	11.1	0.0	0.0	0.0	0.0	50.0
Number of strains (n)	517	61	54	33	24	11	11	9	9	7	6	3	3	2

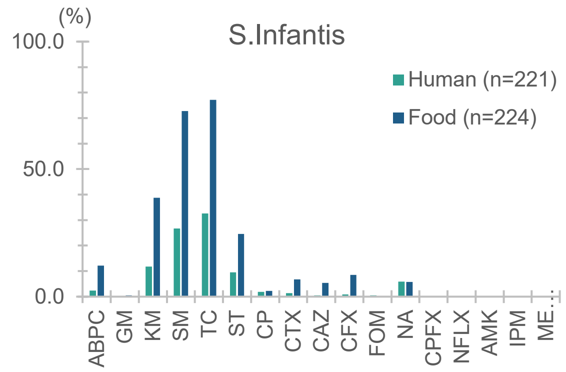
A3: Antimicrobial resistance in food

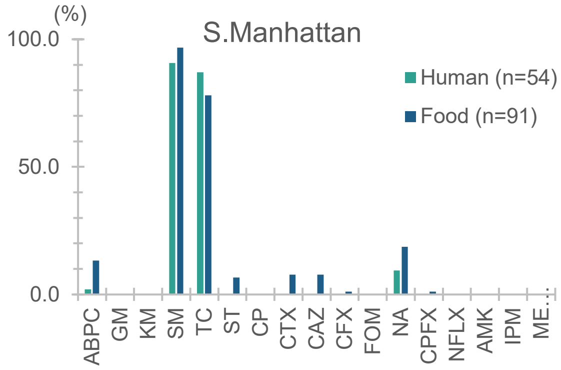
Salmonella **spp.**

When comparing the top 10 serotypes of human-derived strains to the top 5 serotypes of food-derived strains, three common serotypes (*S.* Schwarzengrund, *S.* Infantis, *S.* Manhattan) were identified. A high similarity degree in resistance trends to various antimicrobial agents was observed between human-derived and food-derived strains. This strongly suggests a significant association between human-derived resistant strains (approximately 40% of *S.* Infantis isolates, and the majority of *S.* Schwarzengrund and *S.* Manhattan isolates) and food-derived resistant strains.



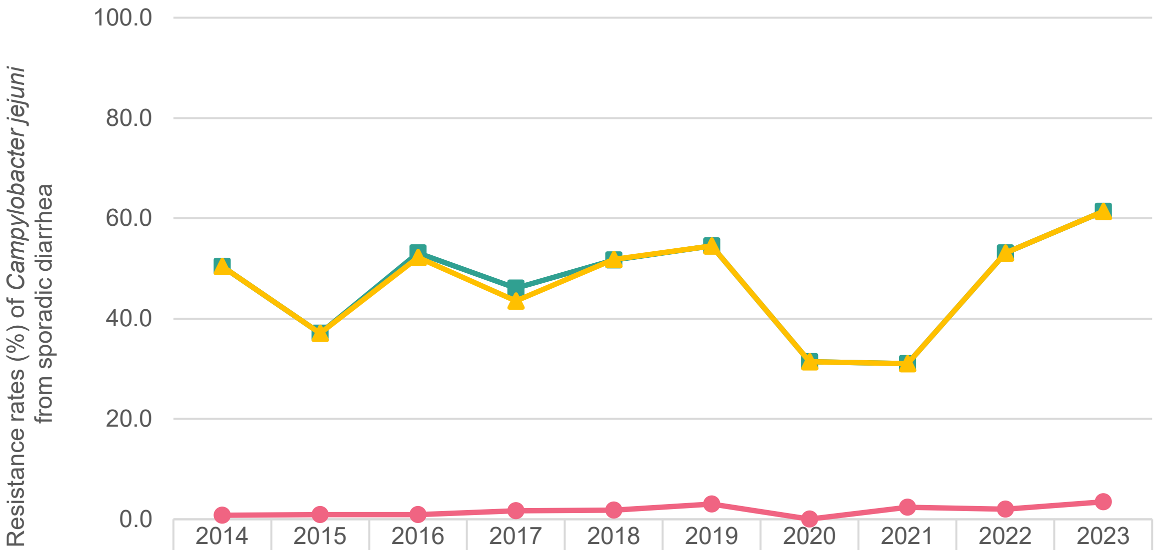






Campylobacter spp.

The graphs below show the resistance rates of *Campylobacter jejuni* and *Campylobacter coli* isolated from sporadic diarrhea patients in Tokyo from 2014 to 2023. In 2023, like 2022, the sample size was small, with only 57 strains of *C. jejuni* and 3 strains of *C. coli* analyzed. The resistance rate of *C. jejuni* to ciprofloxacin (CPFX) was 61.4 %, showing an increase compared to 2022. The resistance rate to erythromycin (EM) was 3.5 %. The resistance rate to CPFX in *C. coli* was 33.3 %.



	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
EM	0.8	0.9	0.9	1.7	1.8	3.0	0.0	2.4	2.0	3.5
NA	50.4	37.1	53.1	46.1	51.7	54.5	31.4	31.0	53.1	61.4
CPFX	50.4	37.1	52.2	43.5	51.8	54.5	31.4	31.0	53.1	61.4
samples	125	116	113	115	110	132	86	42	49	57

A4: Environmental Antimicrobial-Resistant Bacteria

Antimicrobial agents used in the treatment of infectious diseases, along with antimicrobial-resistant bacteria capable of withstanding them, are excreted from humans and animals and enter wastewater systems, ultimately accumulating in wastewater treatment plants. Consequently, wastewater treatment plants serve as critical interfaces linking humans, animals, and the environment, and represent important surveillance sites for understanding the dissemination of antimicrobial resistance genes and antimicrobial residues into the environment.

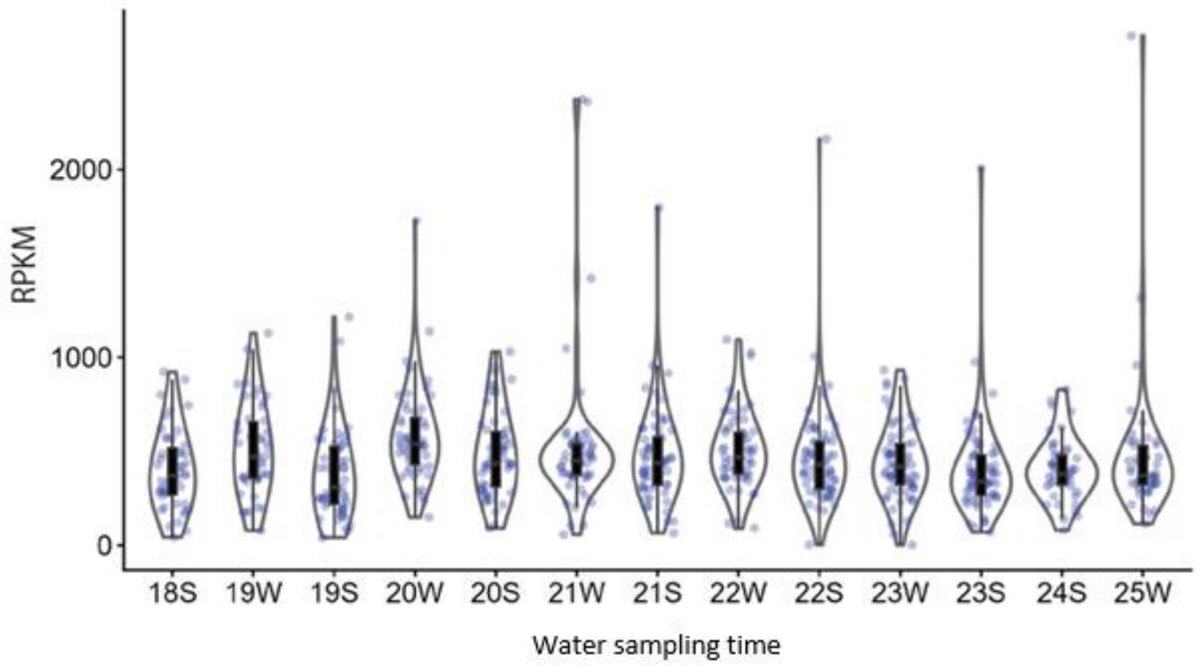
To date, no nationwide quantitative assessment has been conducted to determine the extent of the release of resistance genes and antimicrobial agents into the environment. In this study, with the cooperation of municipalities across Japan, our research team analyzed effluent from wastewater treatment plants twice yearly—in summer and winter—to quantify the diversity and abundance of resistance genes, as well as the types and concentrations of residual antimicrobial agents.

Our analyses indicate a possible increase in certain resistance genes in treated effluent, along with the presence of antimicrobial agents commonly used in clinical practice. However, the potential impact of these findings on human and animal health remains unclear.

Continued monitoring is essential for building a data framework on environmental antimicrobial resistance (environmental AMR) in Japan and for informing the development of effective strategies to combat AMR.

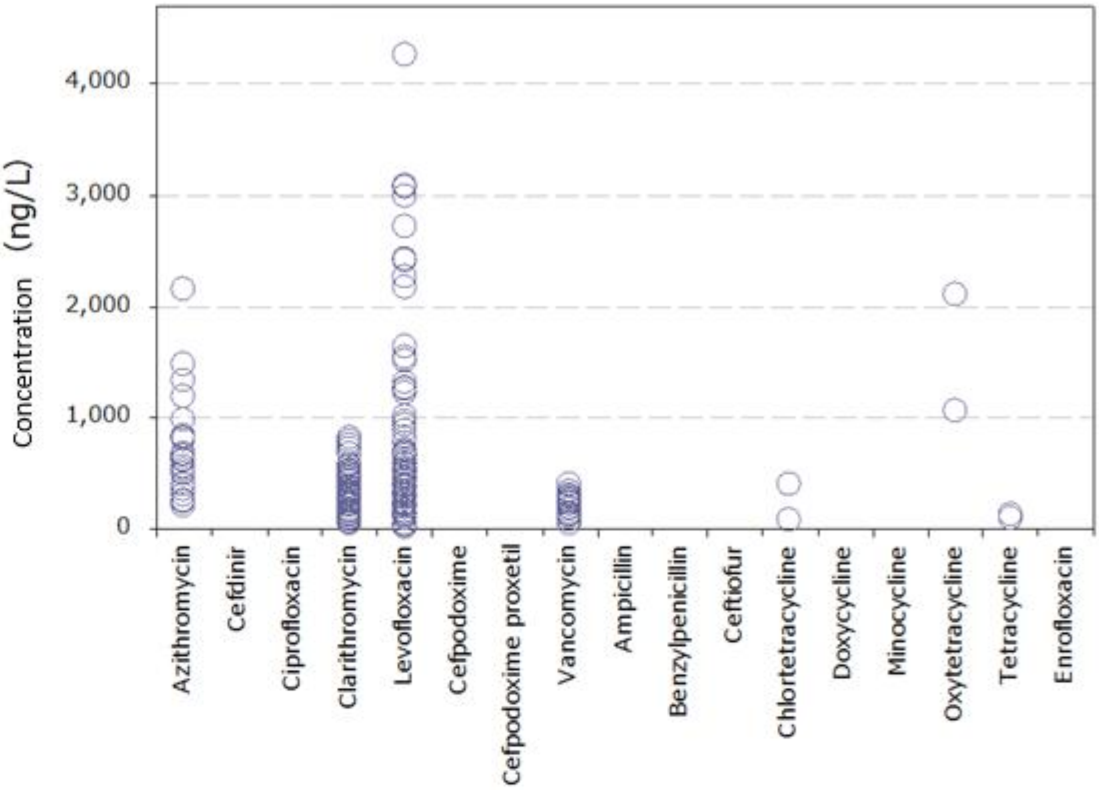
A4.1 Metagenomic DNA-Seq analysis of wastewater treatment plant effluent

From 2018 to 2025, treated effluent samples collected from municipalities were analyzed to detect antimicrobial resistance genes. The graph depicts the number of resistance genes detected in each sample across the different sampling periods. The abundance of detected genes is presented as RPKM values, which normalize for gene length and total sequencing depth. Although minor fluctuations were observed, antimicrobial resistance genes were consistently detected over the study period.



A4.2 Analysis of residual antimicrobials in treated effluent from wastewater treatment plants

The concentrations of residual antimicrobial agents in treated effluent samples collected from municipalities during summer 2024 and winter 2025 are presented. Values below the detection limit of the analytical system are not shown. Clarithromycin, levofloxacin, azithromycin, and vancomycin were detected at frequencies of 98%, 96%, 42%, and 31%, respectively, with mean concentrations of 301, 741, 177, and 40 ng/L. Comparisons between the two sampling periods revealed that clarithromycin and levofloxacin concentrations in winter 2025 were two- to threefold higher than in summer 2024.



A5: Genome comparison of Antimicrobial-resistant Bacteria: Exploring the relationships between humans, animals, food, and the environment

The Action Plan (2016-2020) calls for the analysis of antimicrobial resistance transmission factors present in humans, animals, food, and the environment, as well as studies on the relatedness of transmission processes, as part of the efforts to establish an integrated One Health surveillance system. This approach has been carried out into the new Action Plan (2023-2027). This paper presents the results of analyzing the interrelationships of resistant bacteria across various sectors, based on genome comparisons of resistant strains.

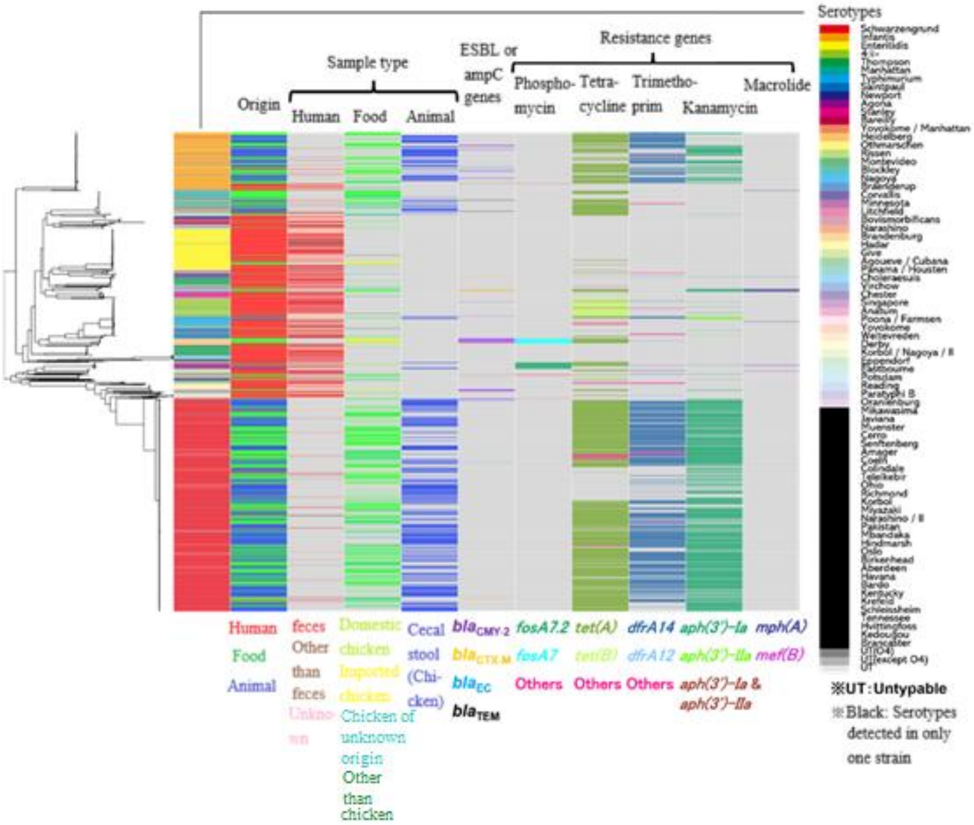
A5.1 Comparative genomics of antimicrobial-resistant bacteria derived from humans, food, and animals

Genome analysis was conducted on strains of *Salmonella* (non-typhoidal *Salmonella* spp.), *Campylobacter* spp. and *Escherichia coli* (*Enterococcus* spp.) to investigate the extent of genomic similarity between human-, food- and animal-derived strains. This was explored through a comparison of genomic nucleotide sequence data.

The results revealed that in *Salmonella*, for serotypes Blockley and Agona, highly related strains harboring the same resistance genes were identified in human-derived strains isolated from patients with infectious enteritis and foodborne illness, as well as in food-derived strains. Although rare, these findings suggest the potential for the transmission of resistance gene-harboring strains from food to humans.

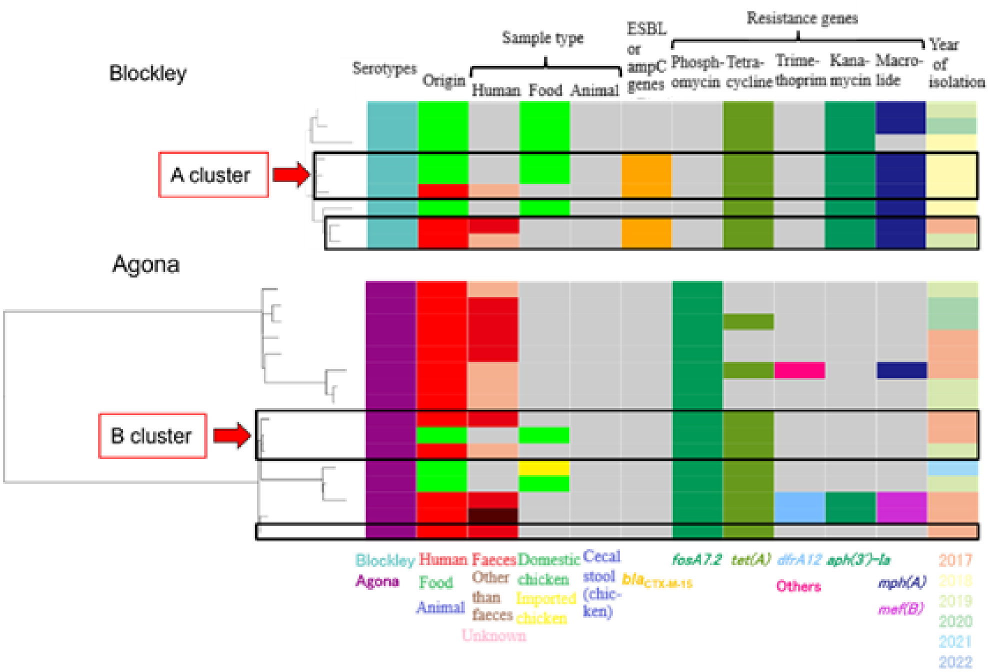
In *Campylobacter*, for both *C. jejuni* and *C. coli*, no closely related strain combinations suggestive of transmission between humans and food or animals were found when comparing human-derived strains with food-derived or animal-derived strains. Furthermore, when comparing the distribution of Clonal Complex (CC) or Sequence Type (ST) across sources, no clear similarities were observed between the different sources for either species.

In enterococci, it was confirmed that both *E. faecium* and *E. faecalis* do not share the same ST between human- and food-derived strains.



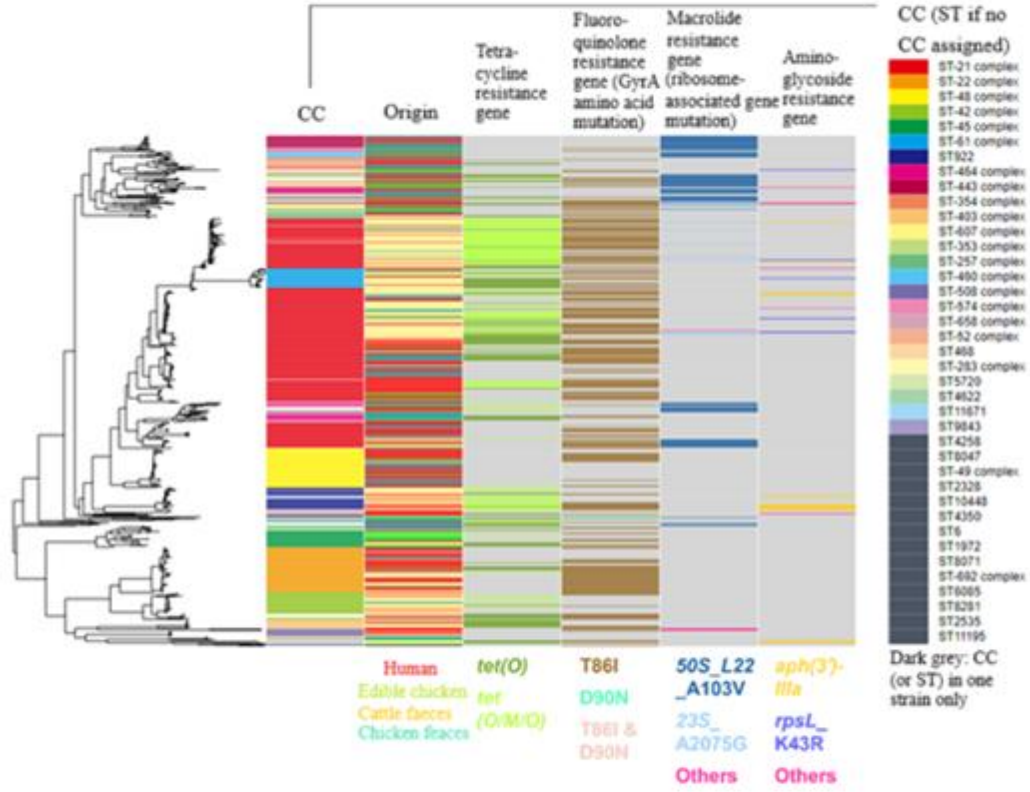
Relationship Between Humans, Food, and Animals Based on Genome Comparisons of Non-typhoidal Salmonella spp. Strains

The grouping of 1,613 strains of non-typhoidal *Salmonella* spp. based on genome similarity is depicted in a phylogenetic tree (on the left). Additionally, the bacterial characteristics (such as serotype, source, sample type, and the presence or absence of resistance genes) are color-coded and plotted on the right. This shows to what extent strains harboring key resistance genes are present within human-derived, food-derived, and animal-derived strains, and how they are distributed on the phylogenetic tree. For example, it is evident that the strains are clearly grouped by serotype based on genome similarity. It was observed that some food-derived and animal-derived strains are mixed within the human-derived group, and conversely, some human-derived strains are mixed within the food-derived and animal-derived groups.



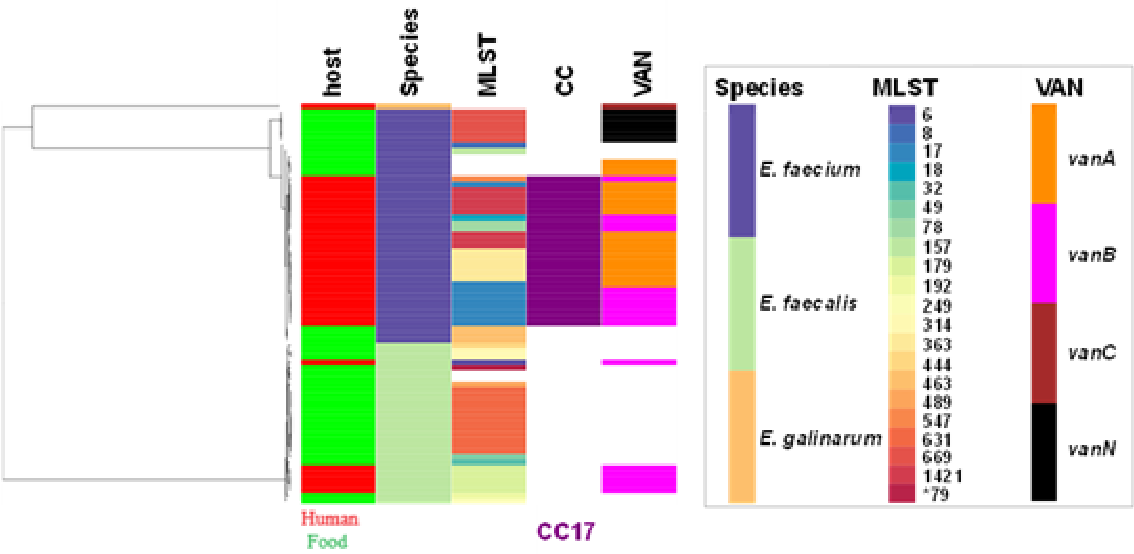
Human-derived and food-derived strains exhibiting common characteristics found in Salmonella serotypes Blockley and Agona

Within the Salmonella serotypes Blockley and Agona, strains with highly similar genomes and identical characteristics (antimicrobial resistance genes) were identified (Cluster A and Cluster B). The presence of both human-derived and food-derived strains within each cluster suggests the potential transmission of resistant strains to humans through food.



Relationship Between Humans, Food, and Animals Based on Genome Comparisons of *Campylobacter jejuni* Strains

The grouping of 249 human-derived strains, 48 food-derived strains (from chicken), and 338 animal-derived strains of *C. jejuni* based on genome similarity is depicted in a phylogenetic tree (on the left). Additionally, bacterial characteristics (such as CC, source, and the presence or absence of resistance genes) are color-coded and plotted on the right. No closely related strain combinations suggesting transmission of resistant strains between humans and food or animals were identified.



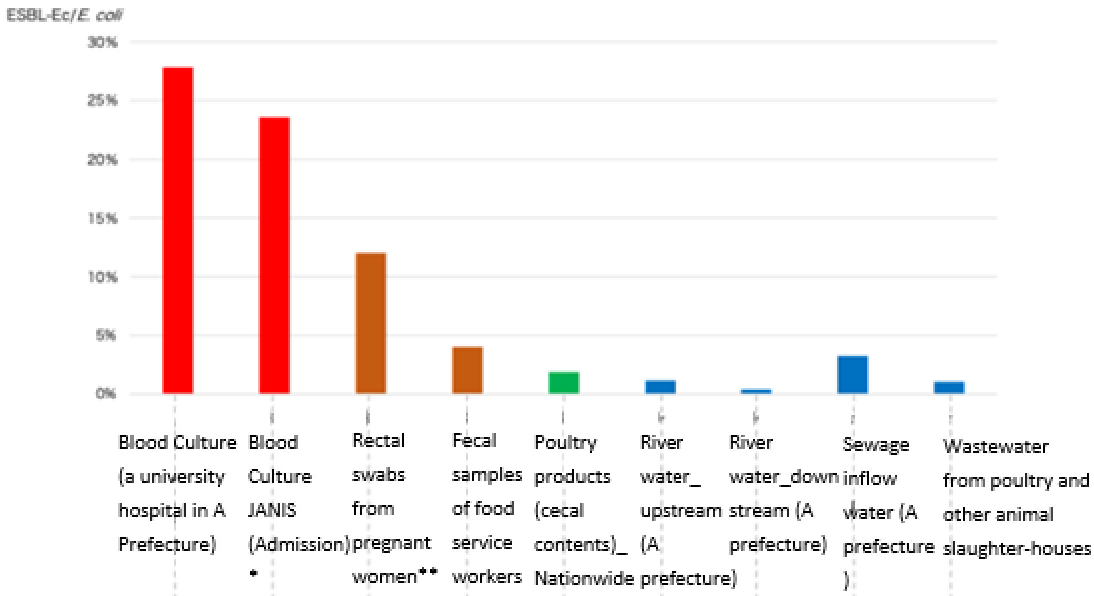
Relationship Between Humans, Food, and Animals Based on Genome Comparisons of *Enterococcus* spp. Strains

The phylogenetic tree, based on genome similarity, groups 38 food-derived *Enterococcus* spp. strains and 34 human-derived vancomycin-resistant strains (on the left). Additionally, the source (human or food), species, MLST (strain type), CC (whether part of the specific group CC17), and VAN (presence or absence of vancomycin resistance genes) of each strain are color-coded and plotted on the right. Within *E. faecium* and *E. faecalis*, human-derived vancomycin-resistant strains and food-derived strains were separated based on strain phylogeny. It was confirmed that human-derived vancomycin-resistant strains did not share the same ST as food-derived strains.

A5.2 The Antimicrobial Resistance (AMR) One Health Surveillance in coordination with the WHO surveillance (Tricycle Project)

Using ESBL-producing *Escherichia coli* (ESBL-Ec) as a key indicator, we calculated the proportion of ESBL-Ec among *Escherichia coli* in the three sectors—human, food, and environment - for each country. Furthermore, we performed molecular characterization and epidemiological analyses of the obtained isolates and conducted comparative assessments among regions and across sectors.

By collecting and analyzing isolates from the three sectors, we clarified the distribution of ESBL-Ec among humans, the environment, and food within the country. The proportion of ESBL-Ec was higher in human blood–derived specimens than in specimens from pregnant women, possibly reflecting differences in antimicrobial use. The proportion of ESBL-Ec in environmental samples was 3.27% in wastewater inflow. In contrast, the proportion of ESBL-Ec among isolates from poultry cecal contents, used as a food-sector indicator, was 1.88%.



	Blood Culture (a university hospital in A Prefecture)	Blood Culture JANIS (Admission) *	Rectal swabs from pregnant women**	Fecal samples of food service workers	Poultry products (cecal contents)_ Nationwide	River water_ upstream (A prefecture)	River water_down stream (A prefecture)	Sewage inflow water (A prefecture)	Wastewater from poultry and other animal slaughter-houses
2019	74	26,004		311	128				
2020	111	26,687		281	121	29	185	1,754	574
2021	97	25,849			145	211	127	4,395	1,843
2022	108	26,058	133		142	11	72	1,191	
2023		26,991			155	206	190	1,266	956

(Number of *E. coli*)

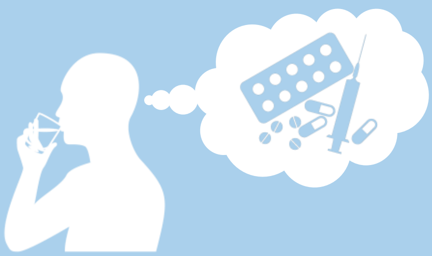
* Blood Culture_JANIS (Admission): CTX resistance *E. coli*/*E. coli* (%)

** Number of ESBL-Ec-positive pregnant women/Total number of pregnant women (%)

The proportion of ESBL-Ec among the total E. coli isolates

The years of analysis are indicated below the bar graph for each sample.

Section B Antimicrobial Usage



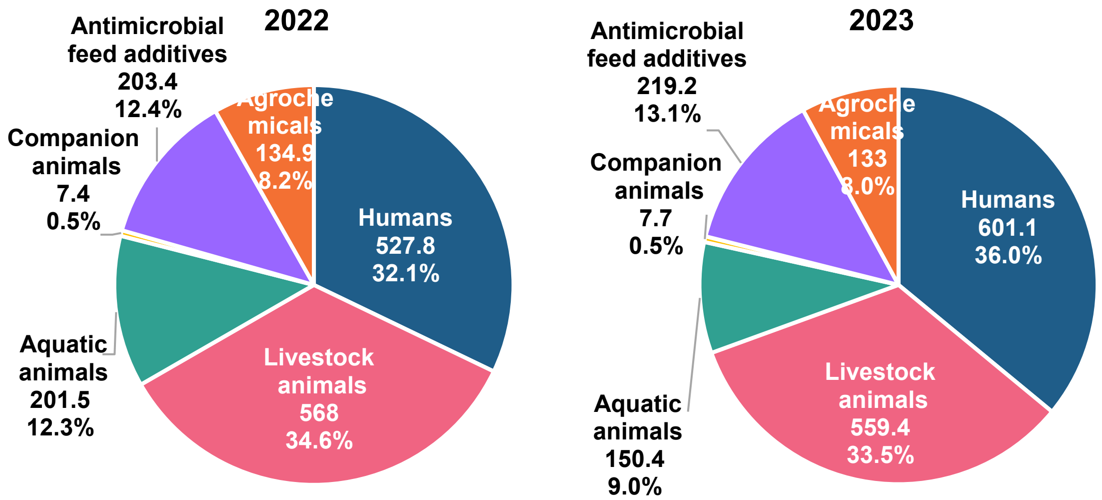
Section B:
Antimicrobial Usage

B1: Current Volume of Use of Antimicrobials in Japan

The proportion of antimicrobial usage by field within the overall antimicrobial use (2023)

In 2023, the antimicrobial usage (or sales volume) in Japan by field (humans, livestock animals, aquatic animals , companion animals, feed additives, and agrochemicals) was highest for humans at 601.1 t (36.0%), followed by livestock animals at 559.4 t (33.5 %).

The usage of important antimicrobials for human medicine constitutes approximately 4% of the total usage in livestock animals, which is equivalent to about 1% of the overall antibiotic usage, thus remaining relatively low. In addition, important antimicrobials for human medicine are not used in aquatic animals, feed additives and agrochemicals.

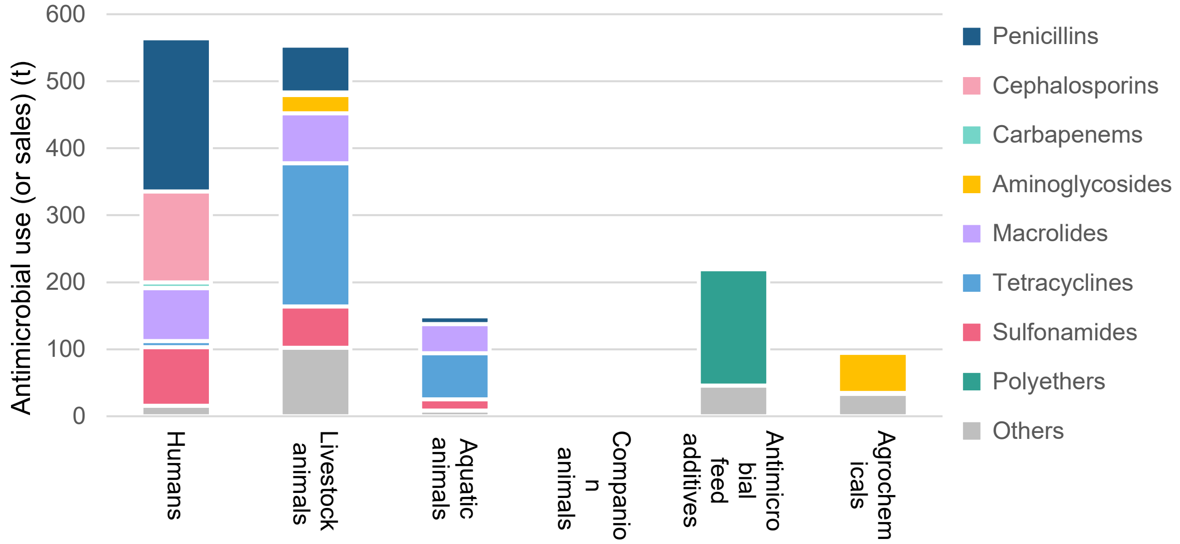


*The units of the values in the pie chart are tons

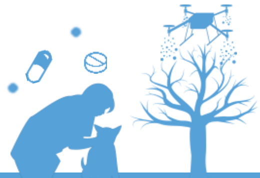
Current antimicrobial use by field (2023)

In 2023, the most used (or sold) antimicrobial classes in Japan by field were penicillins in humans (228.9 t), tetracyclines in livestock animals (213.9 t), and polyethers* in antimicrobial feed additives (173.4 t).

*Ingredients not used in human medicine.



Antimicrobial use (or sales) (t)
600
500
400
300
200
100
0
Humans
Livestock animals
Aquatic animals
Companion animals
Antimicrobial feed additives
Agrochemicals
Penicillins
Cephalosporins
Carbapenems
Aminoglycosides
Macrolides
Tetracyclines
Sulfonamides
Polyethers
Others

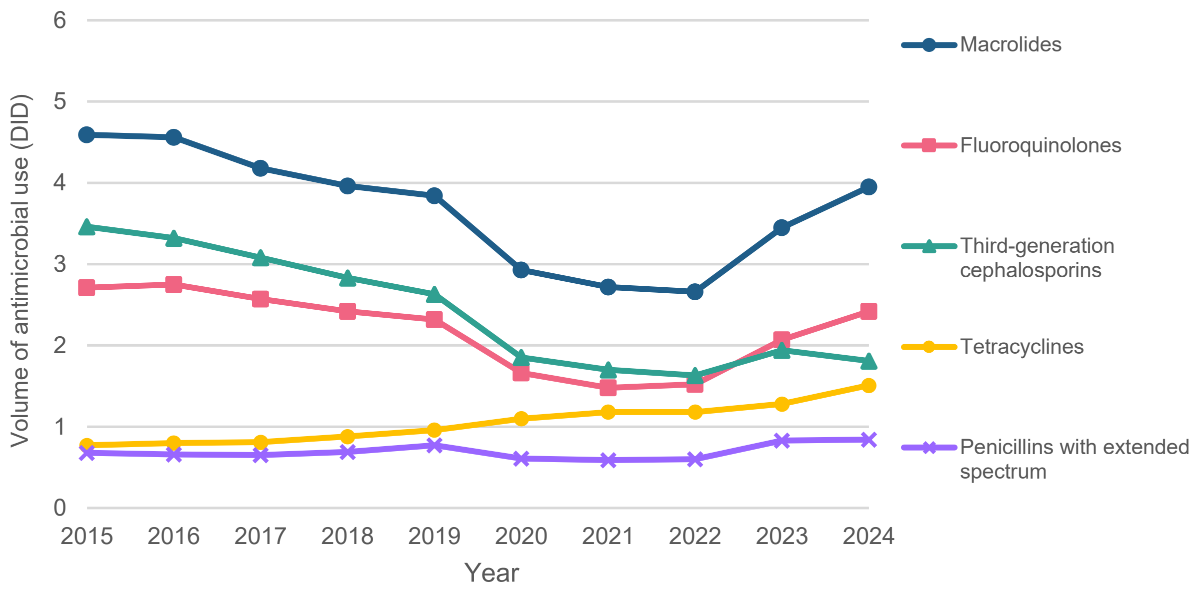


B2: Current Volume of Use of Antimicrobials by Field

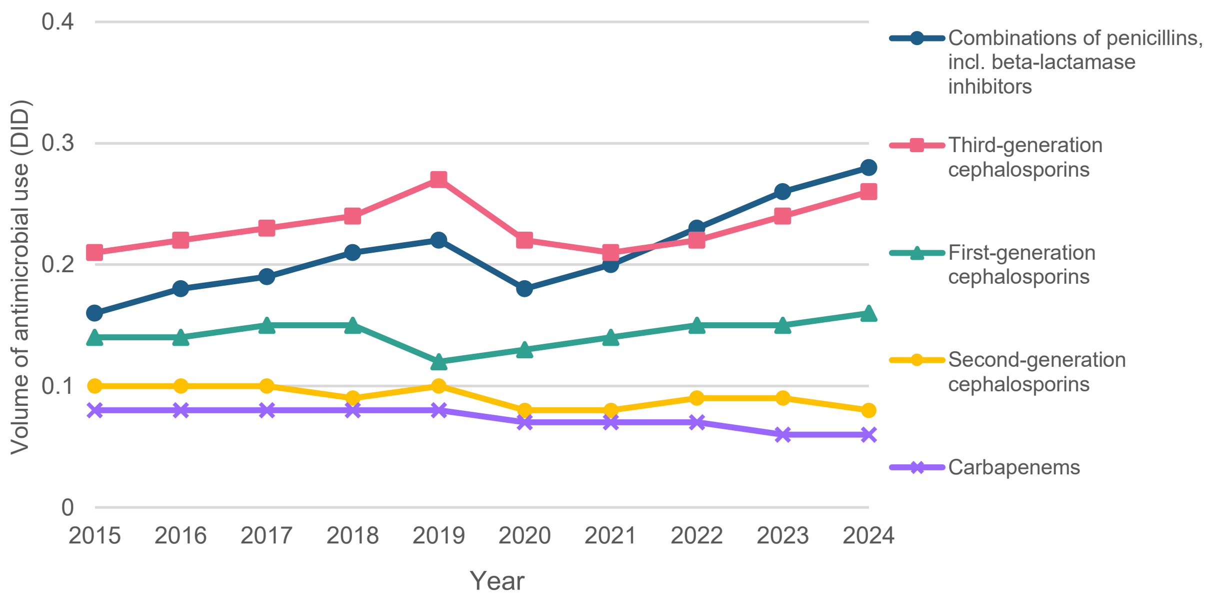
B2.1 The use of antimicrobial agents in humans by class

- In 2024, the use of oral antimicrobial accounted for 11.91 DID (91.9 %) of total antimicrobial use, with macrolides (3.95 DID), fluoroquinolones (2.42 DID) and third-generation cephalosporins (1.81 DID).
- The usage of injectable carbapenems decreased by 9.0 % in 2024 compared to 2020.

Five most used oral antimicrobials in 2015-2024



Five most used injectable antimicrobials in 2014-2024

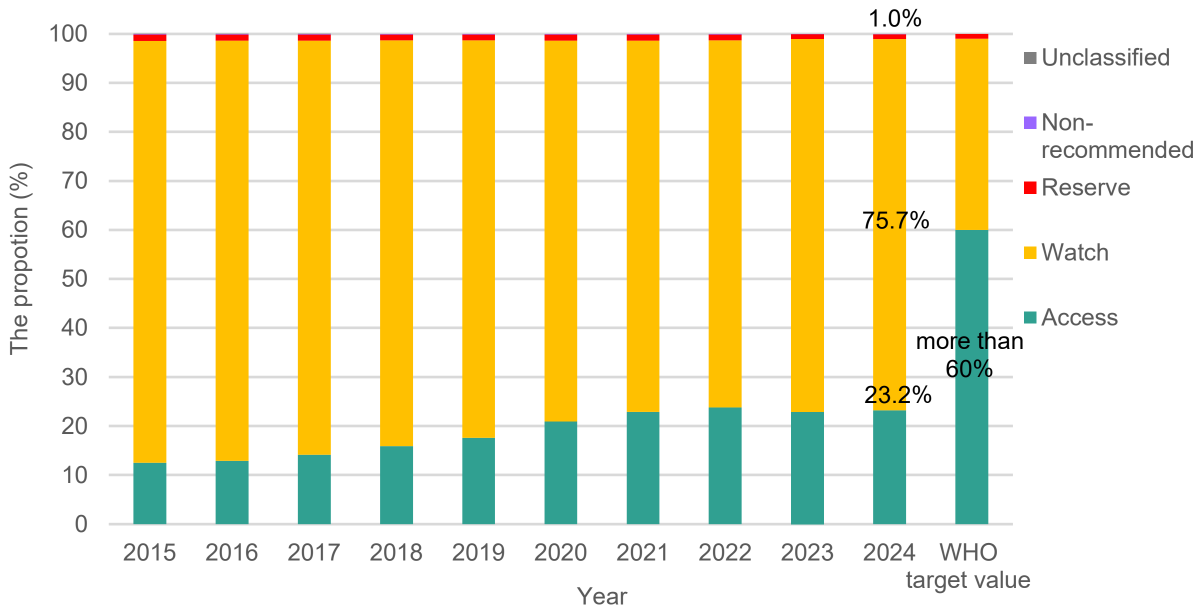


B2.2 Usage of antimicrobials classified under AWaRe

Trends in antimicrobial use by AWaRe classification

The AWaRe classification is an antimicrobial categorization system adapted from the antibiotic classification included in the 20th edition of the WHO Model List of Essential Medicines, and is used as an indicator for appropriate antimicrobial use. Taking into account concerns regarding the development of antimicrobial resistance, antibiotics are categorized into Access, Watch, Reserve, Not Recommended, and Unclassified groups.

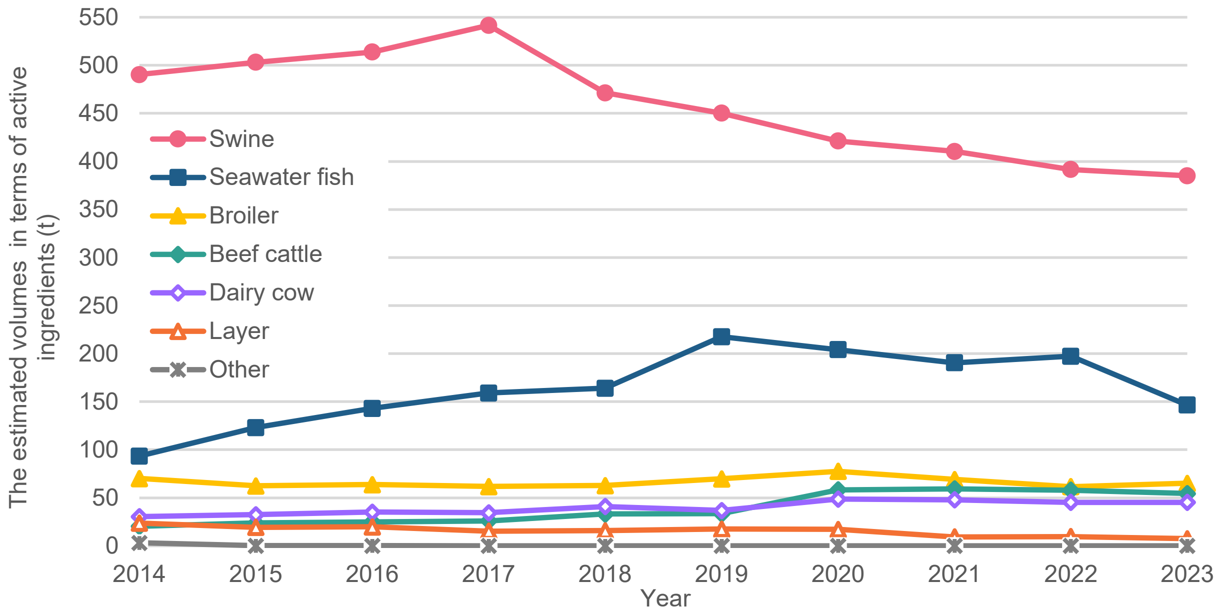
WHO aims for antibiotics classified as "Access" to account for more than 60% of all antimicrobial use. Compared to other countries, Japan tends to have a lower proportion of antimicrobials classified as "Access". However, over time, this proportion has gradually increased from 12.5% in 2015 to 23.2% in 2024, while the proportion of antimicrobials classified as "Watch" has decreased from 86.1% to 75.7%.



B2.3 The amount of antimicrobial use for animals

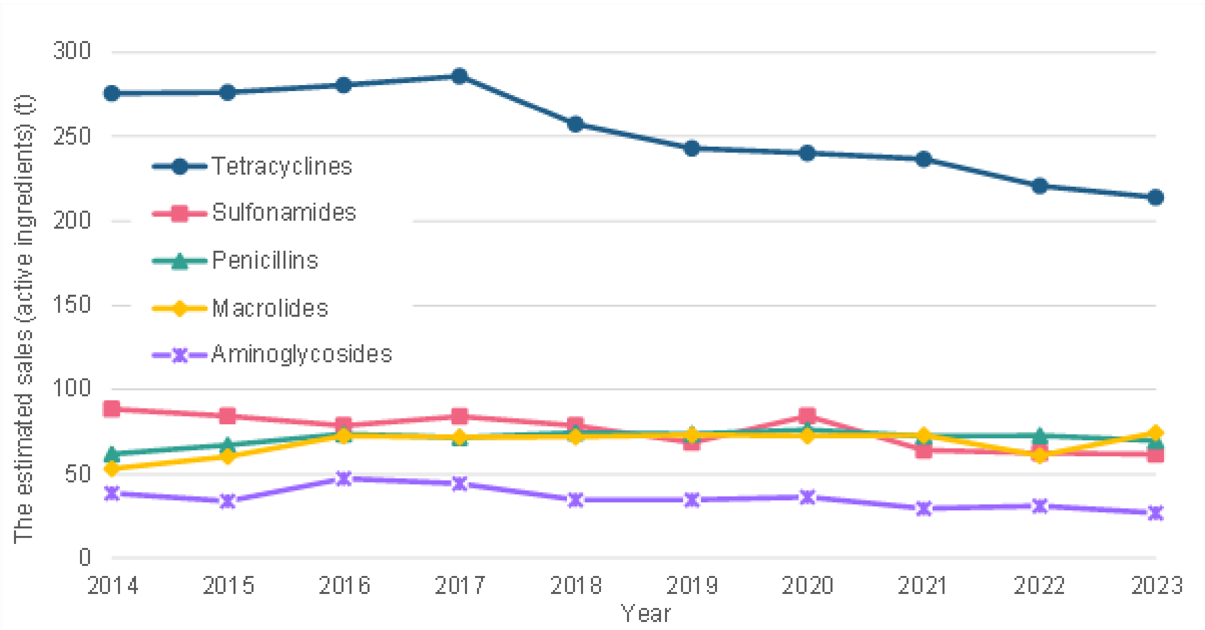
Estimated usage of veterinary antimicrobials by animal species (as active ingredient equivalent) (t)

The estimated sales volume by animal species (calculated as active ingredient equivalent) was highest for swine, followed by seawater fish. Since 2018, the sales volume for swine has decreased.



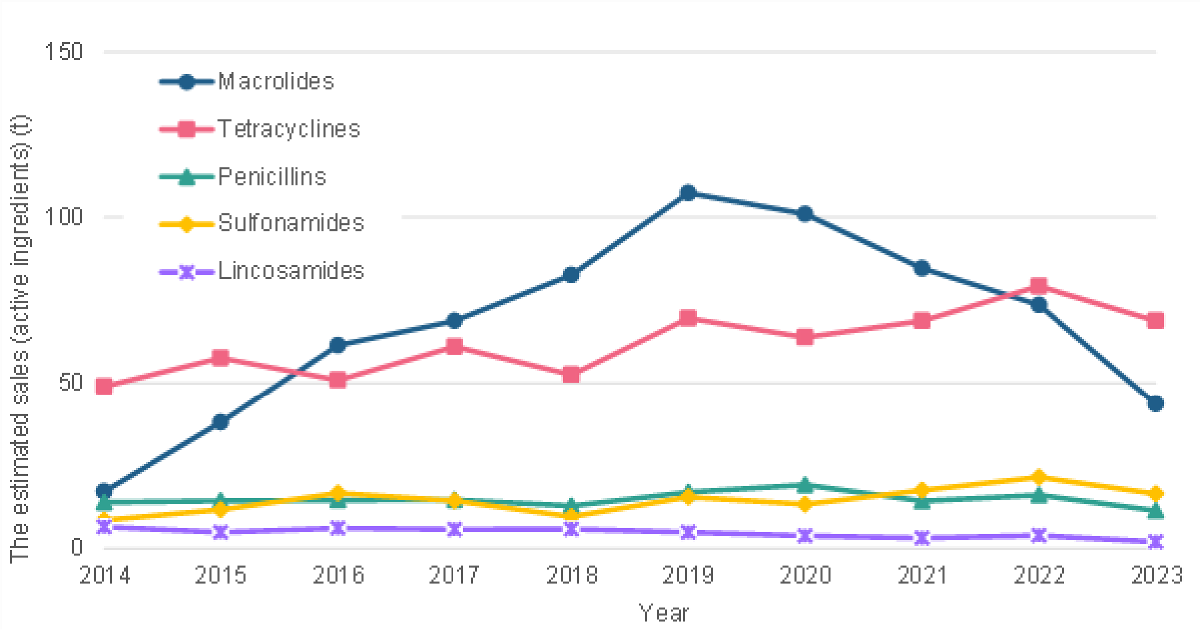
Top five antimicrobials for livestock animals (cattle, swine, horses, chickens and others)

The antimicrobial class with the highest sales volumes was tetracyclines, accounting for from 38.2% to 43.1% of antimicrobials for livestock animals. However, in 2023 the sales volume for tetracyclines was the lowest since 2014, at 213.9 t. This decrease is likely largely attributed to the reduction in usage in swine.



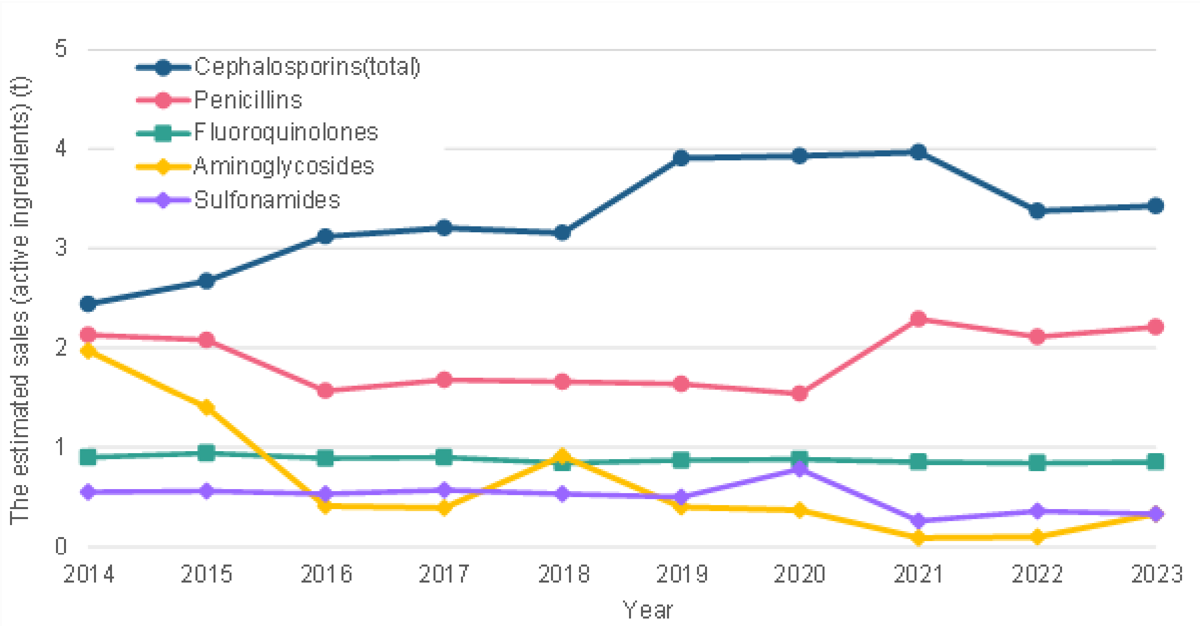
Top five antimicrobials for aquatic animals (seawater fish, freshwater fish, and ornamental fish)

Macrolide antimicrobials showed a notable increase primarily from 2015 to 2019, which may be attributed to their use in treating type II α-hemolytic lactococcosis that have been occurring since around 2013. The usage decreased from 2020 onward, suggesting that improvements in vaccines and other measures may have been effective.



Top five antimicrobials for companion animals (dogs and cats)

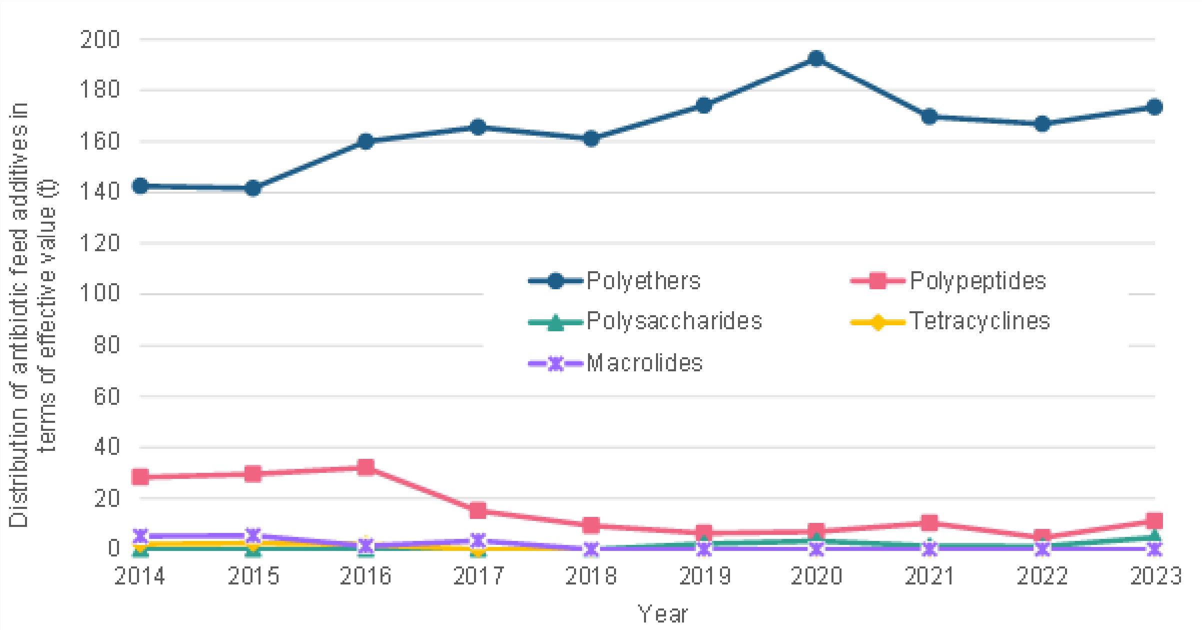
The graph below shows the trend in the veterinary antimicrobials for companion animals. The most sold antimicrobials were first-generation cephalosporins, followed by penicillins.



B2.4 Distribution volume of antimicrobial feed additives

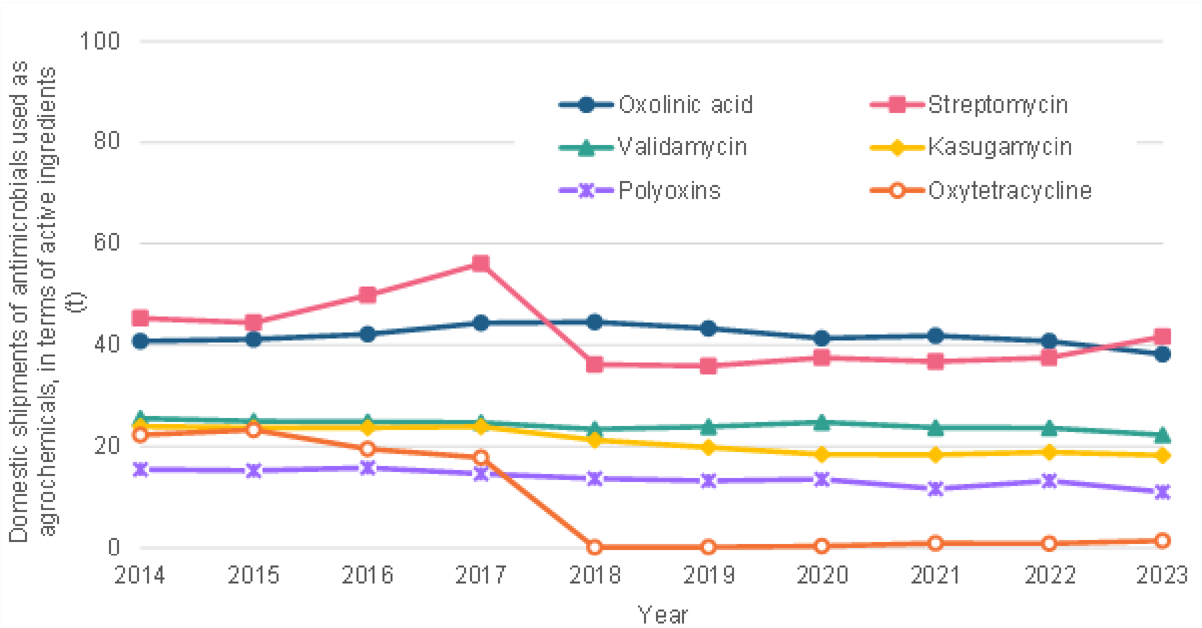
The distribution volume increased slightly from 203.3 t in 2022 to 219.2 t in 2023. It is noteworthy that the designation of the polypeptide colistin, the macrolide tyrosine, and two tetracyclines as feed additives was revoked in July 2018, May 2019 and December 2019, respectively, and thus, these antimicrobials feed additives have not been distributed since their revocation.

* Polyethers are not used in human medicine.



B2.5 The domestic shipment volume of antimicrobials used as agrochemicals

The domestic shipment volume of antimicrobials used as agrochemicals decreased significantly in 2018 for streptomycin and oxytetracycline but remained largely stable in other years. The domestic shipment volume of other antimicrobials has remained steady.



Section C Nosocomial Infections

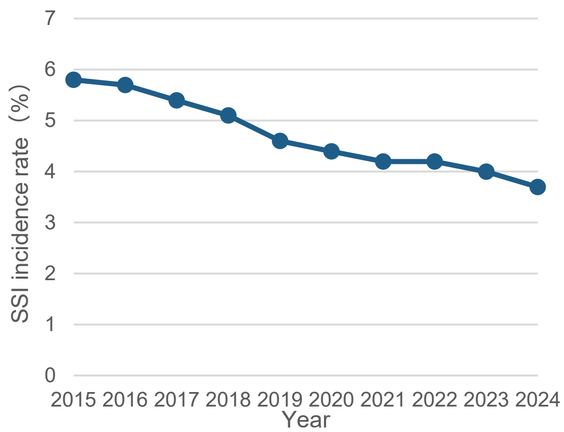
Section C:
Nosocomial Infections

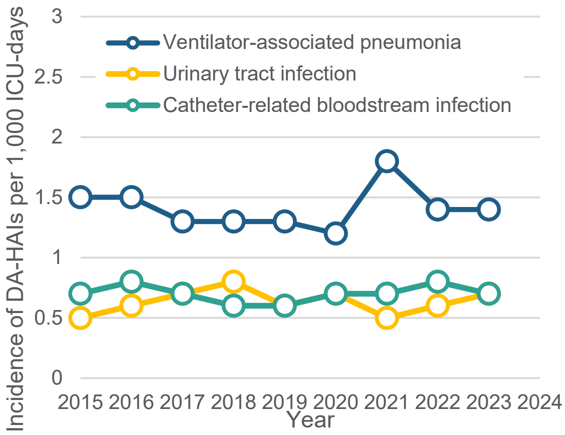
C1: Antimicrobial-resistant bacteria in healthcare-associated infection (HAI)

C1.1 The occurrence of healthcare-associated infections (HAIs)

The incidence of surgical site infections (SSI) has shown a decreasing trend since 2015 (below left diagram). In 2024, out of 407,650 surgical operations conducted in 903 facilities, there were 15,274 SSI cases (incidence rate 3.7 %).

The incidence rate of ventilator-associated pneumonia has fluctuated between 1.2 and 1.8/1,000 ICU admission days over the past 10 years, with a rate of 1.4/1,000 ICU admission days in 2024. The incidence rate of urinary tract infections has ranged from 0.5 to 0.8/1,000 ICU admission days, while that of catheter-related bloodstream infections has fluctuated between 0.6 and 0.8/1,000 ICU admission days. All of these have shown slight increases and decreases over time. (below right diagram)

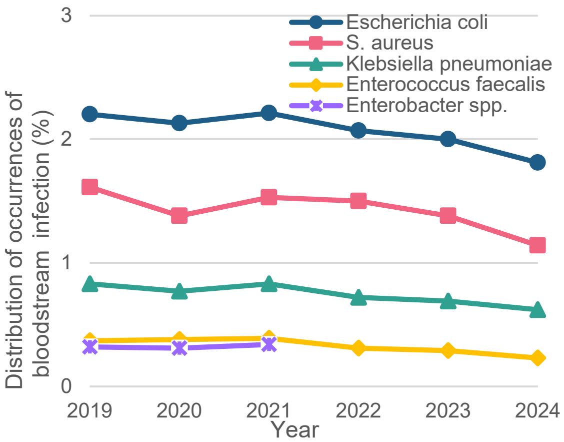


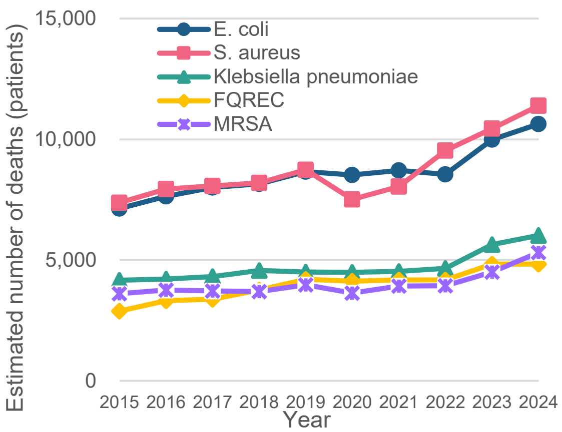


C1.2 Survey of infection management, infection control and disease burden in hospitals

The incidence rate of pathogens detected from blood samples in 2024, measured as the number of cases per 10,000 patient-days (incidence rate of bloodstream infections) was highest for *Escherichia coli* (1.81, IQR: 0.60-2.86), followed by *S. aureus* (1.14, IQR: 0.39-2.09), and *Klebsiella pneumoniae* (0.62, IQR: 0.00-1.18).

In 2024, the estimated number of deaths due to *S. aureus* was the highest at 11,388 (95% CI: 8,958-13,904), followed by *E. coli* with 10,635 deaths (95% CI: 8,475-12,897), and *Klebsiella pneumoniae* with 6,015 deaths (95%CI: 4,567-7,530).





※*S. aureus* includes MRSA; *E. coli* includes FQREC and/or 3CREC, with FQREC and 3CREC calculated independently based on resistance to each respective antimicrobial agent; and *Klebsiella pneumoniae* includes 3CRKP

C1.3 Survey of infections at the Medical long-term care wards/hospitals and facilities for the elderly

Medical long-term care wards/hospitals

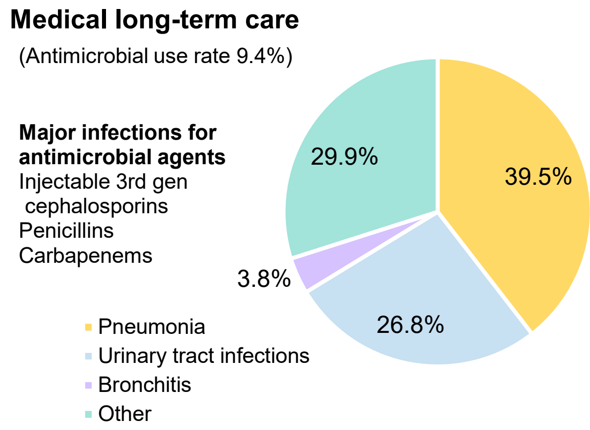
A Point Prevalence Survey (PPS) was conducted in January 2020 by randomly selected medical care facilities with medical long-term care wards from the Japan Association of Medical and Care Facility member institutions. The antibacterial use rate was 9.4% (630 antimicrobial users among 6,729 inpatients).The most common infections were “pneumonia” with 199 cases (39.5%), ”urinary tract infection” with 135 cases (26.8%), and ”bronchitis” with 19 cases (3.8%). The main frequently used antimicrobials were injectable third-generation cephalosporins, penicillin combinations with beta-lactamase inhibitors, and carbapenems.

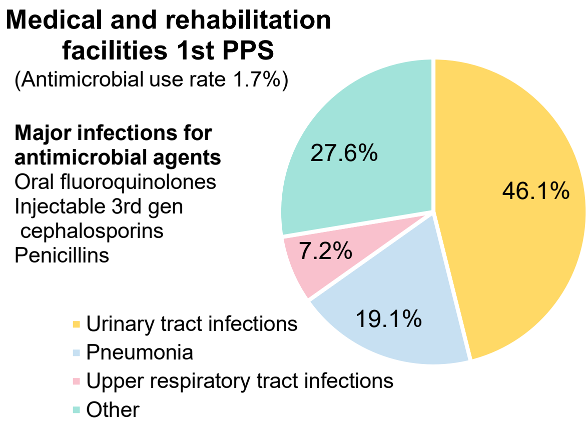
Long-term care facilities for the elderly

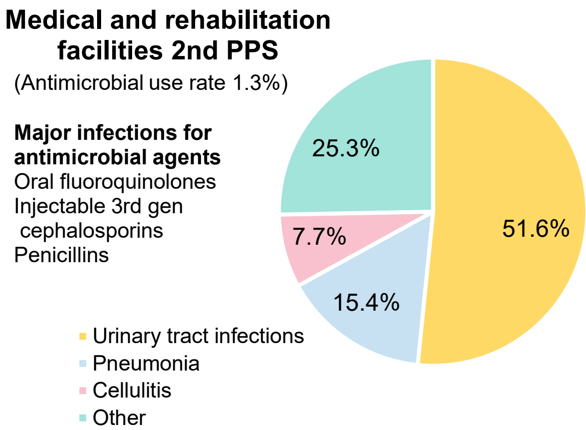
A Point Prevalence Survey (PPS) was conducted by randomly selecting facilities from the Japan Association of Geriatric Health Services Facilities member institutions. In the first PPS, conducted in February 2019, showed an antimicrobial use rate of 1.7% (172 antimicrobial users out of 10,148 residents). The top common infections were "urinary tract infections" with 70 cases (46.1%), "pneumonia" with 29 cases (19.1%), and "upper respiratory tract infections" with 11 cases (7.2%). In the second PPS, conducted in February 2022, showed an antimicrobial use rate of 1.3% (110 antimicrobial users out of 8,291 residents). The most common infections were "urinary tract infections" with 47 cases (51.6%), "pneumonia" with 14 cases (15.4%), and "cellulitis" with 7 cases (7.7%). In both surveys, the antimicrobials primarily used for urinary tract infections were fluoroquinolones and those for pneumonia were injectable third-generation cephalosporins.

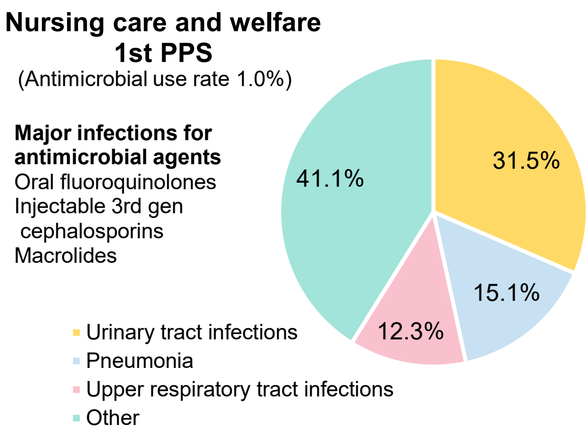
Welfare facilities for the elderly requiring long-term care (special nursing homes for the aged)

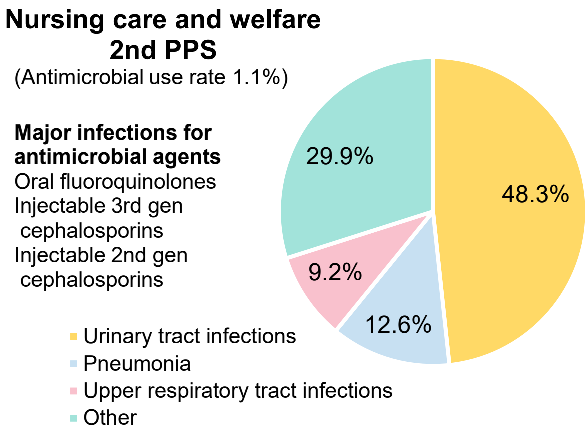
A Point Prevalence Survey (PPS) was conducted by randomly selecting facilities from member institutions of the Japan Association of National Council of Social Welfare Facilities for the Elderly. The first PPS, conducted in March 2020 showed an antimicrobial use rate of 1.0% (94 antimicrobial users out of 9,044 residents). The most common infections were "urinary tract infections" with 23 cases (31.5%), "pneumonia" with 11 cases (15.1%), and "upper respiratory tract infections" with 9 cases (12.3%). The antimicrobials primarily used for urinary tract infections were fluoroquinolones, and those for pneumonia were injectable third-generation cephalosporins. The second PPS, conducted from February to March 2024 showed an antimicrobial use rate of 1.1% (108 antimicrobial users out of 10,255 residents). The most common infections were "urinary tract infections" with 42 cases (48.3%), "pneumonia" with 11 cases (12.6%), and "upper respiratory tract infections" with 8 cases (9.2%). The antimicrobials primarily used for urinary tract infections and pneumonia were fluoroquinolones,


Medical long-term care
(Antimicrobial use rate 9.4%)
Major infections for antimicrobial agents
Injectable 3rd gen cephalosporins
Penicillins
Carbapenems
29.9%
39.5%
3.8%
26.8%
Pneumonia
Urinary tract infections
Bronchitis
Other


Medical and rehabilitation facilities 1st PPS
(Antimicrobial use rate 1.7%)
Major infections for antimicrobial agents
Oral fluoroquinolones
Injectable 3rd gen cephalosporins
Penicillins
27.6%
46.1%
7.2%
19.1%
Urinary tract infections
Pneumonia
Upper respiratory tract infections
Other

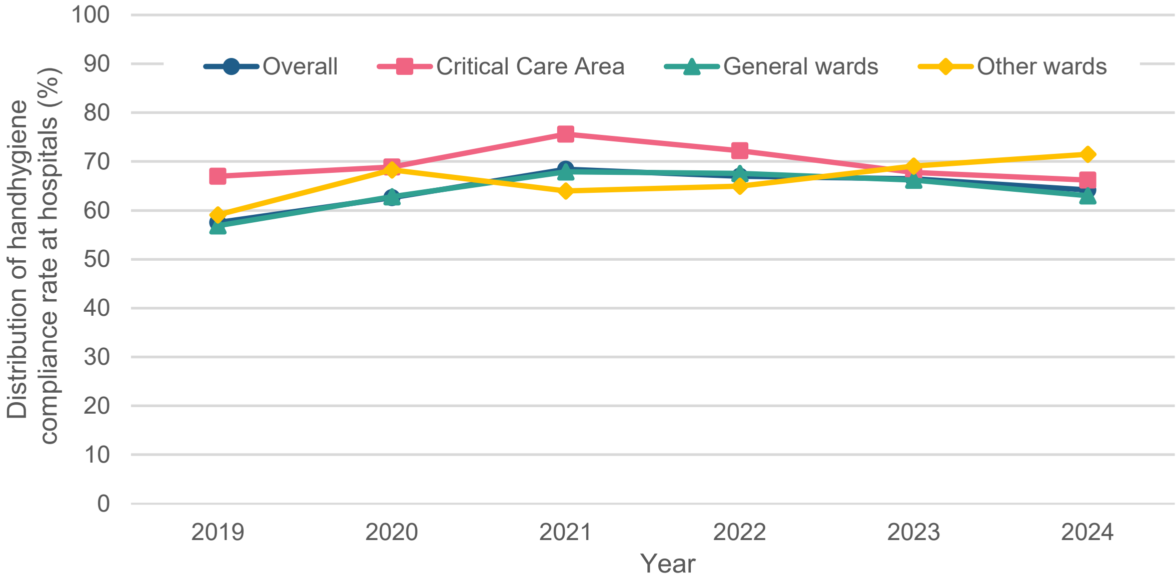

Medical and rehabilitation facilities 2nd PPS
(Antimicrobial use rate 1.3%)
Major infections for antimicrobial agents
Oral fluoroquinolones
Injectable 3rd gen cephalosporins
Penicillins
25.3%
51.6%
7.7%
15.4%
Urinary tract infections
Pneumonia
Cellulitis
Other

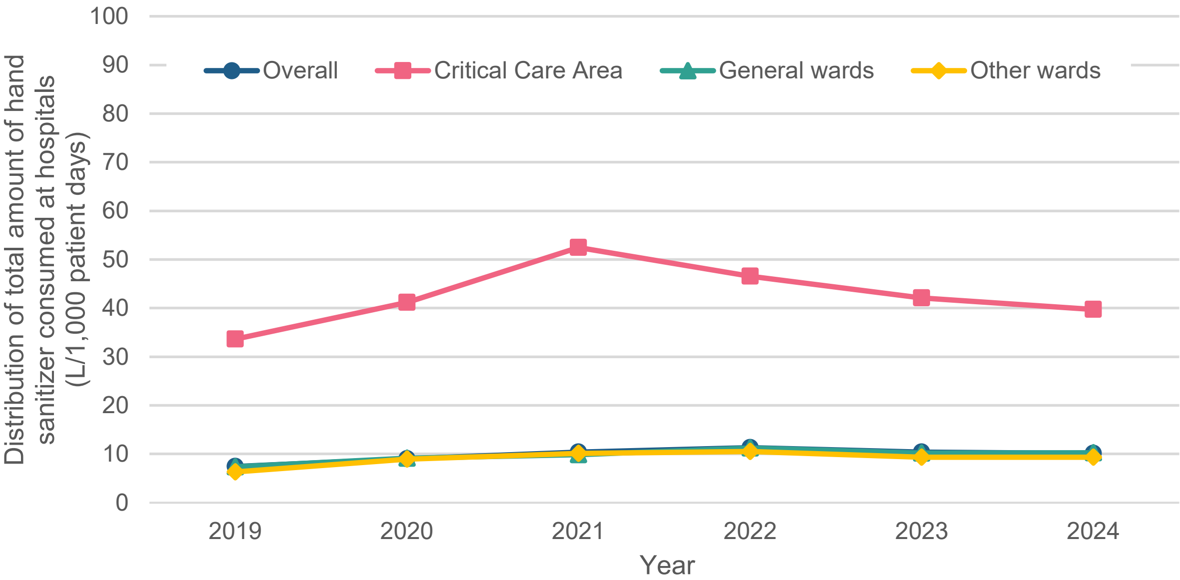

Nursing care and welfare 1st PPS
(Antimicrobial use rate 1.0%)
Major infections for antimicrobial agents
Oral fluoroquinolones
Injectable 3rd gen cephalosporins
Macrolides
41.1%
31.5%
15.1%
12.3%
Urinary tract infections
Pneumonia
Upper respiratory tract infections
Other


Nursing care and welfare 2nd PPS
(Antimicrobial use rate 1.1%)
Major infections for antimicrobial agents
Oral fluoroquinolones
Injectable 3rd gen cephalosporins
Injectable 2nd gen cephalosporins
29.9%
48.3%
9.2%
12.6%
Urinary tract infections
Pneumonia
Upper respiratory tract infections
Other

C2: The status of hand hygiene practice

The hand hygiene compliance rate (in 2024, n=134) was 64.2% overall, while a higher rate of 66.2% in the critical care wards (n=51) compared to general wards. The hand sanitizer consumption per 1,000 patient-days (2024, n=1,476) was 10.09 L (IQR: 6.12-14.84) overall, and 39.15 L (IQR: 24.81-63.19) in the critical care wards (n=493), showing a higher usage compared to general wards. The use of hand hygiene products has shown an increasing trend since 2019, reflecting an improvement in hand hygiene awareness due to COVID-19 infection control measures. However, the rate showed a downward trend in 2022.





Section D
Attitude Surveys on Antimicrobial Resistance

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Attitude Surveys on Antimicrobial Resistance

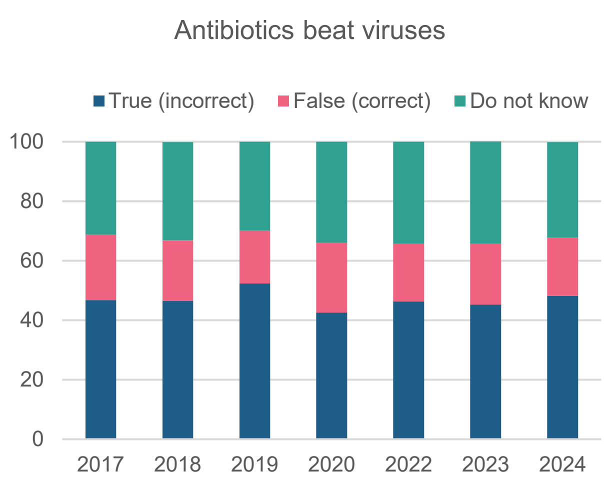
D1：Surveys of the general public

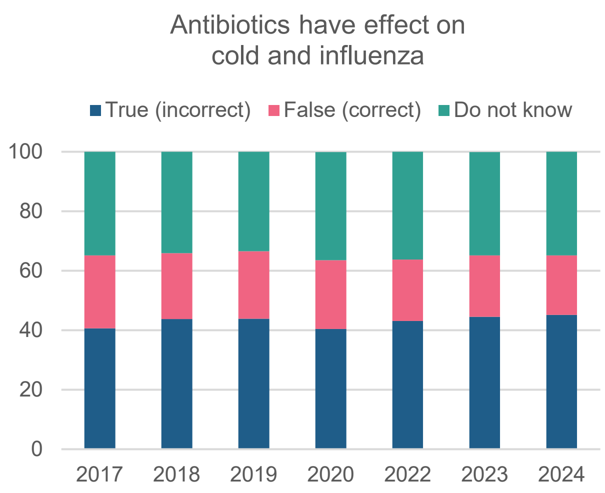
Public awareness surveys on antimicrobial resistance were conducted online in March 2017, February 2018, September 2019, September 2020, October 2022, October 2023, and December 2024.

*Survey participants were monitors registered with INTAGE Research Inc (excluding medical professionals): the 2017 survey had 3,390 valid responses, the 2018 survey 3,192, the 2019 survey 3,218, the 2020 survey 3,200, the 2022 survey 3,193, the 2023 survey 3,202, and the 2024 survey 3,213.

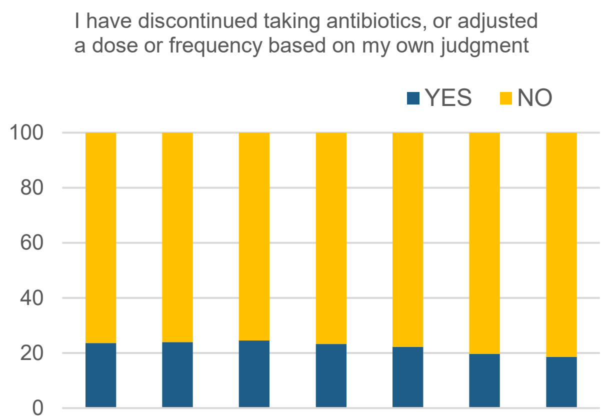
Surveys of attitudes among the public (%)

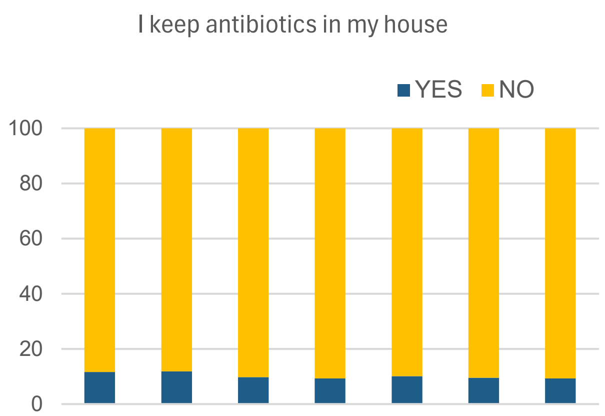
Approximately 40% of respondents answered "true” to the statements "antibiotics beat viruses" or "antibiotics have effect on cold and influenza".





Regarding the use of antibiotics, approximately 20% respondents reported that they “discontinued taking antibiotics based on their own judgment”, while approximately 10% responded that they “kept the remaining antibiotics at home”.





Section D:

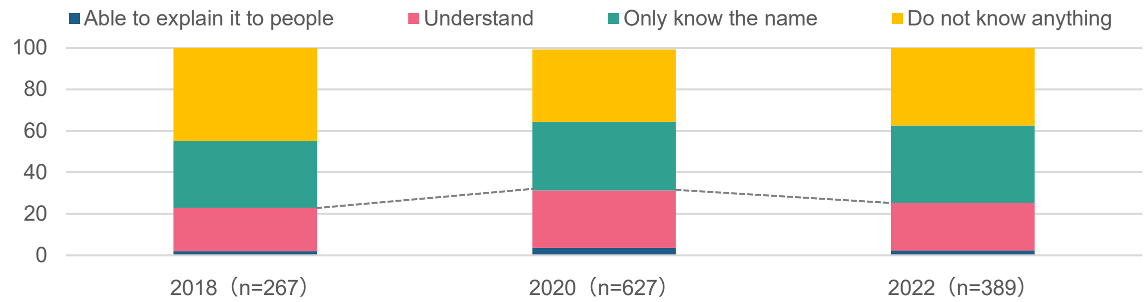
Attitude Surveys on Antimicrobial Resistance

D2: Surveys of healthcare providers

The joint committee on appropriate use of outpatient antibiotics of the Japanese Society of Chemotherapy and the Japanese Association for Infectious Diseases conducted a survey on awareness among physicians working in clinics in 2018, from September to October 2020, and from December 2022 to February 2023. The survey questionnaires were distributed to 3,000 randomly selected clinics nationwide, and questionnaires were filled out and returned through mail.

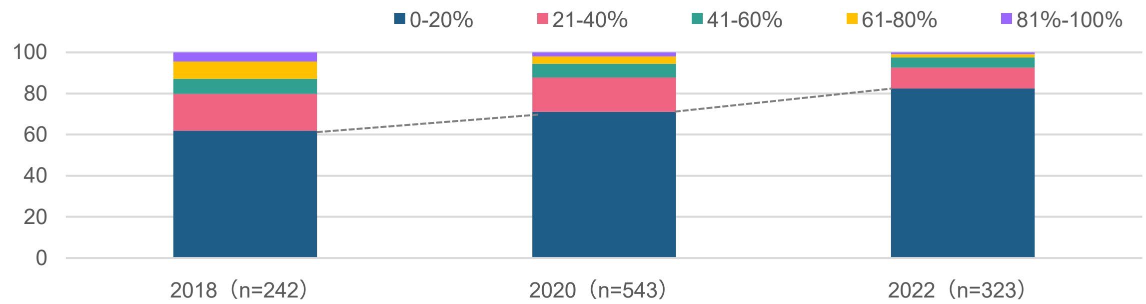
Awareness of the National Action Plan on AMR (%)

In the 2022 survey, compared to 2020, the awareness of the National Action Plan on AMR decreased, with the percentage of respondents answering, "can explain it to people" and "understand it" combined decreasing from 31.3% to 25.2%.



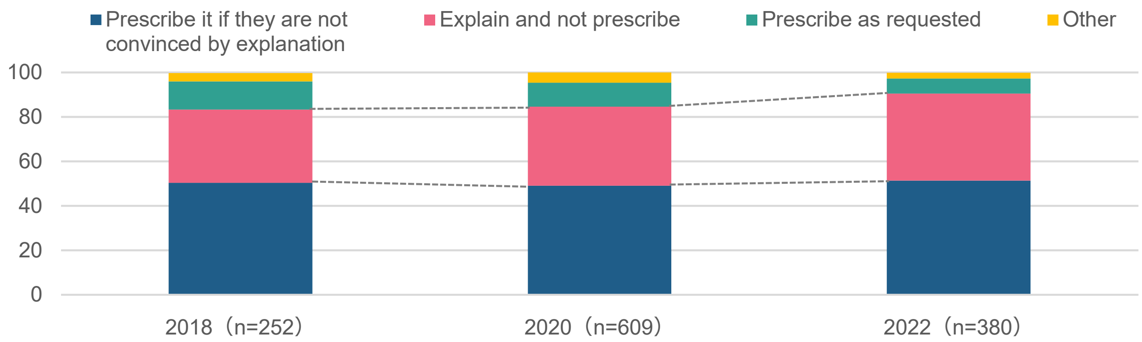
Percentage of prescribing antimicrobials when diagnosing a common cold (%)

The proportion of antimicrobial prescriptions for common cold showed a decrease, with the percentage of respondents indicating “0-20%” rising from 71.1% to 82.4%, suggesting a reduction in prescription rates.



Response when a patient, or their family members, diagnosed with a common cold request for an antimicrobial agent (%)

In response to requests for antimicrobial prescriptions, 39.2% of respondents answered that they would "explain and not prescribe," while 6.8% and 51.3% answered that they would "prescribe as requested" and "prescribe if not satisfied after explanation," respectively. These results were nearly the same as those of the previous survey.



Prescribe it if they are not convinced by explanation
Explain and not prescribe
Prescribe as requested
Other
100
80
60
40
20
0
2018（n=252）
2020（n=609）
2022（n=380）

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Ministry of Agriculture, Forestry and Fisheries	Ministry of Land, Infrastructure, Transport and Tourism

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