One Health Report on **Antimicrobial Utilisation and Resistance, 2023**

One Health Antimicrobial Resistance Workgroup,
Singapore

One Health Report on Antimicrobial Utilisation and Resistance in Singapore, 2023

This Report was compiled by the One Health AMR Workgroup (OH AMRWG) and is jointly published by:

- Communicable Diseases Agency (CDA)
- National Environment Agency (NEA)
- National Parks Board (NParks)
- PUB, Singapore's National Water Agency (PUB)
- Singapore Food Agency (SFA)

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Suggested citation: One Health Antimicrobial Resistance Workgroup Singapore (2025). One Health Report on Antimicrobial Utilisation and Resistance 2023. Singapore.

Date of publication: 23 Dec 2025

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Acknowledgments

The One Health AMR Workgroup thanks the following committees and institutions and their staff for provision and analyses of surveillance data:

- National Antimicrobial Resistance Control Committee (NARCC)
- National Antimicrobial Resistance Expert Panel (NAREP)
- National Antimicrobial Stewardship Expert Panel (NASEP)
- Centre for Animal & Veterinary Sciences, NParks
- National Centre for Food Science, SFA
- Environmental Health Institute, NEA
- Agency for Care Effectiveness, MOH
- Alexandra Hospital
- Changi General Hospital
- KK Women's and Children's Hospital
- Khoo Teck Puat Hospital
- National University Hospital
- Ng Teng Fong General Hospital
- Tan Tock Seng Hospital
- Singapore General Hospital
- Sengkang General Hospital
- Gleneagles Hospital
- Mount Elizabeth Hospital
- Mount Elizabeth Hospital (Novena)
- Mount Alvernia Hospital
- Parkway East Hospital
- Raffles Hospital
- Thomson Medical Centre
- Farrer Park Hospital
- National Healthcare Group (NHG) polyclinics
- National University Health System (NUHS) polyclinics
- Singapore Health Services (SingHealth) polyclinics

List of Abbreviations

AMR	Antimicrobial Resistance
AMRCO	Antimicrobial Resistance Coordinating Office
AMRWG	Antimicrobial Resistance Workgroup
AMU	Antimicrobial utilisation
ANIMUSE	WOAH's Global Database on ANImal antiMicrobial USE (ANIMUSE)
ARB	Antibiotic resistant bacteria
ARG	Antibiotic resistant genes
ASP	Antimicrobial stewardship programme(s)
AST	Antibiotic susceptibility test/testing
ATC	Anatomical Therapeutic Chemical
AVS	Animal & Veterinary Service, NParks
CAVS	Centre for Animal & Veterinary Sciences, NParks
CDA	Communicable Diseases Agency
CFU	Colony-forming unit
CIP	Ciprofloxacin
CLSI	Clinical and Laboratory Standards Institute
CP-CRE	Carbapenemase-producing carbapenem-resistant Enterobacterales
CPE	Carbapenemase-producing Enterobacterales
CR	Carbapenem-resistant
CRE	Carbapenem-resistant Enterobacterales
CRO	Ceftriaxone
CTA	Countries, Territories & Areas
CTX	Cefotaxime
DDD	Defined Daily Dose
DID	DDD/ 1000 inhabitants/ day
EHI	Environment Health Institute, NEA
EPA	United States Environmental Protection Agency
ESBL	Extended spectrum beta-lactamase
EUCAST	European Committee on Antimicrobial Susceptibility Testing
FIB	Faecal indicator bacteria
GI	Gastrointestinal
GLASS	Global Antimicrobial Resistance Surveillance System
GP	General practitioner
HIC	High Income Countries
HIV	Human Immunodeficiency Virus
HPB	Health Promotion Board
ID	Infectious Disease
IPM	Imipenem
IQR	Interquartile range
MDR	Multi-drug resistant
MEM	Meropenem
MIC	Minimum Inhibitory Concentration
MMP	Market Monitoring Programme
MOH	Ministry of Health

MRSA	Methicillin-resistant *Staphylococcus aureus*
MRSP	Methicillin-resistant *Staphylococcus pseudintermedius*
NAFTEC	Nanyang Technological University Food Technology Centre
NARCC	National Antimicrobial Resistance Control Committee
NCFS	National Centre for Food Science, SFA
NCID	National Centre for Infectious Diseases
NEA	National Environment Agency
NParks	National Parks Board
NPHL	National Public Health Laboratory
NTU	National Technological University
NUS	National University of Singapore
WOAH	World Organisation for Animal Health
PUB	Public Utilities Board, Singapore's National Water Agency
QMRA	Quantitative microbial risk assessment
SDG	Sustainable Development Goals
SFA	Singapore Food Agency
TNRM	Trap-Neuter-Release/Rehome-Manage
VRE	Vancomycin-resistant Enterococci
WGS	Whole Genome Sequencing
WHO	World Health Organization

Executive Summary

Surveillance serves to monitor the levels of antimicrobial resistance (AMR) in the affected sectors and to track the consumption of antimicrobials by humans and animals. This provides important data and evidence needed to assess risks, guide policy decisions and measure the impact of interventions. Surveillance therefore forms a core strategy of Singapore's National Strategic Action Plan on AMR.

This One Health report updates on key findings from national AMR and antimicrobial utilisation (AMU) surveillance programmes up to the end of 2023. The last report can be accessed at One Health Report on Antimicrobial Utilisation and Resistance, 2021

NEW in this edition:

- One Health surveillance – a comparison of antimicrobial resistance of *Escherichia coli* in human, animal, food production and environmental sectors
- One Health risk assessment study of coastal environments and aquaculture
- Environmental surveillance – a study of extended spectrum beta-lactamase producing (ESBL) *E. coli* (ESBL-Ec) in coastal and linked waterways.

ANTIMICROBIAL UTILISATION

In the human health sector, the antimicrobials most utilised by acute care hospitals (public and private) in 2023 were beta-lactams and beta-lactamase inhibitors, fluoroquinolones, tetracyclines, third- and fourth-generation cephalosporins, and antifungals. The primary care sector utilised mainly beta-lactams and beta-lactamase inhibitors, followed by tetracyclines and macrolides and lincosamides.

Overall utilisation of antimicrobials in the human health sector increased in 2023, after a decline from 2019 to 2021. The COVID-19 pandemic was likely a contributing factor to this trend; post-pandemic monitoring showed that the overall utilisation of antimicrobials had returned to similar pre-COVID levels. Similarly, total reported antibiotic sales increased in 2022 and 2023 from 2019-2021, contributed largely by sales to private sector outpatient clinics.

In the animal health sector, tetracyclines, fluoroquinolones and penicillins were the most reported antimicrobial drugs sold for veterinary use in 2023, consistent with past trends. The aquaculture sector remained the largest consumer among the animal sectors. Sales for ornamental fish use was segmented for the first time, with sales to the ornamental fish industry exceeding that to the food fish industry in 2023.

ANTIMICROBIAL RESISTANCE

Singapore's **Sustainable Development Goals indicators for AMR** (SDG 3.d.2) decreased in 2023 compared to 2022: The proportion of *E. coli* resistant to third-generation cephalosporins in blood samples was on a declining trend at 23.8% in 2023, while and that of methicillin-resistant *Staphylococcus aureus* in 2023 was 23.6, down from 35.7% in 2022.

Resistance across One Health - An early attempt to integrate resistance profiles for *E. coli* across sectors compared resistance proportions (%R) to third-generation cephalosporins, fluroquinolones and carbapenems as well as the prevalence of ESBL phenotype across sectors. Compared to human clinical isolates recovered from hospitalised patients, resistance rates to third-generation cephalosporins (cefotaxime and ceftazidime) and fluoroquinolones (ciprofloxacin) from non-human populations were relatively low. Carbapenem (meropenem) resistance was not detected in *E. coli* from wildlife, stay dogs and farm samples. ESBL-Ec was more frequently recovered from imported poultry products than from other sample types and sampling locations across sectors.

In human healthcare settings, overall resistance rates of pathogens under monitoring were mostly stable. A gradual increasing trend in the incidence of ciprofloxacin-resistant *E. coli* and *Klebsiella pneumoniae* was observed in acute care hospitals, while approximately 40% of *E. coli* in both inpatient and outpatient (polyclinic) samples were resistant to ciprofloxacin. MRSA rates were overall on a decreasing trend in inpatient settings, with about 20% of *S. aureus* isolates being MRSA in 2023. In outpatient samples, 16.5% of *Staphylococcus aureus* isolates were MRSA. *E. coli* and *K. pneumoniae* isolated from outpatient urine samples were most frequently resistant to ampicillin (>50%) and nitrofurantoin (almost 80%), respectively. While low, the incidence and types of carbapenem-producing Enterobacterales continue to be closely monitored in acute care hospitals: the most frequently detected carbapenemases in 2023 were OXA-type beta-lactamase (OXA), New Delhi metallo-beta-lactamase-mediated carbapenemase (NDM) and *Klebsiella pneumoniae* carbapenemase (KPC).

On local farms, the detection of *Salmonella enterica* serovar Enteritidis (<0.5%) and *Salmonella enterica* serovar Typhimurium (< 3.7%) in local poultry farms continued to remain low from 2021 to 2023. *Salmonella* isolates were most frequently resistant to ampicillin and tetracycline, while consistently low proportions of isolates (<10%) resistant to high priority critically important antibiotics, such as carbapenems, quinolones and third-generation cephalosporins, were observed throughout the past years. Similarly, low levels of resistance to third-generation cephalosporins (cefotaxime and ceftazidime) were observed among *E. coli* isolated from local farms.

In food products, the detection rates of *Salmonella* in raw food products from both import, including animals imported for slaughter (chickens, ducks and pigs), and retail sectors were <0.23% and <0.1% respectively between 2022 and 2023. *Salmonella* was most commonly detected in raw poultry products relative to other raw food types. Overall, antimicrobial resistance rates in *Salmonella* isolates declined between the periods of 2020-2021 and 2022-2023. Of *Salmonella* isolates tested, 23.1% to 28.2% were resistant to cephalosporins such as cefotaxime and ceftazidime. Among the food categories tested, ESBL-Ec was detected most commonly in raw poultry products, with detection rates of approximately 45% in 2022 and 55% in 2023.

In the animal health sector, *E. coli* and *K. pneumoniae* isolates from free-roaming dogs and wildlife demonstrated lower antimicrobial resistance rates and multidrug resistance compared to those from sick companion animals. *K. pneumoniae* isolates demonstrated minimal resistance beyond ampicillin, while low isolation rates of MRSA and MRSP also suggest limited circulation among the free-roaming dog population. These findings indicate that Singapore's free-roaming dogs and wildlife currently pose a relatively low AMR risk to public health, though continued surveillance remains essential to monitor for emerging resistance trends.

In the environment sector, a study of local waterways and coastal waters demonstrated consistently low levels of ESBL-Ec and *Enterococcus* spp. in recreational coastal waters. The varying patterns of microbial presence and AMR profiles observed across different sites underscore the need for systematic risk assessment. Differences may be attributed to distinct environmental profiles of waterways and coastal waters, including the discharge of antimicrobials and ARB from various sources, which may exert varying selective pressures on antibiotic resistance patterns. Average (geometric mean) of *Enterococcus* counts at coastal sites remained below the guideline value for primary contact activities, and were lower in coastal sites than in waterways across all land-use categories. Among *Enterococcus* isolates, erythromycin resistance was most prevalent (25 – 29% of isolates) followed by tetracycline resistance, affecting 6-12% of isolates. These findings provide a foundation for quantitative microbial risk assessment (QMRA) for the evaluation of potential human health risks.

Introduction

Surveillance is one of five core strategies of Singapore's National Strategic Action Plan on Antimicrobial Resistance (AMR) (see Textbox 1). Surveillance of AMR and antimicrobial utilisation (AMU) provide important data for monitoring trends, assessing risks, guiding policy decisions and measuring their impact.

The first *One Health Report on Antimicrobial Utilisation and Resistance, 2017,* was published in 2019 as a step towards an integrated surveillance system in Singapore. This fourth report updates on key findings in the human, animal, food and environment sectors up to 2023. Data from key populations and surveillance sites will contribute towards the formulation of science- and risk-based targets to further drive AMR control efforts.

Surveillance structure

National AMR and AMU surveillance and monitoring programmes in Singapore are implemented by the national agencies responsible for human health, animal health, food and environment. These sectors are in turn supported by participating hospitals, laboratories and other parties providing data to the relevant sector authorities. Data sharing and reporting across sectors is centrally coordinated by the AMR Workgroup (Figure 1).

Human health – Surveillance has been instituted in public hospitals since 2011, and in private hospitals since 2017. The incidence of priority drug-resistant organisms and utilisation of important antimicrobials are routinely monitored by all acute care hospitals in Singapore under a national programme overseen by the National Antimicrobial Resistance Control Committee (NARCC; Textbox 2). Antibiotic susceptibility testing (AST) is carried out by the hospitals' microbiology laboratories, while the National Public Health Laboratory of the Communicable Diseases Agency (CDA) serves as the national reference laboratory for examining new and emerging resistance. Data analysed and compiled by NARCC are reported annually to the Ministry of Health (MOH) and hospitals for monitoring and control. Singapore also partipates in the Global Antimicrobial Surveillance System (GLASS), which collects AMR data on the WHO priority pathogens[1] in humans. On-going national surveillance programmes for HIV, gonorrhea and tuberculosis are beyond the scope of this report.

Animal Health – The monitoring of priority drug-resistant organisms in local poultry and ruminant farms is undertaken by the National Parks Board (NParks) and the Singapore Food Agency (SFA). NParks' Centre for Animal & Veterinary Sciences (CAVS) conducts active AMR surveillance in free-roaming dogs and passive AMR surveillance in wildlife, sick companion and aquatic animals. Data on antimicrobial sales for veterinary use are collected yearly by NParks and reported to the World Organisation for Animal Health (WOAH) on the global database on ANImal antiMicrobial USE (ANIMUSE).

Food – Monitoring of antimicrobial-resistant foodborne bacteria has been in place since 2010 as part of the national food safety surveillance programme, with a focus on *Salmonella* spp. Surveillance and

[1] *E. coli, K. pneumoniae, A. baumannii, S. aureus, Streptococcus pneumoniae, Salmonella spp, Shigella spp, Neisseria gonorrhoeae*

antimicrobial susceptibility testing of AMR foodborne bacteria are conducted by SFA's National Centre for Food Science (NCFS). SFA's efforts for AMR monitoring in the food chain includes establishing baseline data on the prevalence of resistance to antimicrobial agents in commensal bacteria and food-borne pathogens based on stratified random sampling across the food chain particularly at import, slaughterhouses, local farms and retail levels.

Environment – National surveillance programmes for drug-resistant organisms in the enviroment are jointly developed by NEA and PUB. NEA conducts studies to examine the presence and patterns of resistance in environmental bacteria found in various natural and man-made environments. PUB conducts studies to examine the presence and risks of antibiotic resistant bacteria and genes in urban waters in collaboration with local research institutions.

National Coordination – The One Health AMR Workgroup (AMRWG, see Textbox 1) coordinates the sharing of AMR and AMU data across sectors. This work is supported by the AMR Coordinating Office (AMRCO) of the CDA. The longer-term goal is to build an integrated approach for national AMR and AMU surveillance in Singapore that would better elucidate the prevalence and transmission routes of AMR pathogens across sectors.

Textbox 1

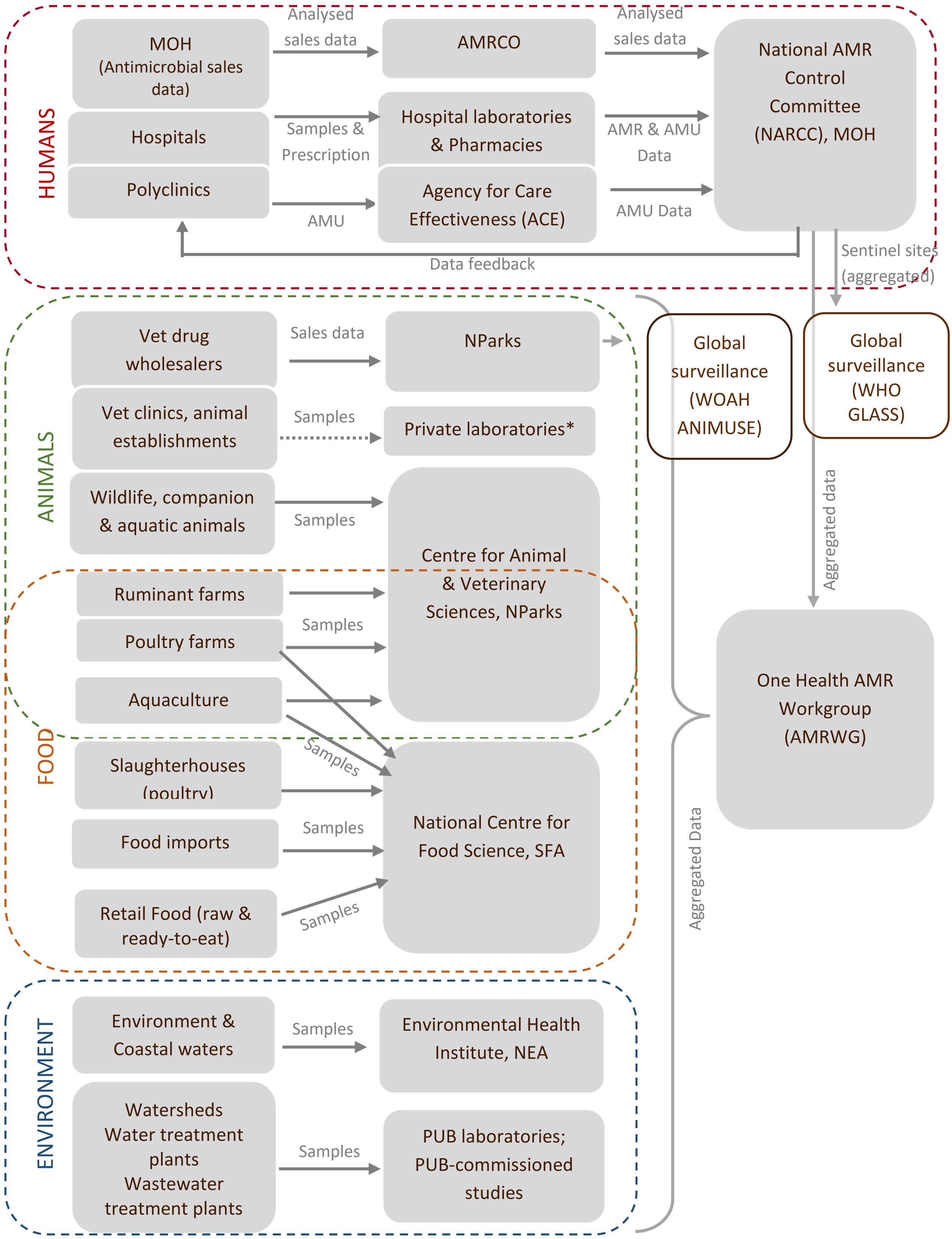
Singapore's National Strategic Action Plan on AMR

The National Strategic Action Plan on AMR (NSAP) was first launched in November 2017 and updated on 12 November 2025. The updated NSAP (NSAPv2) aims to prevent the emergence and reduce the spread of drug-resistant organisms, and preserve the effectiveness of antimicrobials through a One Health approach, protecting human, animal and environmental health in Singapore through five core strategies: Communication and Education, Surveillance and Risk Assessment, Research and Evidence, Prevention and Control of Infection, and Optimisation and Stewardship of antimicrobials. The NSAPv2 is supported by a Monitoring and Evaluation (M&E) Framework which tracks the implementation of the NSAPv2, and effectiveness in fulfilling the mission.

Implementation of the NSAP is overseen by the One Health AMR Workgroup (OH AMRWG), a multi-sectoral committee comprised of representatives from the Communicable Diseases Agency (CDA), National Environment Agency (NEA), National Parks Board (NParks), PUB, Singapore's National Water Agency (PUB) and the Singapore Food Agency (SFA). The Antimicrobial Resistance Coordinating Office (AMRCO) of the CDA serves as Secretariat to the OH AMRWG.

Singapore's NSAP may be found at:
AMR and the National Strategic Action Plan on AMR | Communicable Diseases Agency.

Figure 1. Overview of AMR & AMU surveillance and monitoring in Singapore



*Veterinary clinics may choose to send their samples to the national laboratory (CAVS) or to private laboratories. Data from these private laboratories currently do not contribute to national surveillance.

Human and Animal Populations

Singapore's population in 2023 was 5.92 million[2]. The population is served by 19 acute care hospitals[3] of which 10 are public facilities that account for approximately 80% of hospital admissions. Another nine private acute care hospitals[8] account for the remaining admissions that include a sizeable proportion of international patients. In Singapore, primary care is provided through 25 public polyclinics and 2,493 general practitioner clinics[3] run by private sector general practitioners (GP). The polyclinics meet about 20% of the total primary care demand[4].

Pet ownership in Singapore is on the rise. The number of dogs licensed by the NParks increased from 59,000 in 2011 to 90,000 in 2023. There are currently 112 veterinary centres registered with NParks. The non-food producing animal population consists of approximately 183,700[5] registered dogs and cats, 1,240[6] horses, and 95,300 pet birds.

As a highly urbanised country with low local agricultural production, Singapore is highly dependent on food imports. More than 90% of food is imported from over 180 countries and regions[7]. Singapore has a small, but thriving and increasingly important food fish aquaculture industry, which currently accounts for about 7% of local food fish consumption. Three chicken layer farms producing approximately 30% of local consumption of table eggs. The population of food animals in Singapore and production outputs are presented in Table 1.

Table 1. Production of food animals, eggs and fish, Singapore 2023

Type	No. of farms	Total population	Production (% national consumption)
Chicken layers	3[7]	≈3,000,000[7]	685 million eggs (31.9%)[8]
Quail layers	2[7]	155,000[7]	≈30 million eggs (100%)[7]
Dairy cattle	2[7]	121[7]	-
Dairy goats	1[7]	848[7]	-
Farmed food fish	98 sea-based[7] 33 land-based[7]	Not applicable	4,100 tonnes (7.3%)[7]
Ornamental fish farms	40[9]	NA	NA

[2] www.singstat.gov.sg
[3] www.moh.gov.sg/resources-statistics/singapore-health-facts/health-facilities, 2023
[4] Primary Healthcare Services, www.moh.sg
[5] Source of owned cat population estimates: Euromonitor; Source of owned dog estimates: NParks
[6] Source: World Animal Health Information System (WAHIS), WOAH
[7] SFA annual report, 2023/2024
[8] Singapore Food Statistics 2023, SFA
[9] Source: NParks

PART I. ANTIMICROBIAL UTILISATION

Antimicrobial Utilisation in Humans

Antimicrobial Utilisation in Acute Care Hospitals

NARCC (Textbox 2) monitors the utilisation of important antimicrobial groups, such as broad-spectrum penicillins, third- and fourth-generation cephalosporins, fluoroquinolones and carbapenems. Public hospitals have been reporting AMU data since 2011, and private hospitals since 2017. This report includes data from nine public and eight private acute care hospitals currently contributing AMU data to NARCC. This report presents data from when private hospital data became available in 2017; data on public hospital utilisation from 2011 to 2016 are available in the earlier reports.

Utilisation by acute care hospitals is typically reported in DDD per 1,000 inpatient days. DDD is calculated based on prevailing values published by WHO[10]; adjustments to DDD values by WHO should therefore be taken into consideration when interpreting AMU trends presented in DDD. These limitations notwithstanding, the use of DDD is a commonly accepted and practical way to measure antimicrobial consumption. The use of inpatient days as a denominator allows for a measurement of the antibiotic consumption (DDD per 1,000 inpatient days) to be obtained and normalises consumption across hospitals of different sizes.

Antimicrobial Stewardship Programmes (ASP) were established in all public hospitals in 2011 with the aim of improving patient outcomes, optimising antimicrobial use and reducing the emergence of AMR through a system of audits and feedback. The rates of appropriate antibiotic prescribing and the acceptance rates of ASP interventions are monitored by MOH through NARCC.

Textbox **2**

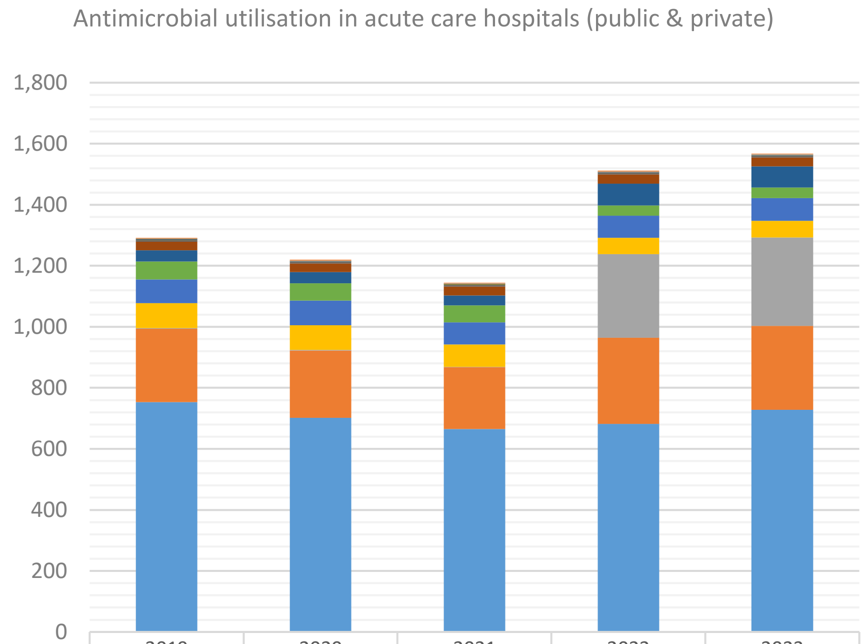
National AMR Control Committee (NARCC)

The National AMR Control Committee (NARCC) is appointed by the Ministry of Health (MOH) to oversee AMR and AMU surveillance in the human health sector. NARCC is represented by all acute care hospitals and assists MOH in developing strategies to control the emergence and spread of AMR. NARCC is supported by two expert panels: The National Antimicrobial Resistance Expert Panel (NAREP), and the National Antimicrobial Stewardship Expert Panel (NASEP). The expert panels, comprising microbiologists, infectious disease physicians and pharmacists from public healthcare institutions, advise on issues related to surveillance of antimicrobial resistant organisms and antimicrobial utilisation. NARCC collects AMR and AMU data every 6 months from hospital laboratories and antimicrobial stewardship teams. Data compiled and analysed by NARCC are provided to the MOH and senior management of hospitals annually. The data are used to monitor trends in hospitals and implement control measures where appropriate.

[10] https://www.whocc.no/atc_ddd_index/

In 2023, NARCC monitored the utilisation of 45 antimicrobials under 14 NARCC-defined groups (Appendix I.I). The five groups of antimicrobials most utilised by public and private acute care hospitals in 2023 were beta-lactams and beta-lactamase inhibitors, fluoroquinolones, tetracyclines, third- and fourth-generation cephalosporins, and antifungals (Figure 2). The increase in tetracyclines reported for 2022 was due to the initiation of tetracycline monitoring in that year.

Figure 2. Antimicrobial utilisation in acute care hospitals (public and private combined) in Singapore, for all antimicrobials under monitoring from 2019 - 2023



	2019	2020	2021	2022	2023
Others	3.3	3.4	3.5	3.25	2.83
Novel Beta Lactams and Beta-Lactamase Inhibitors	0.4	0.8	0.7	1.19	1.55
Cephalosporins, 5th gen	1.1	0.7	0.5	0.66	0.78
Polymyxins	1.6	0.8	0.8	0.48	0.57
Cephalosporins, 2nd gen	1.6	1.2	2.2	1.43	1.48
Monobactam	4.8	5.0	5.3	5.53	5.06
MRSA/VRE agents	28.2	28.3	28.7	29.86	29.21
Carbapenems	37.2	36.6	32.6	71.40	69.81
Lincosamides	58.2	56.7	55.4	33.68	34.63
Antifungals	78.1	81.2	73.0	72.30	74.09
Cephalosporins, 3rd & 4th gen	82.1	81.4	73.8	53.44	54.63
Tetracyclines	1.7	1.2	1.1	274.34	289.59
Fluoroquinolones	240.8	220.4	202.2	281.88	275.44
Beta Lactams and Beta-Lactamase Inhibitors	752.9	702.3	665.0	682.22	727.84

Note: Not all antimicrobials used in hospitals are monitored. The following antimicrobials were introduced for monitoring in 2019: **Beta lactams and Beta-Lactamase Inhibitors:** Amoxicillin-clavulanate, oral and ampicillin-sulbactam, IV; **Novel Beta lactams and Beta-Lactamase Inhibitors:** oral ceftolozane-tazobactam, IV; **Monobactam**: aztreonam, IV ; **Cephalosporin, second generation:** cefoxitin, IV; **Cephalosporin third and fourth generation:** cefixime, oral; cefoperazone, IV; cefotaxime, IV; ceftibuten, oral; **Cephalosporin, fifth generation:** ceftaroline, IV; **MRSA/VRE agents:** teicoplanin, IV; tedizolid, IV and oral. In 2020: **Novel Beta lactams and Beta-Lactamase Inhibitors:** Ceftazidime-avibactam, IV. In 2022, Tetracyclines: doxycycline, IV and oral; eravacycline, IV; minocycline, IV and oral; Tetracycline, oral. The full list of antimicrobials monitored may be found at Appendix I.

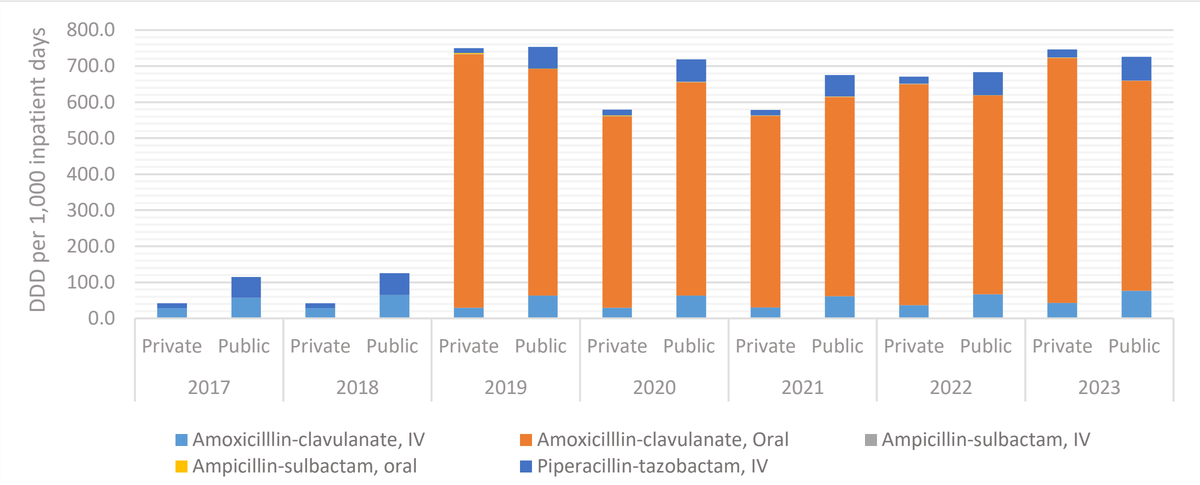
Overall utilisation of antimicrobials by acute care hospitals increased from 2021 to 2023, after a decline from 2019 to 2021. The COVID-19 pandemic was a likely contributing factor to this trend, as evidenced by post-pandemic monitoring which showed overall utilisation of antimicrobials had returning to pre-COVID levels.

Some differences in utilisation patterns were observed between public and private hospitals (Figures 3 – 9). This report does not examine reasons for these differences, recognising that the contributing factors are multi-factorial: including, but not limited to, differences in patient case-mix, hospital drug formulary and operating models. Furthermore, data sources are not uniform across all hospitals. Therefore, attempts to draw conclusions from this limited dataset alone should be avoided.

Beta-lactams and beta-lactamase inhibitors

Beta-lactams and beta-lactamase inhibitors were the most utilised group in both public and private acute care hospitals. Within this group of antimicrobials, oral amoxicillin-clavulanate was the most heavily used of all antimicrobials monitored in 2023. Average utilisation of oral amoxicillin-clavulanate was slightly higher in private hospitals than in public hospitals, at 678.7 DDD per 1000 inpatient days in private hospitals and 582.1 DDD per 1,000 inpatient days in public hospitals (Figure 3).

Figure 3. Utilisation of beta-lactams and beta-lactamase inhibitors in public and private acute care hospitals, 2017-2023

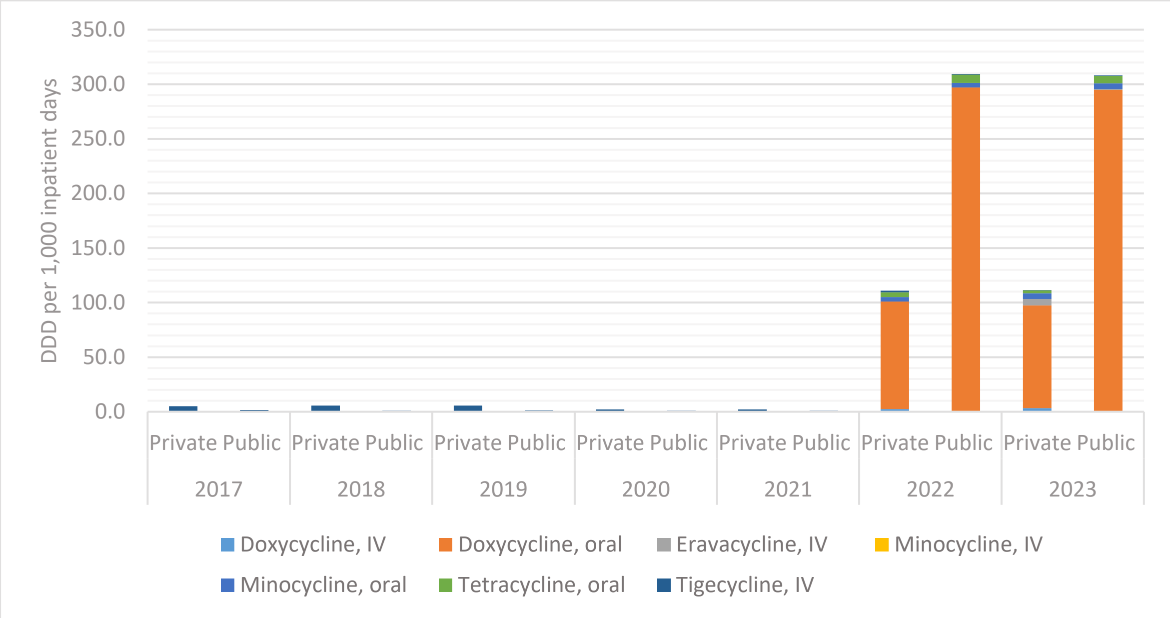


Notes: Amoxicillin-clavulanate, oral; ampicillin-sulbactam, IV and oral were included for monitoring from 2019.

Tetracyclines

Tetracyclines were the next most utilised group of antimicrobials, with oral doxycycline being the most used, followed by oral minocycline. While fluroquinolones were previously reported as the second most utilised group in 2021, the changes in utilisation trends in 2023 were influenced by additional antimicrobials from the tetracycline group (doxycycline IV and oral, eravacycline IV, minocycline IV and oral, and tetracycline oral) being monitored from 2022 onwards. Oral doxycycline utilisation was higher in public hospitals than private hospitals, at 294.6 DDD and 94.3 DDD per 1,000 inpatient days respectively. Oral minocycline utilisation was similar in both private and public hospitals, at 5.2 DDD per 1,000 inpatient days (Figure 4).

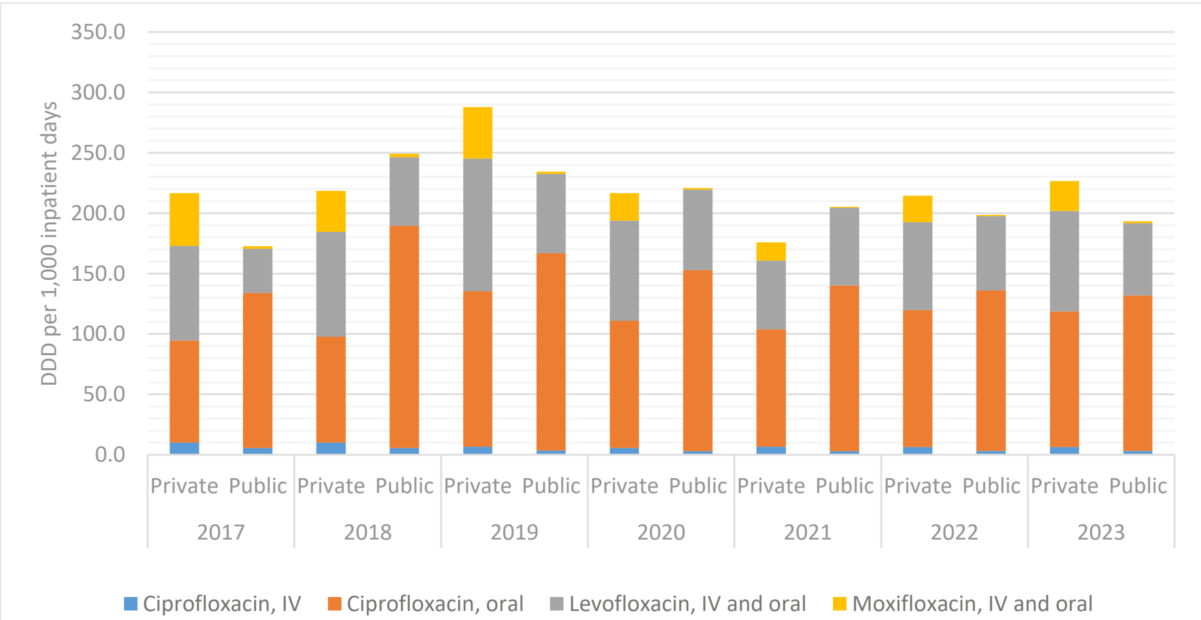
Figure 4. Utilisation of tetracyclines in public and private acute care hospitals, 2017-2023



Fluoroquinolones

Fluoroquinolones were the third most utilised group of antimicrobials, contributed largely by oral ciprofloxacin utilisation. Oral ciprofloxacin utilisation was higher in public hospitals than private hospitals, at 128.7 DDD and 112.4 DDD per 1,000 inpatient days respectively. Moxifloxacin utilisation was higher in private hospitals than in public hospitals from 2017 to 2023, at 25.0 DDD compared with 1.7 DDD per 1,000 inpatient days in 2023 (Figure 5).

Figure 5. Utilisation of fluoroquinolones in public and private acute care hospitals, 2017-2023

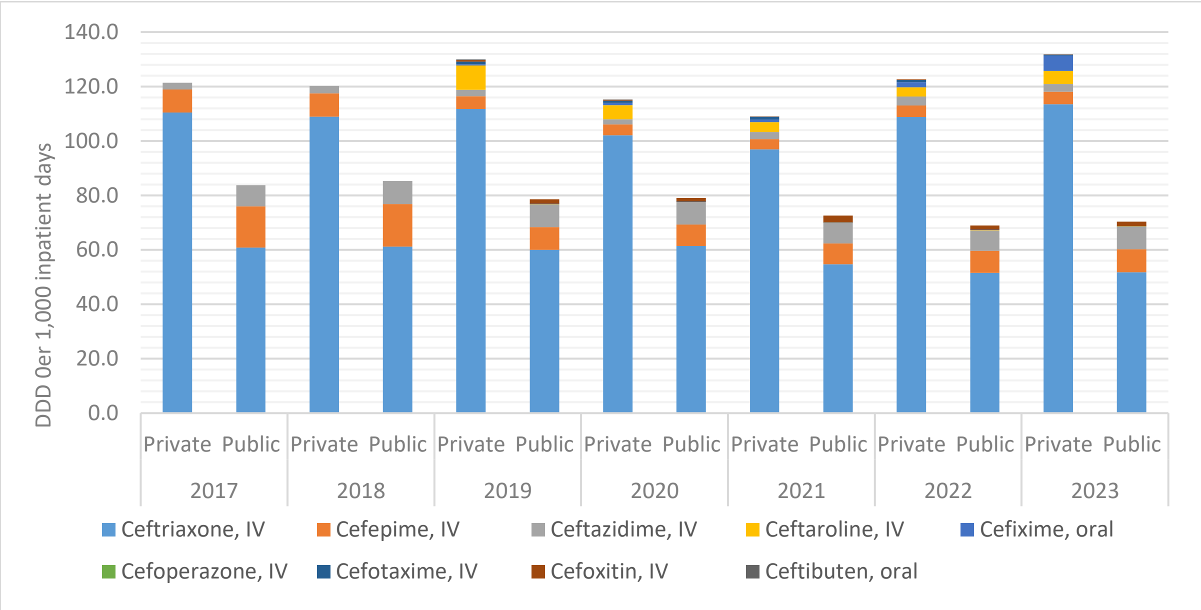


Note: Outpatient utilisation was included in public hospitals data from 2018.

Cephalosporins

Third- and fourth-generation cephalosporins were the fourth most utilised group, of which ceftriaxone was the most used. Private hospital utilisation of cephalosporins was higher than that of public hospitals in 2023. Ceftaroline, a fifth-generation cephalosporin, was used mainly in the private sector, though its utilisation was generally low (Figure 6).

Figure 6. Utilisation of cephalosporins in public and private hospitals, 2017-2021

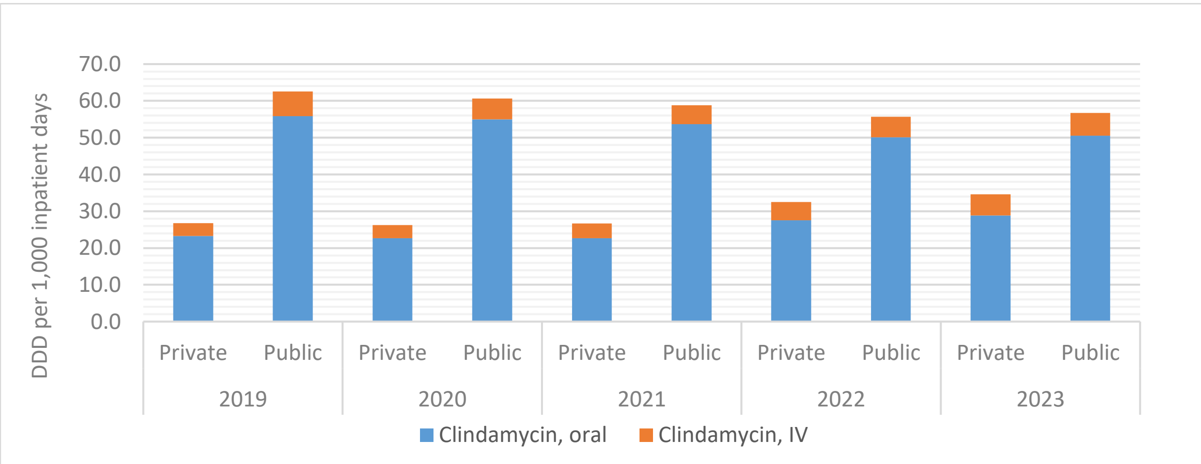


Note: Revised DDD assignment for IV cefepime from 2g to 4g in 2019 may have contributed to observed reduction in utilisation for that year.

Lincosamides

Monitoring of lincosamides, specifically clindamycin, was introduced in 2019. Utilisation of oral clindamycin was higher in public hospitals than in private hospitals (Figure 7).

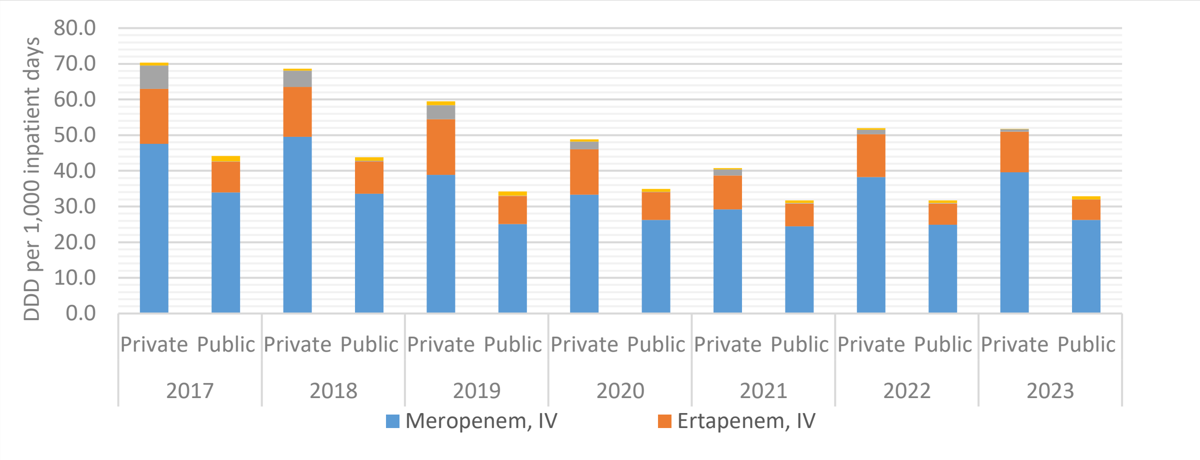
Figure 7. Utilisation of lincosamides in public and private hospitals, 2019 – 2023



Carbapenems

Both private and public hospitals demonstrated declining carbapenem utilisation from 2017 to 2023. The use of carbapenems was higher in private hospitals than public hospitals. Meropenem remains the most widely used carbapenem. In 2023, utilisation of meropenem in private hospitals was 39.5 DDD per 1,000 inpatient days while public hospital utilisation was 26.2 DDD per 1,000 inpatient days. Doripenem is used mainly in private hospitals, while imipenem has limited utilisation in both public and private hospitals (Figure 8).

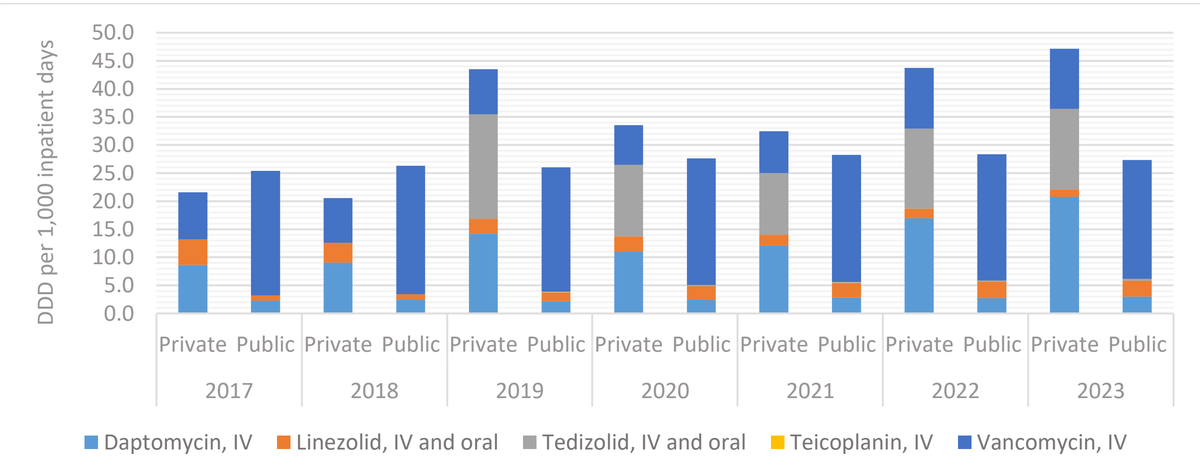
Figure 8. Utilisation of carbapenems in public and private acute care hospitals, 2017-2023



MRSA and VRE agents

This group includes vancomycin, daptomycin, linezolid, tedizolid and teicoplanin. Overall utilisation of this group of antimicrobials was higher in private than public hospitals (Figure 8). Daptomycin and tedizolid were used more by private hospitals while vancomycin was used more widely by public hospitals. Tedizolid and teicoplanin were introduced for monitoring in 2019; the utilisation of tedizolid was 14.3 DDD per 1,000 inpatient days in private hospitals compared to 0.2 DDD per 1,000 inpatient days in public hospitals, while teicoplanin was not used by any hospital during the period of reporting (Figure 9).

Figure 9. Utilisation of MRSA & VRE agents in public and private acute care hospitals, 2017-2023

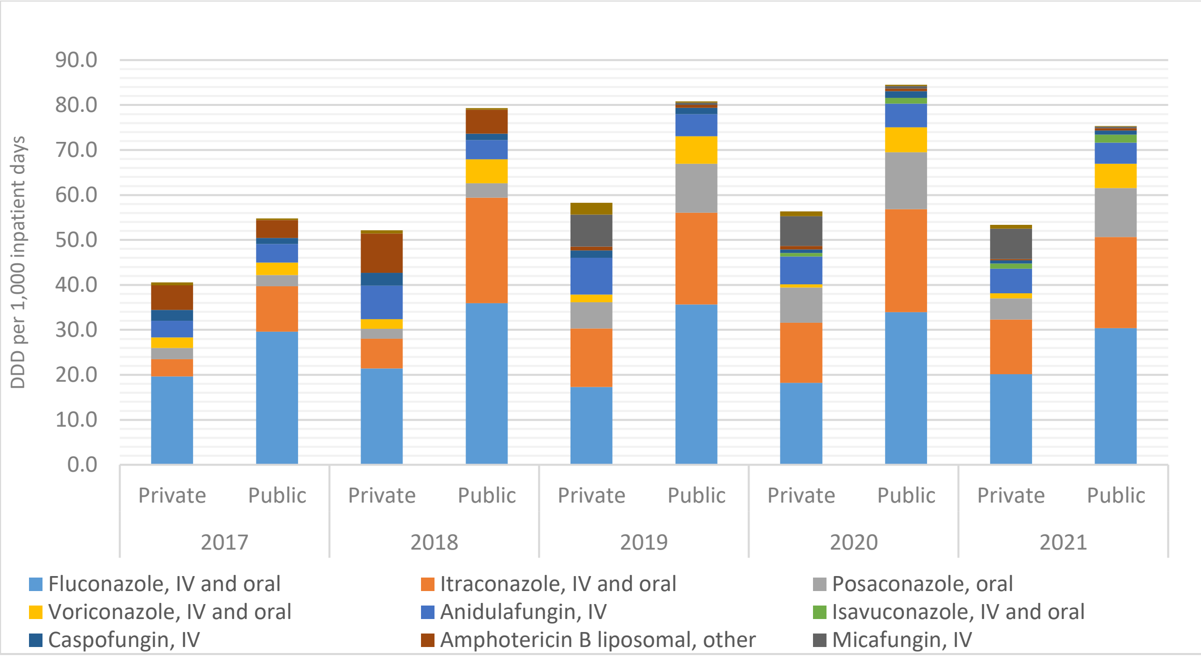


Note: The use of teicoplanin and tedizolid were monitored from 2019.

Antifungals

Fluconazole was the most utilised antifungal from 2017 to 2023. Overall utilisation of antifungals was higher in public than private hospitals (Figure 10). Micafungin, included for monitoring in 2019, was used mainly in private hospitals, while the use of itraconazole and fluconazole was higher in public hospitals. As WHO does not set a specific DDD value for liposomal amphotericin B, a local DDD of 300mg was applied in 2019, accounting for the apparent reduction in the utilisation of liposomal amphotericin B after 2018.

Figure 10. Utilisation of antifungals in public and private acute care hospitals, 2017-2023



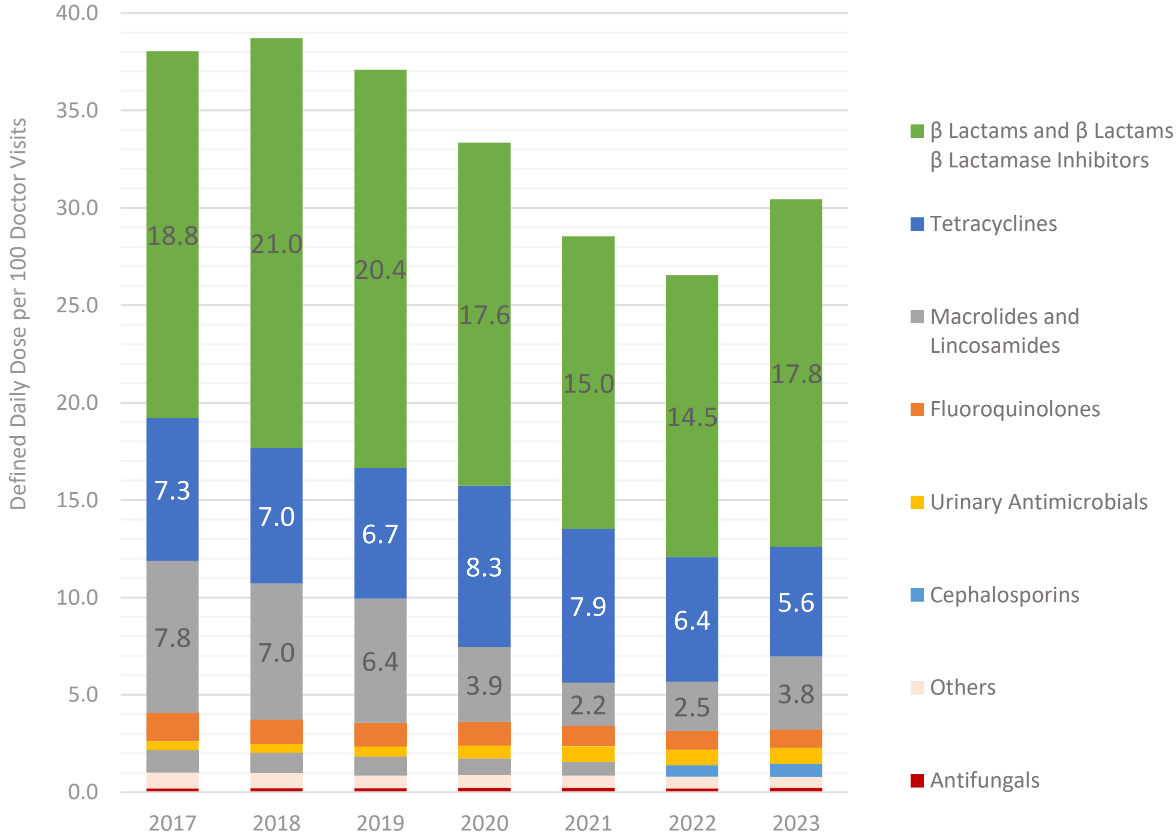
Note: 1. In 2019, DDD of oral posaconazole was updated from 0.8g to 0.3g; DDD of liposomal amphotericin B was updated from 35mg to a local DDD of 300mg. 2. Data on Micafungin IV was collected from 2019; data on isavuconazole, IV and Oral was collected from 2020.

Antimicrobial utilisation in primary care settings (polyclinics)

Polyclinics in Singapore serve as public sector primary care clinics. In 2023, there were a total of 25 polyclinics distributed throughout the country providing services including acute and chronic care to approximately 20% of the outpatient community. Utilisation rates were measured in DDD per 100 doctor visits for eight groups of antimicrobials (Figure 11).

A decline in the utilisation of oral antimicrobials from 2018 to 2022 was observed, followed by an increase in 2023 (Figure 11). In 2023, beta-lactams and beta-lactamase inhibitors (17.8 DDD per 100 doctor visits) were the most utilised antimicrobial group, followed by tetracyclines (5.6 DDD per 100 doctor visits) and macrolides and lincosamides (3.8 DDD per 100 doctor visits). Overall, these three antimicrobial groups with the highest utilisation in the polyclinics have remained consistent across the years.

Figure 11. Antimicrobial utilisation in Singapore's polyclinics, from 2017 – 2023



β Lactam and β Lactam β Lactamase Inhibitors: Phenoxymethylpenicillin (penicillin v), Amoxicillin-Clavulanate, Amoxicillin, Cloxacillin**; Tetracyclines:** Doxycycline, Tetracycline; **Macrolides & Lincosamides:** Azithromycin, Clarithromycin, Clindamycin, Erythromycin ethylsuccinate/stearate; **Fluoroquinolones:** Ciprofloxacin; **Cephalosphorins**: Cefalexin, Cefuroxime; **Urinary Antibiotics:** Nitrofurantoin; **Other Antibiotics:** Metronidazole, Co-trimoxazole; **Antifungal:** Nystatin

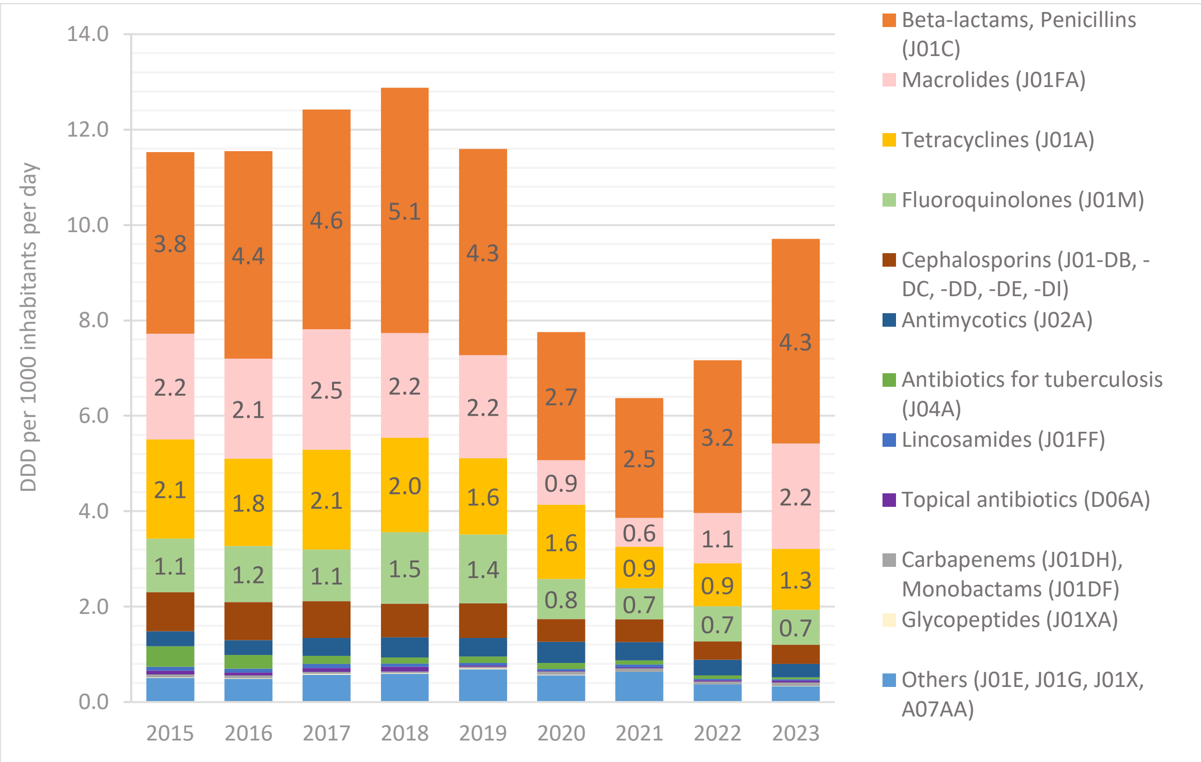
Data Source: MOH Singapore

Antimicrobial sales for human use

Sales data[11] serve as an additional reference to antimicrobial utilisation trends. Sales data is a more readily available source of data and may be used as a general reference to antimicrobial consumption trends. National antimicrobial consumption is typically reported as DDD per 1,000 inhabitants per day or DID (**Error! Reference source not found.**Annex I: Methodology). The main category of a ntimicrobials tracked are those classified under Anatomical Therapeutic Chemical (ATC) code J01 – Antibacterials for systemic use.

In 2021, the sales of beta-lactams, penicillins (mainly amoxicillin-beta lactamase inhibitors) remained the highest. This was followed by macrolides (mainly clarithromycin) and tetracyclines (mainly doxycycline). We observed an increasing trend in total reported sales volume of J01 antibiotics in 2022 and 2023, with a total of 9.7 DID in 2023 (Figure 12), contributed by an increase in sales to private sector outpatient clinics (Figure 13). Clinic sales remained the highest among the four main channels, namely, clinics, pharmacy, hospitals and others (Figure 13). Clinics include all private dispensing clinics (GPs and specialists) and specialists dispensing clinics within private hospitals. Based on 2023 data, it is postulated that the COVID-19 pandemic was the main contributing factor to the decline in sales observed between 2020 to 2021.

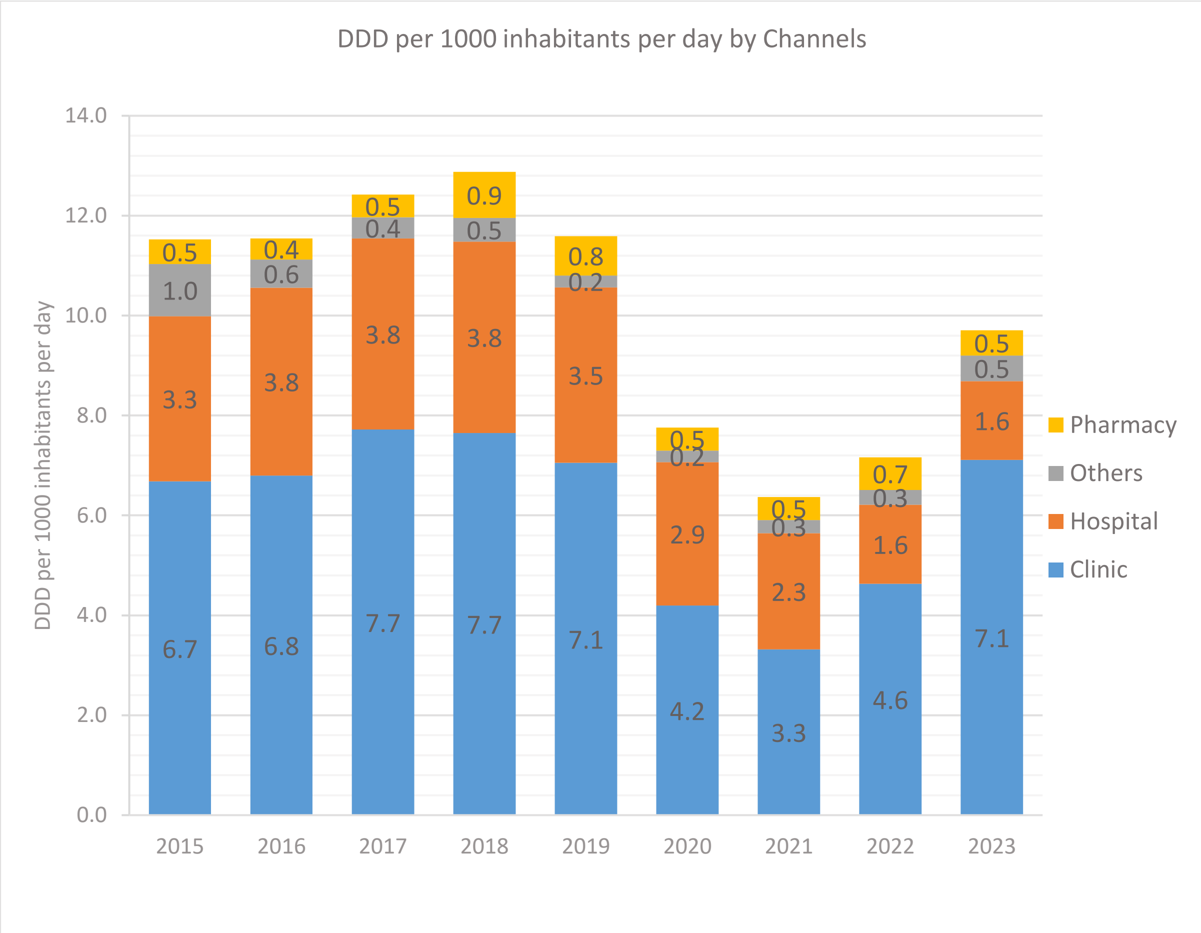
Figure 12. Total sales of antimicrobials, 2015 – 2023, by antimicrobial class (in DDD per 1000 inhabitants per day; DID)



[11] Data source: MOH Singapore

Note: DID of the three most sold classes of antimicrobials are indicated within the columns. The total annual reported sales for the year in DID are indicated above each column. Data: IQVIA National Sales Audit. Source: MOH Singapore.

Figure 13. Total sales of antimicrobials by sales channel 2015 – 2023 (in DDD per 1000 inhabitants per day; DID)



Channels: **Pharmacy** - All pharmacies e.g. chain and solo pharmacies; **Others** - Polyclinics and other institutions like nursing homes, social service centres, community hospitals, including central procurement data;; **Hospital** - Restructured/public hospitals, private hospitals (excluding chain pharmacies); **Clinic** - All private dispensing clinics (GPs and Specialists) including specialists dispensing clinics within private hospitals. Data: IQVIA National Sales Audit. Source: MOH Singapore.

The data reported here are based solely on private market research sales quantities and should be interpreted in context: The total DDD per 1000 inhabitants/day (DID) calculated from this dataset may underestimate true national consumption due to its incomplete coverage of generic antimicrobials. Furthermore, sales data may not correlate well with utilisation data, since not all antimicrobials sold may be utilised within the period of sales data reporting. Nevertheless, in the absence of national-level utilisation data, sales data enables the monitoring of trends across different healthcare settings. As we increase the comprehensiveness of local AMU data collection, we will be better able to draw associations between sales and consumption/utilisation patterns.

DID data based on antimicrobial sales is reported to the WHO Global Antimicrobial Resistance and Use Surveillance System (GLASS)-AMU platform.

Antimicrobial Utilisation in Animals

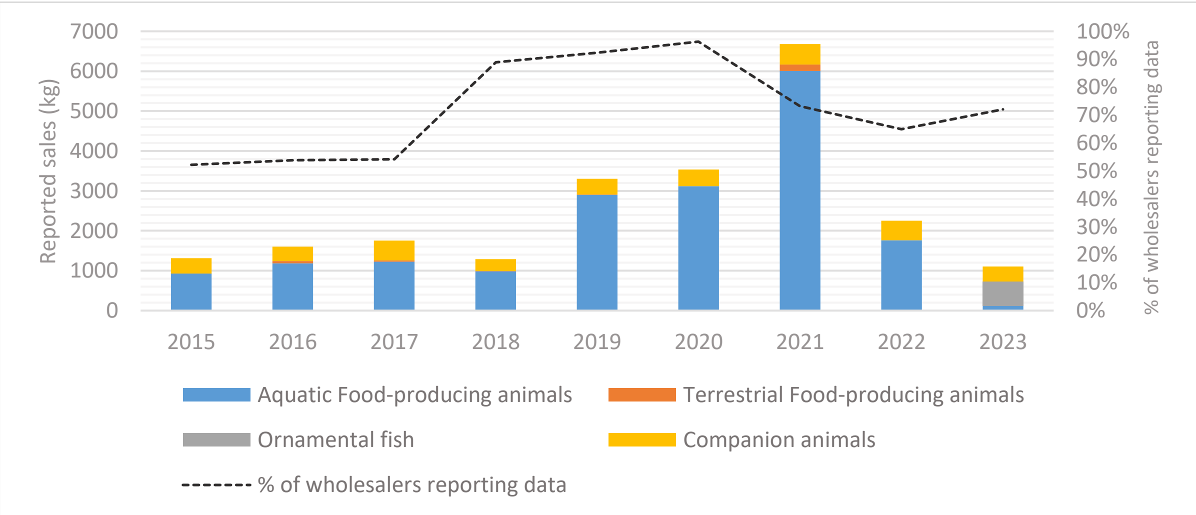
Antimicrobials serve an important role in veterinary medicine in the prevention and treatment of animal diseases. Preservation of antimicrobials is crucial to maintain drug efficacy and minimise both food security and animal health and welfare concerns in the event of a disease outbreak. In Singapore, the use of antimicrobials for growth promotion in food-producing animals is prohibited. Additionally, certain antimicrobials and substances, such as chloramphenicol, polymyxins, avoparcin, beta-agonists and nitrofurans, are prohibited for use in local food-producing animals and in animal feed. The use of antimicrobials in local commercial chicken farms throughout the laying period is also disallowed to prevent the presence of antimicrobial residues in table eggs intended for human consumption. These prohibitions are supported by a robust residue monitoring programme and post-market surveillance.

Antimicrobial Sales for Veterinary Use

Singapore has been reporting data on sales of antimicrobials for animal use to the World Organisation for Animal Health (WOAH) annually since 2015. Sales data collected serve as a proxy for antimicrobial utilisation in animals. Overall, the total quantity of antimicrobial sales recorded decreased from 1318.2 kg in 2015 to 1103 kg in 2023 (Figure 14), largely due to a decrease in import of antimicrobials by two major importers owing to a combination of farm closures and a successful vaccination strategy for managing disease.

From 2015 to 2020, NParks collected sales data through a voluntary survey of wholesalers supplying human antimicrobials to the animal sector for off-label use, of which 26 out of 27 (~96%) surveyed in 2020 had provided their responses. Since 2021, NParks expanded its survey to include additional companies supplying veterinary antimicrobials to the animal sector so as to improve representativeness of AMU data collected. Of these companies, 65 out of 92 companies (~72%) surveyed in 2023 provided their responses.

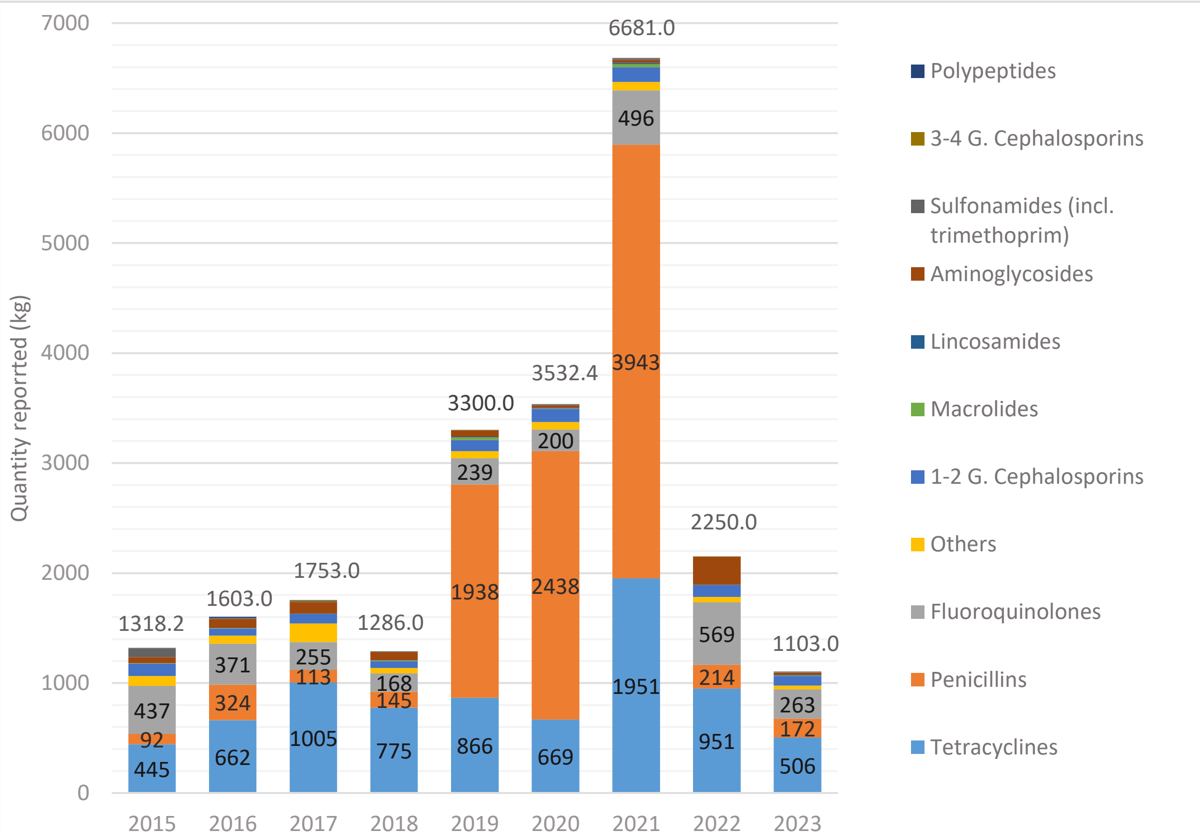
Figure 14. Annual reported sales (kg) of antimicrobial drugs in animal sector, 2015 – 2023*



*The data under 'Aquatic Food-producing animals' from 2015 – 2022 comprises antimicrobials sold to both food fish and ornamental fish sectors.

Tetracyclines, fluoroquinolones and penicillins were the most reported antimicrobial drugs sold for veterinary use from 2015 to 2023 (accounting for approximately 74% to 96% of total antimicrobial quantity sold) (Figure 15). The general trend from 2015 to 2023 revealed that tetracycline was the largest antimicrobial class reported, followed by fluoroquinolones and penicillins. The exception was from 2019 to 2021 where penicillins was the largest antimicrobial class sold, likely to manage multiple disease outbreaks in farmed food fish at that time. In 2022, with increased implementation of vaccination as a disease prevention strategy and improved biosecurity measures on food fish farms, a decrease in sales of penicillins for veterinary use was observed.

Figure 15. Annual reported sales (kg) of antimicrobial drugs in the animal sector, by antimicrobial class, 2015 to 2023



Note: Numbers above bars denote total quantities reported for the year in kg.

Aquaculture

The aquaculture industry in Singapore comprises both ornamental fish and food fish sectors. The majority of local food fish farms employ traditional farming methods, although there is a small but growing segment of progressive farms which are more technology driven. Amongst the animal sectors, this sector (both food fish and ornamental fish) purchased the highest reported amounts of tetracycline, fluoroquinolones (enrofloxacin) then penicillins (by weight) (Figure 16). Antimicrobial usage is further compounded by the limited availability of tropical food fish vaccines worldwide, and reduced cost-effectiveness of vaccination for smaller holdings. Data on sales to the food fish and ornamental fish industries were segregated in 2023. In 2023, sales to the ornamental fish industry were higher than sales to the food fish industry (Figure 16).

Terrestrial livestock

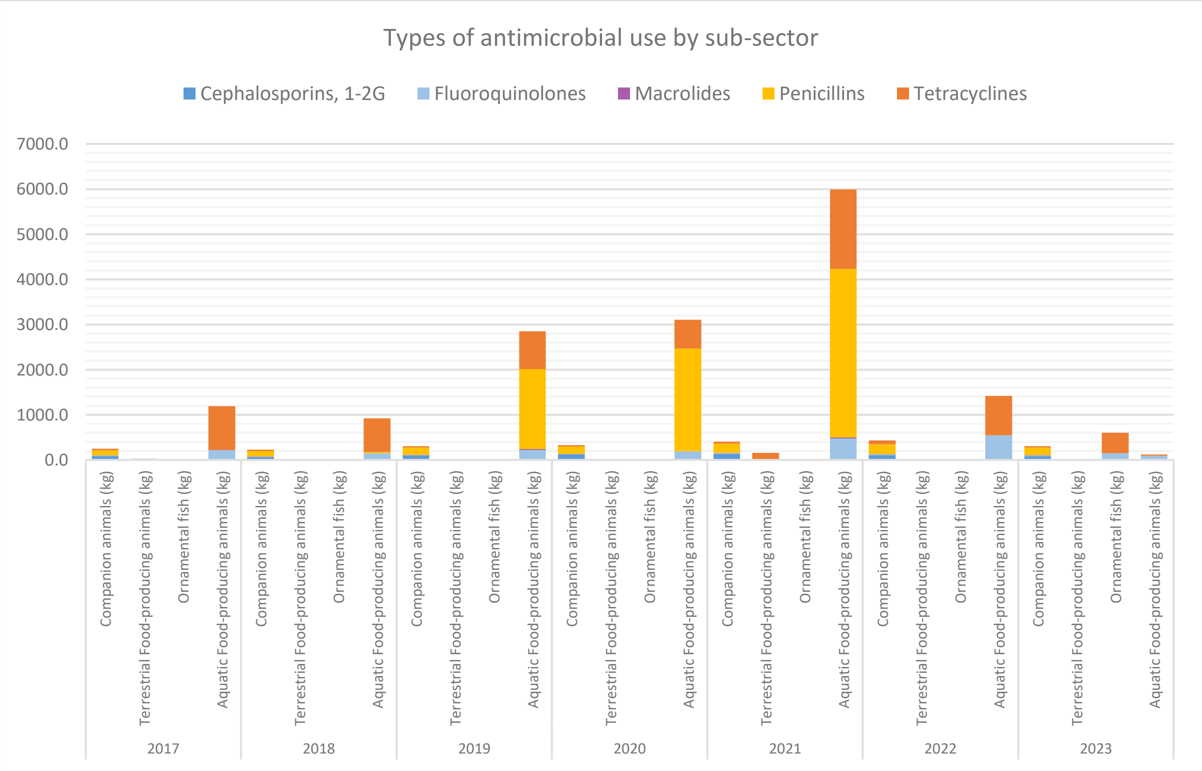
Sales of antimicrobials to terrestrial livestock remain low despite the highly intensive nature of local chicken layer farms. This reflects the mature state of the chicken layer industry here, characterised by adherence to good animal husbandry practices, effective biosecurity measures to prevent disease introduction, routine vaccination programmes for disease prevention and good compliance to antibiotic restrictions.

Companion animals

Sales of antimicrobials to the companion animal sector has generally remained stable over the years, despite the growing number of companion animals. The number of licensed dogs in Singapore has increased by almost 45% from about 62,000 in 2015 to 90,000 in 2023 and the cat population is also increasing. The number of veterinarians in companion animal practice and the number of companion animal veterinary clinics have also correspondingly increased to 112 in 2023.

Despite the growing pet population and industry, the stable sales of antimicrobials suggest responsible prescribing and use of antimicrobials in this sector. Other contributing factors include good animal husbandry and management practices of animal owners and caregivers, and improved uptake and awareness of preventative care, such as vaccination, anti-parasitic treatments, and regular health checks.

Figure 16. Quantities of antimicrobials per animal sector for the 5 classes with highest reported sales, from 2017 to 2023. *



*The data under 'Aquatic Food-producing animals' from 2015 – 2022 comprises antimicrobials sold to both food fish and ornamental fish sectors.

PART II. ANTIMICROBIAL RESISTANCE

One Health AMR and Risk Assessment

This chapter presents an early attempt to compare data on pathogen-drug combinations common across two or more sectors, as a step towards more integrated analysis. The current data are drawn from existing surveillance programmes (described in later chapters) which are subject to sector-specific objectives and at present, insufficient to correlate across sectors. Over time, we expect to expand the list of cross-sector organisms and harmonise methodologies across sectors to enable more meaningful comparisons and analyses.

This chapter also shares highlights of a One Health assessment of ARBs and ARGs coastal waters and aquaculture systems in Singapore, in conjunction with chemical contaminants that may drive antimicrobial resistance.

Resistance of *E. coli* across sectors

E. coli is monitored by the human, animal, food production and environmental sectors, hence the logical target for integration efforts. We compare resistance proportions (%R) to three classes of medically important antimicrobials: third-generation cephalosporins (represented by cefotaxime and ceftazidime), fluroquinolones (represented by ciprofloxacin) and carbapenems (represented by meropenem) (Figures 17-19). In addition, proportions of isolates with the ESBL phenotype (i.e. ESBL-Ec) are also compared (Figure 20).

Compared to human clinical samples obtained from hospitalised patients, resistance frequencies to third-generation cephalosporins and ciprofloxacin in sampled non-human populations were relatively low. Meropenem resistance was not detected in *E. coli* from wildlife and stay dogs, as well as in farm samples, the latter consistent with lack of its use in food production systems (Figures 56, Figures 42-44). ESBL-Ec was most frequently recovered from imported poultry products (36.5 – 55.8% of *E. coli* isolates). In human clinical samples, the ESBL phenotype was indicated by resistance to third-generation cephalosporin (ceftriaxone) and detection ranged from 23.2 – 24.9% from 2023-2024 (Figure 29a).

For specific %R to other antimicrobials, refer to the relevant chapters on sectoral surveillance.

Data limitations – Human health surveillance is passive and based on clinical isolates, which are not routinely tested for the ESBL phenotype. Resistance of non-ESBL *E. coli* is not currently monitored under food and environmental sectors' surveillance programmes.

Figure 17. Comparison of *E. coli* resistant to third generation cephalosporins (cefotaxime and ceftazidime) across sectors

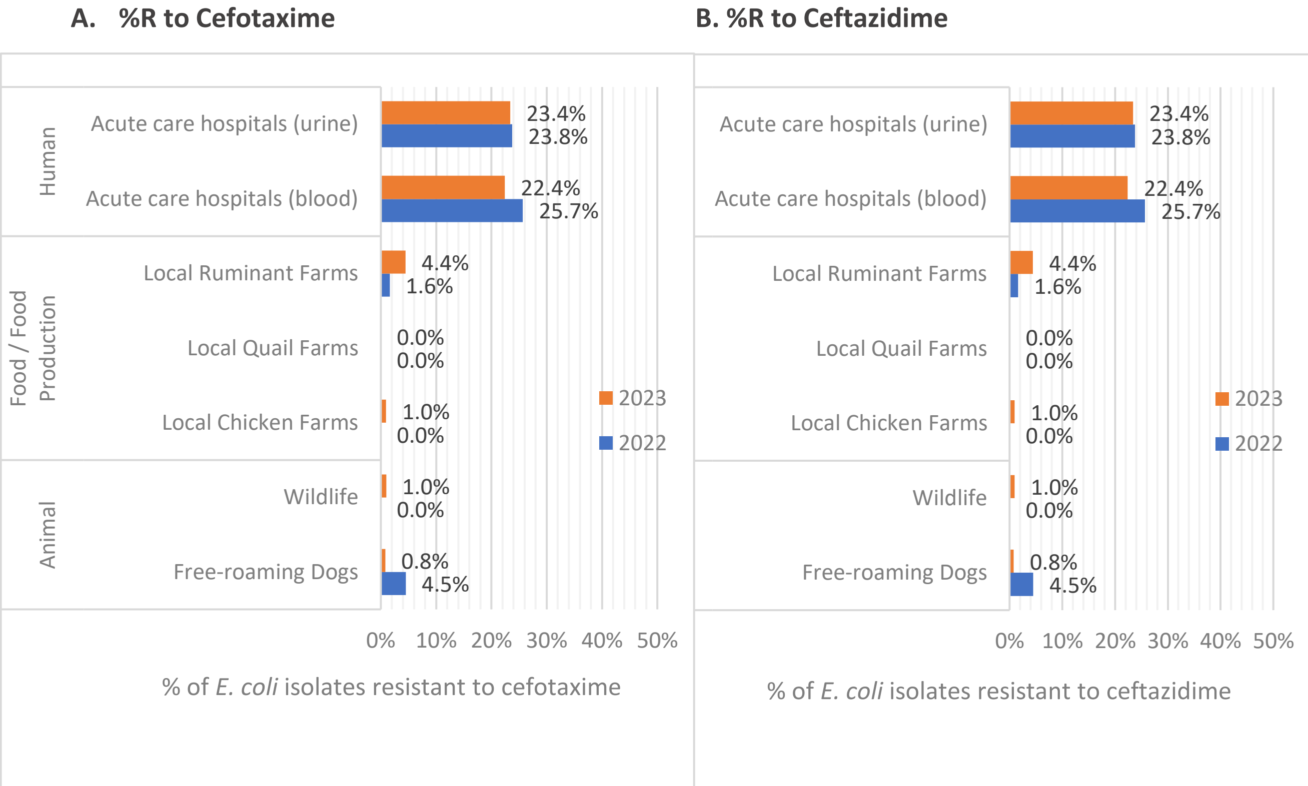


Figure 18. Comparison of *E. coli* ciprofloxacin resistance proportions across sectors

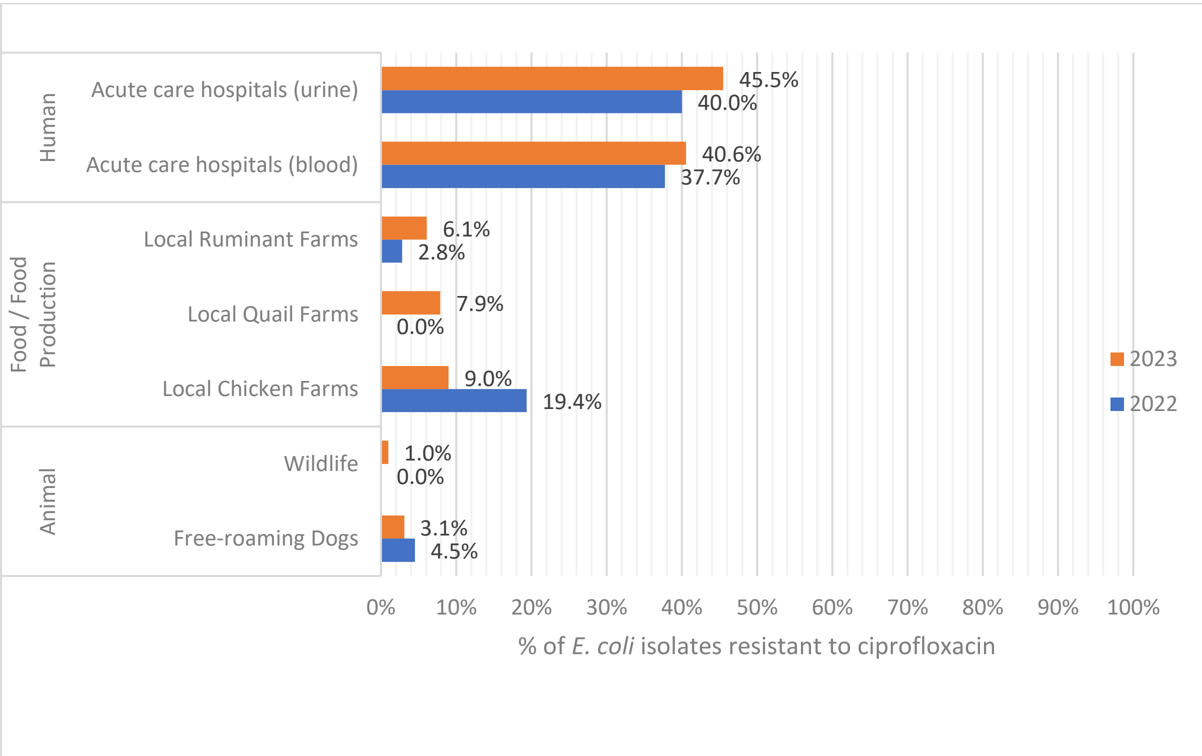


Figure 19. Comparison of *E. coli* meropenem resistance proportions across sectors

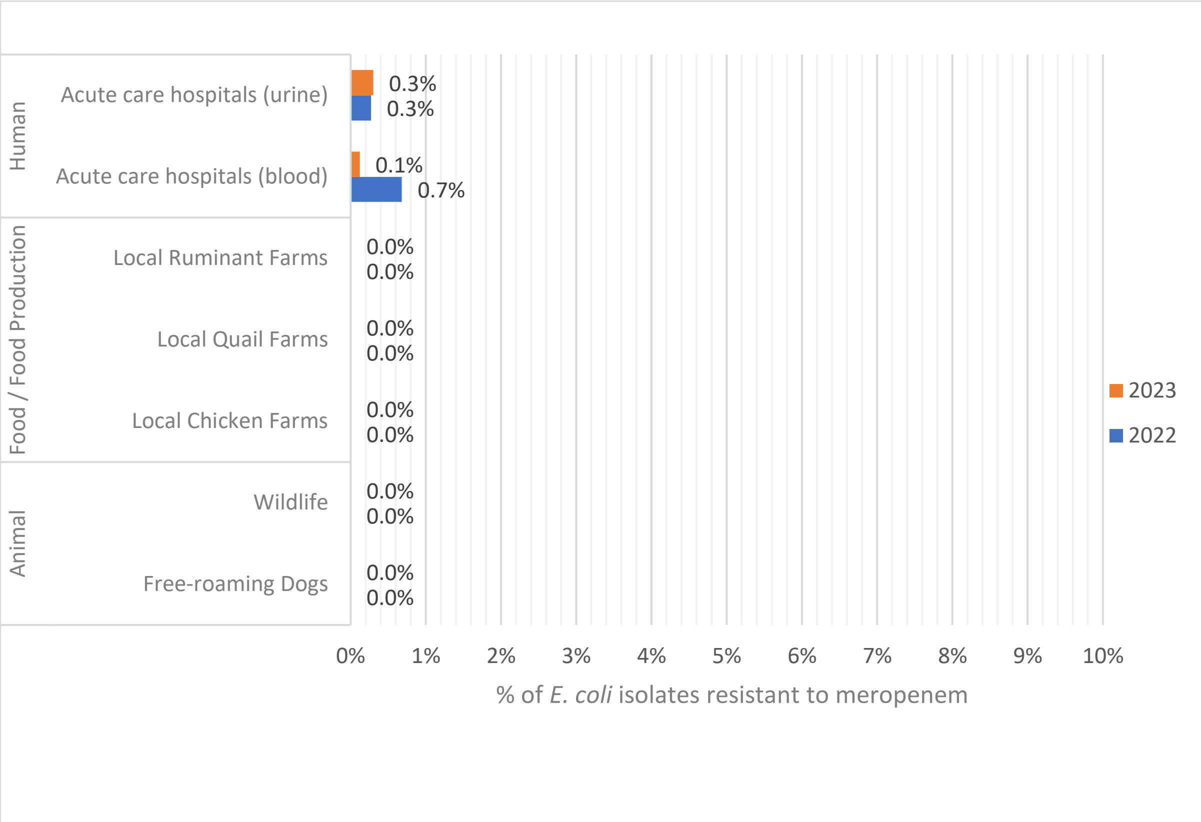
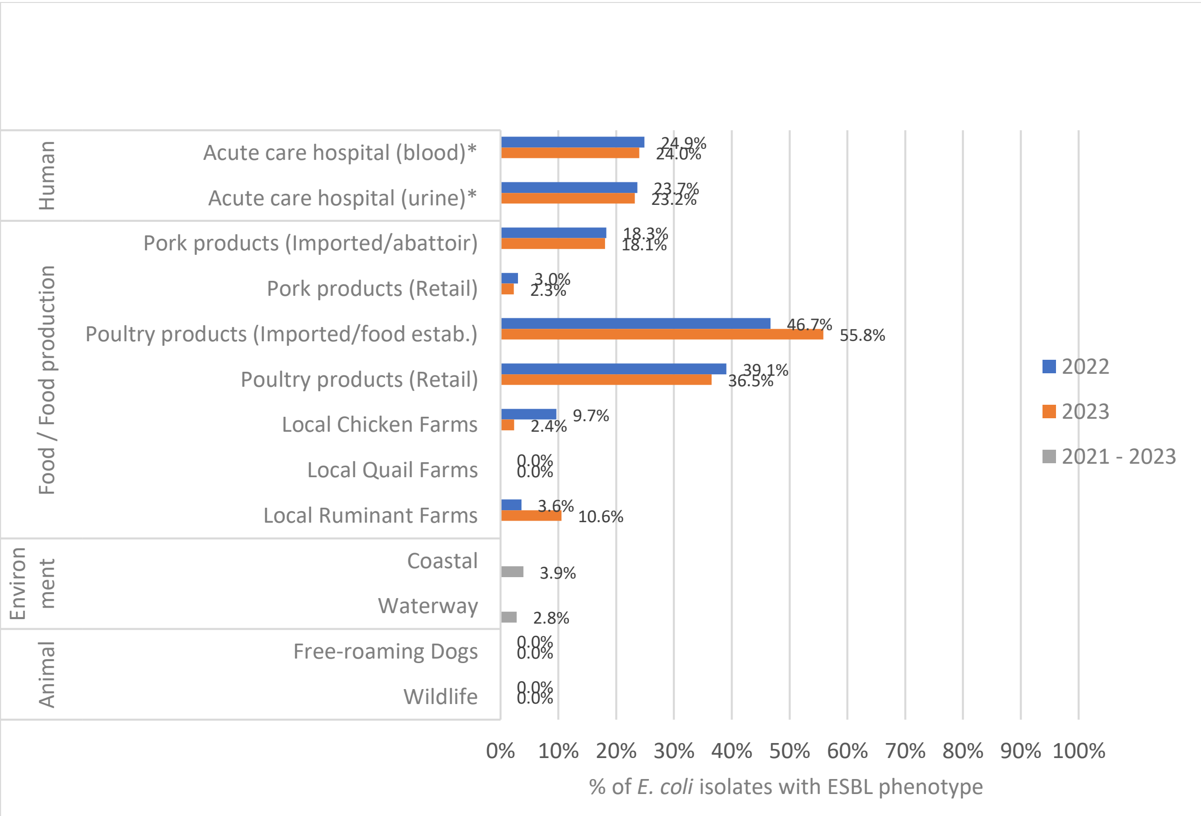


Figure 20. Comparison of ESBL-producing *E. coli* proportions across sectors



Scientific Study: Assessing antimicrobial resistance risks in coastal waters and aquaculture systems in Singapore

A floating fish farm in the waters off Singapore (Photo: The Fish Farmer)

There were 98 sea-based food fish farms in 2023 (Table 1). Amongst the animal sectors, the aquaculture industry (both ornamental fish and food fish sectors) reported highest sales volumes (in kg) of tetracycline, fluoroquinolones and penicillins (Figure 16).

To better understand risks to coastal waters and aquaculture systems, SFA in collaboration with the Nanyang Technological University and National University of Singapore, conducted a spatial temporal study of AMR in these environments, in conjunction with an assessment of chemical contaminants that could act as selective pressures for AMR. The study compared two different aquaculture settings used in Singapore: open cage farm and recirculating aquaculture system (RAS). Field monitoring and samples collection were conducted monthly at 12 sampling sites around the coastal waters of Singapore over a 1-year period from January 2022 to January 2023.

The study set out to (i) investigate the prevalence and co-occurrence of antibiotic-resistant bacteria (ARB), antibiotic resistance genes (ARGs), antibiotics (AB) and various associated chemical compounds at study sites; (ii) explore contributing factors to development and propagation of AMR in the coastal environment; and (iii) assess the AMR risks based on the three AMR determinants: ARB, ARGs and AB. Highlights of the research findings are presented here, with the full study by Goh et al (2024) available at https://doi.org/10.1016/j.watres.2024.122353.

This study identified significant variations in AMR patterns between open cage farm and RAS: Antibiotic-resistant *Vibrio* was more prevalent in RAS water and sediment samples, while specific ARGs (*qepA, blaCTX− M, bacA*) were more abundant in fish from the RAS. The closed loop nature of RAS likely promotes nutrients and organic matter accumulation, creating hotspots for ARB, HGT and ARGs. Chemical contaminants varied across different sites, which were influenced by anthropogenic activities. Higher levels of chemical contaminants were observed in the open cage farm due to greater exposure to external contamination sources. In addition, environmental and seasonal variations also significantly shaped the distribution of ARGs and chemical contaminants in coastal ecosystems.

Hierarchical cluster analysis, based on microbial, chemical and environmental data, revealed three distinct clusters shaped by location, time, and aquaculture activities. The lack of strong correlations between ARGs and chemical compounds suggest that concentrations of chemical compounds in the coastal environment may be too low to exert significant selective pressures for resistance. However, special attention should be given to the contaminants, ERY-H2O and Cu, which were detected at relatively high concentrations and could contribute selective pressure on AMR.

These findings suggest that the structural and operational differences between RAS and open cage farms significantly impact the AMR landscape, with implications for the management and design of aquaculture operations to mitigate the risk of AMR propagation. While the levels of most chemical contaminants were relatively low and pose minimal immediate risks, the potential long-term impact of these trace chemicals on the emergence of AMR warrants consideration. Prolonged exposure of microbes to small quantities of these chemicals could potentially act as a source of selective pressure. This sustained low-level exposure may gradually drive the evolution of resistance mechanisms in microbial populations. It would be essential to explore and monitor the long-term effects of these trace chemicals in the environment to fully understand their role in the emergence and spread of AMR.

Finally, a multifaceted risk assessment approach using methodologies such as the multiple antibiotic resistance (MAR) index, comparative AMR risk index (CAMRI) and Risk quotient (RQ) underscored the complexity of AMR risks. The authors emphasised the importance of employing multidimensional approaches in AMR management to address the complexity and variability of resistance patterns, while highlighting the need for globally standardised methods for detecting AMR determinants.

Reference:

Goh SG, You L, Ng C, Tong X, Mohapatra S, Khor WC, Ong GHM, Aung KT, Gin KY. A multi-pronged approach to assessing antimicrobial resistance risks in coastal waters and aquaculture systems. Water Research 266 (2024) 122353. https://doi.org/10.1016/j.watres.2024.122353

Antimicrobial Resistance in Human Health

AMR surveillance in hospitals

NARCC collects data on seven important pathogens isolated from clinical samples from acute care hospitals: *E. coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii, Staphylococcus aureus, Enterococcus faecium* and *Enterococcus faecalis*. In addition to specific pathogen-drug combinations, NARCC monitors the incidence density rates of *Clostridioides difficile*, which is associated with antimicrobial overuse (Refer to Appendix 1: Methodology for Table of drug-pathogen combinations and sample types). This report includes data from nine public and eight private acute care hospitals currently contributing AMR data to NARCC.

E. coli and ***K. pneumoniae*** are monitored for resistance to three important antibiotic classes:

i. Ceftriaxone resistance (or an equivalent third-generation cephalosporin) is an indicator for extended-spectrum beta-lactamase (ESBL), and cephalosporinases. These resistance mechanisms usually result in patients needing treatment with carbapenems, which are very broad-spectrum, second- or later-line antibiotics.

ii. Ciprofloxacin resistance is a marker for fluoroquinolone resistance and can potentially be correlated with widespread fluoroquinolone use in the community as well as in hospitals.

iii. Carbapenem resistance (defined as meropenem or imipenem non-susceptibility) is an emerging concern because infections caused by carbapenem-resistant organisms typically require treatment with other last-line antibiotics. Resistance mechanisms include carbapenemase production, and a combination of ESBL or AmpC production with porin loss. Carbapenemases are beta-lactamases with the ability to hydrolyse penicillins, cephalosporins, monobactams and carbapenems.

P. aeruginosa is an opportunistic pathogen which can cause serious community-acquired and nosocomial infections and is of particular concern in neutropaenic patients. *P. aeruginosa* is also a relatively frequent coloniser of medical devices, such as in-dwelling catheters, and can harbour multiple antibiotic resistance mechanisms. *P. aeruginosa* is monitored for resistance to carbapenems (imipenem or meropenem).

A. baumannii is an important cause of nosocomial infections including pneumonia, urinary tract, bloodstream, catheter and wound infections. *Acinetobacter* is intrinsically resistant to a broad range of antimicrobials. Multi-drug resistant (MDR) *A. baumannii* (defined here as concurrent resistance to imipenem/meropenem, ciprofloxacin, and amikacin) is therefore monitored as infections are more likely to require treatment with polymyxin B or colistin, which are considered last-line antibiotics.

S. aureus is a frequent coloniser of the skin and mucosa. *S. aureus* more commonly causes skin infections but can also spread through the bloodstream and cause a broad range of severe conditions such as pneumonia, endocarditis and osteomyelitis. Methicillin-resistant *S. aureus* (MRSA) is of particular concern due to their resistance to more effective first-line antibiotics used to treat ordinary staphylococcal infections.

Enterococci constitute a part of the normal intestinal microbiota in humans and animals. Most human enterococci infections are caused by *E. faecalis* and *E. faecium.* Enterococci are intrinsically resistant to many groups of antimicrobials, with severe and penicillin-resistant infections typically treated with vancomycin. *E. faecalis* and *E. faecium* are monitored for resistance to vancomycin. Presence of vancomycin resistance further restricts treatment choice.

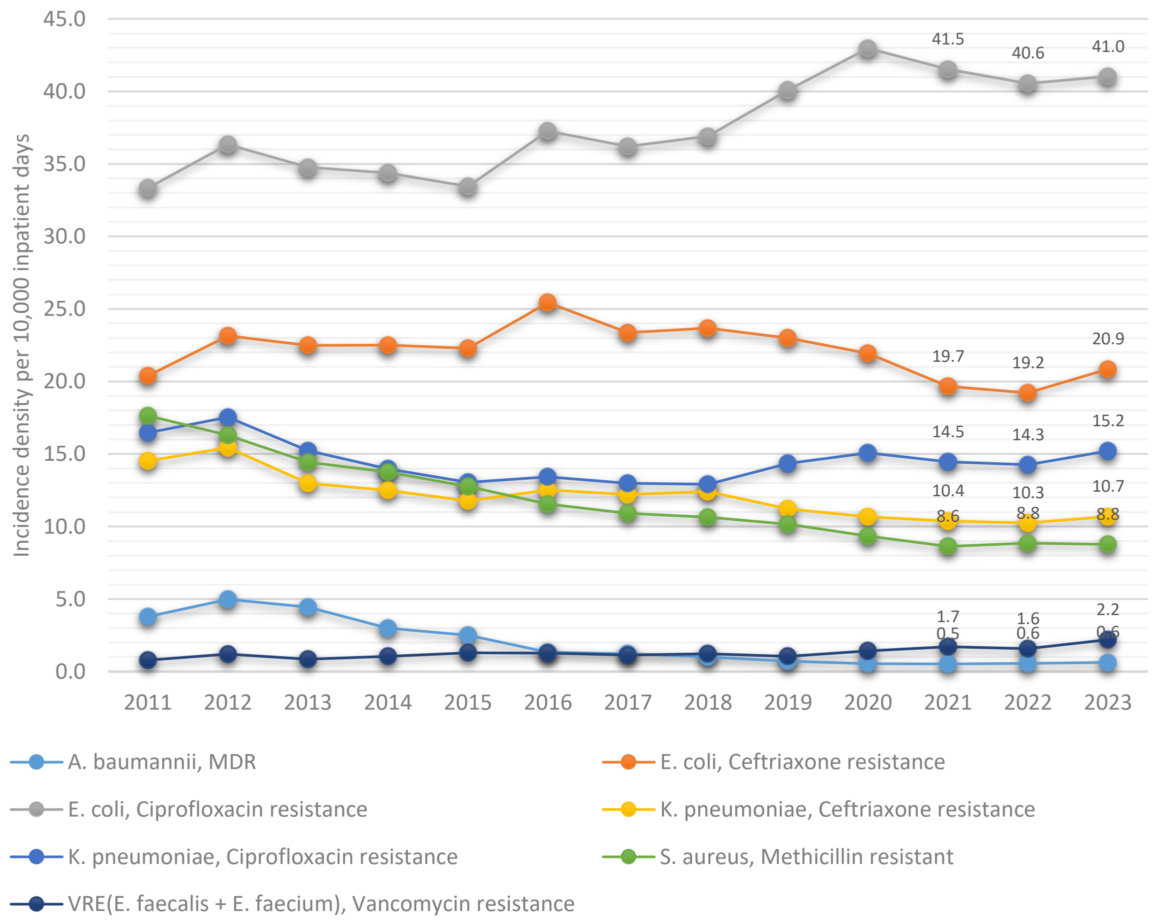
Incidence density trends

Incidence density is measured as the number of clinical isolates per 10,000 inpatient days. The use of inpatient days as a denominator allows for normalisation across hospitals of different size and patient load.

Public hospital trends

Since 2012, we have observed an overall decreasing trend in the incidence density of MRSA in public hospitals, which appears to have stabilised over the past three years (Figure 21). The declining rate corresponds with the implementation of antimicrobial stewardship programmes in public hospitals in 2011 and is also attributed to the continual enhancement of infection control measures in hospitals. However, increasing trends in the incidence of ciprofloxacin-resistant *E. coli* and *K. pneumoniae* were observed (Figure 21), despite a steady decline in ciprofloxacin and overall fluoroquinolone use in public hospitals (Figure 5).

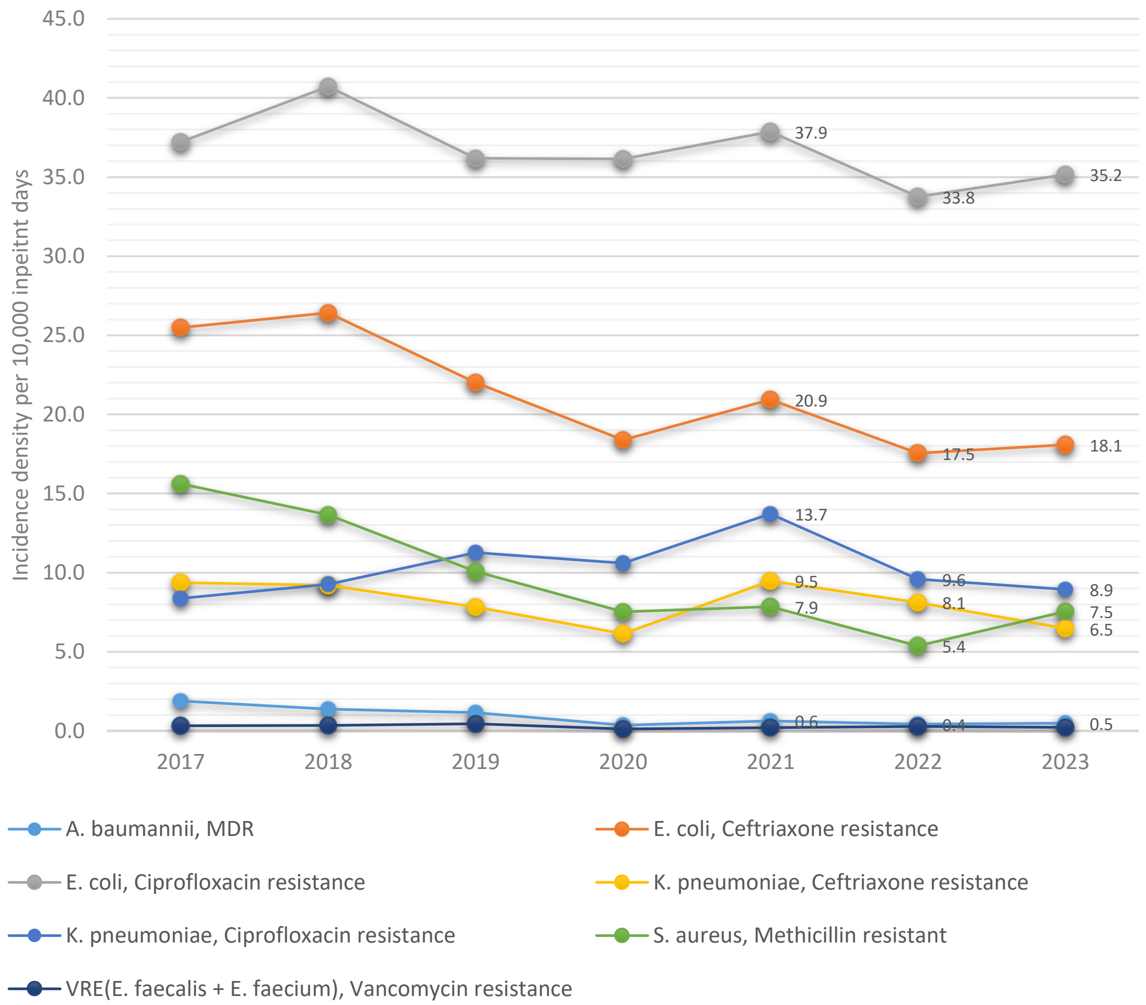
Figure 21. Incidence density of priority AMR organisms in public hospitals, all clinical isolates, 2011 – 2023



Private hospital trends

Overall decreasing trends of ceftriaxone- and ciprofloxacin-resistant *K. pneumoniae* incidences were observed in private hospitals (Figure 22), with an uptick in the incidence of MRSA and ciprofloxacin-resistant *E. coli* in 2023 compared to 2022.

Figure 22. Incidence density of priority AMR organisms in private hospitals, all clinical isolates, 2017 – 2023



Carbapenem-resistant Enterobacterales (CRE)

Carbapenem-resistant *Enterobacterales* (CRE), particularly carbapenemase-producing CRE (CP-CRE), are of particular importance due to their resistance to a wide range of antibiotics and the challenges associated with treating patients with CP-CRE infections. This group of pathogens includes the meropenem or imipenem-resistant strains of *E. coli* and *K. pneumonia.*

The incidence rate of carbapenem-resistant *A. baumannii* has been declining, but that of carbapenem-resistant *E. coli* has crept up in both public and private hospitals (Figure 23 and 24) in 2023 compared to 2022. The most frequently detected carbapenemases in Singapore (all acute care hospitals) were OXA-type beta-lactamase (OXA), New Delhi metallo-beta-lactamase-mediated carbapenemase (NDM) and *Klebsiella pneumoniae* carbapenemase (KPC; Figure 25). To further stratify carbapenemase detection in Singapore, imipenem-resistant Pseudomonas (IMP), verona integron-encoded metallo-lactamase (VIM), and imipenem-hydrolysing beta-lactamase (IMI; Figure 20) were included for monitoring in 2023.

Figure 23. Trends in incidence density of carbapenem (meropenem or imipenem)-resistant organisms in public hospitals, all clinical isolates, 2011 – 2023

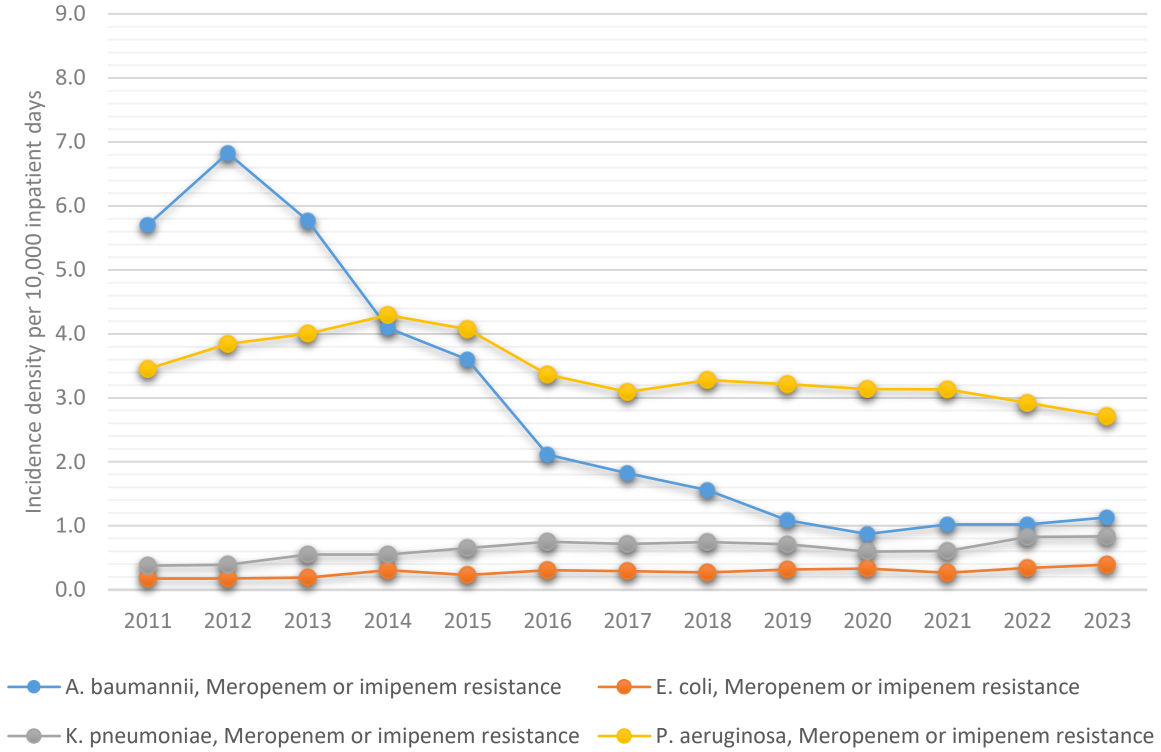


Figure 24. Trends in incidence density of carbapenem (meropenem or imipenem)-resistant organisms in private hospitals, all clinical isolates, 2017 – 2023

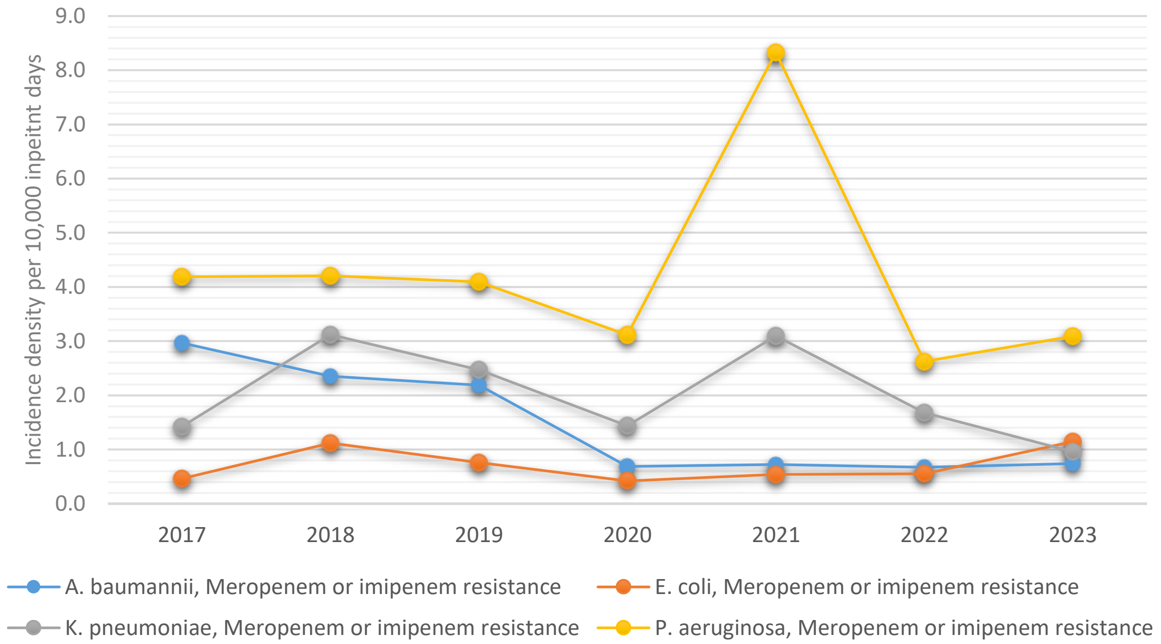
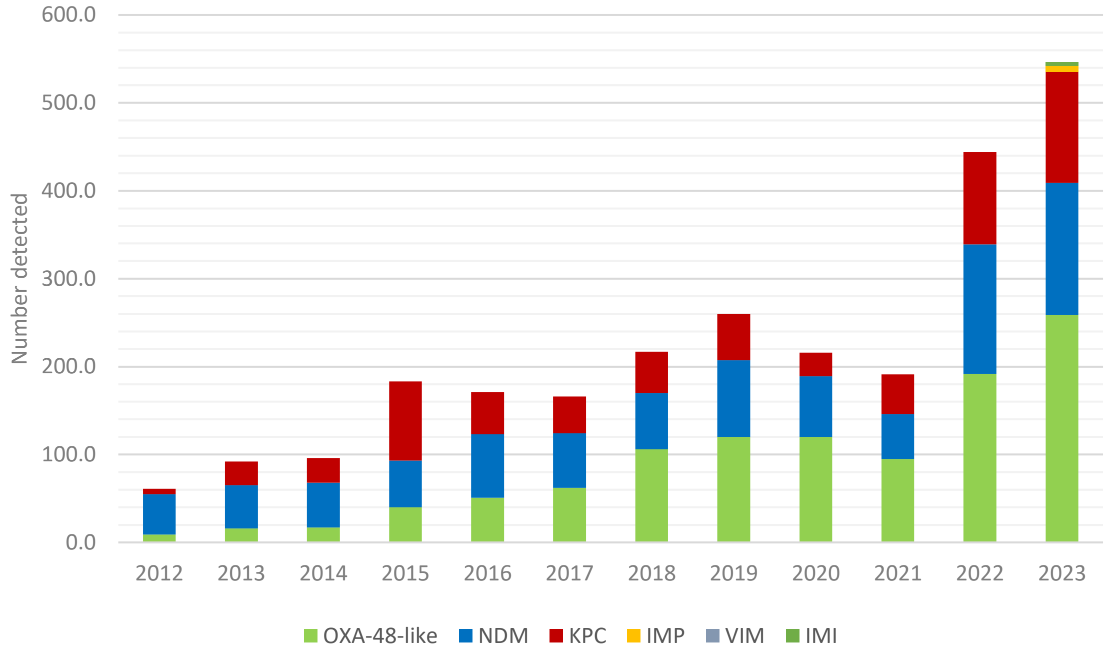


Figure 25. Carbapenemases detected in clinical isolates from all acute care hospitals, 2012 – 2023



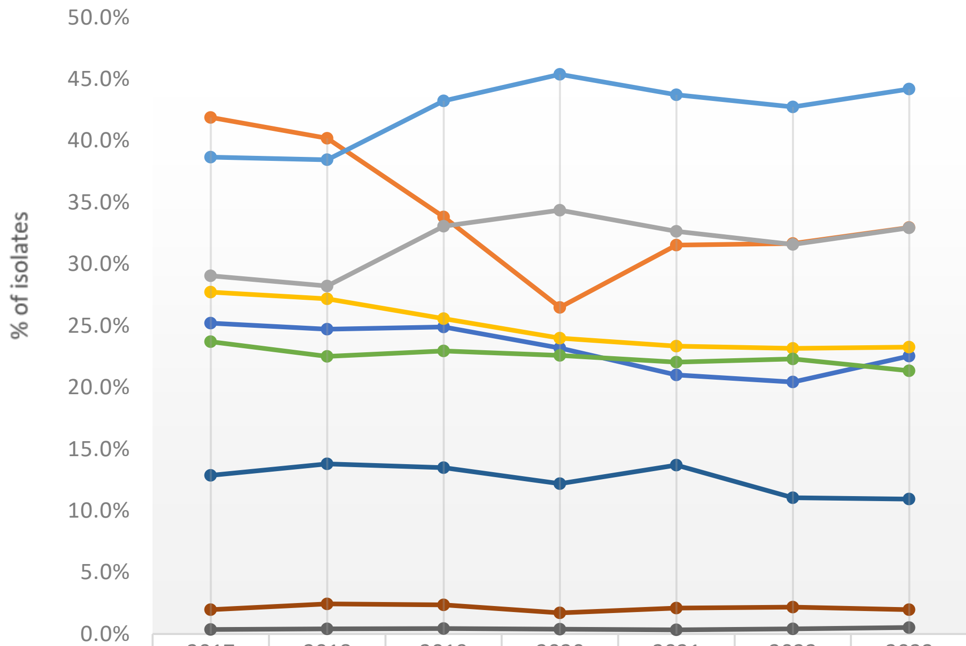
Note: Due to limited data on CPE types in the private sector, data for public and private hospitals are presented together.

Resistance percentage (%R)

The resistance percentage (%R) measures the proportion of isolates that are tested as being resistant to a specified antimicrobial, based on CLSI or EUCAST breakpoints. For NARCC's purposes, resistant isolates include those of intermediate susceptibility.

From 2017 to 2023, the average %R of most priority AMR pathogens in acute care hospitals have either decreased or remained stable, except for ciprofloxacin-resistant *E. coli* and *K. pneumoniae*, which were on an increasing trend (Figure 21). Over 40% of *E. coli* are resistant to ciprofloxacin and approximately one-third of *A. baumanii* isolates are resistant to carbapenems (meropenem or imipenem) (Figure 26), although its incidence has declined significantly in public hospitals since 2012 (Figure 23).

Figure 26. Trends in resistance percentages (%R) of priority pathogen-drug combinations, all clinical isolates from all acute care hospitals, 2017 to 2023



	2017	2018	2019	2020	2021	2022	2023
A. baumannii, Meropenem or imipenem resistance	41.9%	40.2%	33.8%	26.5%	31.5%	31.7%	33.0%
E. coli, Ceftriaxone resistance	25.2%	24.7%	24.9%	23.2%	21.0%	20.4%	22.5%
E. coli, Ciprofloxacin resistance	38.7%	38.4%	43.2%	45.4%	43.7%	42.7%	44.2%
E. coli, Meropenem or imipenem resistance	0.4%	0.4%	0.4%	0.4%	0.3%	0.4%	0.5%
K. pneumoniae, Ceftriaxone resistance	27.7%	27.2%	25.6%	24.0%	23.3%	23.2%	23.3%
K. pneumoniae, Ciprofloxacin resistance	29.1%	28.2%	33.1%	34.4%	32.6%	31.6%	32.9%
K. pneumoniae, Meropenem or imipenem resistance	2.0%	2.4%	2.4%	1.7%	2.1%	2.2%	2.0%
P. aeruginosa, Meropenem or imipenem resistance	12.9%	13.8%	13.5%	12.2%	13.7%	11.1%	10.9%
S. aureus, Methicillin resistant	23.7%	22.5%	22.9%	22.6%	22.0%	22.3%	21.3%

Note: Resistant isolates include those of intermediate susceptibility.

AMR surveillance in primary care

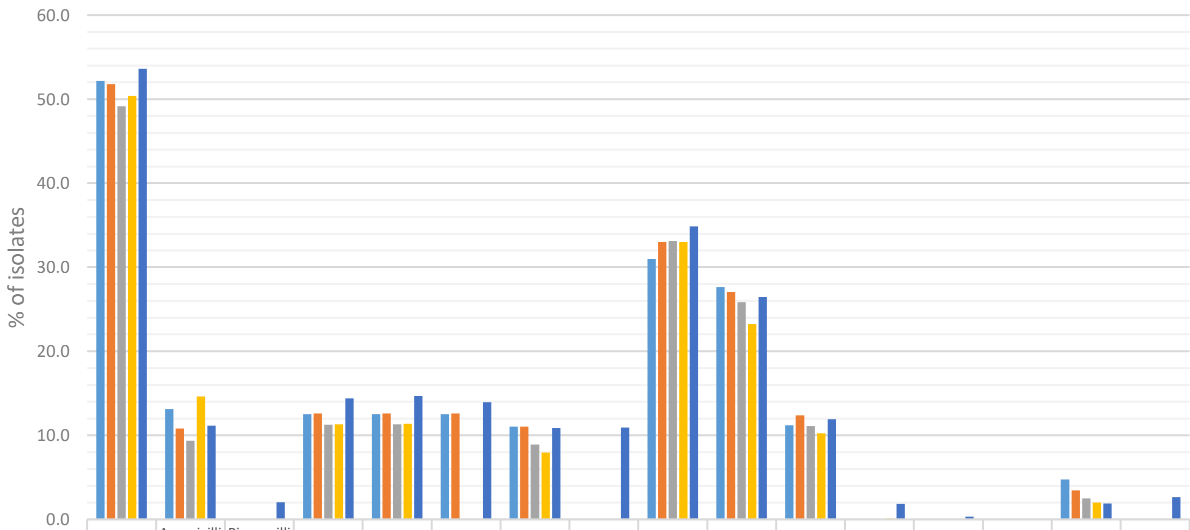
Approximately 20% of the primary healthcare needs are served by 25 polyclinics distributed across the country. In 2019, the AMRCO embarked on systematic and annual collection of data on the resistance profiles (including those of intermediate susceptibility) of *E. coli* and *K. pneumoniae* in urine samples, and *S. aureus* in clinical samples, to better understand resistance levels of key community pathogens.

Overall, average resistance levels remained generally stable from 2019 to 2023. In 2023, *E. coli* displayed the highest resistance to ampicillin (53.6%), ciprofloxacin (34.9%) and co-trimoxazole (26.5%) (Figure 27). *K. pneumoniae* displayed the highest resistance to nitrofurantoin (78.7%) and ciprofloxacin (22.8%) (Figure 28), while 16.5% of *S. aureus* isolates (20 out of 121 isolates) were MRSA (as defined by resistance to cloxacillin; Figure 29). The latter was an increase from 11.3% in 2022 (16 out of 142 isolates).

Of note, the overall number of carbapenemase producers remained low from 2019 (3 among a total of 706 *K. pneumoniae* and 4,894 *E. coli* isolates tested) to 2023 (8 among 971 *K. pneumoniae* and 5,332 *E. coli* tested). Continued surveillance of resistance rates in the polyclinics is beneficial to provide a proxy measure of community resistance rates over time.

There was an expansion on the list of susceptibility profiles collected from 2023. This includes data on ceftazidime- and piperacillin-tazobactam-resistance for *E. coli* and *K. pneumoniae* isolates, and fosfomycin-resistance for *E. coli*. For *S. aureus*, data on additional antibiotics tested were collected for penicillin, oxacillin, cefoxitin and doxycycline.

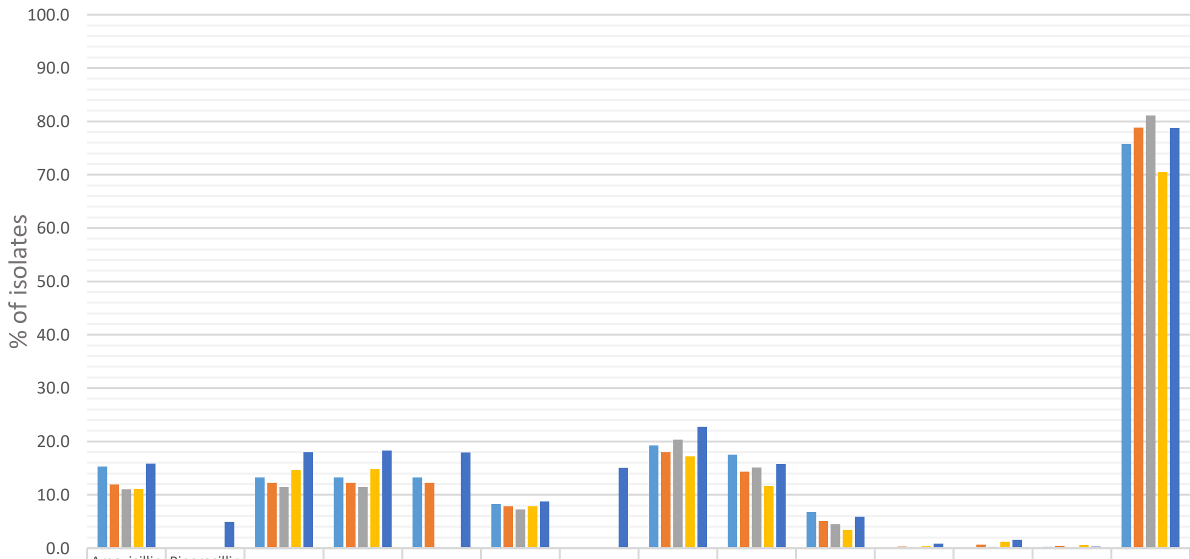
Figure 27. Resistance percentage (%) of *E. coli* from polyclinic urine samples, 2019-2023



	Ampicillin	Amoxicillin-Clavulanate	Piperacillin-tazobactam	Cefuroxime (oral)	Cephalexin	Cefazolin	Ceftriaxone	Ceftazidime	Ciprofloxacin	Co-trimoxazole	Gentamicin	Amikacin	Ertapenem	Meropenem	Nitrofurantoin	Fosfomycin
2019	52.1	13.1		12.5	12.5	12.5	11.0		31.0	27.6	11.2	0.1	0.0	0.1	4.8	
2020	51.8	10.8		12.6	12.6	12.6	11.0		33.0	27.1	12.4	0.1	0.1	0.1	3.4	
2021	49.1	9.3		11.3	11.3	0.0	8.9		33.1	25.8	11.1	0.1	0.0	0.0	2.5	
2022	50.4	14.6		11.3	11.4		8.0		33.0	23.2	10.2	0.1	0.1	0.1	2.0	
2023	53.6	11.1	2.1	14.4	14.7	14.0	10.9	10.9	34.9	26.5	11.9	1.9	0.3	0.1	1.9	2.6

Note: Data on ceftazidime, piperacillin-tazobactam and fosfomycin was collected from 2023.

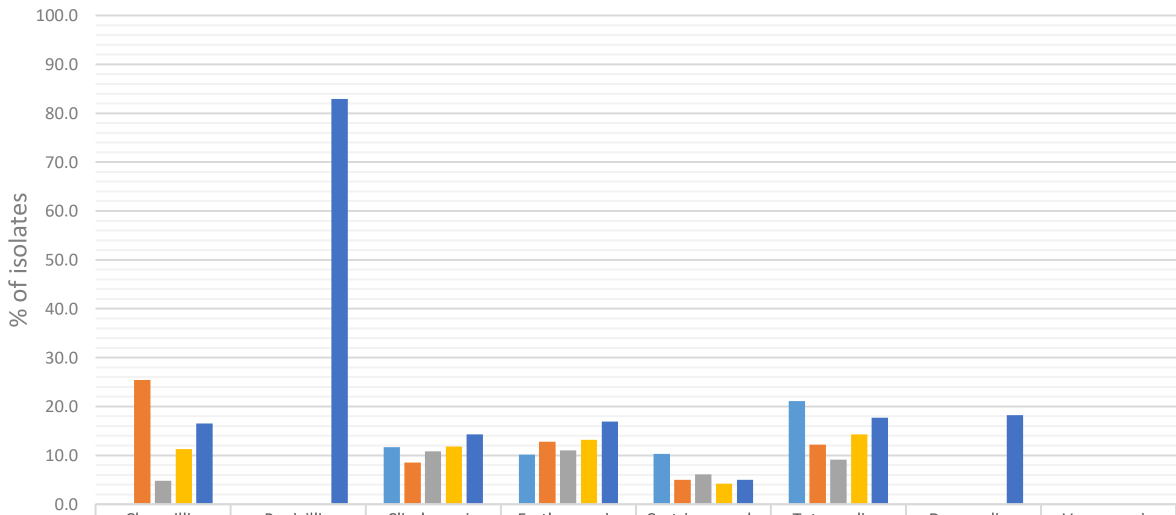
Figure 28. Resistance percentage (%) of *K. pneumoniae* from polyclinic urine samples, 2019-2023



	Amoxicillin-Clavulanate	Piperacillin-tazobactam	Cefuroxime (oral)	Cephalexin	Cefazolin	Ceftriaxone	Ceftazidime	Ciprofloxacin	Co-trimoxazole	Gentamicin	Amikacin	Ertapenem	Meropenem	Nitrofurantoin
2019	15.3		13.3	13.3	13.3	8.3		19.3	17.5	6.8	0.1	0.0	0.3	75.8
2020	11.9		12.2	12.2	12.2	7.9		18.0	14.3	5.1	0.3	0.6	0.4	78.8
2021	11.1		11.5	11.5		7.3		20.3	15.1	4.5	0.0	0.2	0.0	81.1
2022	11.1		14.6	14.8		7.9		17.2	11.6	3.4	0.4	1.2	0.6	70.5
2023	15.9	4.9	18.0	18.3	17.9	8.8	15.0	22.8	15.8	5.9	0.8	1.6	0.3	78.7

Note: Data on ceftazidime and piperacillin-tazobactam were collected from 2023.

Figure 29. Resistance percentage (%) of *S. aureus* in clinical samples from polyclinics, 2019-2023



	Cloxacillin	Penicillin	Clindamycin	Erythromycin	Co-trimoxazole	Tetracycline	Doxycycline	Vancomycin
2019			11.7	10.2	10.3	21.1		0.0
2020	25.4		8.5	12.8	5.0	12.2		0.0
2021	4.8		10.8	11.0	6.1	9.1		0.0
2022	11.3		11.8	13.2	4.2	14.3		0.0
2023	16.5	82.9	14.3	16.9	5.0	17.7	18.2 *	0.0

Notes: * denotes less than 30 isolates were tested for the specific drug-pathogen combination. Blanks denote unavailability of data for the year indicated. Data on penicillin, oxacillin, cefoxitin and doxycycline were collected from 2023; oxacillin and cefoxitin have been excluded from this chart.

Participation in Global Antimicrobial Resistance and Use Surveillance System (GLASS-AMR)

GLASS-AMR[12] was launched by the WHO in 2015 as a collaborative global effort to provide a standardised approach to the collection, sharing and analysis of AMR data.

As of 2023, GLASS collected aggregated country data on six priority specimens (blood, stool, urine, genital, pharyngeal and anorectal swabs), and eight organisms (*E. coli, K. pneumoniae, Acinetobacter* spp., *S. aureus, Streptococcus pneumoniae, Salmonella* spp., *Shigella* spp., *Neisseria gonorrhoea)*, stratified by age group, gender, and origin of infection (hospital vs community). Singapore enrolled in GLASS-AMR in September 2019, with the AMRCO and the NPHL appointed by MOH as the national coordinating centre and the AMR reference laboratory, respectively.

Resistance profiles

Aggregate data from four sentinel sites were submitted to GLASS in 2022 and 2023. Sites comprised three public acute care hospitals which provided data on blood, urine and stool samples, and one outpatient sexual health clinic providing data on genital, pharyngeal and anorectal swab samples for gonorrhoea.

The resistance profiles of GLASS pathogens detected in Singapore's sentinel hospitals are presented in Figures 30 and 31 in terms of resistance percentages (%R). The resistance profile of *N. gonorrhoea* isolates is shown as Figure 32. Only pathogen-drug combinations of at least 10 isolates with AST done are shown in the charts below.

Overall, percentage resistance rates were generally stable in 2022 and 2023, similar to rates in 2021 and 2022.[13]

The full global and country-level data are available on the GLASS visualisation dashboard at worldhealthorg.shinyapps.io/glass-dashboard/. For details on GLASS methodology and data limitations, please refer to Global Antimicrobial Resistance and Use Surveillance System (GLASS) (who.int).

[12] www.who.int/glass/en/
[13] One Health Report on AMR and AMU, 2021

Figure 30. Resistance (%) of drug-resistant pathogens isolated from (a) blood and (b) urine samples in sentinel hospitals, Singapore 2022 - 2023

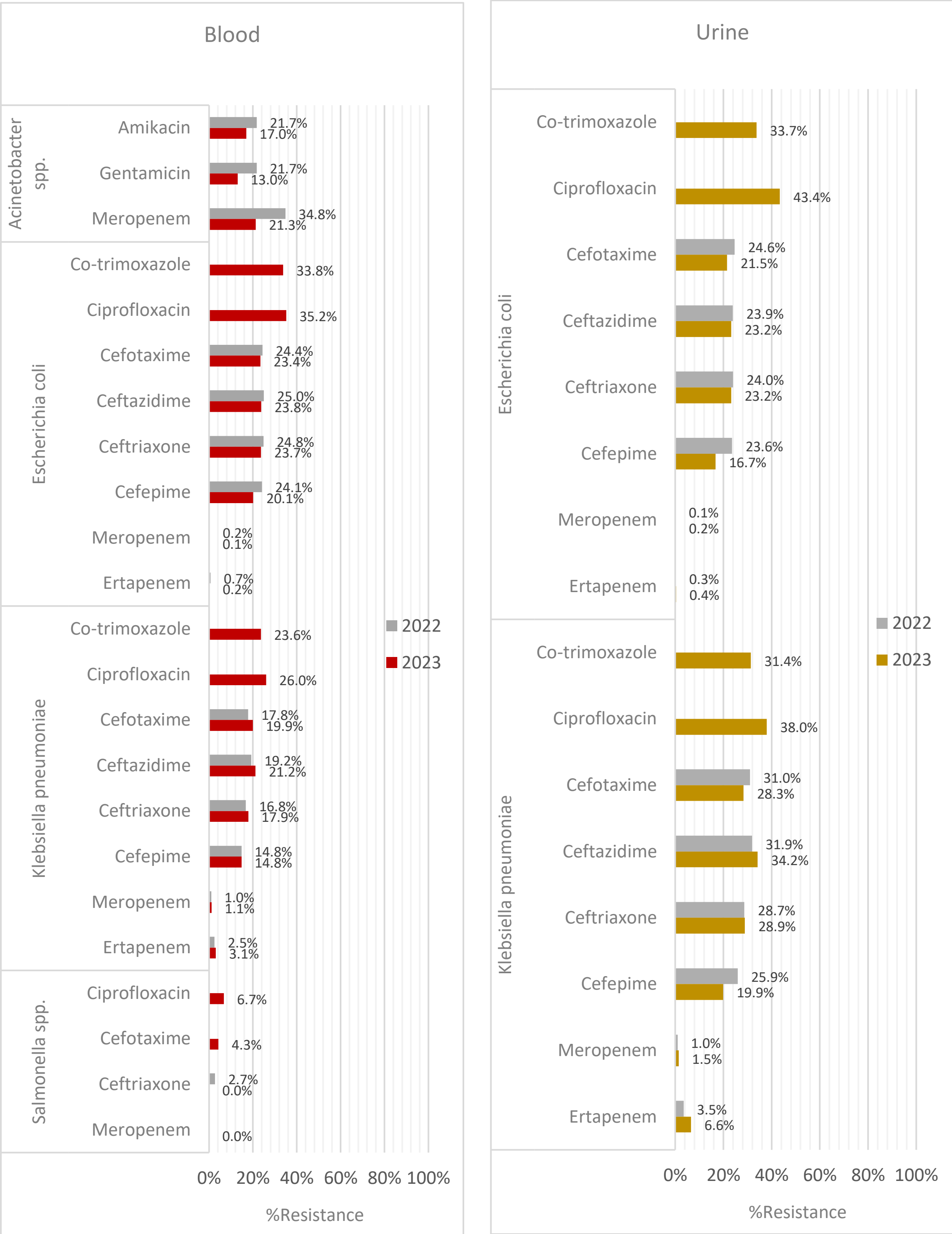


Figure 31. Resistance (%) of drug-resistant Salmonella spp isolated from stool samples in sentinel hospitals, Singapore 2022 - 2023

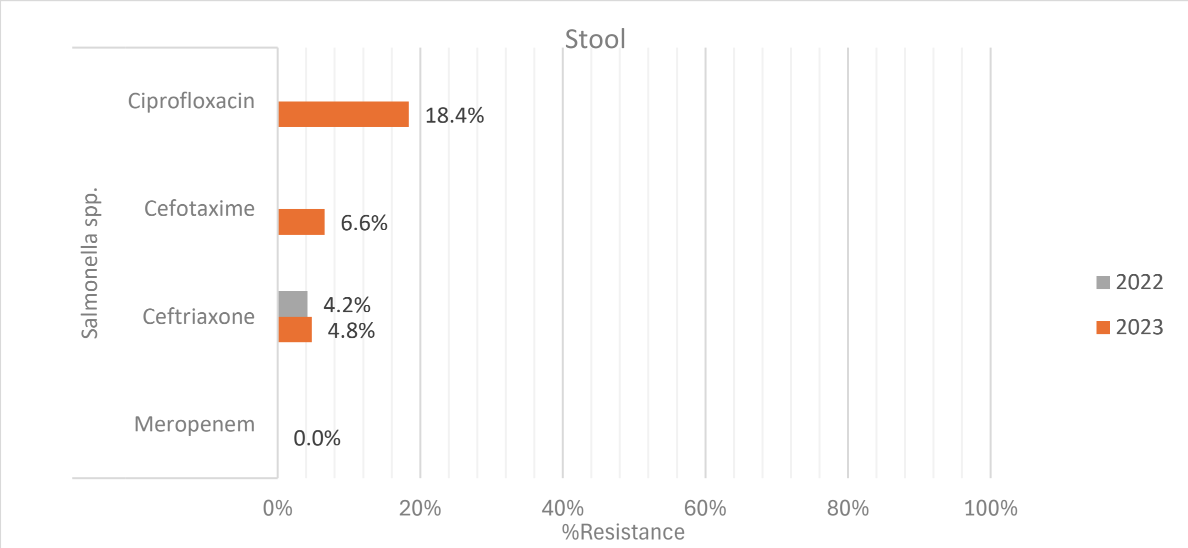
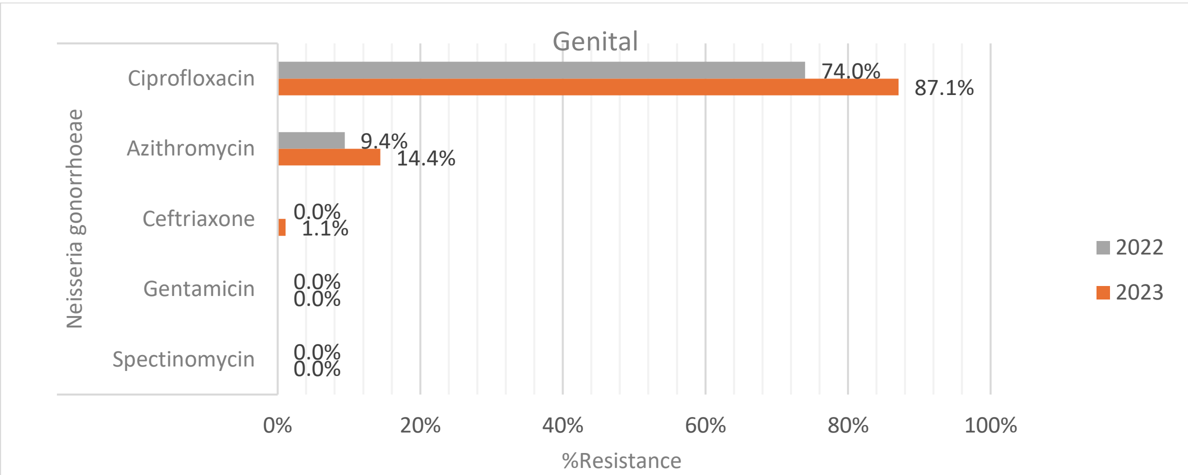


Figure 32. Resistance (%) of drug-resistant *N. gonorrhoea*, Singapore 2022 - 2023

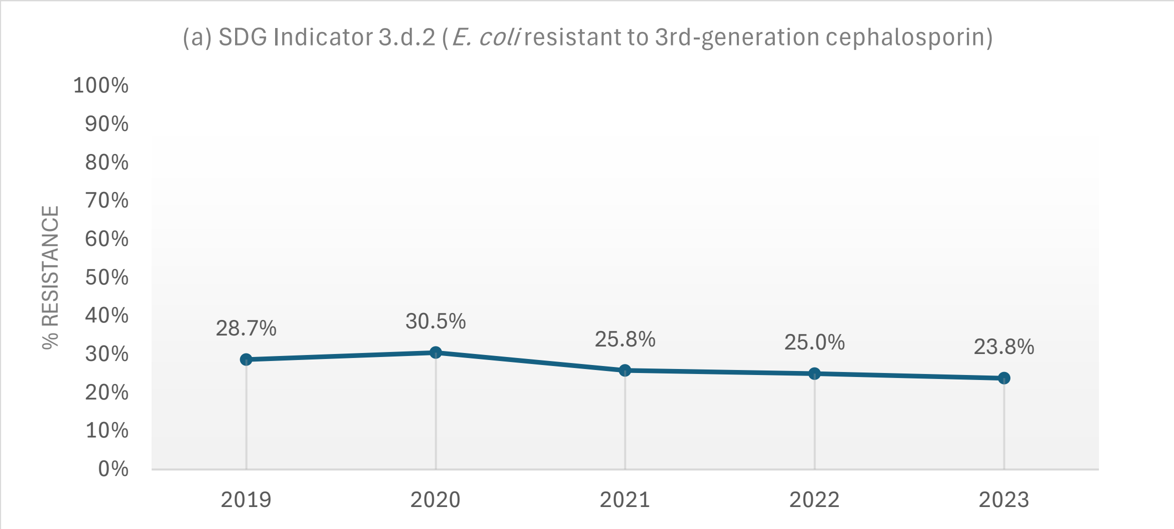


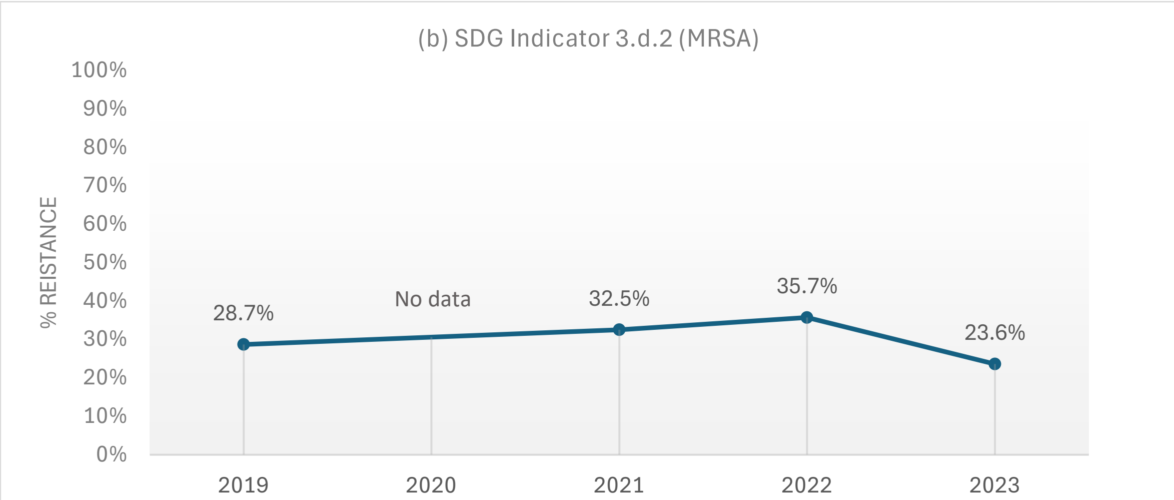
Sustainable Development Goal (SDG) AMR indicators

AMR indicators for Sustainable Development Goal (SDG) 3, which is "To ensure healthy lives and promote well-being for all at all ages", measure reduction in the frequency of bloodstream infection among hospital patients due to (i) *E. coli* resistant to 3rd-generation cephalosporin (e.g., ESBL- *E. coli*) and (ii) MRSA. Methicillin-resistance in *S. aureus* is calculated by resistance to oxacillin and/or cefoxitin and by taking the maximum resistance value where both antibiotics were tested. The AMR SDG indicators are derived from data from sentinel hospitals in Singapore contributing to GLASS.

The frequency of bloodstream *E. coli* resistant to third-generation cephalosporins was observed to be on a declining trend from 30.5% in 2020 to 23.8% in 2023 (Figure 33.a). The frequency of bloodstream methicillin-resistant *Staphylococcus aureus* in 2023 was 23.6%, down from 35.7% in 2022 (Figure 33.b).

Figure 33. Percentage resistance of (a) *E. coli* resistant to 3rd-generation cephalosporin (e.g., ESBL-*E. coli*) and (b) methicillin-resistant *S. aureus* (MRSA) among patients seeking care and whose blood sample is taken and tested





Note: Observations based on < 10 BCIs with AST, are excluded from the plot. Data on the MRSA indicator was not available in 2020.

Caveats:

(i) Data for these indicators are obtained from only three of 19 acute care hospitals in Singapore and therefore lacks representativeness for the country as a whole. Efforts are on-going to increase the number of sentinel sites to improve the representativeness of Singapore's data.

(ii) GLASS data records substantial differences in the number of patients that pathogens were isolated from and large variations on country coverage. These impact the quality and relevance of the national antibiotic resistance frequencies. Hence, while GLASS data provide useful estimates for benchmarking, national resistance levels may be non-representative and should therefore be interpreted cautiously.

The GLASS SDGs AMR Indicator dashboard is found at worldhealthorg.shinyapps.io/glass-dashboard/.

Antimicrobial Resistance in Bacteria in the Food Chain

The national AMR surveillance programme for the food chain covers local food-producing animals, animals imported for slaughter, food imports and retail food products. The programme aims to assess the potential impact of AMR in the food chain on consumers and food handlers. The programme covers the testing of common foodborne bacteria, particularly *Salmonella* spp. and *E. coli*, for resistance against clinically and epidemiologically important antimicrobial agents. Efforts are also made to examine the prevalence and AMR profiles of ESBL *E. coli* in the food chain. The trends presented in this report may reflect the risk-based sampling methodology in some food chain points, which prioritises surveillance of higher-risk sources.

Salmonella spp. is a major cause of food-borne illness worldwide and in Singapore. Salmonellosis, the infection by non-typhoidal strains of *Salmonella* spp., is a notifiable disease in Singapore. The incidence of Salmonellosis has generally been on a downward trend since 2016, with 1265 cases of salmonellosis reported in 2023 compared with 2214 in 2016 [14]. Out of over 2000 different serovars of *Salmonella enterica*, Enteritidis and Typhimurium are the main serovars associated with non-typhoidal Salmonellosis in Singapore[15,16]. *Salmonella enterica* serovars are naturally present in the digestive tracts of many animals but are most frequently isolated from poultry and its associated products. *Salmonella* spp. is monitored for specific resistance as well as multi-drug resistance (MDR), defined as resistance to three or more classes of antimicrobials.

E. coli are ubiquitous commensal bacteria found in all warm-blooded animals. *E. coli* in the gut may be exposed to antimicrobials from various sources, potentially becoming reservoirs for transferable resistance determinants in the animal or human gut [17]. The bacteria also serve as indicators for resistance in different reservoirs along the food chain. As most AMR phenotypes from animal populations are present in commensal bacteria, the effects of AMU and AMR trends are more accurately reflected in commensal bacteria than in food-borne pathogens[18]. Most strains of *E. coli* are non-pathogenic but have the potential to transfer resistance determinants to pathogenic Gram-negative bacteria. Hence, *E. coli* are monitored for specific resistance as well as MDR. ESBL *E. coli* are of specific concern due to their concurrent resistance to many other antibiotics.

Key findings from surveillance of these organisms in the food supply chain are presented here.

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[14] Communicable Diseases Agency, Singapore. Weekly Infectious Diseases Bulletin. https://safe.menlosecurity.com/https://www.cda.gov.sg/resources/weekly-infectious-diseases-bulletin-2023/

[15] Salmonellosis, non-typhoidal. In: Ooi PL, Boudville I, Chan M, Tee N, eds. Communicable diseases control. Singapore: S-FETP, 2020; 264-266.

[16] Aung, K.T., et al. Characterisation of Salmonella Enteritidis ST11 and ST1925 Associated with Human Intestinal and Extra-Intestinal Infections in Singapore. Int. J. Environ. Res. Public Health. 2022, Vol. 19, p. 5671.

[17] Food and Agriculture Organisation of the United Nations (FAO), 2019. *Regional Antimicrobial Resistance Monitoring and Surveillance Guidelines Volume 1 (Monitoring and surveillance of antimicrobial resistance in bacteria from healthy food animals intended for consumption*.

[18] European Food Safety Authority (EFSA), 2018. The European Union summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2016. *EFSA Journal,* 16(2), 5182.

Antimicrobial resistance in *Salmonella*

In healthy production animals

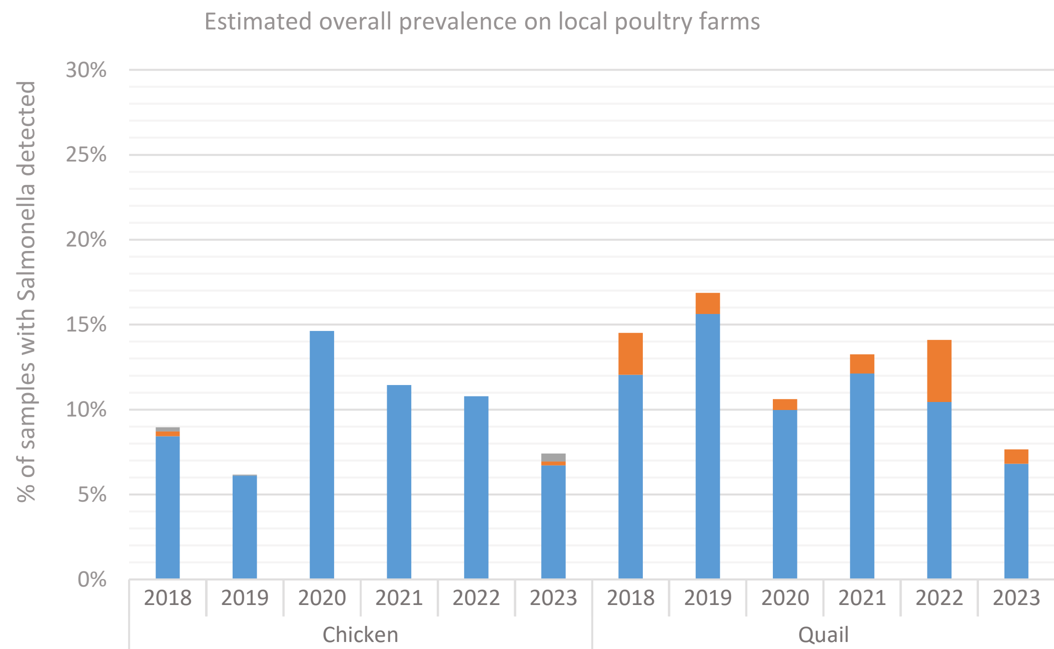
The prevalence and AMR profiles of *Salmonella* in local chicken and quail farms have been monitored since 2008. The surveillance programme was administered by NParks from 2008 to June 2021, and by SFA since July 2021. Surveillance of the ruminant (dairy goat and cattle) farms was initiated in November 2017 and remains under the purview of NParks.

Isolates from farm samples were subjected to AST by microbroth dilution using the Sensititre™ Asia Surveillance Plates for *Salmonella/E. coli* (see Appendix II. AMR Methodology) and applying CLSI M100 breakpoints. These plates were adopted in 2020 to enable harmonisation with other ASEAN regional laboratories for more comparable analyses of AMR in food animals in the region. In applying the Sensititre™ Asia Surveillance Plates, trimethoprim and sulfamethoxazole resistance were monitored separately from 2020, compared to monitoring in combination prior to 2020. The results of combination testing are available in previous editions of the One Health Report.

Salmonella from local poultry farms

Overall, the prevalence of *Salmonella enterica* serovars Enteritidis and Typhimurium on local poultry farms continued to remain low (Figure 34) with no *Salmonella* Enteritidis detected from 2020 to 2022. Other *Salmonella* spp. detected mostly comprised serovars belonging to Group C and E.

Figure 34. Estimated overall prevalence of *Salmonella* spp. in local poultry farms, 2018 – 2023



	Chicken 2018	Chicken 2019	Chicken 2020	Chicken 2021	Chicken 2022	Chicken 2023	Quail 2018	Quail 2019	Quail 2020	Quail 2021	Quail 2022	Quail 2023
S. Enteritidis	0.2%	0.1%	0.0%	0.0%	0.0%	0.5%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
S. Typhimurium	0.3%	0.0%	0.0%	0.0%	0.0%	0.2%	2.5%	1.3%	0.6%	1.1%	3.7%	0.8%
Other Salmonella	8.4%	6.1%	14.6%	11.5%	10.8%	6.7%	12.1%	15.6%	10.0%	12.1%	10.4%	6.8%

Farm type and year sampled

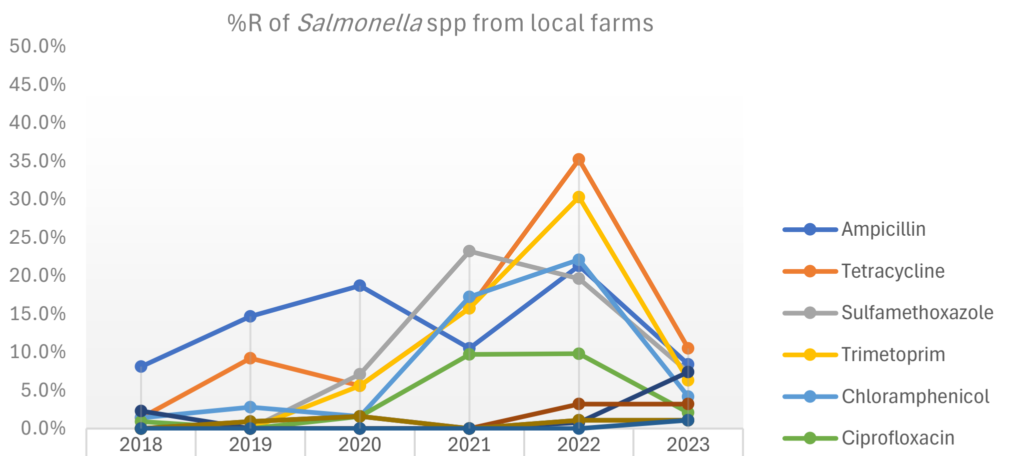
Table 2. Numbers of samples tested and *Salmonella* spp. isolates obtained from poultry farm surveillance

Farm		2018	2019	2020	2021	2022	2023
Chicken layer	No. samples tested	2467	1766	1374	1170	1132	1287
	No. of isolates recovered	221	109	201	134	122	95
Quail layer	No. samples tested	365	320	311	264	163	235
	No. of isolates recovered	53	54	66	35	23	18

Resistance profiles of Salmonella from poultry farms

Overall, resistance proportions of isolates from local chicken farms declined in 2023 after increasing from 2020 to 2022 (Figure 35). The percentage of resistance fluctuated between 2018 to 2023 (Figure 36). *Salmonella* isolates from quail farms were more frequently resistant to the antibiotics tested compared to isolates from chicken farms. Isolates from poultry farms were most frequently resistant to ampicillin and tetracycline. Resistance to other high priority critically important antibiotics, such as carbapenems, quinolones and third-generation cephalosporins, remained low.

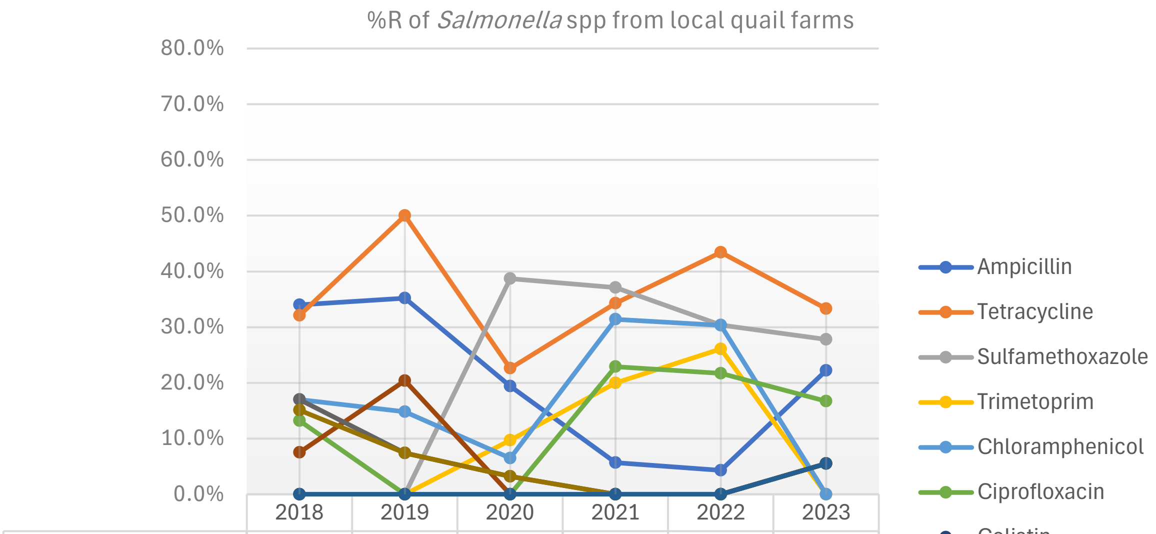
Figure 35. Percentage (%) resistance of *Salmonella* spp. isolated from local chicken farms, 2018-2023



	2018	2019	2020	2021	2022	2023
Ampicillin	8.1%	14.7%	18.7%	10.5%	21.3%	8.4%
Tetracycline	1.4%	9.2%	5.6%	15.7%	35.2%	10.5%
Sulfamethoxazole			7.1%	23.2%	19.6%	7.4%
Trimetoprim			5.6%	15.7%	30.3%	6.3%
Chloramphenicol	1.4%	2.8%	1.6%	17.2%	22.1%	4.2%
Ciprofloxacin	0.9%	0.0%	1.6%	9.7%	9.8%	2.1%
Colistin	2.3%	0.0%	0.0%	0.0%	0.8%	7.4%
Gentamicin	0.0%	0.0%	0.0%	0.0%	3.2%	3.2%
Cefotaxime	0.0%	0.9%	1.6%	0.0%	1.1%	1.1%
Ceftazidime	0.0%	0.9%	1.6%	0.0%	1.1%	1.1%
Meropenem	0.0%	0.0%	0.0%	0.0%	0.0%	1.1%

*Greyed areas denote no available data.

Figure 36. Percentage (%) resistance of *Salmonella* spp. isolated from local quail layer farms, 2018-2023



	2018	2019	2020	2021	2022	2023
Ampicillin	34.0%	35.2%	19.4%	5.7%	4.3%	22.2%
Tetracycline	32.1%	50.0%	22.6%	34.3%	43.4%	33.3%
Sulfamethoxazole			38.7%	37.1%	30.4%	27.8%
Trimetoprim			9.7%	20.0%	26.1%	0.0%
Chloramphenicol	17.0%	14.8%	6.5%	31.4%	30.3%	0.0%
Ciprofloxacin	13.2%	0.0%	0.0%	22.9%	21.7%	16.7%
Colistin	0.0%	0.0%	0.0%	0.0%	0.0%	5.5%
Gentamicin	7.5%	20.4%	0.0%	0.0%	0.0%	5.5%
Cefotaxime	17.0%	7.4%	3.2%	0.0%	0.0%	5.5%
Ceftazidime	15.1%	7.4%	3.2%	0.0%	0.0%	5.5%
Meropenem	0.0%	0.0%	0.0%	0.0%	0.0%	5.5%

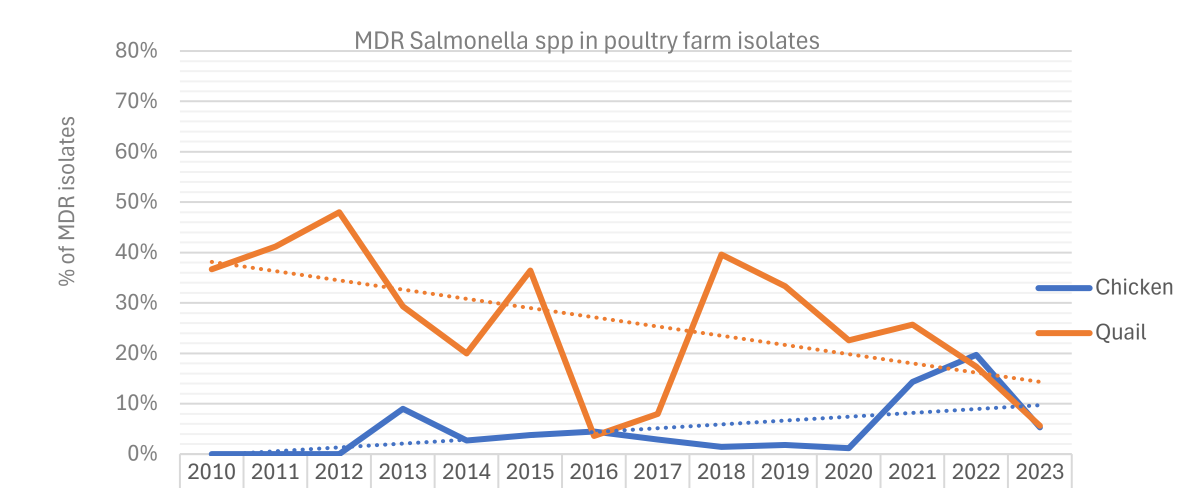
*Greyed areas indicate no data available. The number of isolates recovered in 2022 and 2023 were below the threshold of reliability (<30).

MDR Salmonella in poultry farm animals

MDR *Salmonella* remains a worldwide challenge, particularly when occurring in serovars of public health importance. While the MDR proportions were previously higher in quail farms than chicken farms, the proportion of MDR *Salmonella* spp. in local chicken and quail farms were similar in 2023 (5.3% and 5.6%, respectively). None of the MDR isolates were *S.* Enteritidis or *S.* Typhimurium.

MDR *Salmonella* from local chicken farms from 2010 to 2023 demonstrated a slightly increasing trend, while an overall decreasing trend was observed for MDR *Salmonella* from quail farms (Figure 37). The limited number of quail farm isolates (fewer than 30) in 2022 and 2023 suggests that conclusions should be drawn cautiously.

Figure 37. Proportion of MDR isolates among *Salmonella* spp. from the local poultry farms, 2010 – 2023.



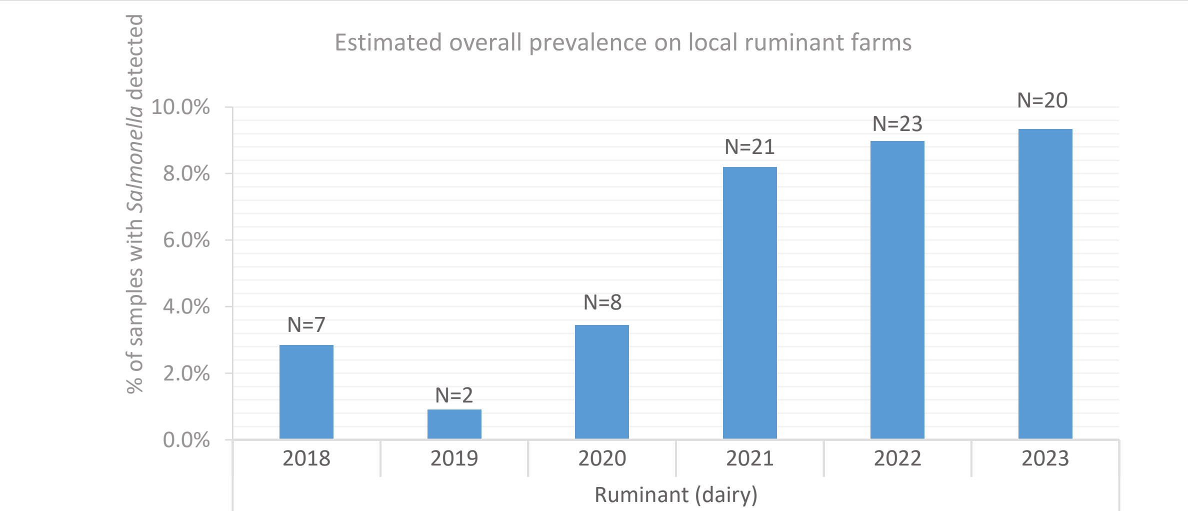
	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Chicken	0.0%	0.0%	0.0%	9.0%	2.7%	3.8%	4.5%	2.9%	1.4%	1.8%	1.2%	14.3%	19.7%	5.3%
Quail	36.7%	41.2%	48.0%	29.3%	20.0%	36.4%	3.6%	8.0%	39.6%	33.3%	22.6%	25.7%	17.4%	5.6%

Note: AST were performed with 11 antimicrobials in 2018 - 2023, whereas AST were performed with four antimicrobials (ampicillin, chloramphenicol, streptomycin and tetracycline) in 2010-2017. The limited number of quail farm isolates (fewer than 30) in 2022 and 2023 suggests that conclusions should be drawn cautiously.

Salmonella from local ruminant farms

Salmonella spp. was infrequently isolated from ruminant (dairy cattle and dairy goat) farm samples, with typically less than 10% recovered in the samples tested; serovars Enteritidis or Typhimurium were not detected (Figure 38). Table 3 shows the total number of samples received from local ruminant farms for isolation of *Salmonella*.

Figure 38. Estimated overall prevalence of *Salmonella* spp. in local ruminant farms, 2018 – 2023



	2018	2019	2020	2021	2022	2023
S. Enteritidis	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
S. Typhimurium	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Other Salmonella	2.8%	0.9%	3.4%	8.2%	9.0%	9.3%

Table 3. Number of *Salmonella* spp isolates obtained from ruminant farm surveillance, 2018-2023

Farm		2018	2019	2020	2021	2022	2023
Ruminant (dairy) (cattle and goat)	No. samples tested	246	219	232	256	256	214
	No. of isolates recovered	7	2	8	21	23	20

Note: Not all isolates were used for subsequent AST.

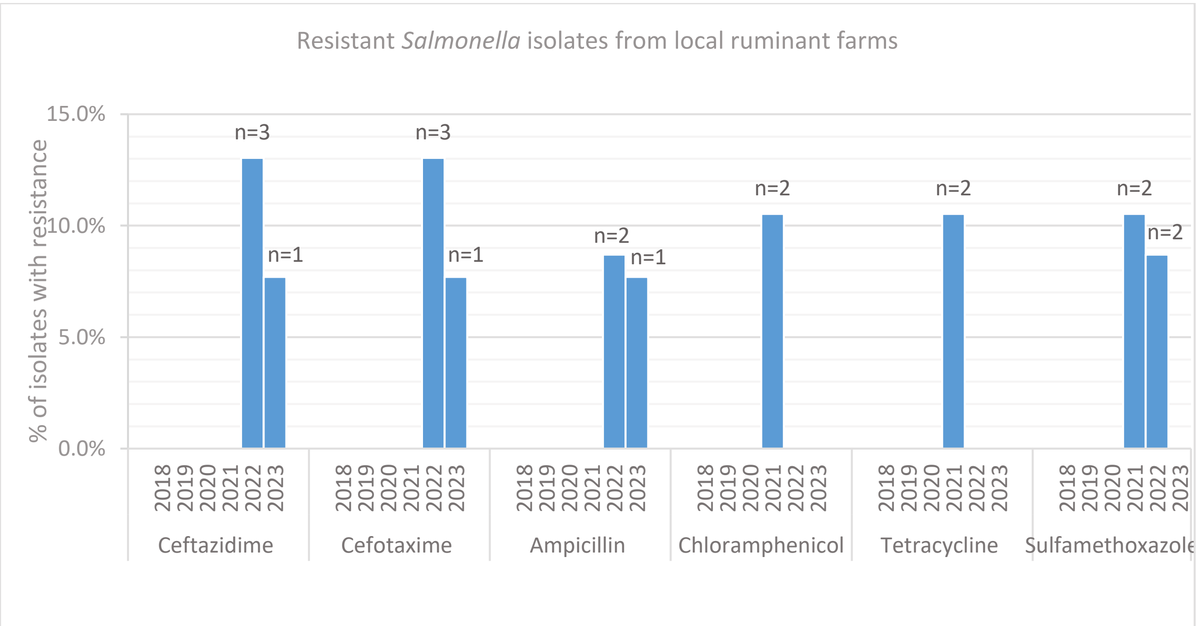
Resistance profiles of Salmonella *from local ruminant farms*

Salmonella spp. isolates from local ruminant farms showed no observable resistance to colistin, ciprofloxacin, gentamicin, meropenem and trimethoprim from 2018 to 2023 (data not shown).

Resistance to third generation cephalosporins (cefotaxime and ceftazidime) was observed in *Salmonella* spp. isolates from 2022 to 2023 (Figure 39). Further investigation is warranted to determine if these isolates are ESBL-producing. The limited sample size precludes the identification of representative trends from these observations. Continued surveillance of these farms is recommended to monitor any potential spread of ESBL-producing bacteria.

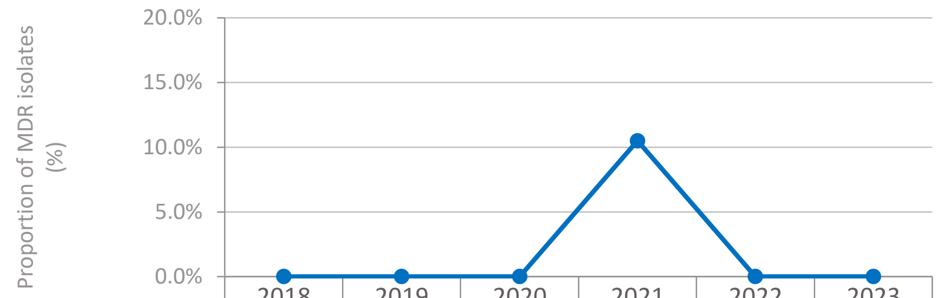
Salmonella spp. isolated from local ruminant farms demonstrated no multi-drug resistance across all years from 2018 to 2023, except for the year 2021, with 2 out of 19 isolates (10.5%) showing MDR to chloramphenicol, sulfamethoxazole and tetracycline (Figure 40).

Figure 39. Percentage of *Salmonella* spp. with resistance, isolated from local ruminant farms in 2018 - 2023 (n = number of isolates with resistance).



*Antimicrobials with no observable resistance (colistin, ciprofloxacin, gentamicin, meropenem, trimethoprim) were not shown in the chart.

Figure 40. Proportion of MDR isolates among *Salmonella* spp. from the local ruminant farms, 2018 – 2023.



	2018	2019	2020	2021	2022	2023
Ruminant (dairy) farms	0.0%	0.0%	0.0%	10.5%	0.0%	0.0%

In Imported and Retail Food Products

Salmonella in Imported food

Detection rates of Salmonella in imported raw food products (including products from local slaughterhouses)

Under SFA's import control surveillance programme, 568 *Salmonella* isolates were obtained from 7665 (7.4%) imported raw food products comprising meat and seafood (beef, chicken mutton/lamb, pork, fish and other seafood) as well as poultry and pork products from local slaughterhouses tested in 2022 and 2023. The numbers of samples tested in 2020 and 2023 are shown in Table 4.

Table 4. Number of imported raw food product (including products from local slaughterhouses) tested in 2020 - 2023 for *Salmonella* spp.

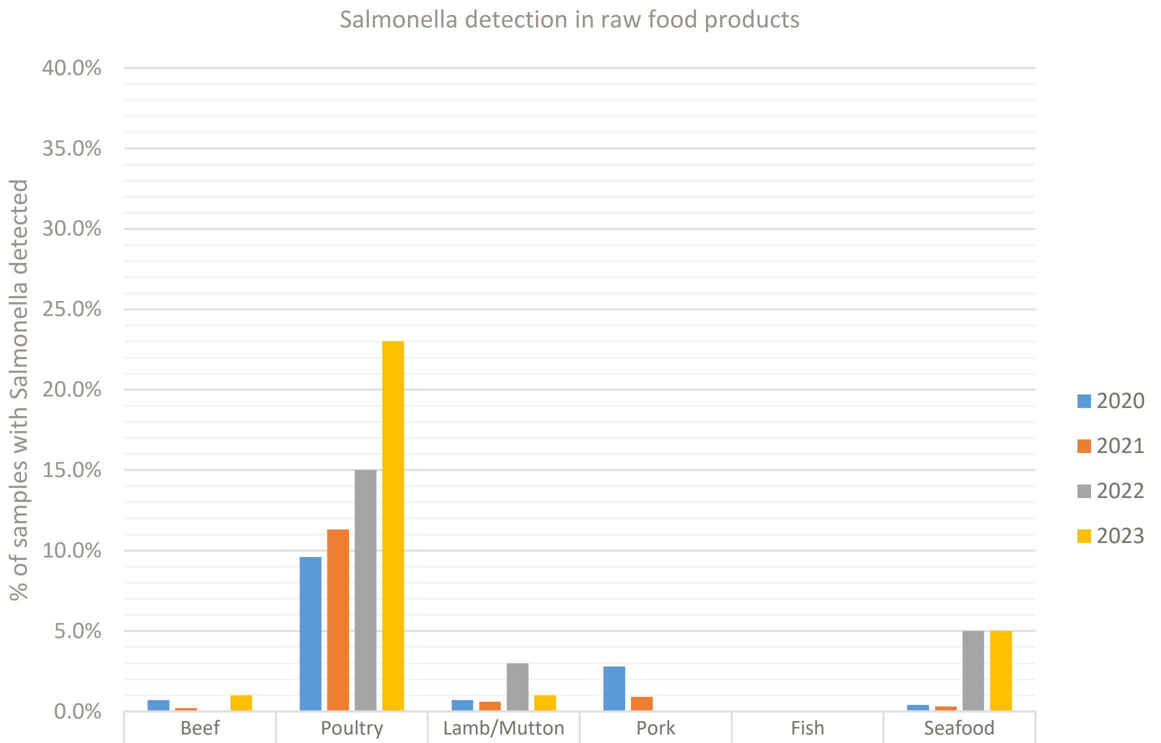
	Beef	Poultry	Lamb/Mutton	Pork	Fish	Seafood	Total samples tested
2020	1184	1132	427	834	132	279	3988
2021	1372	1272	354	964	136	384	4482
2022	1048	1396	277	816	67	386	3990
2023	1076	1183	307	622	62	425	3675

The prevalence of *Salmonella* spp. was relatively higher in raw poultry and pork products compared to other raw meats and seafood products (Figure 41).

The average detection rate of *Salmonella* in poultry and pork in 2022-2023 (13.5%, 541 isolates from 4017 samples) was higher than that for 2018-2019[19] (6.7%; 488 isolates from 7296 samples) and 2020-2021[13] (10.6%, 430 isolates from 4202 samples). Of 541 *Salmonella* isolates from poultry and pork in 2022-2023, 87.4% (389/541) were obtained from raw chicken meat products.

[19] One Health Report on AMR and AMU, 2019

Figure 41: Percentage (%) of *Salmonella* spp. detected in imported raw food products (including products from local slaughterhouses), 2020-2023



	Beef	Poultry	Lamb/Mutton	Pork	Fish	Seafood
2020	0.7%	9.6%	0.7%	2.8%	0.0%	0.4%
2021	0.2%	11.3%	0.6%	0.9%	0.0%	0.3%
2022	0.0%	15.0%	3.0%	0.0%	0.0%	5.0%
2023	1.0%	23.0%	1.0%	0.0%	0.0%	5.0%

Resistance profile of Salmonella isolates from imported raw food products (including products from local slaughterhouses)

Salmonella isolates were subjected to AST by microbroth dilution applying CLSI breakpoints (M100, 30th Edition). Tests for Minimum Inhibitory Concentration (MIC) were performed with 10 classes of 11 antimicrobials (ampicillin, cefotaxime, ceftazidime, ciprofloxacin, chloramphenicol, colistin, gentamicin, meropenem, sulfamethoxazole, tetracycline and trimethoprim) using the Sensititre™ Asia Surveillance Plates for *Salmonella/E. coli* (see Appendix II. AMR Methodology). *Salmonella* spp. serovars was determined by serotyping and/or Whole Genome Sequencing (WGS).

Over 60% of Salmonella isolates tested were resistant to tetracycline, sulfamethoxazole and ampicillin. Among the isolates examined, resistance to cephalosporin antibiotics including cefotaxime and ceftazidime was observed in 23.1% to 28.2% of the isolates. Resistance rates showed a slight decline in 2022-2023 when compared to the 2020-2021 (Figure 42). The number of isolates tested are shown in Table 5.

Figure 42. Percentage (%) of antibiotic-resistant *Salmonella* spp. isolated from imported raw food products (including products from local slaughterhouses), 2018 - 2023

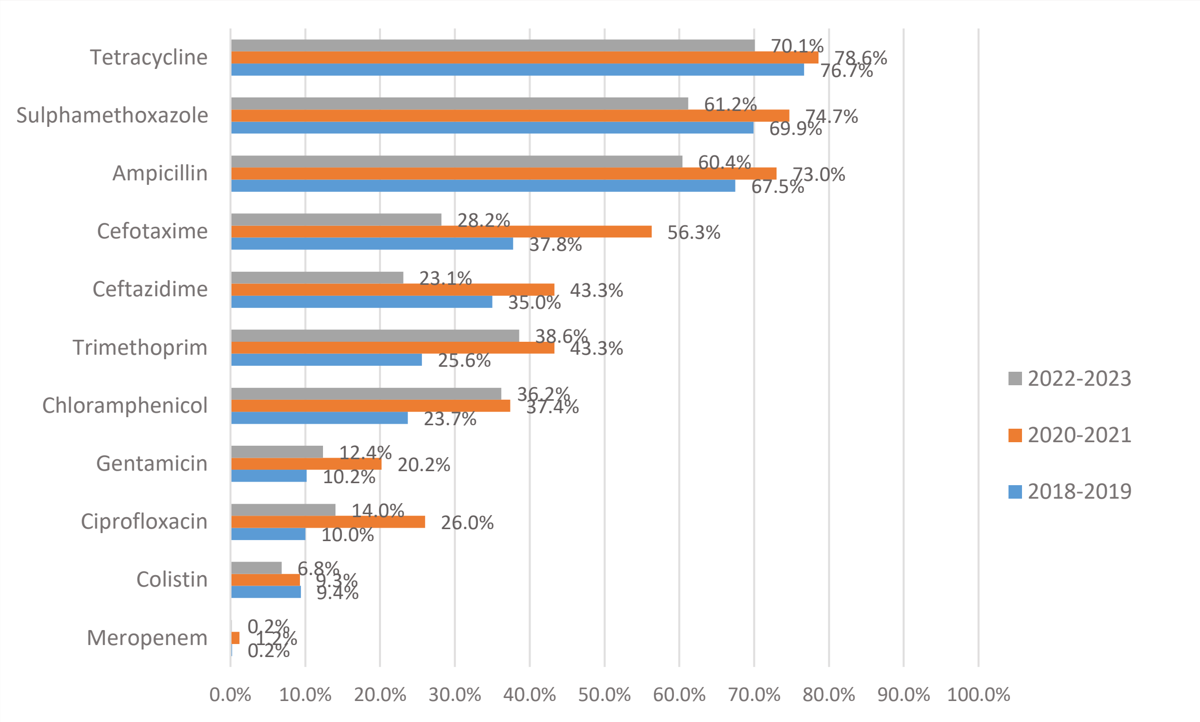


Table 5. Number of *Salmonella* isolates detected in imported raw poultry (chicken and duck) and pork products (including products from local slaughterhouses), 2018-2023

	Chicken	Duck	Pork	Total
2018 - 2019	311	61	117	489
2020 - 2021	318	46	66	430
2022- 2023	389	84	68	541

MDR Salmonella in chilled and frozen chicken products

Among 389 Salmonella isolates from imported chilled and frozen chicken meat products in 2022 and 2023, 64.0% of the isolates tested were found to be MDR (Table 6).

Table 6. Percentage (%) of MDR *Salmonella* in imported chicken meat products, 2018 – 2023

Product type	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**
Imported raw chilled chicken products (including products from local slaughterhouses)	67.8% (40/59)	73.2% (41/56)	55.0% (22/40)	89.0% (73/82)	50.0% (37/73)	73.2% (120/164)
Imported frozen chicken products	74.1% (80/108)	79.5% (70/88)	64.6% (64/99)	89.7% (87/97)	65.2% 60/92	54.4% 31/57

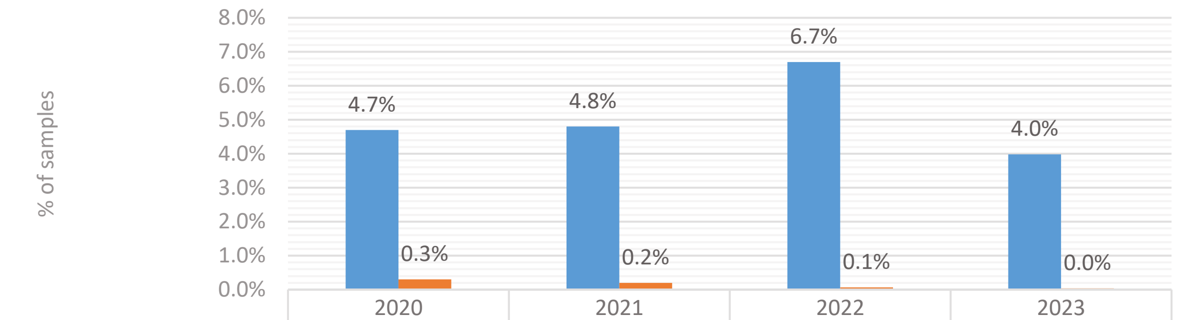
Note: MIC tests using Sensititre™ Asia Surveillance Plates for *Salmonella/E. coli* were introduced in 2018. Due to changes in methodology, 2018-2021 data are not trended with MDR *Salmonella* data reported for 2011-2017.

Salmonella from retail food products

Under the Market Monitoring Programme (MMP), SFA monitors Cooked/Ready-To-Eat (RTE) food prepared and/or sold at retail food premises (e.g., hawker centres, restaurants, coffee shops, caterers and food courts) as well as food products from wet markets, supermarkets and online marts. SFA also monitors raw food products (beef, chicken mutton/lamb, pork, fish and other seafood) from wet markets and supermarkets under its MMP and AMR surveillance programme.

Overall, the detection of *Salmonella* in raw food products remained relatively stable at retail (approximately 5.0%) from 2020-2023 (Figure 43), where similar rates were observed in 2018 and 2019 [19], and in 2020 and 2021(Table 7).

Figure 43. Percentage (%) of *Salmonella* spp. detected in Raw Products and Cooked/RTE food at retail, 2020 – 2023



	2020	2021	2022	2023
Raw Products	4.7%	4.8%	6.7%	4.0%
Cooked/RTE products	0.3%	0.2%	0.1%	0.0%

Table 7. Number of Raw food and Cooked/RTE products tested for *Salmonella* spp. in 2020-2023

	Raw Food Products	Cooked/RTE food products
2020	1204	1658
2021	3021	4547
2022	2414	4003
2023	2767	4379
4-year Total	9406	14,587
No. of isolates obtained	473	20
Detection rate	5.0%	0.14%

Resistance profiles of Salmonella from retail food products

The antibiotic resistance profiles of a total of 276 *Salmonella* isolated from retail food products in 2022 and 2023 were examined, comprising 271 isolates from raw food products and 5 isolates from cooked/RTE products. There was an overall decrease in the resistance rates of isolates to most antibiotics tested in 2022-2023, as compared to 2020-2021.

Of the isolates tested from retail raw food products, over 60% were resistant to tetracycline and ampicillin (Figure 44). In addition, more than 40% of isolates were resistant to trimethoprim, sulfamethoxazole, chloramphenicol and 20% to cephalosporins. Compared to data in the 2019 and 2021 reports, the overall percentage of isolates resistant to antimicrobials had decreased in 2023. The proportion of antimicrobial resistant isolates from cooked/ready-to-eat food products appeared to rise during 2022-2023; nevertheless, the small sample size (n=5) fell below the threshold required for reliable statistical interpretation (Figure 45). Surveillance testing found 66.3% and 59.8% of *Salmonella* isolates from retail raw chilled chicken meat products to be MDR in 2022 and 2023 respectively. MDR Salmonella was also isolated from raw frozen chicken meat products, but numbers were too few to provide reliable estimates of MDR rates (Table 8).

Figure 44. Percentage (%) of antibiotic-resistant *Salmonella* spp. isolates from retail raw food products, 2020 - 2023

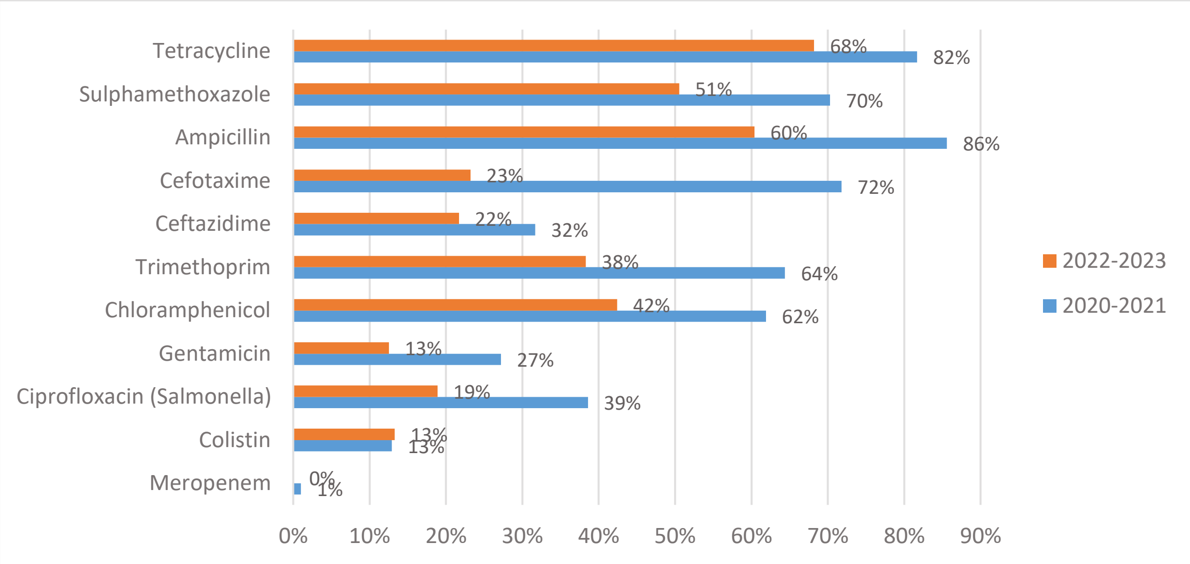
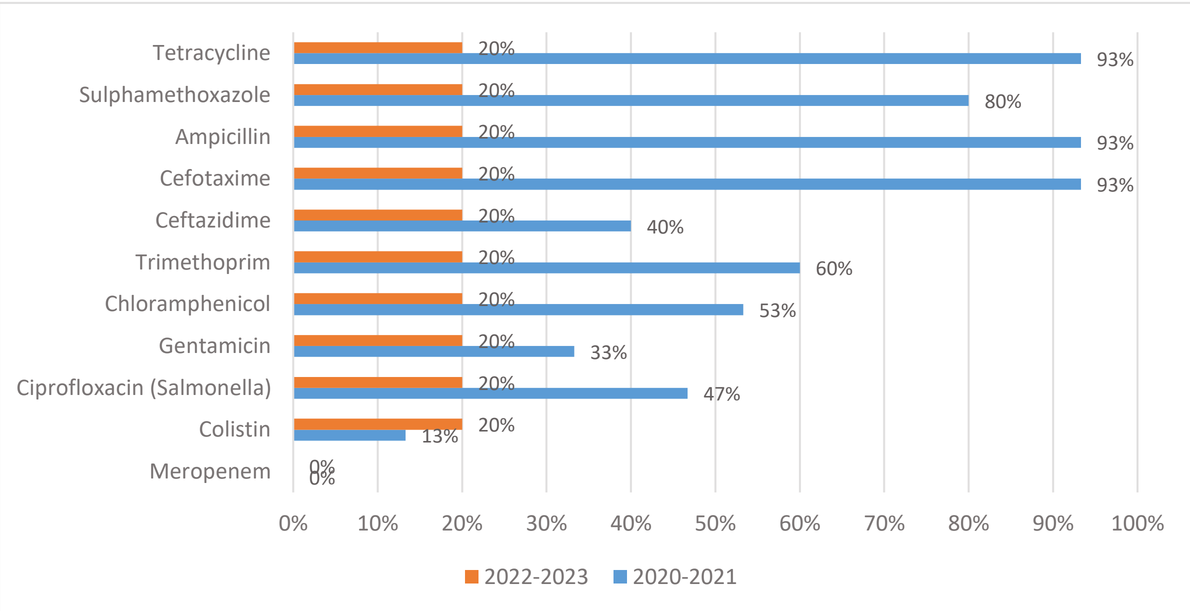


Figure 45. Percentage (%) of antibiotic-resistant *Salmonella* spp. isolates* from Cooked/RTE food products at retail, 2020 - 2023



*Sample size n=5. One isolate demonstrated resistance to 10 of the 11 tested antibiotics, representing 20% of the sample.

Table 8. Percentage (%) of MDR *Salmonella* in retail raw chicken meat products, 2020 - 2023

Product type	**2017-2018**[19]	**2020**	**2021**	**2022**	**2023**
Retail chilled chicken products	50.9% (108/204)	51.4% (19/37)	9.9% (8/81)	66.0% (35/53)	59.8% (49/82)
Retail frozen chicken products		100% (4/4)^	66.7% (4/6)^	92.9% (13/14)^	100% (5/5)^

Note: MIC tests using Sensititre™ Asia Surveillance Plates for *Salmonella/E. coli* were introduced in 2018. Due to changes in methodology, 2020-2021 data are not trended with MDR *Salmonella* data reported for 2011-2019.
^ Number of isolates recovered were below the threshold of reliability.

Antimicrobial resistance in *E. coli*

In healthy production animals

Monitoring of AMR profiles of indicator *E. coli* from local poultry and ruminant farms was introduced in November 2017. *E. coli* was isolated from more than 95% of healthy local farm animals in 2022 and 2023 (Table 9), which is not surprising as *E. coli* are commensal bacteria.

Table 9. Percentage prevalence of *E. coli* and the number of *E. coli* isolates from local farm samples (in parentheses), 2018 – 2023.

Farm	2018	2019	2020	2021	2022	2023
Chicken	79.0% (387/490)	81.1% (241/297)	93.6% (468/500)	94.0% (311/331)	98.4% (62/63)	97.7% (211/216)
Quail	95.5% (84/88)	91.7% (88/96)	84.8% (78/92)	92.5% (74/80)	100% (6/6)	95.0% (42/44)
Ruminant (dairy)	93.6% (161/172)	96.3% (211/219)	94.3% (230/244)	95.7% (245/256)	98.4% (250/254)	98.9% (212/214)

Note: Not all isolates were used for subsequent AST

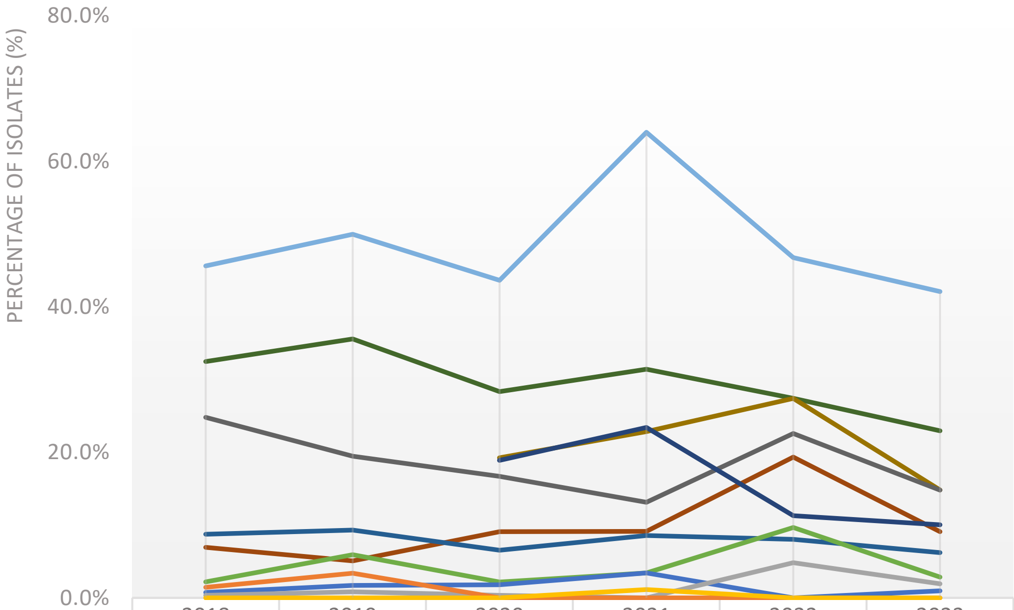
Resistance profiles of *E. coli*

<u>Chicken farms</u>

From 2018 to 2023, the overall percentage resistance to most antimicrobials tested were relatively stable for most antimicrobials, with a decreasing trend in resistance to ampicillin (Figure 42). The spike in resistance to tetracycline in 2021 was consistent with the increased tetracycline AMU reported in the same year for the terrestrial food producing animal sector (Figure 16). The percentage resistance to tetracycline subsequently tapered off in 2022 and 2023 to levels similar to those in previous years, following a decrease in the AMU for tetracycline.

E. coli isolates in 2022 (n=62) and 2023 (n=209), were most frequently resistant to tetracycline, followed by ampicillin, trimethoprim and nalidixic acid. All isolates examined in 2022 and 2023 were susceptible to colistin and meropenem. Low levels of resistance to third generation cephalospoins (cefotaxime and ceftazidime) were observed (Figure 46); additional testing would be required to determine if these are ESBL-producing.

Figure 46. Percentage resistance of *E. coli* isolated in local chicken farms, 2018-2023



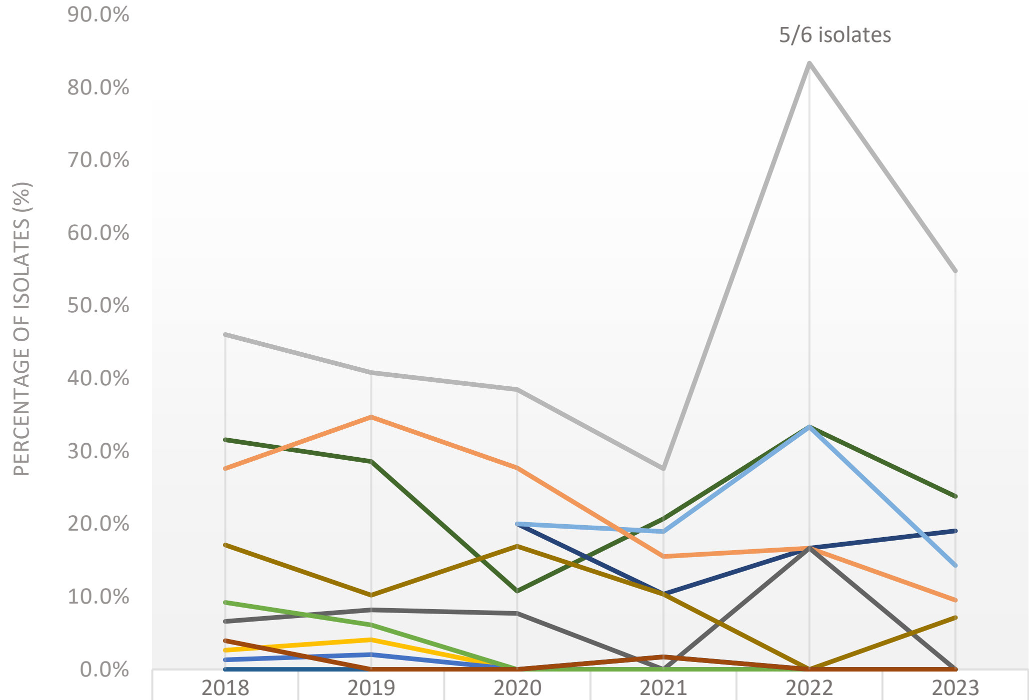
	2018	2019	2020	2021	2022	2023
Tetracycline	45.6%	50.0%	43.6%	64.0%	46.8%	42.1%
Ampicillin	32.5%	35.6%	28.4%	31.4%	27.4%	23.0%
Trimethoprim			19.3%	22.9%	27.4%	14.8%
Nalidixic acid	24.8%	19.5%	16.7%	13.1%	22.6%	14.8%
Ciprofloxacin	6.9%	5.1%	9.1%	9.1%	19.4%	9.1%
Sulfamethoxazole			18.9%	23.4%	11.3%	10.0%
Chloramphenicol	8.8%	9.3%	6.5%	8.6%	8.1%	6.2%
Cefotaxime	2.2%	5.9%	2.2%	3.4%	9.7%	2.9%
Ceftazidime	0.7%	1.7%	1.8%	3.4%	0.0%	1.0%
Gentamicin	0.4%	0.8%	0.4%	0.0%	4.8%	1.9%
Colistin	1.5%	3.4%	0.0%	0.0%	0.0%	0.0%
Meropenem	0.0%	0.0%	0.0%	1.1%	0.0%	0.0%

Note: Starting in 2020, the monitoring of resistance uses the Sensititre™ Asia Surveillance Plates (ASSECAF and ASSECB; see Appendix 2), which monitors trimethoprim and sulfamethoxazole resistance separately.

<u>Quail farms</u>

Consistent with data from the chicken farms, tetracycline resistance was also the most prevalent for *E. coli* isolates from local quail farms (Figure 47). In 2022, tetracycline resistance was detected in five of the six isolates examined, representing 83.3% of the tested samples. However, the substantially reduced sample size for quail surveillance in 2022 (n=6) may not accurately reflect resistance patterns on the quail farms. Despite this limitation, tetracycline resistance levels in 2023 remained elevated (54.8%) compared to earlier years. Continued monitoring will determine if this represents a temporary fluctuation or an upward trend in AMR development within the quail farming sector.

Figure 47. Percentage resistance of *E. coli* isolated in local quail farms, 2018-2023

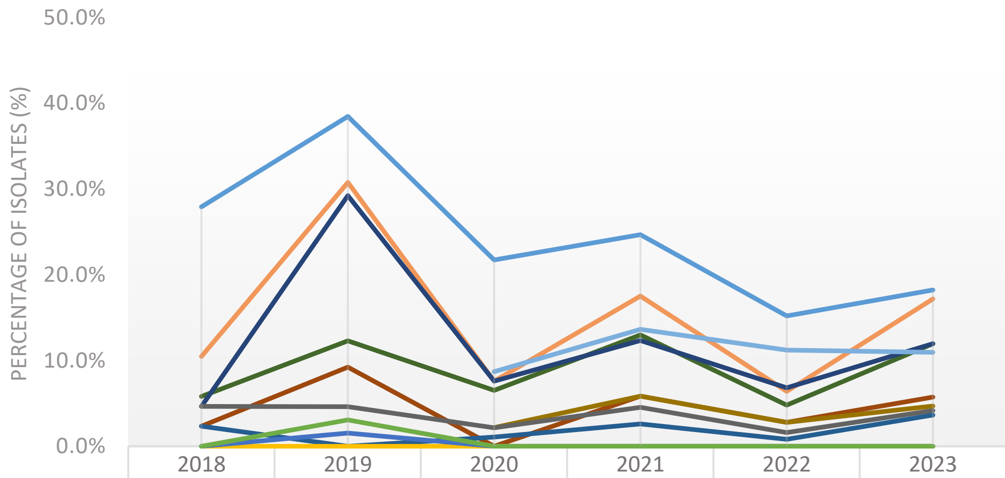


	2018	2019	2020	2021	2022	2023
Tetracycline	46.1%	40.8%	38.5%	27.6%	83.3%	54.8%
Ampicillin	31.6%	28.6%	10.8%	20.7%	33.3%	23.8%
Trimethoprim			20.0%	10.3%	16.7%	19.0%
Sulfamethoxazole			20.0%	19.0%	33.3%	14.3%
Nalidixic acid	27.6%	34.7%	27.7%	15.5%	16.7%	9.5%
Chloramphenicol	6.6%	8.2%	7.7%	0.0%	16.7%	0.0%
Ciprofloxacin	17.1%	10.2%	16.9%	10.3%	0.0%	7.1%
Gentamicin	2.6%	4.1%	0.0%	0.0%	0.0%	0.0%
Ceftazidime	1.3%	2.0%	0.0%	0.0%	0.0%	0.0%
Cefotaxime	9.2%	6.1%	0.0%	0.0%	0.0%	0.0%
Meropenem	0.0%	0.0%	0.0%	1.7%	0.0%	0.0%
Colistin	3.9%	0.0%	0.0%	1.7%	0.0%	0.0%

Ruminant farms

The *E. coli* isolates from ruminant farms demonstrated alternating fluctuations of AMR levels for most antimicrobials over the years (Figure 48). Notably, a general decreasing trend was observed for tetracycline resistance, with levels below 20% in 2022 and 2023. The isolates were most frequently resistant to tetracycline and ampicillin. Since 2020, all *E. coli* isolates were consistently susceptible to colistin, gentamicin and meropenem. Resistance to third-generation cephalosporins (cefoxatime and ceftazidime) was detected in several isolates. Further testing would be required to confirm if these are ESBL-producing strains.

Figure 48. Percentage resistance of *E. coli* isolated in local ruminant farms, 2018-2023

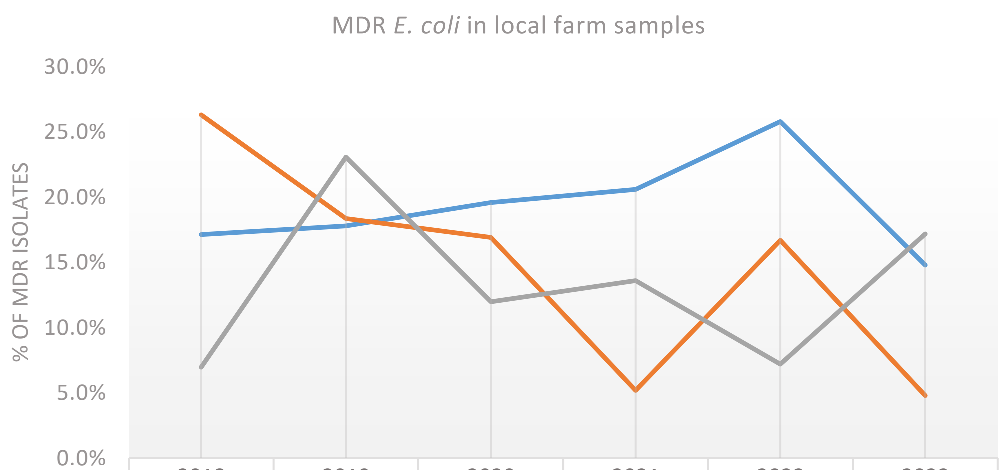


	2018	2019	2020	2021	2022	2023
Tetracycline	27.9%	38.5%	21.7%	24.7%	15.2%	18.2%
Ampicillin	10.5%	30.8%	7.6%	17.5%	6.4%	17.2%
Cefotaxime	5.8%	12.3%	6.5%	13.0%	4.8%	12.0%
Nalidixic acid	4.7%	29.2%	7.6%	12.3%	6.8%	12.0%
Sulfamethoxazole			8.7%	13.6%	11.2%	10.9%
Ciprofloxacin	2.3%	9.2%	0.0%	5.8%	2.8%	5.7%
Trimethoprim			2.2%	5.8%	2.8%	4.7%
Ceftazidime	4.7%	4.6%	2.2%	4.5%	1.6%	4.2%
Chloramphenicol	2.3%	0.0%	1.1%	2.6%	0.8%	3.6%
Meropenem	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Gentamicin	0.0%	1.5%	0.0%	0.0%	0.0%	0.0%
Colistin	0.0%	3.1%	0.0%	0.0%	0.0%	0.0%

MDR *E. coli*

The percentage of MDR *E. coli* isolated from local farms (chicken, quail, ruminant) remained consistently below 30% throughout the period from 2018 to 2023 (Figure 49). In chicken farms, a gradual increase in MDR *E. coli* prevalence was observed from 2018 to 2022, before declining to 14.8% in 2023. There was a decrease in MDR *E. coli* prevalence to 5.2% in 2021 for local quail farms, with levels remaining at 4.8% in 2023. The elevated percentage observed in 2022 at 16.7% for quail farms should be interpreted with caution, as this figure was derived from only six isolates and may not provide a representative assessment of the broader population. In local ruminant farms, MDR *E. coli* prevalence fluctuated across the years, with the most recent data showing a prevalence of 17.2% in 2023.

Figure 49. Proportion of MDR *E. coli* isolates in local farm samples, 2018 - 2023.



	2018	2019	2020	2021	2022	2023
Chicken	17.2%	17.8%	19.6%	20.6%	25.8%	14.8%
Quail	26.3%	18.4%	16.9%	5.2%	16.7%	4.8%
Ruminant (dairy)	7.0%	23.1%	12.0%	13.6%	7.2%	17.2%

In Imported and Retail Food Products

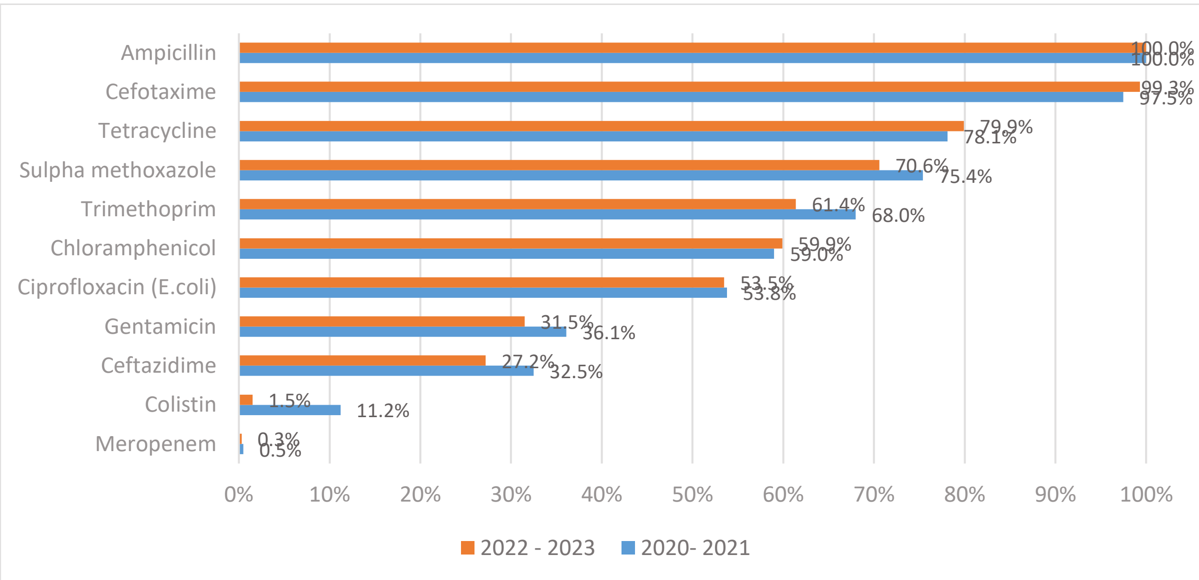
ESBL-Ec in Imported Raw Food Products (including products from local slaughterhouses and aquatic farms)

ESBL-Ec can be found in food-producing animals and may also be present in food products due to extraneous contamination along the food supply chain, such as during handling or processing. Under SFA's AMR surveillance programme, a total of 738 ESBL-Ec isolates were obtained from 4568 imported (including products from local slaughterhouses and aquatic farms) raw food products (beef, chicken mutton/lamb, pork, fish and other seafood) tested in 2022 and 2023. ESBL-Ec was most frequently isolated from imported products (including products from local slaughterhouses) and retail raw poultry products (Table 10), with detection rates over 45% in 2022 and over 55% in 2023. In comparison, prevalence of ESBL-Ec in imported products (including products from local slaughterhouse) and retail pork and pork products were lower, ranging from 2.3% to 18.3% in 2022 and 2023 respectively. The resistance proportions of ESBL-Ec isolates in 2022-2023 were similar to those in 2020-2021 (Figure 50).

Table 10. Percentage of *ESBL*-Ec detection in poultry and pork products, 2020 – 2023

Product type	2020	2021	2022	2023
Imported products (including products from local slaughterhouses) poultry (chicken and duck)	53.3% (105/197)	38.0% (184/485)	46.7% (311/666)	55.8% (277/496)
Retail poultry (chicken and duck) products	59.4% (98/165)	39.4% (180/457)	39.0% (145/371)	36.5% (172/471)
Imported pork products (including products from local slaughterhouse)	4.1% (5/122)	5.7% (10/176)	18.3% (24/131)	18.0% (13/72)
Retail pork products	4.3% (6/140)	8.8% (33/375)	3.0% (11/366)	2.3% (8/352)

Figure 50. Percentage (%) of antibiotic resistant ESBL-Ec isolates from imported (including products from local slaughterhouses and aquatic farms) raw food products, 2020 -2023



Extended Spectrum Beta-lactamase-producing E. coli (ESBL-Ec) in Retail Food Products

Under the SFA's AMR surveillance programme in 2022 and 2023, a total of 368 ESBL-Ec isolates were obtained from 2709 samples of retail raw food products (beef, chicken mutton/lamb, pork, fish and other seafood). Among the isolates tested, over 70% were resistant to ampicillin, cefotaxime, tetracycline and sulfamethoxazole, trimethoprim and chloramphenicol, similarly to the period of 2020-2021 (Figure 51). Retail food products had higher rates of detection of ESBL-Ec E than products sampled upstream at points of import, local slaughterhouses and aquatic farms (Table 11).

Figure 51. Percentage (%) of antibiotic resistant ESBL Ec isolates from retail raw food products, 2020-2023

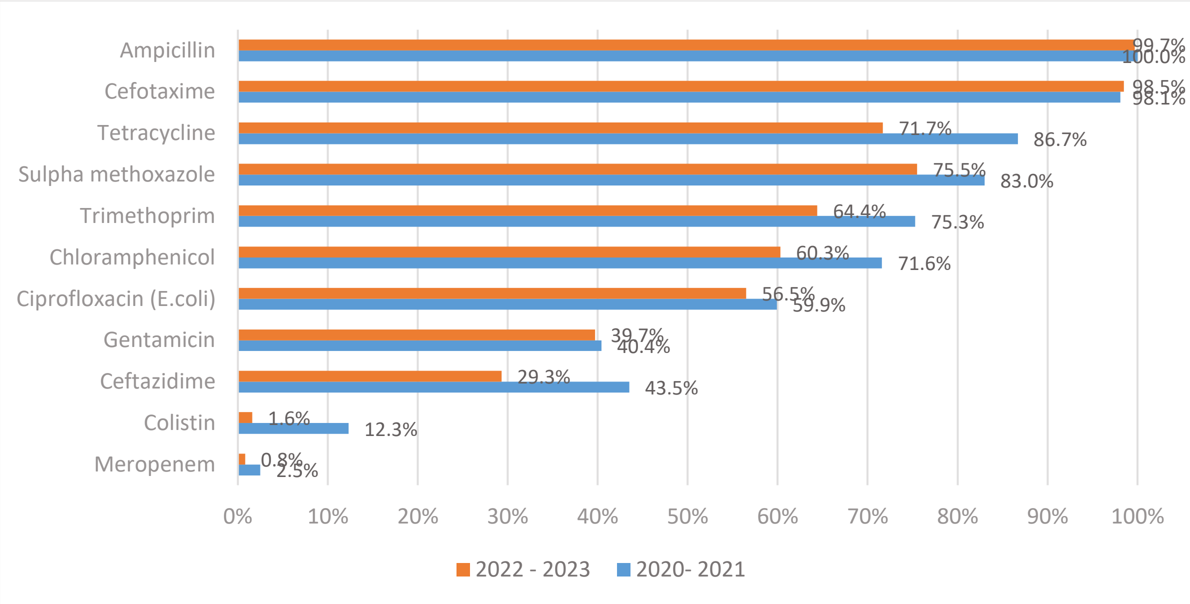


Table 11. Percentage (%) of ESBL-Ec detection in imported raw food products (including products from local slaughterhouses and aquatic farms) vs retail raw food products, 2020 – 2023.

Source type	2020	2021	2022	2023
Imported raw food products (including products from local slaughterhouses and aquatic farms)	15.7% (117/745)	13.6% (249/1830)	20.0% (343/1714)	13.8% (395/2854)
Retail raw food products	22.3% (98/439)	17.5% (226/1289)	13.3% (170/1278)	13.8% (198/1431)

Antimicrobial Resistance in Bacteria from Companion Animals and Wildlife

AMR surveillance in companion animals

AMR has implications for both human and animal populations. Despite the frequent use of antimicrobials in companion animals and their regular contact with humans, the role of companion animals in AMR remains inadequately understood[20]. National AMR surveillance programmes in companion animals are therefore essential, focusing on bacteria of concern to public and animal health. NParks' surveillance of companion animals comprises both passive and active surveillance, and includes *E. coli*, *Klebsiella pneumoniae*, methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant *Staphylococcus pseudintermedius* (MRSP). Bacteria isolated are subjected to AST against clinically and epidemiologically important antimicrobial agents according to CLSI standards (Appendix II).

E. coli is ubiquitous in the intestinal tract of humans and animals. The organism can acquire various AMR genes, leading to the emergence of MDR strains. Resistant *E. coli* in companion animals pose a potential risk of transmission to humans, especially through close contact.

K. pneumoniae, an opportunistic pathogen causing infections in various hosts, including companion animals, presents challenges due to its ability to develop resistance to multiple antibiotics, including beta-lactams. Most *K. pneumoniae* exhibit intrinsic resistance towards ampicillin due to the presence of the chromosomal SHV gene which encodes a beta-lactamase enzyme that breaks down ampicillin. Besides beta-lactamase production, *K. pneumoniae* may employ multiple antimicrobial resistance mechanisms, such as biofilm formation, upregulation of efflux pumps, and reduced outer membrane permeability to antibiotics. These diverse resistance mechanisms enable *K. pneumoniae* to develop resistance across multiple antibiotic classes.

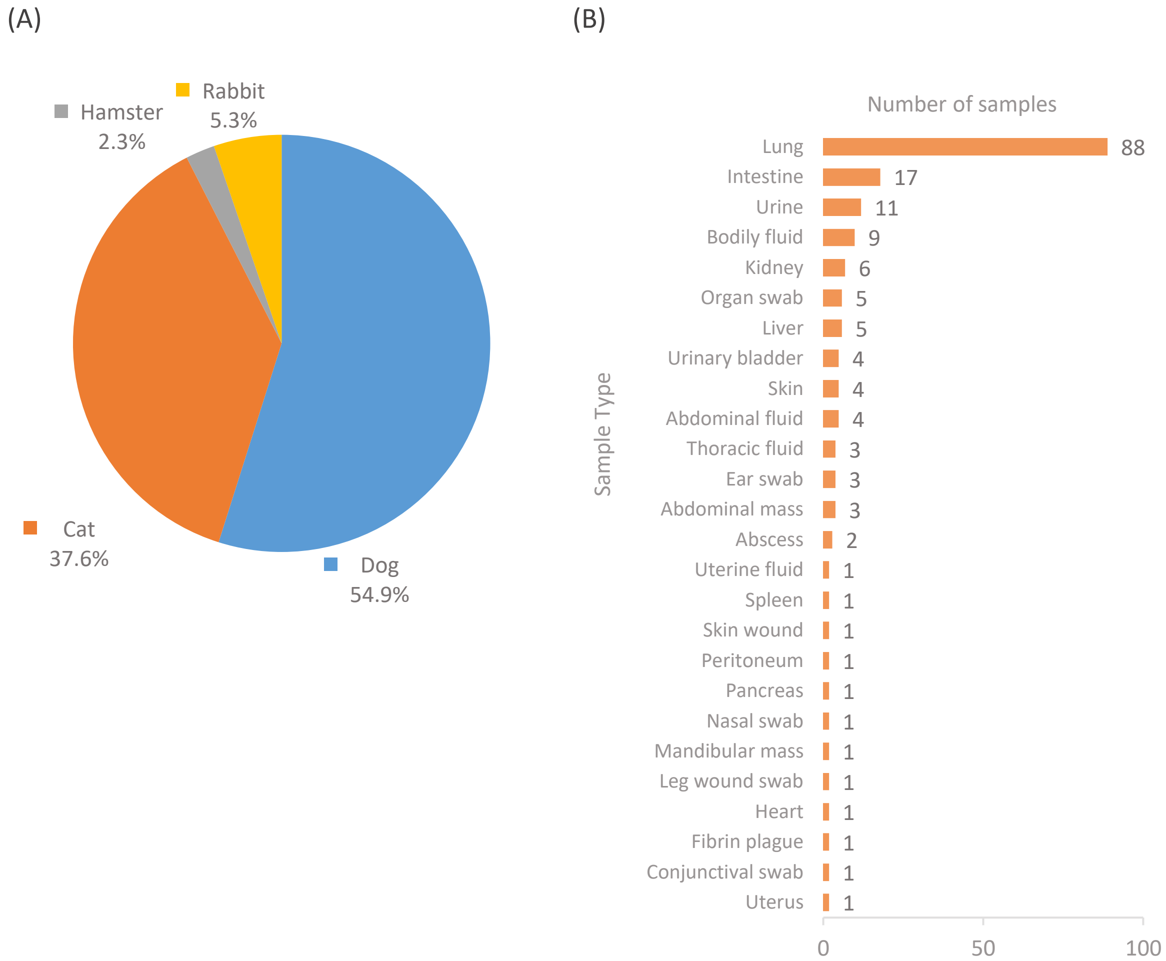
MRSA and **MRSP** are frequently associated with skin, wound, or surgical site infections, otitis, and urinary tract infections in cats and dogs. While MRSA is often acquired from humans, serving as potential bacterial reservoirs, MRSP is more commonly isolated in dogs and cats. MRSP tends to colonise dogs, posing a risk of zoonotic transmission. Although human infections of MRSP are rare[21], both MRSA and MRSP are concerning due to limited treatment options for infections by these organisms and the potential for transmission between animals and humans. MRSA/P characteristically exhibit resistance to many common antibiotics. Infections by MRSA and MRSP are therefore harder to treat.

[20] Damborg P., Broens E.M., Chomel B.B., Guenther S., Pasmans F., Wagenaar J.A., Weese J.S., Wieler L.H., Windahl U., Vanrompay D., et al. Bacterial Zoonoses Transmitted by Household Pets: State-of-the-Art and Future Perspectives for Targeted Research and Policy Actions. J. Comp. Pathol. 2016;155:S27–S40.
[21] Reflection paper on meticillin-resistant *Staphylococcus pseudintermedius*. EMA/CVMP/SAGAM/736964/ 2009 Committee for Medicinal Products for Veterinary Use (CVMP), 20 September 2010.

Sick companion animals

NParks conducts passive AMR surveillance on sick companion animals, focusing on *E. coli*, *K. pneumoniae*, MRSA and MRSP from clinical samples submitted by veterinarians. In 2022 and 2023, the samples were mainly collected from dogs, followed by cats, and rabbits (Figure 52A), similar to the distribution in 2020 and 2021. Lung (50.2%), intestine (9.7%) and urine (6.3%) were the most common sample types received by the laboratory (Figure 52B).

Figure 52. Distribution of samples for passive AMR surveillance on sick companion animals by (A) species and (B) sample type, 2022-2023.



<u>*E. coli, K. pneumoniae* and MRSP in companion animals</u>

In 2022, *E. coli* and *K. pneumoniae* were isolated from 48 (70.6%) and 16 (23.5%) companion animals, respectively. In 2023, *E. coli* and *K. pneumoniae* were obtained from 49 (75.4%) and 19 (29.2%) companion animals, respectively. Few *S. aureus* and *S. pseudintermudius* isolates were obtained from the passive surveillance: Less than 10 MRSA and MRSP were isolated per year from 2018 to 2023. A total of 3 MRSP were isolated in 2022 and 2023, while there were no MRSA isolates obtained in this period (Table 12).

Table 12. Proportion (%) of *E. coli, K. pneumoniae* and MRSA/P isolated from sick companion animal samples and the respective number of isolates (in parentheses), 2018-2023.

Farm	2018	2019	2020	2021	2022	2023
E. coli	-	-	49.3% (33/67)	35.0% (14/40)	70.6% (48/68)	75.4% (49/65)
K. pneumoniae	-	-	11.9% (8/67)	10.0% (4/40)	23.5% (16/68)	29.2% (19/65)
MRSA/P	5.7% (9/158)	6.3% (4/63)	7.5% (5/67)	7.5% (3/40)	2.9% (2/68)	1.5% (1/65)

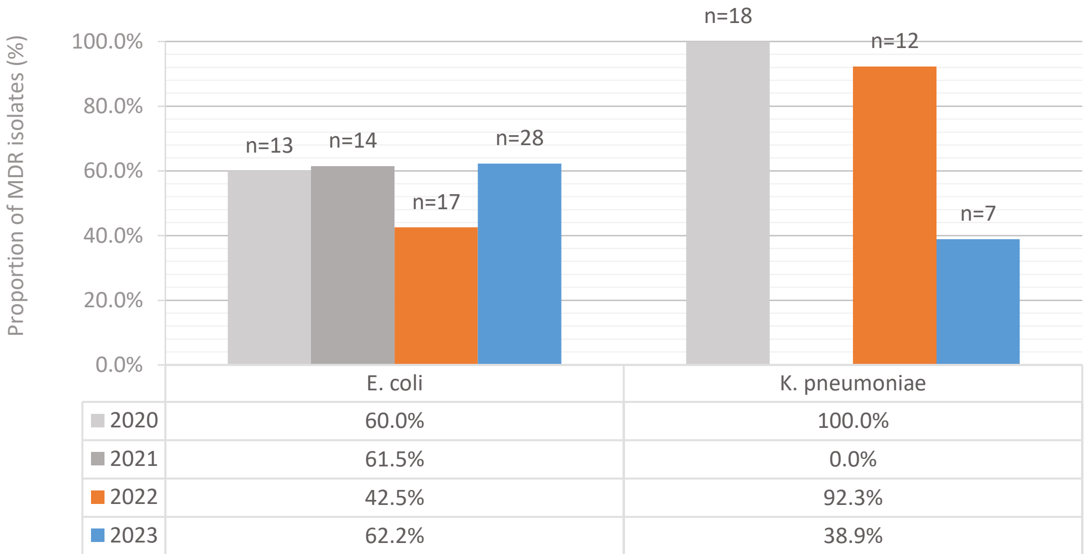
Note: Not all isolates were used for subsequent AST.

Resistance profiles of companion animal isolates

<u>MDR rates of *E. coli* and *K. pneumoniae* isolated from companion animals</u>

The proportion of MDR *E. coli* isolates from companion animals were 42.5% (17/40 isolates) and 62.2% (28/45 isolates) in 2022 and 2023, respectively (Figure 53). The proportion of MDR *K. pneumoniae* isolated from companion animals were 92.3% (12/13 isolates) and 38.9% (7/18 isolates) in 2022 and 2023 respectively. However, the number of isolates (<30) fall below the threshold of reliability for estimating resistance proportions.

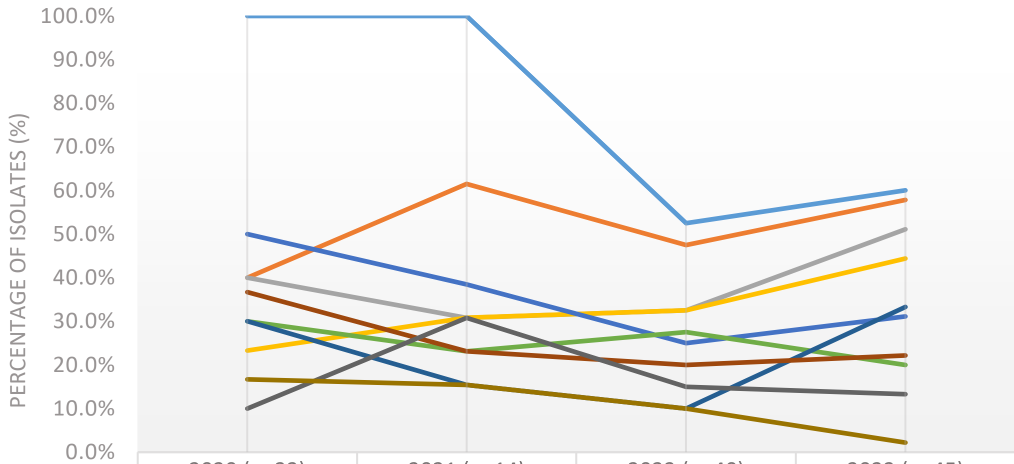
Figure 53. Proportion of MDR *E. coli* and *K. pneumoniae* in sick companion animals, 2018-2023 (n = number of MDR isolates)



<u>*E. coli* from sick companion animals</u>

E. coli isolates from sick companion animals were most frequently resistant to ampicillin (Figure 54). This correlates with the reported AMU trends in the companion animal sector, where penicillins comprised the largest class of antimicrobials across the years (Figure 16). *E. coli* resistant to ampicillin reduced from 100% in 2020 and 2021 to 52.5% in 2022 and 60.0% in 2023. All *E. coli* isolates were susceptible to colistin and meropenem (data not shown).

Figure 54. Percentage resistance of *E. coli* isolated from sick companion animals, 2020-2023 (n= number of isolates tested per year)



	2020 (n=33)	2021 (n=14)	2022 (n=40)	2023 (n=45)
Ampicillin	100.0%	100.0%	52.5%	60.0%
Tetracycline	40.0%	61.5%	47.5%	57.8%
Sulfamethoxazole	40.0%	30.8%	32.5%	51.1%
Trimethoprim	23.3%	30.8%	32.5%	44.4%
Nalidixic acid	50.0%	38.5%	25.0%	31.1%
Cefotaxime	30.0%	23.1%	27.5%	20.0%
Chloramphenicol	30.0%	15.4%	10.0%	33.3%
Ciprofloxacin	36.7%	23.1%	20.0%	22.2%
Gentamicin	10.0%	30.8%	15.0%	13.3%
Ceftazidime	16.7%	15.4%	10.0%	2.2%

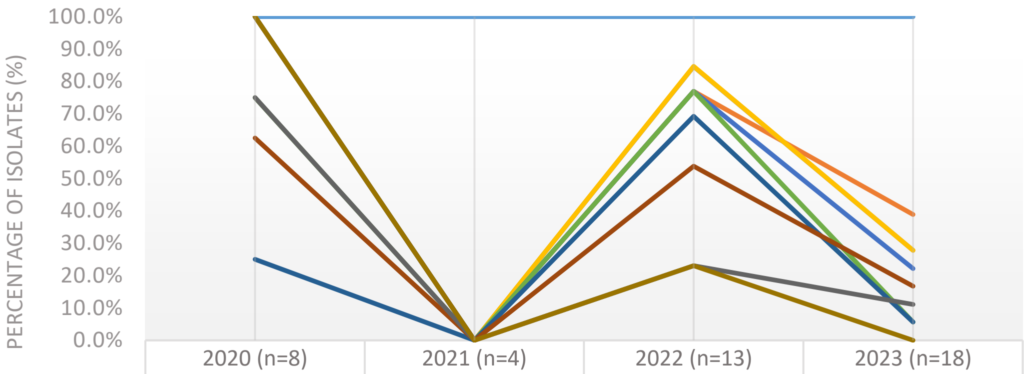
Note: Antimicrobials with no observable resistance (colistin and meropenem) were not shown on the graph.

<u>*K. pneumoniae* from sick companion animals</u>

All *K. pneumoniae* isolated from sick companion animals in 2022 (n=13) and 2023 (n=18) were resistant to ampicillin, consistent with the intrinsic resistance conferred by the chromosomal SHV gene. In 2022, 84.6% of the *K. pneumoniae* isolates were also resistant to sulfamethoxazole and tetracycline, 76.9% were resistant to trimethoprim, ciprofloxacin and ceftazidime, 69.2% of the isolates were resistant to cefotaxime, 53.8% were resistant to gentamicin, and 23.1% were resistant to nalidixic acid and chloramphenicol (Figure 55).

For 2023, resistance rates among isolates were generally lower than 2022, with the majority of antimicrobials exhibiting resistance percentages below 40%. All isolates from 2020 to 2023 demonstrated complete susceptibility to colistin and meropenem (data not shown).

Figure 55. Percentage resistance of *K. pneumoniae* isolated from sick companion animals, 2020-2023 (n= number of isolates tested per year)



	2020 (n=8)	2021 (n=4)	2022 (n=13)	2023 (n=18)
Ampicillin	100.0%	100.0%	100.0%	100.0%
Trimethoprim	100.0%	0.0%	76.9%	38.9%
Sulfamethoxazole	100.0%	0.0%	84.6%	27.8%
Tetracycline	100.0%	0.0%	84.6%	27.8%
Ciprofloxacin	100.0%	0.0%	76.9%	22.2%
Ceftazidime	75.0%	0.0%	76.9%	5.6%
Cefotaxime	25.0%	0.0%	69.2%	5.6%
Gentamicin	62.5%	0.0%	53.8%	16.7%
Nalidixic acid	75.0%	0.0%	23.1%	11.1%
Chloramphenicol	100.0%	0.0%	23.1%	0.0%

Note: Antimicrobials with no observable resistance (colistin and meropenem) were not shown on the graph.

<u>MRSP from sick companion animals</u>

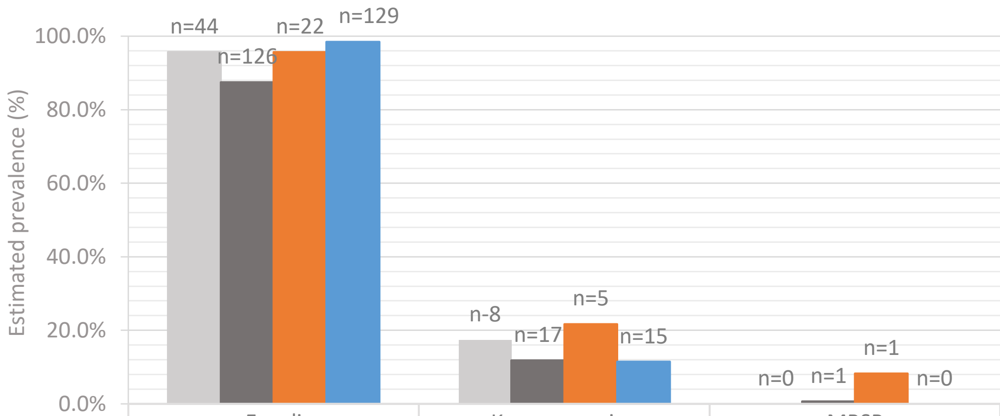
MRSA/P prevalence in clinical samples remained low in 2022-2023, with only three MRSP and no MRSA detected. As expected, all MRSP isolates were multidrug resistant. In 2022, both clinical MRSP isolates exhibited resistance to pradofloxacin, cefovecin, marbofloxacin, enrofloxacin, erythromycin, doxycycline, chloramphenicol, penicillin, tetracycline and oxacillin. One isolate was also resistant to clindamycin, trimethoprim/sulfamethoxazole and gentamicin. The single MRSP isolate from 2023 exhibited resistance to all the above-mentioned antimicrobials except for gentamicin. All three MRSP isolates from both 2022 and 2023 were susceptible to nitrofurantoin.

AMR surveillance on free-roaming dogs

In 2020, NParks embarked on an active AMR surveillance programme targeting *E. coli*, *K. pneumoniae*, MRSA and MRSP in healthy free-roaming dogs across Singapore. Singapore has an estimated population of 2,200 free-roaming dogs that inhabit locations close to human communities. Since 2018, free-roaming dogs have been sterilised and either rehomed or released into the environment under NParks' nationwide Trap-Neuter-Release/Rehoming-Manage (TNRM) Programme.

Free-roaming dogs were sampled from those admitted into the TNRM programme. In 2022, *E. coli* and *K. pneumoniae* were isolated from 22 (95.7%) and five (21.7%) free-roaming dogs, respectively (Figure 56). Out of the 12 *S. pseudintermedius* isolated in free-roaming dogs in 2022, one (8.3%) was MRSP. In 2023, *E. coli* and *K. pneumoniae* were isolated from 129 (98.5%) and 15 (11.5%) free-roaming dogs, respectively. All five *S. pseudintermedius* isolated in free-roaming dogs in 2023 were found susceptible to methicillin (oxacillin). *Staphylococcus aureus* and MRSA were not isolated in free-roaming dogs in 2022 and 2023.

Figure 56. Estimated prevalence of *E. coli, K. pneumoniae* and MRSP in local free-roaming dog populations, 2020-2023 (n = number of samples with bacteria isolated).



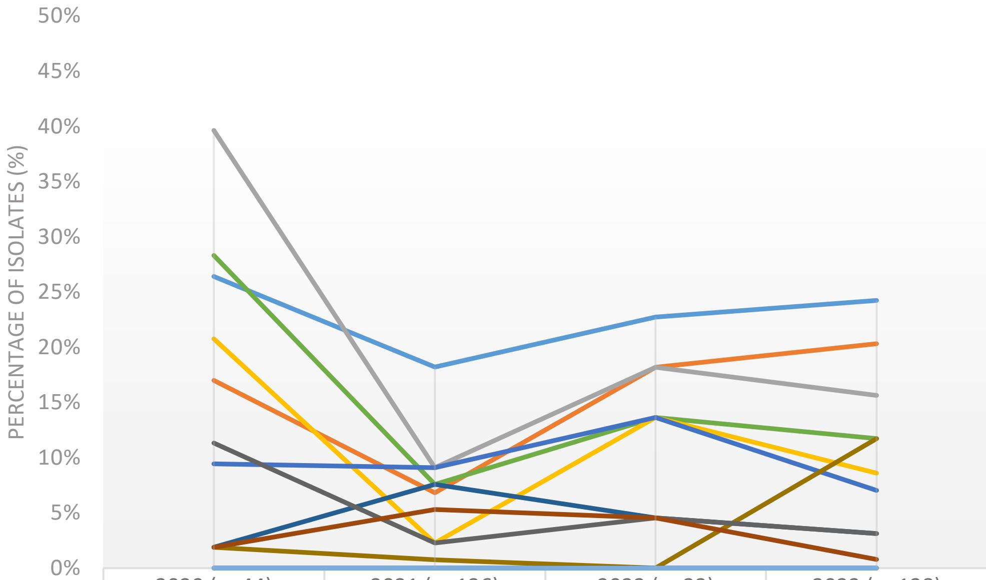
	E. coli	K. pneumoniae	MRSP
2020	95.7%	17.4%	0.0%
2021	87.5%	11.8%	0.7%
2022	95.7%	21.7%	8.3%
2023	98.5%	11.5%	0.0%

<u>Drug-resistant *E. coli* and *K. pneumoniae* in free-roaming dogs</u>

E. coli isolated in 2022 (n=22) and 2023 (n=128) from free-roaming dogs exhibited highest percentage resistance to ampicillin (22.7% in 2022 and 24.2% in 2023), followed by sulfamethoxazole and tetracycline (Figure 57). Isolates were fully susceptible to colistin and meropenem. The higher proportion of *E. coli* resistant to ampicillin relative to other antimicrobials was consistent with reports elsewhere, such as in Thailand[22] and Japan[23]. *K. pneumoniae* isolated from free-roaming dogs in 2022 exhibited resistance to ampicillin but were fully susceptible to cefotaxime, ceftazidime, colistin, gentamicin and meropenem (Figure 57). In 2023, the resistance percentage for ampicillin decreased to 78.6% and isolates were fully susceptible to all other antimicrobials except for cefotaxime (7.1%) and ceftazidime (7.1%).

The resistance percentages of *E. coli* and *K. pneumoniae* isolated from free-roaming dogs (Figures 57 and 58) were generally lower than those from sick companion animals (Figures 49 and 50). As with past years, few MDR *E. coli* and *K. pneumoniae* were recovered from free-roaming dog samples (Figure 59).

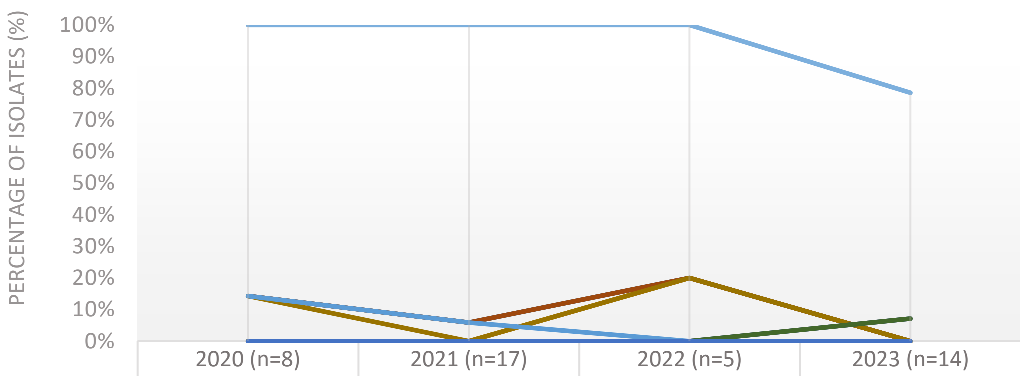
Figure 57. Percentage resistance of *E. coli* isolated from free-roaming dogs, 2020-2023



	2020 (n=44)	2021 (n=126)	2022 (n=22)	2023 (n=128)
Ampicillin	26.4%	18.2%	22.7%	24.2%
Sulfamethoxazole	17.0%	6.8%	18.2%	20.3%
Tetracycline	39.6%	9.1%	18.2%	15.6%
Trimethoprim	28.3%	7.6%	13.6%	11.7%
Chloramphenicol	20.8%	2.3%	13.6%	8.6%
Nalidixic acid	9.4%	9.1%	13.6%	7.0%
Gentamicin	1.9%	0.8%	0.0%	11.7%
Cefotaxime	1.9%	7.6%	4.5%	3.1%
Ciprofloxacin	11.3%	2.3%	4.5%	3.1%
Ceftazidime	1.9%	5.3%	4.5%	0.8%
Meropenem	0.0%	0.0%	0.0%	0.0%
Colistin	0.0%	0.0%	0.0%	0.0%

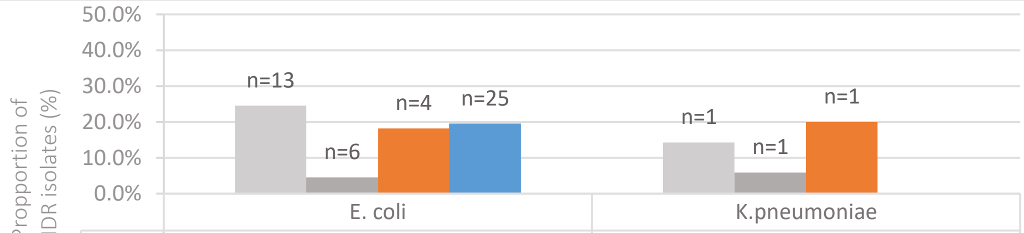
[22] Buranasinsup et al, 2023. Prevalence and characterisation of antimicrobial-resistant *Escherichia coli* isolated from veterinary staff, pets and pet owners in Thailand. Journal of Infections and Public Health, 16(1):194-202
[23] Hata et al, 2022. Surveillance of antimicrobial *Escherichia coli* in Sheltered dogs in the Kanto Region of Japan. Sci Rep, 12:773.

Figure 58. Percentage resistance of *K. pneumoniae* isolated from free-roaming dogs, 2020-2023



	2020 (n=8)	2021 (n=17)	2022 (n=5)	2023 (n=14)
Ampicillin	100.0%	100.0%	100.0%	78.6%
Nalidixic acid	0.0%	0.0%	20.0%	0.0%
Sulfamethoxazole	14.3%	5.9%	20.0%	0.0%
Ciprofloxacin	0.0%	0.0%	20.0%	0.0%
Tetracycline	14.3%	5.9%	20.0%	0.0%
Trimethoprim	14.3%	0.0%	20.0%	0.0%
Cefotaxime	0.0%	0.0%	0.0%	7.1%
Ceftazidime	0.0%	0.0%	0.0%	7.1%
Chloramphenicol	14.3%	5.9%	0.0%	0.0%
Colistin	0.0%	0.0%	0.0%	0.0%
Gentamicin	0.0%	0.0%	0.0%	0.0%
Meropenem	0.0%	0.0%	0.0%	0.0%

Figure 59. Proportion of MDR *E. coli* and *K. pneumoniae* in local free-roaming dog populations, 2020-2023 (n=number of MDR isolates)



	E. coli	K.pneumoniae
2020	24.5%	14.3%
2021	4.5%	5.9%
2022	18.2%	20.0%
2023	19.5%	0.0%

<u>MRSP in free-roaming dogs</u>

The sole MRSP isolate from a free-roaming dog in 2022 was resistant to penicillin, oxacillin, enrofloxacin, marbofloxacin, pradofloxacin, erythromycin, doxycycline and tetracycline, intermediately resistant to gentamicin, and susceptible to cefalotin, cefovecin, clindamycin, nitrofurantoin and trimethoprim (data not shown). The low isolation rates of MRSA/P from free-roaming dogs represent a favourable finding from a public health perspective, as it suggests limited circulation of these multidrug-resistant pathogens in the community animal population.

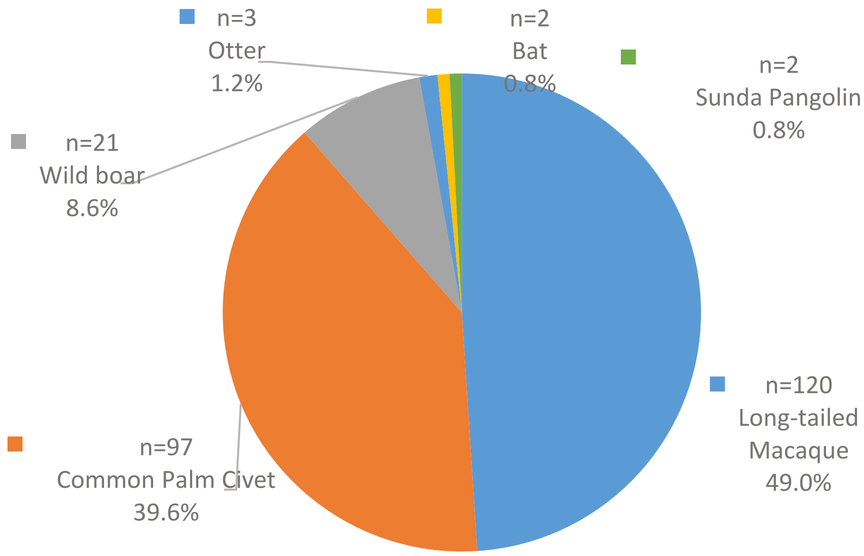
AMR surveillance in wildlife

AMR in wildlife is a growing concern due to its potential impact on ecosystem health and public health[24]. Wildlife can serve as reservoirs of AMR, harbouring resistant bacteria that may be transferred to other animals or humans. Despite an increasing awareness of this issue, there remains a lack of knowledge in this field, hindering our understanding of the dynamics of AMR among wildlife populations. [25,26]

NPark's wildlife AMR surveillance is passive and targets *E. coli* isolated from wild animals. *E. coli*, being a common bacterium found in the intestines of many animals, is often the target bacterium for studying AMR in wildlife.[27] Monitoring AMR in wildlife can aid our understanding of AMR transmission pathways in Singapore's small island state context where urban and non-urban areas lie in close proximity, and where necessary, guides the development of strategies to mitigate the spread of AMR from wildlife to other environments, and vice versa.

In 2022 and 2023, samples were collected opportunistically from a total of 245 animals. The total number of samples collected were higher than the total for 2020 and 2021 (n=109) The highest number of samples were obtained from the long-tailed macaque (49.0%), followed by common palm civet (39.6%), wild boar (8.6%), otter (1.2%), bat (0.8%) and pangolin (0.8%) (Figure 60). Bacteria isolated were subjected to AST against clinically and epidemiologically important antimicrobial agents.

Figure 60. Distribution of samples for passive AMR surveillance on wildlife, 2022-2023



[24] Arnold, K. E., Williams, N. J., & Bennett, M. (2016). 'Disperse abroad in the land': the role of wildlife in the dissemination of antimicrobial resistance. *Biology Letters*, *12*(8), 20160137.
[25] Huijbers PMC, Blaak H, de Jong MCM, Graat EAM, Vandenbroucke-Grauls CMJE, Husman AMDR. 2015 Role of the environment in the transmission of antimicrobial resistance to humans: a review. *Environ. Sci. Technol.* **49**, 11 993–12 004. (doi:10.1021/acs.est.5b02566)
[26] Greig J, Rajic A, Young I, Mascarenhas M, Waddell L, LeJeune J. 2015 A scoping review of the role of wildlife in the transmission of bacterial pathogens and antimicrobial resistance to the food chain. *Zoonoses Public Health* **62**, 269–284. (doi:10.1111/zph.12147)
[27] Lagerstrom, K. M., & Hadly, E. A. (2021). The under-investigated wild side of *Escherichia coli:* genetic diversity, pathogenicity and antimicrobial resistance in wild animals. *Proceedings of the Royal Society B*, *288*(1948), 20210399.

Resistance profile of E. coli from wildlife samples

E. coli was isolated from 113/128 (88.3%) and 106/117 (90.6%) wild animals in 2022 and 2023, respectively (Figure 61A). Of these, three *E. coli* isolated in 2022 and six *E. coli* isolated in 2023 were found to be MDR (Figure 61B). MDR *E. coli* in 2022 were isolated from a long-tailed macaque, common palm civet and otter. While in 2023, three MDR *E. coli* were each isolated from long-tailed macaques and common palm civets.

AST of *E. coli* isolated in wildlife in 2022 and 2023 revealed distinct AMR patterns; they were less frequently resistant (below 9%) to antimicrobials tested (Figure 62) compared to *E. coli* from food-producing and companion animals. All isolates were susceptible to meropenem. Isolates from 2022 were all susceptible to ceftazidime, ciprofloxacin and gentamicin. In 2023, some *E. coli* isolates were resistant to ceftazidime (1.0%), ciprofloxacin (1.0%) and gentamicin (1.0%). 2.7% of the isolates in 2022 and 5.8% of the isolates in 2023 were resistant to trimethoprim (Figure 62).

Figure 61. Proportion of (A) *E. coli* and (B) MDR *E. coli* isolated from wildlife, 2020-2023

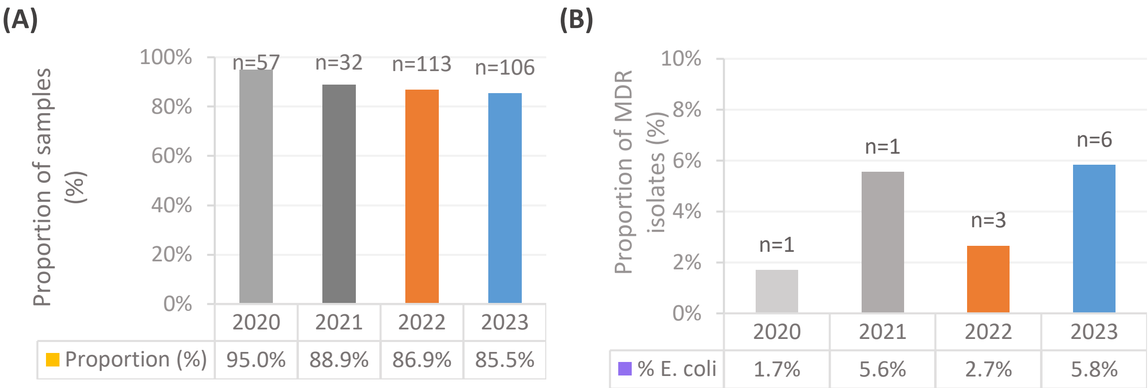
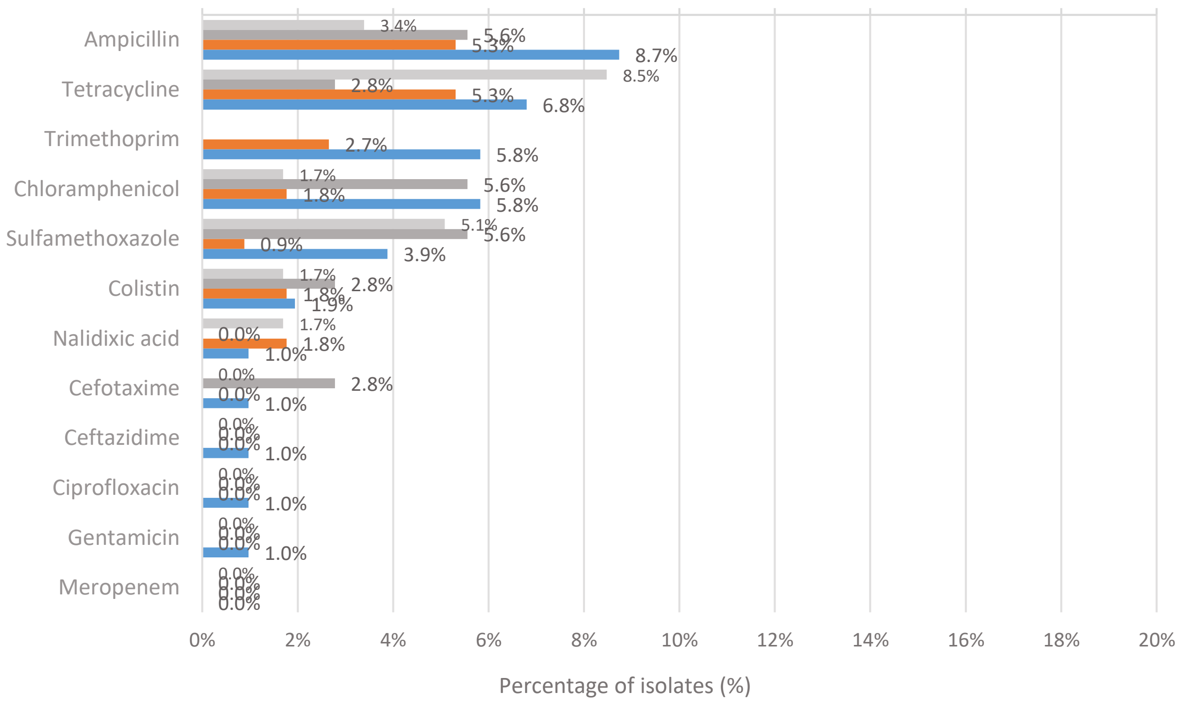


Figure 62. Percentage resistance of *E. coli* isolated from wildlife, 2020-2023



Summary

NParks' surveillance of sick companion animals, free-roaming dogs and wildlife provides insights into resistance patterns across key bacterial pathogens and commensals, focusing on *E. coli*, *K. pneumoniae* and MRSA/P.

The AMR surveillance programme for free-roaming dogs and wildlife yielded encouraging findings from a public health perspective: Rates of MDR and specific resistance were generally lower for bacteria isolated from healthy free-roaming dogs and wildlife compared to those from sick companion animals. Sick companion animals were more likely to have undergone prior antibiotic therapies, resulting in greater development of bacterial resistance, highlighting the relationship between antimicrobial use and resistance development in veterinary practice. The consistently lower resistance rates in free-roaming dogs and wildlife reflects reduced antimicrobial exposure in these populations. The low isolation rates of MRSA and MRSP also suggest limited circulation among the free-roaming dog population.

Further study would be needed to assess the impact of AMR in wildlife on public and animal health over a longer time frame. This underscores the importance of refining the ongoing monitoring programme, such as having more regular AMR testing alongside information on geographic distributions, to better understand and address AMR dynamics in wildlife.

Antimicrobial Resistant Bacteria in the Environment

AMR in environmental settings has emerged as a significant public health concern[28]. Aquatic ecosystems have been recognised as potential reservoirs and transmission pathways for antibiotic-resistant bacteria (ARB) and antibiotic resistance genes (ARGs). These environmental niches may facilitate the persistence, evolution and dissemination of AMR, potentially impacting human and animal health through various exposure routes[29].

NEA has conducted several studies aimed at assessing the prevalence and distribution of AMR in diverse waterbodies, including beaches, waterways and coastal sites. A previous time-limited study carried out in March 2021 revealed the absence of ESBL-Ec in water samples from six recreational beaches[30].

Building on this, a spatio-temporal study was conducted from 2021 to 2023, comprising 28 coastal sites and 34 waterway sites. These sites generally receive surface run-offs from various land-uses including agriculture, industrial, residential and recreational areas. The sampling plan and study design were detailed in the OH report on AMU and AMR, 2021[30].

Antimicrobial resistant bacteria in coastal water and linked waterways

Prevalence of ESBL-Ec in coastal waters and linked waterways (2021 – 2023)

Following the earlier study at six recreational beaches[30], the study carried out over 2021-2023 showed similar results, with no ESBL-Ec detected in recreational coastal sites (Figure 63), although ESBL-Ec were identified from 2.4% of *E. coli* isolates from upstream recreational waterways. The percentages of ESBL-Ec detected in coastal waters and waterways at recreational, residential and agricultural sites were generally low (< 4.7%), except at industrial areas (11.5%). These levels are comparable with other studies where 4.2% of ESBL-Enterobacteriaceae was found in the eastern Adriatic Sea in Croatia[31] and 15.5% of ESBL-Ec was detected in a river system in China[32].

For sites receiving run-offs from residential and recreational land uses, the percentage of ESBL-Ec was significantly higher in waterways compared to coastal sites ($p < 0.05$). Conversely, industrial areas showed a significantly higher percentage of ESBL-Ec in coastal sites compared to waterways ($p < 0.05$).

[28] Hernando-Amado, S., Coque, T.M., Baquero, F. and Martínez, J.L. (2020) Antibiotic Resistance: Moving From Individual Health Norms to Social Norms in One Health and Global Health. Frontiers in Microbiology Volume 11 - 2020.

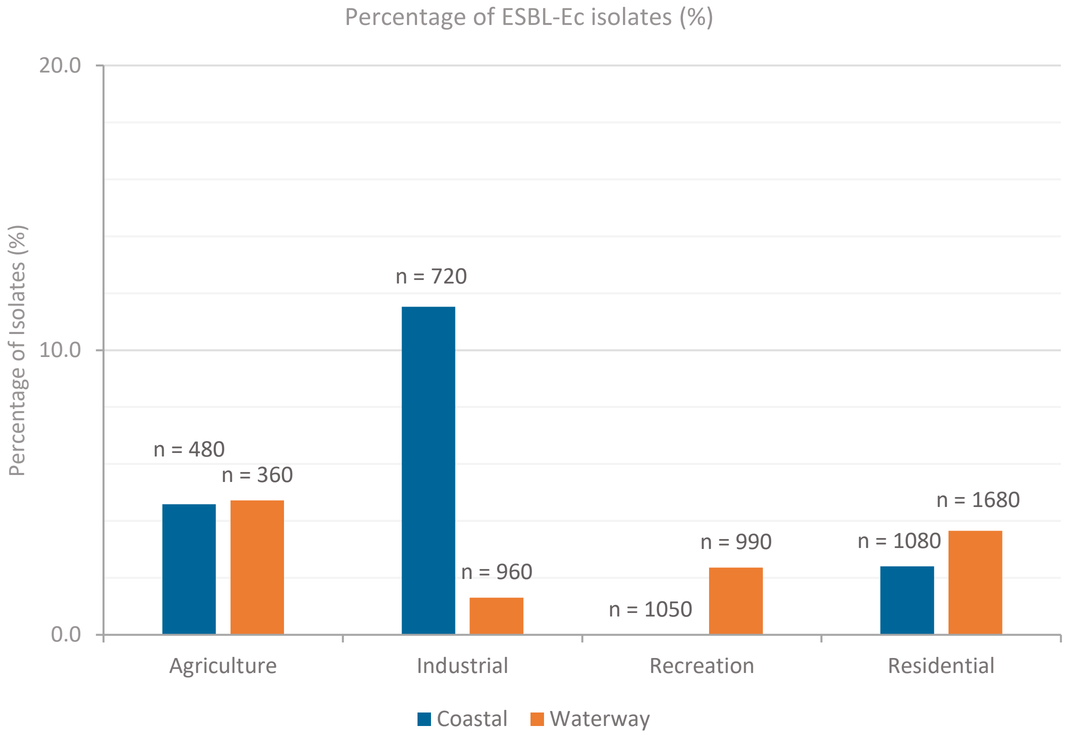
[29] Larsson, D.G.J., Gaze, W.H., Laxminarayan, R. and Topp, E. (2023) AMR, One Health and the environment. Nature Microbiology 8(5), 754-755.

[30] One Health Report on AMU and AMR, 2021

[31] Maravić, A., Skočibušić, M., Cvjetan, S., Šamanić, I., Fredotović, Ž. and Puizina, J. (2015) Prevalence and diversity of extended-spectrum-β-lactamase-producing Enterobacteriaceae from marine beach waters. Marine Pollution Bulletin 90(1), 60-67.

[32] Li, Q., Zou, H., Wang, D., Zhao, L., Meng, M., Wang, Z., Wu, T., Wang, S. and Li, X. (2023) Tracking spatio-temporal distribution and transmission of antibiotic resistance in aquatic environments by using ESBL-producing Escherichia coli as an indicator. Journal of Environmental Management 344, 118534.

Figure 63. Percentage of ESBL-Ec isolates from coastal waters and waterways across different land-use categories.



Note: The data label on top of each bar indicates the total number of isolates screened for ESBL-Ec.

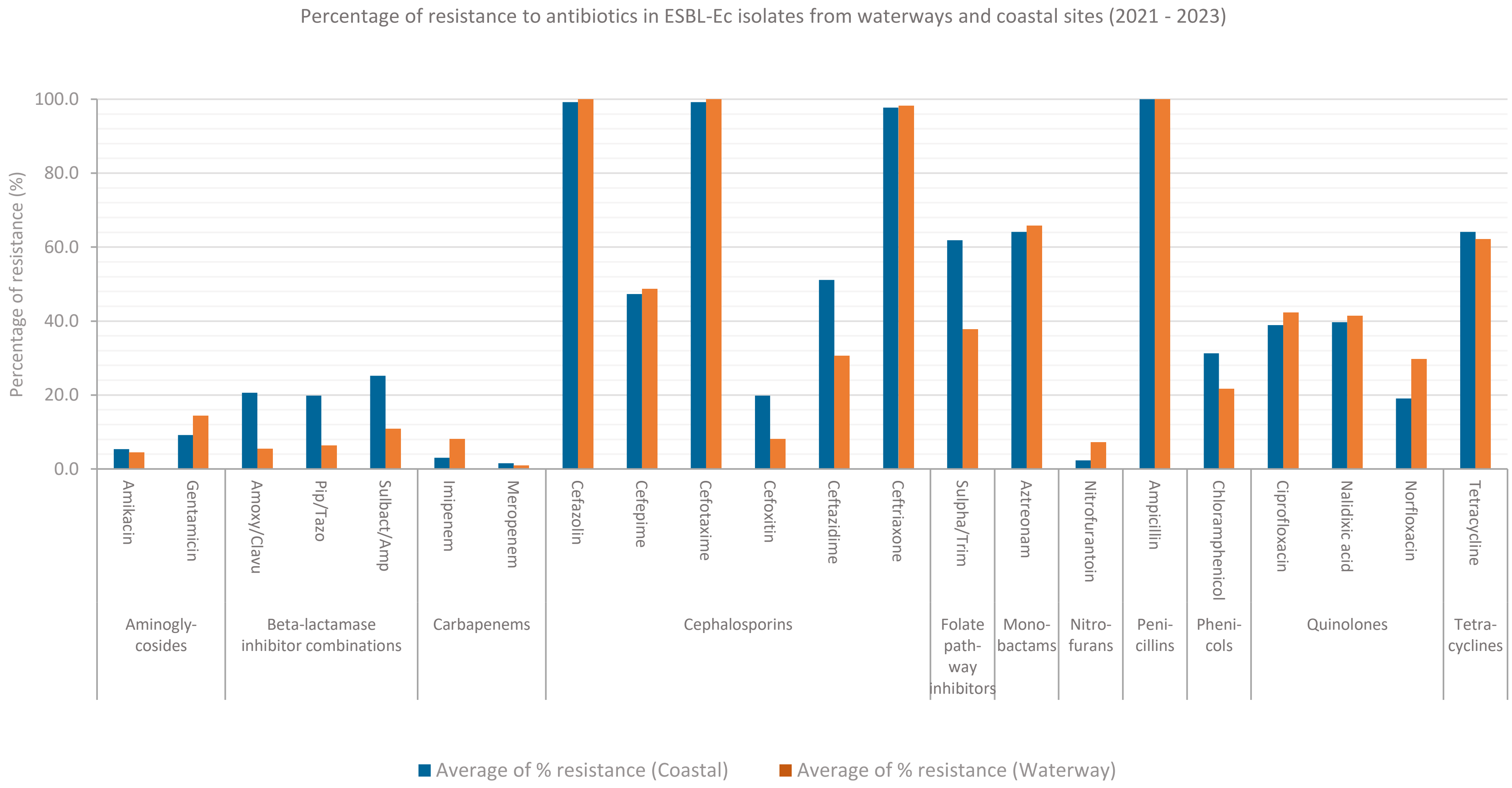
Antibiotic resistance profiles of ESBL-Ec isolates from coastal waters and linked waterways (2021 – 2023)

A total of 242 ESBL-Ec isolates (111 isolates from waterways and 131 isolates from coastal sites) were screened for their antibiotic susceptibility profiles (Figure 64).

Almost all ESBL-Ec isolates were resistant to ampicillin, cefazolin, cefotaxime and ceftriaxone (≥ 98%). This is expected as ESBL-producing organisms are, by definition, resistant to most beta-lactam antibiotics, including penicillins, cephalosporins and monobactam aztreonam. A substantial proportion (>62%) of ESBL-Ec isolates exhibited resistance to tetracycline, which is a broad-spectrum antibiotic effective against both Gram-positive and Gram-negative bacterial infections.

Coastal sites showed a higher proportion of ESBL-Ec isolates resistant to beta-lactamase inhibitor combinations, specific cephalosporins (cefoxitin and ceftazidime), sulfamethoxazole/trimethoprim and chloramphenicol compared to waterways. This difference may be attributed to the distinct environmental profiles of waterways and coastal waters, particularly the biotic and abiotic factors which may exert varying selective pressures on antibiotic resistance patterns.

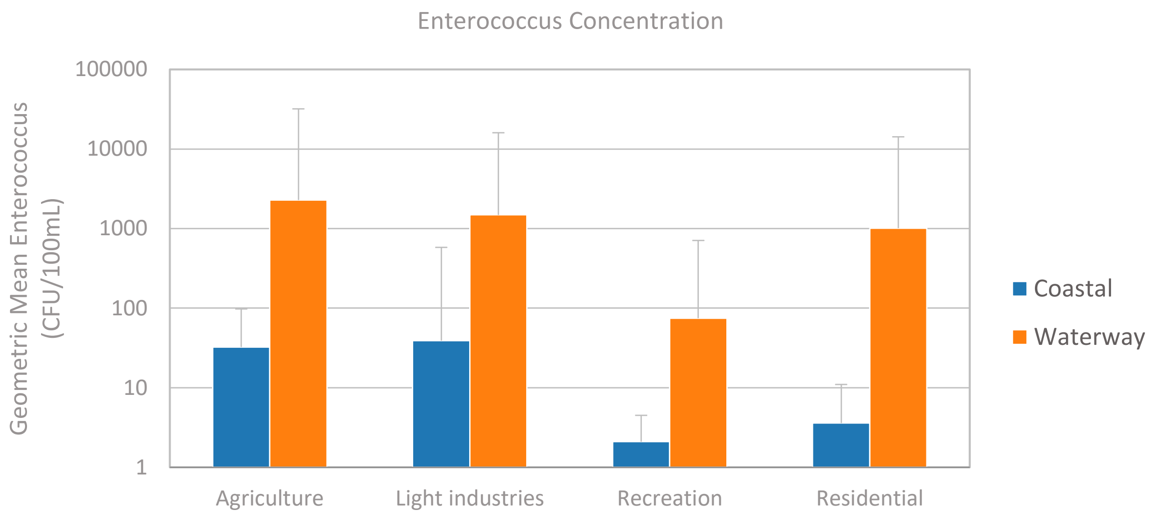
Figure 64. Antibiotic resistance profiles of ESBL-Ec isolates from coastal waters and waterways.



Occurrence of Enterococcus spp. in coastal waters and linked waterways (2021 – 2023)

Figure 65 illustrates the geometric mean *Enterococcus* spp. concentration in coastal sites and waterways across different land-use categories. *Enterococcus* counts were significantly higher in waterways compared to their coastal counterparts ($p < 0.001$). The average (geometric mean) *Enterococcus* concentrations at coastal sites remained below the guideline value for primary contact activities (200 CFU/100mL). However, coastal sites in light industrial areas experienced occasional spikes in Enterococcus spp. concentrations, despite the average (geometric mean) remaining within acceptable limits. These sites are not designated for primary contact recreational activities.

Figure 65. Geometric mean *Enterococcus* spp. concentration in coastal waters and waterways.



Antibiotic resistance profiles of Enterococcus isolates from coastal waters and linked waterways (2021 – 2023)

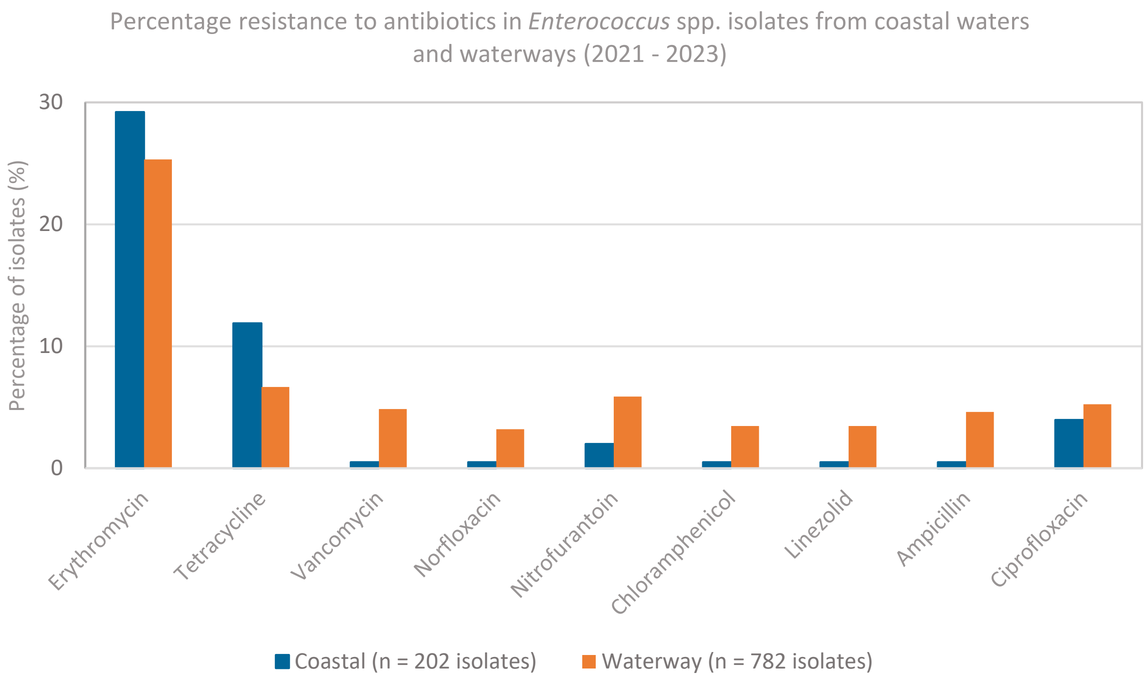
Antibiotic susceptibility testing was conducted on 984 enterococci isolates, comprising *E. faecalis* and *E. faecium* species, obtained from aquatic environments (782 isolates from waterways and 202 isolates from coastal sites). The resistance profiles against a panel of antibiotics were tested and are presented in Figure 66.

Analysis of the antibiotic resistance patterns of these *Enterococcus* isolates revealed that erythromycin resistance was most prevalent, with 25 – 29% of isolates exhibiting resistance. Tetracycline resistance was the second most common, affecting 6-12% of isolates. The high resistance to erythromycin observed in *Enterococcus* spp. corroborate with findings from the previous study examining recreational beach water, beach sand and drainage water samples [33]. The elevated prevalence of tetracycline-resistant *Enterococcus* at coastal sites corresponds with the increasing use of tetracycline in aquaculture settings [29]. While isolates from coastal sites showed a higher proportion of resistance to both erythromycin and tetracycline compared to waterways, analysis of the remaining antibiotics showed that *Enterococcus* isolates from waterways exhibited a higher percentage of

[33] One Health Report on AMU and AMR, 2019

resistance than those from coastal sites. Nevertheless, with the exception of erythromycin and tetracycline, the proportion of isolates resistant to other antibiotics were all under 6%.

Figure 66. Antibiotic resistance profiles of enterococci isolates from coastal waters and waterways.



Summary

Collectively, this study provided insights on the spatio-temporal prevalence of AMR in coastal waters and waterways, highlighting unique differences in species abundance and their respective antimicrobial resistant profiles. While recreational coastal waters demonstrated consistently low levels of ESBL-Ec and *Enterococcus* spp., the varying patterns of microbial presence and AMR profiles observed across different sites underscore the need for systematic risk assessment. These findings establish a crucial foundation for quantitative microbial risk assessment (QMRA), which would enable the evaluation of potential human health risks, particularly in areas showing elevated microbial loads and AMR prevalence. Such risk assessments would be essential in developing evidence-based risk communication strategies and implementing targeted interventions to protect public health.

Appendix I: AMU Methodology

General Information

I. Data on antimicrobial consumption

Antimicrobial consumption in humans

1. **Defined Daily Doses (DDD).** Hospitals report utilisation on a six-monthly basis using defined daily doses (DDD) per 1,000 inpatient days. DDD is the average daily maintenance dose for a drug's main indicated use in adults and is a standard determined by the WHO. The DDD is the assumed average maintenance dose per day for a medicine used for its main indication in adults. The DDD is a technical unit of use and does not necessarily reflect the recommended or average prescribed dose. The number of DDDs is calculated as follows:

   Number of DDDs = Total grams of active ingredient used / DDD value in grams

   The DDD value is assigned by the WHO only for drugs that already have an Anatomical Therapeutic Chemical (ATC) code. The ATC classification system is the most used method for aggregating data on medicines. Under this system, the active ingredients are classified into different groups according to the organ or system on which they act and their therapeutic, pharmacological and chemical properties.

2. Table I.1. Antimicrobials monitored by NARCC (as of 2021)

Grouping	Antimicrobial Agents (Year included for monitoring)
β Lactams and β-Lactamase Inhibitors (BLBLI)	Amoxicillin-clavulanate, IV Amoxicillin-clavulanate, oral (2019) Piperacillin-tazobactam, IV Ampicillin-sulbactam, IV and oral (2019)[34]
Novel BLBLI	Ceftolozane-tazobactam, IV (2019) Ceftazidime-avibactam, IV (2020)
Monobactam	Aztreonam, IV (2019)
Cephalosporins, 2nd gen	Cefoxitin, IV (2019)
Cephalosporins, 3rd & 4th gen	Cefixime, oral (2019) Cefoperazone, IV (2019) Cefotaxime, IV (2019) Ceftazidime, IV Ceftibuten, oral (2019) Ceftriaxone, IV Cefepime, IV
Cephalosporins, 5th gen	Ceftaroline, IV (2019)

[34] For oral, submitted as the whole strength of ampicillin-sulbactam (sultamicillin) tablet (375mg) as per WHO ATC (ref NASEP NOM 02/20, item 7.1 and NARCC NOM 02/20, item 4.2)

Carbapenems	Imipenem, IV Meropenem, IV Ertapenem, IV Doripenem, IV
Fluoroquinolones[35]	Ciprofloxacin, IV and oral Levofloxacin, IV and oral Moxifloxacin, IV and oral
Polymyxins	Colistin, IV and nebulised use (combined)[36] Polymyxin B, IV
MRSA/VRE agents	Teicoplanin, IV (2019) Vancomycin, IV and oral (combined)[37] Linezolid, IV and oral Tedizolid, IV and oral (2019) Daptomycin, IV
Tetracyclines	Doxycycline, IV and oral (2022) Eravacycline, IV (2022) Minocycline, IV and oral (2022) Tetracycline, oral (2022) Tigecycline, IV
Lincosamides	Clindamycin, IV and oral (2019)
Others	Fosfomycin, IV and oral (2019)
Antifungals	Fluconazole, IV and oral Voriconazole, IV and oral Posaconazole, oral Isavuconazole, IV and oral (2020) Caspofungin, IV Anidulafungin, IV Micafungin, IV (2019) Amphotericin B conventional Amphotericin B liposomal Itraconazole, IV and oral

3. **Data limitations.** (1) *Paediatric use* - DDDs are normally assigned based on use in adults. For medical products approved for use in children, the dose recommendations will differ based on age and weight. DDDs are therefore not ideal for estimating drug utilisation in children. However, for NARCC's purposes, DDD has been applied to both adult and paediatric use. (2) *DDD changes* - DDD is calculated based on prevailing values published by WHO. WHO regularly reviews and updates DDDs because dosages may change over time e.g. due to introduction of new main indications. These changes should be taken into consideration when interpreting AMU trends presented in DDD. (3) *The use of inpatient days as a denominator* allows for a weightage of overall utilisation to be obtained and allows normalisation across hospitals of

[35] For levofloxacin and moxifloxacin, submitted separately according to the route of administration (IV and oral) w.e.f. 2022 (ref NASEP NOM 03/22, item 3.1 and NARCC NOM 03/22, item 4.1)
[36] Submitted as a combined total as some hospitals are unable to differentiate between IV and nebulised use of colistin (ref NARCC NOM 02/20, item 4)
[37] Submitted as a combined total as some hospitals are unable to differentiate between IV and oral use of vancomycin w.e.f. 2022 (ref NARCC NOM 02/20, item 4)

different sizes. However, antimicrobial utilisation includes both inpatient and outpatient sources. Nevertheless, consistent application of the same methodology allows for year-on-year trending.

Antimicrobial consumption in animals

1. Sales data serving as national consumption estimates for the animal sector through are obtained a voluntary survey sent to veterinary drug wholesalers annually. Wholesalers are requested to provide information on the following:
    - Name of antimicrobial product
    - Strength
    - Unit
    - Active ingredient(s)
    - Route of administration
    - End-user the product is supplied to (e.g. Vet clinic, land farm, fish farm etc)
    - Purpose (therapeutic use or growth promotion)
    - Quantity supplied

Quantities (in kg) of the antimicrobials are calculated from the sales data provided and grouped into respective antimicrobial classes, stratified by type of use (veterinary medical use or growth promotion), species group (e.g., food-producing animals and non-food producing animals) and route of administration.

2. Data limitations

    (1) Given the voluntary nature of this survey, not all veterinary drug wholesalers engaged by NParks participated in the survey. Therefore, the data obtained may be an underestimate of the actual number of antimicrobials supplied to and utilised by the animal sector.

    (2) As antimicrobial sales data only serves as a proxy of antimicrobial utilisation in animals, it is insufficient to illuminate consumption patterns and volumes at the level of the end-user (vet clinics, farms). Sales trends should also be interpreted with caution as they do not necessarily correspond with utilisation. Therefore, the collection of comprehensive antimicrobial utilisation data at the level of the end-user remains the most valuable method to determine utilisation trends and guide the development of targeted and effective strategies and interventions.

Appendix II. AMR Methodology

Collection, Identification and susceptibility testing of bacterial isolates

From human specimens

1. **Data collection.** Clinical isolates are counted once in every six-month period per patient. Duplicate isolates from the same patient, sample type and bacterial species collected within each six-month period are excluded. While clinical isolates may include colonisation, they provide a useful indicator for the total AMR burden, which in turn impacts the consumption of hospital resources (e.g., isolation rooms, gowns, gloves and manpower). Bacteraemia rates generally represent true infection. Screening samples are excluded in most instances.
2. **List of priority pathogen-drug combinations and sample types** for surveillance (Table II.1).

Table II.1. NARCC priority pathogens for surveillance

Pathogen	Specific resistance	Specimen types to report
Staphylococcus aureus	Cloxacillin (or equivalent anti-staphylococcal penicillin), vancomycin	(i) All clinical specimens (ii) Blood (for MRSA only)
Escherichia coli	Ceftriaxone (or equivalent 3rd-generation cephalosporin), ciprofloxacin, carbapenem (meropenem or imipenem)	(i) All clinical specimens (ii) Blood
Klebsiella pneumoniae	Ceftriaxone (or equivalent 3rd-generation cephalosporin), ciprofloxacin, carbapenem (meropenem or imipenem)	(i) All clinical specimens (ii) Blood
Pseudomonas aeruginosa	Carbapenem (meropenem or imipenem)	(i) All clinical specimens (ii) Blood
Acinetobacter baumannii	Carbapenem (meropenem or imipenem), MDR[a]	(i) All clinical specimens (ii) Blood (for carbapenem resistance only)
Enterobacterales	Carbapenemase-producing	(i) All clinical specimens (ii) Screening specimens
Enterococcus faecalis, Enterococcus faecium	Vancomycin	(i) All clinical specimens (ii) Blood
Clostridioides difficile	-	(i) All clinical specimens (stool)
Candida auris	-	(i) All clinical specimens (ii) Screening specimens[b] (iii) Blood

[a] Multi-drug resistance for *Acinetobacter spp.* is arbitrarily defined as concurrent resistance to imipenem/meropenem, ciprofloxacin and amikacin

[b] W.e.f. from 2022 data collection

3. **Standards and AST methods.** Clinical isolates are tested for antimicrobial susceptibility by hospitals' clinical microbiology laboratories in accordance with the standards of Clinical & Laboratory Standards Institute (CLSI), European Committee on Antimicrobial Susceptibility Testing (EUCAST), or with the Calibrated Dichotomous Sensitivity (CDS, Australia) method, where applicable. Laboratory and AST methods are determined by hospital laboratories, and include disk diffusion, e-test and MIC methods where appropriate.
4. **Metrics.** The data are presented as (i) incidence density per 10,000 inpatient days and where relevant, (ii) the proportion (%) of resistant clinical isolates. The resistance percentage is typically calculated only when the denominator contains at least 30 isolates to ensure a minimum level of precision in the calculation. For NARCC's purposes, resistant isolates include those of intermediate susceptibility.
5. **Data limitations.** The use of inpatient days as a denominator allows for a measurement of the incidence density (cases per 10,000 inpatient days) to be obtained and allows normalisation across hospitals of different sizes. However, antimicrobial resistance data are obtained from laboratory detection from samples submitted, which may include outpatient sources. Nevertheless, consistent application of the same methodology will allow year-on-year observation of trends.

From animal specimens

1. **Data collection.** Samples collected from the respective AMR surveillance programmes were obtained from veterinarians from NParks or veterinary clinics/hospitals (Table II.2). These samples were then sent to the CAVS for testing. Subsequently, the AST results were compiled and analyzed by the NParks AMR workgroup at least once every six months.

Table II.2. Sampling matrix for the respective AMR surveillance in companion animals and wildlife

Surveillance	Bacteria	Sample Type	Frequency
Free-roaming dogs (active)	(i) *E. coli, K. pneumoniae* (ii) MRSA/MRSP	(i) Faecal or rectal swabs (ii) Ear swabs	Monthly
Sick companion animals (passive)	(i) *E. coli, K. pneumoniae* (ii) MRSA/MRSP	Various sample types (clinical/ post-mortem samples)	Ad-hoc
Wildlife (passive)	*E. coli*	(i) Faecal or rectal swabs (ii) Organs	(i) Monthly (ii) Ad-hoc

2. **Standards & AST methods.** AST were performed on all *E. coli* and *K. pneumoniae* by broth microdilution using the Sensititre ASSECAF and ASSECB plates (Figure II.1). The method and breakpoint interpretations were in accordance with the CLSI and/or EUCAST standards, where applicable. The Sensititre plates contained 15 veterinary important antimicrobials (ampicillin, azithromycin, ceftazidime, cefotaxime, chloramphenicol, ciprofloxacin, colistin, gentamicin,

meropenem, nalidixic acid, sulfamethoxazole, streptomycin, tigecycline, tetracycline, and trimethoprim) from 10 antimicrobial classes.

Figure II.1. Sensititre™ Asia Surveillance Plates ASSECAF (left) and ASSECB (right). [38]

Fig 1. Asia Salmonella/E.coli Plate 1 (ASSECAF) with 10 highest and high priority critically imporatnt antimicrobials in the Regional Panel

Fig 2. Asia Salmonella/E.coli Plate 2 (ASSECB) with the remaining 5 highly important antimicrobials in half plate = 2 isolates per plate

AST were performed on *S. aureus* and *S. pseudintermedius* using VITEK AST GP80 cards. The method and breakpoint interpretations were in accordance with the CLSI and/or EUCAST standards, where applicable. The VITEK GP80 card contained 19 antimicrobials (amoxicillin/clavulanic acid, cefalotin, cefovecin, ceftiofur, chloramphenicol, clindamycin, doxycycline, enrofloxacin, erythromycin, gentamicin, kanamycin, marbofloxacin, nitrofurantoin, neomycin, penicillin, pradofloxacin, oxacillin, tetracycline and trimethoprim/sulfamethoxazole) from 11 antimicrobial classes that are of veterinary importance to companion animals. The isolates were tested for methicillin resistance and specific resistance genes, in particular, the *mecA* gene, which is the most common gene conferring methicillin resistance in staphylococci. Cefoxitin-resistant *S. aureus* carrying the *mecA* gene are identified as MRSA, while oxacillin-resistant *S. pseudintermedius* with the *mecA* gene are identified as MRSP.

3. **Metrics**. The data were presented as (i) prevalence or proportion of samples, (ii) the proportion (%) of MDR bacteria, and (iii) the percentage (%) of resistant isolates. MDR is defined as being resistant to three or more classes of antimicrobials. Resistant isolates did not include those of intermediate susceptibility.

From farms

1. **Data collection.** Samples collected from local farm AMR surveillance were obtained from inspectors from SFA (Table II.3). The testing of *Salmonella* spp. and *E. coli* in the poultry and ruminant farms were under the purview of NParks until Jun 2021. In July 2021, the testing of *Salmonella* spp. in the poultry farms was taken over by SFA. The testing of *Salmonella* spp. and *E. coli* in the ruminant farms and the testing of *E. coli* in poultry farms remained under the purview of NParks. Subsequently, the AST results were compiled and analyzed by the NParks

[38] FAO (2019). Towards transforming AMR surveillance capacities in food and agriculture in Asia, Vol 2. No. 1 (Project OSRO/RAS/502/USA)

AMR workgroup at least once every six months. The AST results from *Salmonella* in the poultry farms were jointly analysed by the NParks and SFA AMR workgroup.

Table II.3. Sampling matrix for AMR surveillance in local farms

Surveillance	Bacteria	Sample Type	Frequency
Poultry (chicken and quail) farms	(i) *Salmonella* spp. (ii) *E. coli*	[Jan 2020 – Jun 2021] Various sample types, including environmental swabs, pooled organs, faeces [Jul 2021 onwards] Pooled drag swabs	Quarterly
Ruminant (cattle and goat) farms	(i) *Salmonella* spp. (ii) *E. coli*	Pooled fecal samples	Quarterly

2. **Standards & AST methods.** AST were performed on all *Salmonella* spp. and *E. coli* by broth microdilution using the Sensititre ASSECAF and ASSECB plates (Figure II.1). The method and breakpoint interpretations were in accordance with the CLSI and/or EUCAST standards, where applicable. The Sensititre plates contained 15 veterinary important antimicrobials from 10 antimicrobial classes.

   Salmonella isolates from farm samples were subjected to AST by microbroth dilution using the SensititreTM Asia Surveillance Plates for Salmonella/E. coli (see Appendix II. AMR Methodology) and applying CLSI M100 breakpoints. Tests for Minimum Inhibitory Concentration (MIC) were performed with 10 classes of 11 antimicrobials (ampicillin, cefotaxime, ceftazidime, ciprofloxacin, chloramphenicol, colistin, gentamicin, meropenem, sulfamethoxazole, tetracycline and trimethoprim) using the SensititreTM Asia Surveillance Plates for Salmonella/E. coli (see Appendix II. AMR Methodology). Salmonella spp. serovars was determined by serotyping and/or Whole Genome Sequencing (WGS).

   CLSI M100 interpretive breakpoints are applied for the surveillance of healthy food-producing animals from the public health perspective. For sick animals, CLSI VET01S interpretative breakpoints are applied for treatment purposes. Where appropriate clinical breakpoints are not available in VET01S, CLSI M100 breakpoints are applied.

3. **Metrics (where applicable)**. The data were presented as (i) prevalence or proportion of samples, (ii) the proportion (%) of MDR bacteria, and (iii) the percentage (%) of resistant isolates. MDR is defined as being resistant to three or more classes of antimicrobials. Resistant isolates did not include those of intermediate susceptibility.

From food samples

1. **Data collection.** SFA's AMR surveillance adopts the FAO's Regional AMR Monitoring and Surveillance Guidelines to ensure a standardised and harmonised protocol for AMR monitoring. This harmonisation also ensures comparability of AMR data to maximise potential value of findings at regional level in future.

2. **Target organisms and samples.** SFA monitors resistance to antimicrobial agents in commensal bacteria and food-borne pathogens from target food and food-producing animals intended for consumption and monitors trends of AMR bacteria (*E. coli* and *Salmonella* spp.) in relevant imported and retail food products, animal feed, food producing animals, as well as farm and food processing environments.

3. **Standards and AST methods.** *Salmonella* spp. and *E. coli* bacteria from food sources, establishments, and retail samples were isolated and tested by SFA according to ISO17025 accredited methods and international standards for microbiological identification and antibiotic susceptibility testing. SFA adopts the CLSI M100 interpretive breakpoints for determining antibiotic susceptibility.

   Tests for MIC were performed with 10 classes of 11 antimicrobials (ampicillin, cefotaxime, ceftazidime, ciprofloxacin, chloramphenicol, colistin, gentamicin, meropenem, sulfamethoxazole, tetracycline and trimethoprim) using the Sensititre™ Asia Surveillance Plates for *Salmonella/E. coli*.

   The Combination Disk Diffusion test (CDT) is based on the capacity of clavulanic acid to inhibit ESBL, and the synergy that is produced in combination with cefotaxime and the combination with ceftazidime. The interpretation of the results is based on the zone size of each cephalosporin alone cefotaxime (CTX), 30µg and ceftazidime (CAZ), 30µg, compared with the discs containing the combination of cephalosporin and clavulanic acid, (Cefotaxime-clavulanic acid (CTX/CA) and Ceftazidime- clavulanic acid (CAZ/CA), 40 ug (30µg/10µg) each. If the zone diameter of the disc with the combination for any or both cephalosporin is higher or equal to 5mm, the result is interpreted as positive for ESBL.

   VITEK® 2 AST-GN79 ESBL Test was used for confirmation of the ESBL phenotype in 2020 and 2021. It is a confirmatory test for those ESBLs inhibited by clavulanic acid, and it utilizes cefepime, cefotaxime, and ceftazidime, with and without clavulanic acid, to determine a positive or negative result.

   Antimicrobial susceptibility testing is carried out by SFA using the Sensititre™ system to determine minimum inhibitory concentration (MIC) in accordance with accredited methodology, adopting FAO's Asia Surveillance plates for *Salmonella/E. coli* (ASSEc) Panel.

   The Asia Surveillance plates for *Salmonella/E. coli* (ASSEc) were designed by FAO in collaboration with Singapore to provide an antibiotic panel consistent with recommendations in the FAO Regional AMR surveillance Guideline #1 (AMR monitoring and surveillance in bacteria from healthy food animals intended for consumption). The ASSEc plates consist of a range of antibiotic dilutions covering the clinical breakpoints, ECOFFs and recommended ranges appropriate for the prescribed bacterial strain. Plate 1 (ASSECAF) consists of the 10 highest priority critically important antimicrobials in the Regional Panel. Plate 2 (ASSECB) consists of the next five highly important antimicrobials in half plate format, such that isolates could be tested per plate. The results are interpreted based on CLSI breakpoints (M100, 30th Edition) and (EUCAST Ver 11.0, 2021) to determine the Minimum Inhibitory Concentration (MIC).

a. **ASSECAF Asia *Salmonella/ E. coli* Sensititre Plate 1**
Antimicrobial panel and interpretive criteria for target bacteria adapted according to FAO (2019).

Antibiotic Panel and Dilution Range			Breakpoints			
No	**Antibiotic**	**Concentration (µg/ml)**	**S**	**I**	**R**	**Interpretative guideline**
1	Azithromycin	0.5-64	≤ 16	-	≥ 32	CLSI M100 30th Edition
2	Nalidixic Acid	1-128	≤ 16	-	≥ 32	
3	Colistin	0.12-16	-	≤ 2	≥ 4	
4	Cefotaxime	0.06-16	≤ 1	2	≥ 4	
5	Streptomycin	1-256	-	-	-	
6	Ampicillin	0.05-128	≤ 8	16	≥ 32	CLSI M100 30th Edition
7	Ceftazidime	0.125-64	≤ 4	8	≥ 16	
8	Gentamicin	0.25-128	≤ 4	8	≥ 16	
9	Meropenem	0.008-8	≤ 1	2	≥ 4	
10	Ciprofloxacin (*E. coli)*	0.015-16	≤ 0.25	0.5	≥ 1	
	Ciprofloxacin (*Salmonella)*	0.015-16	≤ 0.06	0.12-0.5	≥ 1	

b. **ASSECAF Asia *Salmonella/ E. coli* Sensititre Plate 2**

Antibiotic Panel and Dilution range			Breakpoints			
No	**Antibiotic**	**Concentration (µg/ml)**	**S**	**I**	**R**	**Interpretative guideline**
1	Chloramphenicol	1-256	≤ 8	16	≥ 32	CLSI M100 30th Edition
2	Sulfamethoxazole	1-1024	≤ 256	-	≥ 512	
3	Trimethoprim	0.25-256	≤ 8	-	≥ 16	
4	Tetracycline	1-256	≤ 4	8	≥ 16	
5	Tigecycline	0.25-16	≤ 0.5	-	> 0.5	EUCAST Ver 11.0, 2021

4. **Metrics.** Resistance data are presented as proportion of resistant isolates (%R), which is the number of isolates resistant to the specified antimicrobial as a proportion of all isolates tested. For SFA's monitoring, resistant isolates exclude those of intermediate susceptibility.

5. **Data limitations.** Rates of detection in food imports or along the food supply chain do not necessarily correlate with prevalence. Sampling of food products is primarily for food safety purposes and are therefore subject to risk-based sampling. For instance, higher-risk products may be subject to increased sampling. Food sources and product types also vary from year to year. These factors should be taken into consideration when interpreting data and trends.