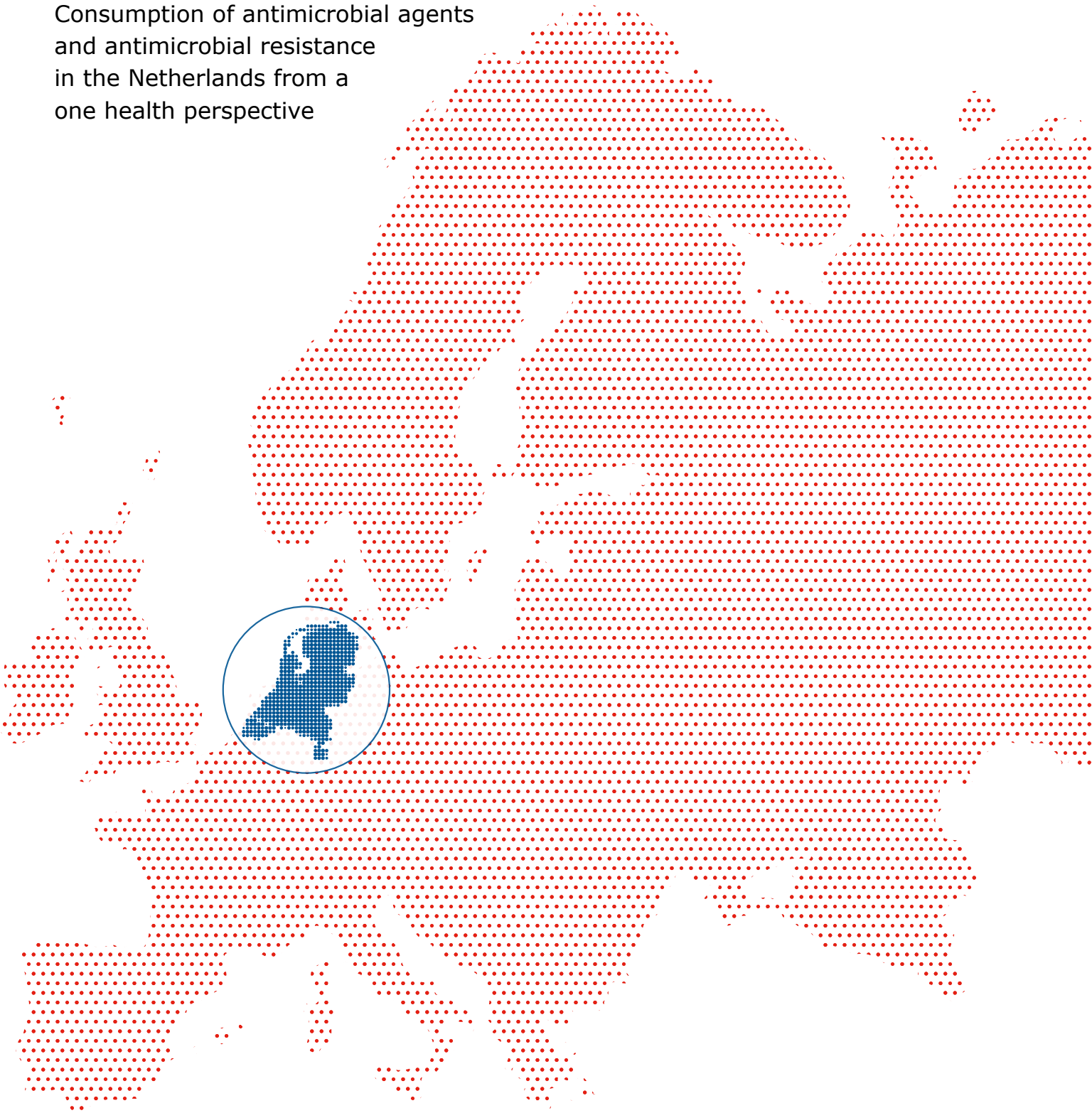
NethMap One Health 2026

Consumption of antimicrobial agents and antimicrobial resistance in the Netherlands from a one health perspective



National Institute for Public Health and the Environment
Ministry of Health, Welfare and Sport

SWAB Stichting Werkgroep Antibioticabeleid

WAGENINGEN UNIVERSITY & RESEARCH

NethMap One Health 2026

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Colophon

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Synopsis

NethMap One Health 2026

Bacteria can become resistant to antibiotics. Infections caused by resistant bacteria are often more difficult to treat. That is why the Netherlands monitors, for each bacterial species, what percentage of bacteria are resistant to each of several antibiotics. The amount of antibiotics used by people and animals each year is also recorded. This is because resistance mainly develops when people or animals are prescribed antibiotics incorrectly and for too long.

Antibiotic resistance in the Netherlands is still lower than in other European countries. However, in recent years – and again in 2025 – an increasing proportion of certain bacteria has become resistant. This increase can be seen throughout Europe. The increase affects, among others, bacteria that can cause serious infections in patients as well as common infections such as bladder infections. As a result of this increase, there is a greater risk of contracting an infection caused by a bacterium that does not respond to the antibiotics normally prescribed.

To prevent the situation from getting worse, research is carried out to identify potential additional control measures. The aim is to investigate whether certain groups of patients are more likely to carry resistant bacteria and, if so, whether patients carrying these bacteria can be identified earlier. This information helps to ensure that people with serious infections receive the right treatment more quickly. This information also helps to prevent resistant bacteria from spreading further among vulnerable people, for example in hospitals. Moreover, it will be explored whether antibiotic treatment guidelines need to be revised to further encourage appropriate antibiotic use.

Hygiene measures, such as handwashing, will of course remain necessary to prevent the spread of resistant bacteria. It also remains essential that all parties involved work together. This is because resistant bacteria are found in humans, animals, food and the environment (the One Health approach).

In 2025, approximately the same quantity of antibiotics was prescribed in GP practices, hospitals and nursing homes as in 2024. However, more antibiotics are prescribed in hospitals than in nursing homes. These quantities also vary within the same type of healthcare institution.
In Dutch livestock farming, antibiotic use fell further in 2025. Following a significant decline since 2009, the amount used has become more and more stable in recent years. Antibiotic resistance in animals has also stabilised, probably mainly as a result of the decline in antibiotic use.

Keywords: one health, ABR, antimicrobial stewardship, antibiotic use, bacteria, infection

Publiekssamenvatting

NethMap One Health 2026

Bacteriën kunnen ongevoelig worden voor antibiotica (resistent). Een infectie met een resistente bacterie is vaak minder goed te behandelen. Daarom wordt in Nederland per bacteriesoort bijgehouden welk percentage resistent is tegen verschillende antibiotica. Ook wordt bijgehouden hoeveel antibiotica mensen en dieren elk jaar gebruiken. Want resistentie ontstaat vooral als mensen of dieren antibiotica verkeerd en te lang krijgen voorgeschreven.

De antibioticaresistentie is in Nederland nog steeds lager dan in andere Europese landen. Maar de afgelopen jaren, en ook weer in 2025, is een steeds groter deel van bepaalde bacteriën resistent geworden. Deze stijging is in heel Europa te zien. Het gaat onder andere om bacteriën die ernstige infecties bij patiënten kunnen veroorzaken. Maar ook veelvoorkomende infecties als een blaasontsteking. Door de stijging is de kans groter om een infectie te krijgen met een bacterie die niet reageert op de standaard voorgeschreven antibiotica.

Om erger te voorkomen wordt onderzocht welke extra maatregelen mogelijk zijn. Zo zal worden bekeken of bepaalde groepen patiënten vaker resistente bacteriën bij zich dragen. En zo ja, of zij eerder kunnen worden gevonden. Deze informatie helpt om mensen met ernstige infecties sneller de juiste behandeling te kunnen geven. En om te voorkomen dat resistente bacteriën zich verder verspreiden onder kwetsbare mensen, bijvoorbeeld in een ziekenhuis. Ook wordt onderzocht of de richtlijnen voor antibioticabehandeling moeten worden aangepast om juist gebruik van antibiotica verder te stimuleren.

Uiteraard blijven hygiënemaatregelen, zoals handen wassen, nodig om te voorkomen dat resistente bacteriën zich verspreiden. Ook blijft het noodzakelijk dat alle betrokken partijen samenwerken. Want resistente bacteriën komen niet alleen bij mensen, maar ook bij dieren, in voeding en in het milieu voor (one health-benadering).

In huisartsenpraktijken, ziekenhuizen en verpleeghuizen is in 2025 ongeveer evenveel antibiotica voorgeschreven als in 2024. Wel worden in ziekenhuizen meer antibiotica voorgeschreven dan in verpleeghuizen. Ook verschillen deze hoeveelheden binnen hetzelfde type zorginstelling.

In de Nederlandse veehouderij is het antibioticagebruik verder gedaald in 2025; na een flinke daling sinds 2009 stabiliseert de hoeveelheid de laatste jaren steeds meer. Ook de antibioticaresistentie bij dieren is gestabiliseerd, wat waarschijnlijk vooral komt door de daling in het gebruik.

Kernwoorden: one health, ABR, antimicrobial stewardship, antibioticagebruik, bacteriën, infectie

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1 Introduction

This is NethMap One Health, the annual report presenting trends in the consumption of antimicrobial agents and antimicrobial resistance in the Netherlands from a One Health perspective. Previously, we presented trends in the human domain (NethMap) back-to-back with trends in the veterinary domain (Maran), but since last year we have changed the structure of the report to achieve a more integrated overview of antimicrobial resistance (AMR) and antimicrobial consumption (AMC) in humans and animals in the Netherlands.

The main aim of surveillance of AMR and AMC in the Netherlands is to halt the emergence and limit the spread of AMR. Key objectives of NethMap One Health are to deliver essential data to medical doctors, veterinarians, and other health professionals to support the development and continuous improvement of evidence-based antibiotic treatment guidelines. Secondly, it acts as a comprehensive knowledge base for authorities, academia, and policymakers, supporting risk assessment and management, and thus facilitating informed decision-making in the prevention and control of resistant bacterial infections. Lastly, AMR and AMC surveillance identifies areas for further research, such as antimicrobial resistance transmission dynamics or possible associations between antimicrobial consumption and resistance.

NethMap One Health is compiled under the editorial supervision of the Dutch Working Group on Antibiotic Policy (SWAB; Stichting Werkgroep Antibiotica Beleid), Wageningen Bioveterinary Research (WBVR) and the National Institute for Public Health and the Environment (RIVM).

The SWAB was founded in 1996 as an initiative of The Netherlands Society for Infectious Diseases, The Netherlands Society of Hospital Pharmacists and The Netherlands Society for Medical Microbiology. SWAB is fully funded by a structural grant from the CIb, on behalf of the Ministry of Health, Welfare and Sports. The SWAB plays a central role in promoting the rational use of antimicrobial agents in the Netherlands. SWAB's primary task is to develop evidence-based guidelines for antimicrobial therapy in humans, thereby supporting clinicians in making informed decisions and contributing to the containment of antimicrobial resistance. In addition, SWAB coordinates antibiotic stewardship activities, facilitates interdisciplinary collaboration and advises policymakers on issues related to antimicrobial stewardship, antimicrobial consumption and antimicrobial resistance.

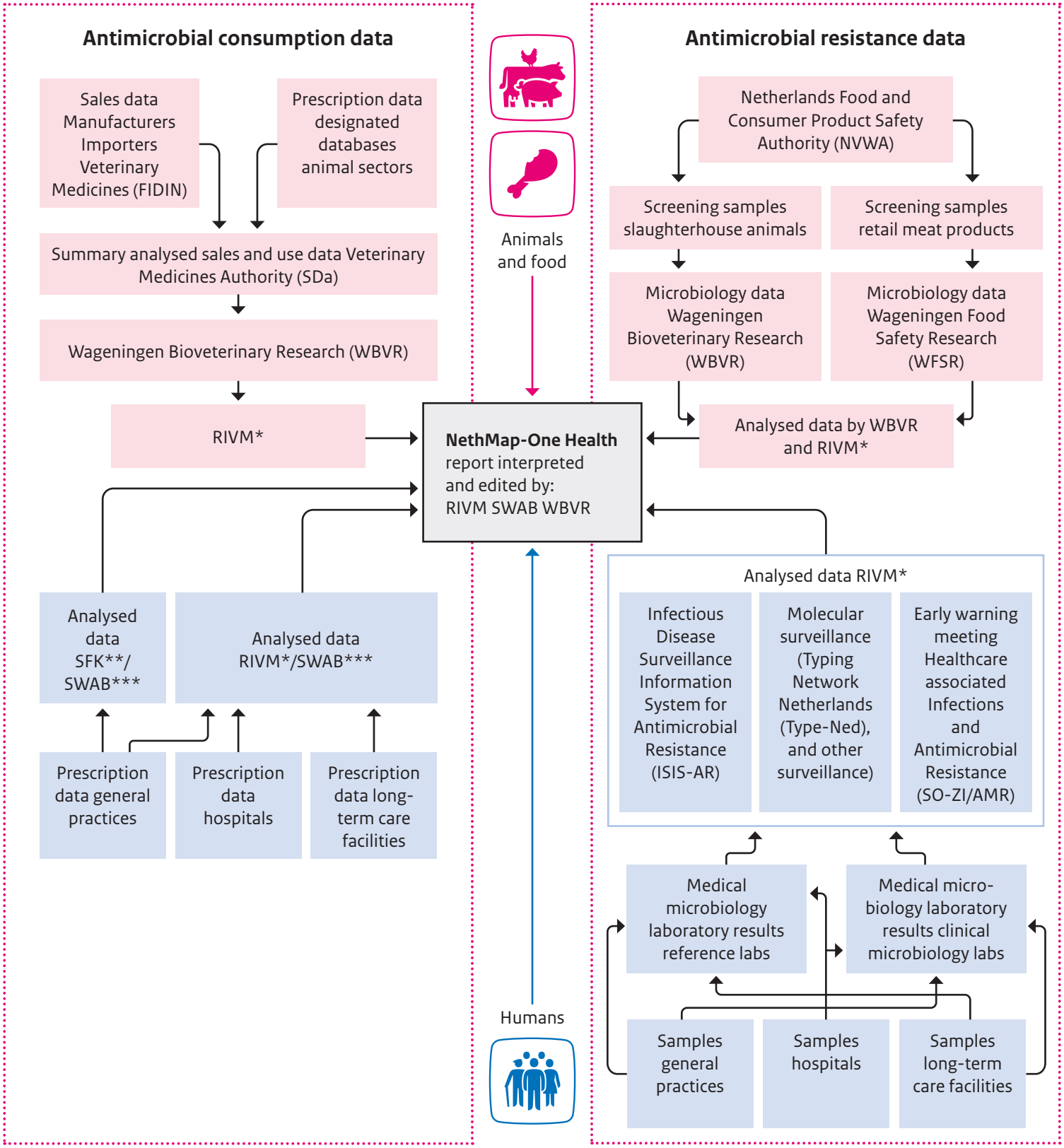
Wageningen Bioveterinary Research (WBVR) monitors and researches antimicrobial resistance in animals in the Netherlands. WBVR conducts surveillance to track resistance trends, investigates the development and spread of resistance, and advises veterinarians and policymakers on antibiotic stewardship. The results from the veterinary domain presented in this report have been generated through collaboration between WBVR, the Food and Consumer Product Safety Authority (NVWA), Wageningen Food Safety Research (WFSR), Veterinary Medicines

Institute (SDa), the Faculty of Veterinary Medicine, Utrecht University (FD) and the Centre for Infectious Disease Control Netherlands (CIb) at the RIVM.

The CIb at the RIVM coordinates surveillance on antimicrobial resistance and consumption in humans in the Netherlands to inform the general public, professionals and policy makers about potential national health threats with regard to antimicrobial resistance and to guide healthcare professionals and policymakers on the control of AMR. Furthermore, the CIb subsidizes surveillance programs that focus on the monitoring of specific pathogens, or specific resistance mechanisms. By collaborating with national and international partners, CIb works to prevent the spread of AMR and protect public health.

Figure 1 provides a schematic overview of the data flows from the general surveillance systems from which the results are presented in this report. All results presented in this report have been made possible through the collaboration of numerous partners in both the human healthcare and veterinary sectors. We are very grateful for the valuable contributions and commitment of all involved parties and express our hope that they are willing to continue their important clinical and scientific support to NethMap One Health and thereby contribute to the general benefit and health of the people.

Figure 1 Flowchart NethMap-One Health



*RIVM Dutch National Institute for Public Health and the Environment
**SFK Foundation for Pharmaceutical Statistics
***SWAB Dutch Working Party on Antibiotic Policy

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2 Extensive summary

This chapter provides a summary of the findings described in this report and relevant conclusions with respect to antimicrobial use, policy and resistance surveillance in both humans and farm animals.

2.1 Most important trends in antimicrobial consumption in humans

Outpatient use

- Total outpatient antibiotic use decreased by 4.2%, from 9.02 DID in 2024 to 8.64 DID in 2025. This is the first decrease since 2021.
- The decrease was mainly seen for doxycycline, amoxicillin and nitrofurantoin. Use of macrolides, lincosamides and sulfonamides with trimethoprim continued to increase slightly.
- Within the fluoroquinolones, the share of levofloxacin increased from 9% in 2019 to 16% in 2025. Ciprofloxacin still accounted for about three quarters of fluoroquinolone use.
- The prescribing quality indicators show wide variation between GP practices. The median number of antibiotic prescriptions decreased by 10% to 251 per 1,000 registered patients.

Inpatient use

- Total systemic antibiotic use in hospitals decreased by 6.4%, from 90.3 to 84.5 DDD per 100 patient-days. This is the second consecutive decrease, but use remains above the 2019 level.
- Fewer hospitals participated than in 2024. About one fifth of the decrease is attributable to the change in participating hospitals.
- Carbapenem use decreased for the first time since 2018 (in DDD per 100 patient-days), but this decrease is largely attributable to the change in participating hospitals.
- Expressed in DDD, flucloxacillin had the largest volume of use, followed by ceftriaxone, cefuroxime and cefazolin.

AWaRe classification

- In 2025, 72.0% of the antibiotics used in the Netherlands were from the Access category, so the European target continues to be met.

Long-term care facilities (LTCFs)

- Antibiotic use in LTCFs decreased by 4.8%, from 53.1 to 50.6 DDD per 1,000 resident-days.
- The largest decrease was seen for macrolides. Use continues to vary widely between facilities.

2.2 Most important trends in antimicrobial consumption in animals

- In 2025, total sales of antimicrobial veterinary medicinal products (AVMPs) amounted to 113 tonnes, a decrease of 6.8% compared with 2024. Compared with 2009, sales have decreased by 77.2%, reflecting the impact of policies to reduce antibiotic use in animals. This long-term downward trend has levelled off in recent years.
- Compared with 2024, antimicrobial use (AMU) decreased by 9.7% in pigs but increased by 24.7% in broilers; the reasons for this increase are still under investigation. AMU in veal calves remained stable at a relatively high level, whereas use in the cattle sector, including dairy cattle, remained low.
- In animals, the use of antibiotics of critical importance to human medicine, particularly third- and fourth-generation cephalosporins, remained low. Sales of polymyxins decreased further in 2025, the reduction since 2011 accumulates to 87%. Fluoroquinolone use also showed a substantial long-term decline, with sales down 91% since 2011. However, 51% of fluoroquinolones sold were used in sectors not yet monitored, highlighting a gap in monitoring coverage.

2.3 Most important trends in antimicrobial resistance and implications for treatment in humans

In this chapter, the extensive summary, we highlight the most relevant trends in antimicrobial resistance and antibiotic use observed in NethMap One Health. These include both changes over time and patterns that have remained stable, where they are particularly important for clinical practice or public health. By drawing attention to these patterns, we primarily aim to indicate areas that may warrant closer observation and ongoing evaluation and, where appropriate, further research to better understand their underlying causes and implications. Over time, such developments may suggest the need to consider adjustments to clinical guidelines or antimicrobial stewardship policies.

2.3.1 General AMR surveillance

2.3.1.1 Descriptive characteristics of ISIS-AR data

- For the 2025 analyses, data of 36 laboratories could be used, resulting in inclusion of data on 518,929 isolates.
- The distribution of laboratories that provided antimicrobial resistance data over the past five years was considerably more balanced across the Netherlands compared to earlier editions of NethMap One Health.

2.3.1.2 General practices

Urinary tract infections – Enterobacterales

- In *Escherichia coli*, resistance levels for **nitrofurantoin** and **fosfomycin**, i.e. respectively first and second choice antibiotics for the treatment of uncomplicated UTI in adults in primary care, remained stable and low (≤2%) over the last five years. These agents therefore remain reliable empirical options. For **trimethoprim**, third choice antibiotic for the treatment of uncomplicated UTI in adults, resistance was 21–22%, unchanged from 2024.

- From 2025 onwards, resistance to **co-amoxiclav** in Enterobacterales can be calculated using the EUCAST breakpoint for oral treatment of uncomplicated UTI. Using this breakpoint, resistance to co-amoxiclav in *E. coli* was 8%.
- Resistance levels for **ciprofloxacin**, first choice antibiotic for the empirical treatment of complicated UTI in adults in primary care, remained stable at 10% for both *E. coli* and *Klebsiella pneumoniae*. Resistance levels for **co-amoxiclav**, second choice antibiotic for the empirical treatment of complicated UTI, were 26% in *E. coli* and 15% in *K. pneumoniae*, essentially unchanged compared to previous years. Resistance levels for **co-trimoxazole**, third empirical choice for this indication, were 19% in *E. coli* and 8% in *K. pneumoniae* and remained stable.
- Combined resistance to **co-amoxiclav**, **ciprofloxacin** and **co-trimoxazole** (multidrug resistance to oral therapy, MDOT) in all Enterobacterales remained low (≤3%).

Skin and soft tissue infections – S. aureus and β-haemolytic Streptococci

- Antibiotic resistance levels in *Staphylococcus aureus* remained relatively low, with resistance to most antibiotics below 5%. **MRSA** was found in 3% of isolates of primary care patients, which was stable over the last five years.
- A continuing and worrisome increase in resistance to **fusidic acid** was found in *S. aureus*, from 18% in 2021 to 30% in 2025. Resistance to **mupirocin** (3%) also showed an increasing trend over the last five years. These percentages may be somewhat inflated by selective sampling, as cultures are usually obtained from patients who have failed topical therapy; nevertheless, the trend is considered real and complicates treatment.
- In β-haemolytic *Streptococcus* group A, continuing the favourable trends observed in 2024, resistance to **doxycycline/tetracycline** (27%) and **co-trimoxazole** (1.9%) showed a significant decreasing trend over the last five years.
- In contrast, in β-haemolytic *Streptococcus* group B, resistance to **erythromycin** (25%), **clindamycin** (15%) and **clindamycin including inducible resistance** (20%) increased significantly over the last five years, with 2025 levels notably higher than in 2024. Resistance to **doxycycline/tetracycline** remained very high (77%). Together, this complicates treatment options for patients with a beta-lactam allergy.

Respiratory infections – S. pneumoniae and H. influenzae

- The proportion of *Streptococcus pneumoniae* isolates in the I-category for **(benzyl)penicillin** was 8% in GP patients, whereas resistance remained very low (0.5%). Resistance to **doxycycline/tetracycline** in *S. pneumoniae* was 9%.
- In *Haemophilus influenzae*, resistance to **co-amoxiclav** was 11% and stable over the years, confirming co-amoxiclav as a reliable treatment option in the majority of cases. Resistance to **doxycycline/tetracycline** (3%) was low and stable; resistance to **ciprofloxacin** was 10%.

2.3.1.3 Outpatient departments

Urinary tract and abdominal infections – Enterobacterales and P. aeruginosa

- For both Enterobacterales and *P. aeruginosa*, resistance levels for all tested antibiotics were higher in isolates of OPD patients compared to resistance levels in isolates from primary care patients, consistent with previous years.
- For the three most important oral antibiotics used in the OPD setting, resistance levels were essentially unchanged over the last five years. Resistance to **co-amoxiclav** was 30% in *E. coli* and 17% in *K. pneumoniae*. Resistance to **ciprofloxacin** was 16% in *E. coli*, 14% in *K. pneumoniae* and 10% in *P. aeruginosa*. Resistance to **co-trimoxazole** was 24% in *E. coli* and 13% in *K. pneumoniae*. In the majority of cases at least one oral treatment option remained available, given the relatively low combined resistance (5% in both *E. coli* and *K. pneumoniae*).
- In *K. pneumoniae*, resistance to **third generation cephalosporins** in 2025 was similar to 2024, but increased significantly over the last five years.

Skin and soft tissue infections – S. aureus and β-haemolytic Streptococci

- Resistance levels in *S. aureus* isolates of OPD patients were generally low and comparable to 2024. **MRSA** was found in 3% of isolates.
- Resistance to **clindamycin including inducible resistance** was 19% and showed a newly significant increasing trend over the last five years. Clindamycin resistance without considering inducible resistance was much lower (3%). According to EUCAST, clindamycin may still be used for short-term therapy in less severe skin and soft tissue infections if tested susceptible, even in the presence of an inducible resistance mechanism.
- In β-haemolytic *Streptococcus* group A, resistance levels were comparable to 2024 and stable over the last five years: **clindamycin including inducible resistance** 8%, **doxycycline/tetracycline** 26% and **co-trimoxazole** 1.8%.
- In β-haemolytic *Streptococcus* group B, no significant trends were identified either. Resistance to **doxycycline/tetracycline** remained very high (75%) and **clindamycin including inducible resistance** was elevated (17%), with the same clinical implication as in primary care: these levels complicate empirical treatment in patients with a beta-lactam allergy.

2.3.1.4 Hospital departments

Inpatient hospital departments (excl. ICU)

Blood, abdominal, urinary tract, skin and respiratory infections – Enterobacterales, P. aeruginosa and Acinetobacter baumannii/calcoaceticus complex

- For *E. coli*, resistance levels in 2025 were largely stable compared to 2024. Resistance to **cefuroxime** was 12% and to **cefotaxime/ceftriaxone** 7%.
- For *K. pneumoniae*, resistance to **third generation cephalosporins** (10%) was similar to 2024, and increased

significantly over the last five years. Resistance to **cefuroxime** was 15%. This means that patients infected with *K. pneumoniae* have a considerable risk of non-adequate empiric treatment with a second or (to a lesser extent) third generation cephalosporin. In case of severe infection, empiric combination therapy with an **aminoglycoside** reduced the likelihood of resistance to 3%. Resistance to **meropenem/imipenem** rose to 0.5% in 2025, continuing its gradual upward trajectory, although absolute levels remain low.

- For *P. aeruginosa*, resistance was relatively low and stable for all antibiotics over the last five years. Empirical treatment with **ceftazidime** for infections potentially caused by *P. aeruginosa* therefore remains adequate.
- For *A. baumannii/calcoaceticus* complex, resistance to **tobramycin** (4%) showed a new significant increasing trend, whereas in 2024 increasing trends had been flagged for meropenem/imipenem, ciprofloxacin and tobramycin collectively. Resistance to **meropenem/imipenem** was 3% and to **ciprofloxacin** 7%, consistent with the previous five years.

Blood, urinary tract, abdominal, skin and respiratory – S. aureus, Enterococci, β-haemolytic Streptococci

- In *S. aureus*, most resistance levels were stable and very similar to OPD findings. Resistance to **clindamycin including inducible resistance** was 18% and, as in the OPD setting, showed a significant increasing trend. This indicates that culture and susceptibility testing are advised before starting treatment with this drug. When inducible clindamycin resistance was ignored, only 3% of isolates were resistant, which indicates that clindamycin may still be used for short-term treatment in less severe skin and soft tissue infections. Resistance to **levofloxacin**, **doxycycline** and **co-trimoxazole** was 4% or less.
- **MRSA** was found in 3% of *S. aureus* isolates of hospitalised patients, which remained stable over the last five years.
- Resistance to **vancomycin** in *Enterococcus faecium* was 0.7% and showed a newly significant increasing trend.
- In β-haemolytic *Streptococcus* group A, resistance to **erythromycin** rose to 14% and now shows a significant increasing trend — a new finding not flagged in 2024. **Clindamycin including inducible resistance** was stable at 10%, while resistance to **doxycycline/tetracycline** increased to 34% without a significant trend.
- In β-haemolytic *Streptococcus* group B, resistance to **doxycycline/tetracycline** remained very high (74%), **clindamycin including inducible resistance** was 18% and **erythromycin** was stable at 23%. In groups C and G, **clindamycin including inducible resistance** was 12%, **doxycycline/tetracycline** 28% and **erythromycin** 15%, all stable.

Blood, urinary tract, abdominal, skin and respiratory – anaerobes

- The previously stable picture for *Bacteroides fragilis* complex was disrupted in 2025: resistance to **metronidazole** increased to 4% and now shows a significant increasing trend. This is a clinically important finding, given that metronidazole is a cornerstone of anaerobic treatment. Resistance to **clindamycin** remained high (16%) and to **co-amoxiclav** stable (9%).
- For *Clostridium perfringens*, resistance to **clindamycin** (63%) remained very high and stable, while resistance to **co-amoxiclav** (2%) and **metronidazole** (3%) was low with no trend flags.

Respiratory infections – S. pneumoniae and H. influenzae

- The proportion of *S. pneumoniae* isolates in the I-category for **(benzyl)penicillin** was 10% in hospital patients, and the significant increasing trend identified in 2024 was confirmed in 2025. Resistance to (benzyl)penicillin remained very low (1.2%). Resistance to **doxycycline/tetracycline** was 8%, lower than in GP patients, most probably due to more frequent use of these antibiotics and/or more selective sampling of isolates in primary care.
- In *H. influenzae*, resistance to **co-amoxiclav** was 14% and stable. Resistance to **cefuroxime** showed a significant increasing trend to 13%, already flagged last year and now confirmed. Resistance to **doxycycline/tetracycline** (3%) and **ciprofloxacin** (8%) was low and stable.

Intensive Care Units

Blood, urinary tract, abdominal, skin and respiratory – Enterobacterales and P. aeruginosa

- For Enterobacterales and *P. aeruginosa*, resistance levels for beta-lactam antibiotics were higher in intensive care unit (ICU) patients than in isolates from non-ICU patients.
- In *E. coli*, resistance to **cefuroxime** was 19% and to **cefotaxime/ceftriaxone** 13%. In *K. pneumoniae*, resistance to **cefuroxime** was 23% and to **cefotaxime/ceftriaxone** 17%. This indicates a continuing pattern of elevated cephalosporin resistance in the ICU compared to other settings, maintaining a high risk of inadequate empirical therapy with second and third generation cephalosporins for both species.
- Empiric combination therapy of **cefuroxime or cefotaxime/ceftriaxone with an aminoglycoside** reduced combined resistance to 3% in *E. coli* and 4% in *K. pneumoniae*, which might be a suitable strategy in case of severe infection. Combination therapy with **ciprofloxacin** was less successful, with combined resistance levels of 9% in *E. coli* and 10% in *K. pneumoniae*.
- Most critically, resistance to **meropenem/imipenem** in *K. pneumoniae* rose to 3% (2% in 2024) and now carries a significant and worrisome increasing trend over the last five years. This escalating carbapenem resistance in *K. pneumoniae* is the most clinically alarming finding in this setting.
- In *P. aeruginosa*, resistance to **piperacillin-tazobactam** showed a newly significant decreasing trend and is now 11% (2024:

14%), where previously this had been highlighted as a concern given its high level compared to other settings. Resistance to **tobramycin** also showed a decreasing trend (1.4%), while **ceftazidime** (10%) and **ciprofloxacin** (9%) were stable.

Blood, urinary tract, skin and respiratory – S. aureus and E. faecium

- **MRSA** in clinical *S. aureus* isolates of ICU patients remained stable at 4% over the last five years.
- The percentage of **vancomycin** resistance in clinical *E. faecium* isolates of ICU patients increased significantly to 0.7% over the last five years.

Blood isolates from inpatient departments (incl. intensive care units)

- In *E. coli* from blood cultures, resistance to **cefuroxime** remained stable at 13%, whereas resistance to **cefotaxime/ceftriaxone** increased significantly to 9% over the last five years. Resistance to **meropenem/imipenem** remained low (0.1%).
- In *K. pneumoniae* from blood cultures, resistance to **cefuroxime** and **cefotaxime/ceftriaxone** was stable between 2024 and 2025, but a worrisome increase was observed over the last five years, to 15% and 12% respectively. A significant increase in resistance to **meropenem/imipenem** (0.9%) was also found over the last five years.
- In June 2026, an expert meeting was organized by RIVM with relevant stakeholders to discuss the epidemiology and potential impact of the (inter)national rise in third-generation cephalosporin-resistant Enterobacterales (3GCR-E).
- Patients with a bloodstream infection with *E. coli* or *K. pneumoniae* thus have a considerable risk of non-adequate empiric treatment with a second or third generation cephalosporin. In case of severe infection, empiric combination therapy with **cefuroxime or cefotaxime/ceftriaxone and an aminoglycoside** reduced the likelihood of resistance to 2% in *E. coli* and 4% in *K. pneumoniae*. Empirical combination therapy with **cephalosporins and ciprofloxacin** appears to provide little additional benefit over treatment with a second or third generation cephalosporin alone (combined resistance 9%).
- After initial intravenous treatment, in patients with *E. coli* or *K. pneumoniae* bacteremia a switch to either **ciprofloxacin**, **co-trimoxazole** or **co-amoxiclav** was most often possible, given the relatively low (≤5%) combined resistance rates for these oral agents.
- In *P. aeruginosa* from blood cultures, resistance to **ceftazidime** (4%), **piperacillin-tazobactam** (7%) and **ciprofloxacin** (9%) remained stable over the last five years.
- **MRSA** was found in 2% of *S. aureus* isolates in blood cultures, the lowest MRSA percentage across all care settings.
- **Vancomycin** resistance was found in 0.6% of *E. faecium* isolates in blood cultures, which was low but increased significantly over the last five years.

Urology services

- Resistance levels in Enterobacterales and *P. aeruginosa* from patients in urology services traditionally have been higher than in non-urology patients. Within urology services, resistance levels were higher in isolates from admitted patients (IPD) than in outpatients (OPD).
- For *E. coli*, resistance to **cefuroxime** was 13% (OPD) and 17% (IPD), and to **cefotaxime/ceftriaxone** 8% (OPD) and 12% (IPD). A new significant increasing trend was identified for **cefotaxime/ceftriaxone/ceftazidime** in *E. coli* from urology IPD patients. Resistance to **ciprofloxacin** and **co-trimoxazole** remains a problem: 19% and 26% in OPD patients and 22% and 29% in IPD patients.
- Although levels were similar to 2024, a worrisome increase in resistance to almost all antibiotics was seen for *K. pneumoniae* from admitted patients over the last five years: resistance to **ciprofloxacin** and **co-trimoxazole** both increased significantly to 20%, resistance to **cefuroxime** increased to 20% and to **cefotaxime/ceftriaxone** to 16%. The increasing trend for **meropenem/imipenem** that was a major concern in urology IPD patients in 2024 is no longer flagged in 2025, a notable and reassuring change.
- Empiric combination therapy in *K. pneumoniae* from admitted urology patients — **cefuroxime + gentamicin** (5%) and **cefotaxime/ceftriaxone + gentamicin** (5%) — reduced the combined failure risk, but both combinations carried increasing trends. This represents a substantial risk in the treatment of severe *K. pneumoniae* infections in this population that warrants close monitoring over the coming years.
- For *P. aeruginosa*, resistance levels were comparable to 2024. Resistance to **ciprofloxacin** was 12% in both OPD and IPD patients. This is clinically important, as **ciprofloxacin** remains the only available oral agent to treat *P. aeruginosa* infections. Resistance to **piperacillin-tazobactam** was 5% in both settings and to **ceftazidime** 3% in IPD patients.

2.3.1.5 Long-term care facilities

- Resistance levels in *E. coli*, *K. pneumoniae* and *P. aeruginosa* urine isolates from selected residents of long-term care facilities (LTCFs) were comparable to resistance levels in OPD and hospital patients, consistent with the pattern observed in previous years.
- Resistance levels for **nitrofurantoin** and **fosfomycin** in *E. coli*, first and second choice antibiotics for the treatment of uncomplicated UTI in adults, remained stable and low (both 3%).
- Resistance levels for **ciprofloxacin**, first choice antibiotic for the empiric oral treatment of complicated UTI in adults, remained stable in *E. coli* (14%), *K. pneumoniae* (13%) and *P. aeruginosa* (9%). Resistance to **co-amoxiclav**, second choice antibiotic for this indication, remained stable in *E. coli* (29%) but decreased significantly to 17% in *K. pneumoniae*. Resistance to **co-trimoxazole**, third choice antibiotic, was stable at 19% in *E. coli* and 11% in *K. pneumoniae*.

- Resistance to **levofloxacin** (14%) in *S. aureus* was much higher than in *S. aureus* from OPD (3%), hospital (3%) and ICU patients (2%). This might result from either selective sampling or intensive use of fluoroquinolones in this setting.
- **MRSA** was found in 3% of *S. aureus* isolates and now carries a significant increasing trend — the first time an increasing MRSA trend has been identified in the LTCF setting.
- Resistance to **clindamycin including inducible resistance** was 20% and also carries a significant increasing trend. **Clindamycin** resistance without inducible mechanisms was 4%, unchanged from 2024. According to EUCAST, **clindamycin** may still be used for short-term therapy in less severe skin and soft tissue infections if tested susceptible, even in the presence of an inducible resistance mechanism.

2.3.2 Specific AMR surveillance

Extended spectrum beta-lactamases

- From 2021 to 2025, the proportion of extended spectrum β-lactamase (ESBL) producing *E. coli* increased significantly in GP patients (5%) and in ICUs (13%). Overall, 6% of 201,185 diagnostic *E. coli* isolates were ESBL-producing, with 7% in OPD and 8% in IPD.
- The proportion of ESBL-producing *K. pneumoniae* increased significantly overall (7%), and specifically in OPD (9%) and IPD (10%). In ICUs the proportion remained high (16%).
- Percentages above 10% in the inpatient setting, combined with the overall increasing trend, are alarming. In June 2026 an expert meeting was organised by RIVM with relevant stakeholders, which concluded that this increase is worrisome and that optimal control requires better insight into the epidemiology and the risk groups for carriage and infection. Research projects will be set up, including investigation of adjustments in empirical treatment policies and infection prevention measures.

Carbapenem-resistant and carbapenemase-producing Enterobacterales

- The prevalence of **carbapenem** resistance in diagnostic isolates of *E. coli* slightly increased between 2021 and 2025 from 0.00% to 0.04%. For *K. pneumoniae*, the prevalence of **carbapenem** resistant strains increased between 2021 and 2025 from 0.09% to 0.30%
- The RIVM received 812 Enterobacterales isolates that produced carbapenemase, which was considerably higher than in previous years.
- The most frequently identified carbapenemase encoding genes in Enterobacterales were $bla_{\text{OXA-48-like}}$ (31%), $bla_{\text{NDM-5}}$ (22%) and $bla_{\text{OXA-48}}$ (16%).
- In 39% of patients, there was a relation with hospitalization abroad for more than 24 hours during the two months prior to sampling.

Carbapenem-resistant and carbapenemase-producing P. aeruginosa

- In 2025, 4% of *P. aeruginosa* in diagnostic isolates were resistant to **carbapenems**.
- For only 14% of **carbapenem**-resistant isolates, information on carbapenemase testing was reported; of these, 14% produced carbapenemase. Of the **carbapenem**-resistant isolates without such test results, 91% were susceptible to **tobramycin**, which explains most of the missing data under the Dutch guideline for detection of highly resistant microorganisms.
- The RIVM received 55 carbapenemase-producing *P. aeruginosa* (CPPA) isolates via Type-Ned. The predominant carbapenemase-encoding allele was $bla_{\text{NDM-1}}$ (37%), followed by $bla_{\text{IMP-1}}$ (30%) and $bla_{\text{VIM-2}}$ (24%). Before the Ukraine/Russia war $bla_{\text{VIM-2}}$ was dominant; the share of $bla_{\text{NDM-1}}$ rose from 7% in 2021 to 37% in 2025.

Carbapenem-resistant Acinetobacter baumannii-calcoaceticus complex

- In 2025, 2% of *A. baumannii-calcoaceticus* complex in diagnostic isolates were resistant to **carbapenems**. The percentage of **carbapenem**-resistant *A. baumannii-calcoaceticus* isolates from inpatient departments increased significantly over the past five years (5%). Differences with section 1.3.1.4 result from inclusion of carbapenemase test results and different sample selection.
- The RIVM received 71 *A. baumannii-calcoaceticus* complex isolates that produced carbapenemase.
- The predominant (49%) carbapenemase-encoding gene combination in *A. baumannii-calcoaceticus* complex was $bla_{\text{OXA-23}}$ and $bla_{\text{OXA-66}}$, and 18% carried a $bla_{\text{NDM-like}}$ carbapenemase.

Methicillin-resistant Staphylococcus aureus (MRSA)

- The overall proportion of routinely collected diagnostic *S. aureus* isolates that were MRSA positive in 2025 was still at a low level of 3%, with 4% in ICUs.
- A strong increase in phenotypic **fusidic acid** resistance was observed among diagnostic MRSA isolates, corresponding to a clear increase in the *fusC* resistance gene.
- During the 2021-2025 surveillance period, there has been a decreasing trend in the proportion of MC0398 in both diagnostic (from 12% to 7%) and screening isolates (from 26% to 10%).
- In 2025, 40% of the diagnostic MRSA-isolates carried the PVL encoding genes, whereas 20% of the screening isolates were PVL-positive.

Vancomycin-resistant E. faecium

- The proportion of VRE in diagnostic *E. faecium* isolates in various healthcare settings in 2025 was still low (0.7% overall, below 1% in all settings), but the increases over the last five years were significant in outpatient departments and intensive care units.
- There are currently no centrally collected molecular typing data for VRE*fm* in the Netherlands, even though WHO lists VRE*fm* in the high-risk category; reliable data on the molecular epidemiology of VRE*fm* in Dutch hospitals are therefore lacking.

Healthcare associated Infections and Antimicrobial Resistance (SO-ZI/AMR)

- In 2025, 67 outbreaks were reported to SO-ZI/AMR, higher than in the previous five years.
- The number of VRE outbreaks (n=18) in hospitals was again notably higher than in previous years.
- In LTCFs the majority of reported outbreaks were MRSA (n=20), substantially more than in 2020–2023 but comparable to 2019 and 2024. In hospitals, 12 MRSA outbreaks were reported, half of them related to paediatric or neonatal wards.

Helicobacter pylori

- Although probably biased towards higher resistance levels due to sampling policies, resistance in *H. pylori* remained high for **metronidazole** (51%) and **levofloxacin** (22%) and **clarithromycin** (59%) over the last five years.
- Resistance to **amoxicillin/ampicillin** (8%) and **doxycycline/tetracycline** (1.0%) traditionally has been low.
- For first-choice combination treatment with **amoxicillin and clarithromycin**, combined resistance was 6% in 2025. If treatment fails, recommended rescue regimens **tetracycline plus metronidazole** (0.7%) and **amoxicillin plus metronidazole** (5%) both remain reliable.

Neisseria meningitidis

- The number of invasive *N. meningitidis* isolates in recent years has nearly reached pre-COVID-19 levels.
- **Penicillin** resistance in *N. meningitidis* isolates is rare (<3%)

Neisseria gonorrhoeae

- The number of gonorrhoea diagnoses reported in 2025 continued to increase, from around 6,000 per year in 2016-2020 to 14,297 in 2025.
- In 2025, **ceftriaxone** resistance was reported for the first time in an imported infection. There was no further transmission following this case in the Netherlands. Although this was only one case, the MIC distribution among all isolates in the Netherlands has shifted towards higher MICs since 2021.
- Resistance to **ciprofloxacin** continues to increase yearly, to 59.7% in 2025. **Azithromycin** resistance decreased to 21.9%.
- **Tetracycline** was added to the panel in 2025 because of the emerging use of **doxycycline** post-exposure prophylaxis (Doxy-PEP), and resistance was 57.1%. At this level, Doxy-PEP is unlikely to reduce gonorrhoea incidence and might increase the incidence of **tetracycline**-resistant gonorrhoea.

Mycobacterium tuberculosis complex

- In 2025, 10% of *M. tuberculosis* isolates contained resistance to one or more **antimycobacterial** drugs, compared with 13.4% in 2024. This mainly concerned **isoniazid** resistance; the alarming increase in **isoniazid** resistance in 2024 was brought under control in 2025.

- The number of multidrug-resistant (MDR) isolates was stable in recent years and represented 2.4% of culture positive cases.

Aspergillus fumigatus and Candida auris

- **Azole** resistance among *A. fumigatus* was 12.5% in five UMCs and 4.2% in five teaching hospitals in 2025. In teaching hospitals this was stable compared with previous years, whereas in UMCs it was higher than in recent years but comparable to 2019, and above the 10% threshold at which initial therapy covering azole resistance is recommended for invasive aspergillosis.
- In 2025, eleven *C. auris* cases were reported by nine hospitals. All were linked to travel and/or hospital admission abroad, all patients were colonised only, and no nosocomial transmission was noted.

Shigella

- Of the 416 *Shigella* isolates in 2025, *S. sonnei* made up 50% and *S. flexneri* 40%. Resistance was high: about 70% to **ampicillin**, 55% to **cotrimoxazole**, and about 37% to **ciprofloxacin**. No **carbapenem** resistance or CPE was found.
- In *S. sonnei*, resistance to **ciprofloxacin** and **third generation cephalosporins** has stayed around 40% since 2023. Resistance and multidrug resistance (MDR) were highest among MSM (men who have sex with men), with MDR in *S. sonnei* usually above 10% in that group. Changes over time come mostly from long-running clusters found by whole-genome sequencing.

2.4 Most important trends in antimicrobial resistance in zoonotic pathogens in humans and animals

Salmonella

- Among **human** *S.* Enteritidis isolates resistance against **fluoroquinolones** is high (49% in 2025), and it has been increasing since 2016, now exceeding the previous peak in 2022.
- In contrast, resistance against **fluoroquinolones** was much lower in *S*. Enteritidis isolates from **layers and broilers** (9% and 26%). Although not specified per serotype, resistance levels to **fluoroquinolones** among isolates from Dutch/EU broiler meat (which are an additional source of SE) was around 52%.
- Among **human** *S.* Typhimurium isolates resistance to **amoxicillin/ampicillin** remained high (29% in 2025), although it appears to have decreased slightly in recent years, while resistance to **cotrimoxazole** was moderate (9%) and has remained relatively stable. Correspondingly, in isolates from **animal** sources the levels of resistance of *S.* Typhimurium and its monophasic variant to **ampicillin**, **sulfamethoxazole** and **tetracycline** were high, especially in pigs (ranging from 29% to 85%).
- In contrast to *S*. Enteritidis, resistance to **fluoroquinolones** was relatively low for *S*. Typhimurium (12%) and its monophasic variant (11%).
- The proportion of ESBL/pAmpC-producing *Salmonella* isolates from humans remained low, with a prevalence of 1.3%

(18/1341) in 2025 (1.4% in 2024); in non-human isolates it was 0.4% (2/545). None of the tested human and non-human *S.* enterica isolates were found to produce carbapenemases.

Campylobacter

- In **human** *Campylobacter* spp. isolates, the level of **ciprofloxacin** and **tetracycline** resistance increased further in 2025 (around 69% and 52%, respectively, compared with 62% and 45% in 2024)
- Resistance to **erythromycin**, first choice antibiotic for campylobacteriosis in humans, remained low among human isolates (<5%; 3.6% in 2025)
- **Poultry and poultry meat** are the most important reservoir and transmission route of campylobacteriosis. Levels of resistance among human isolates correspond with similarly high levels among isolates from broilers and meat thereof.
- Among *C. coli* isolates from **veal calves erythromycin** resistance is notably higher (37%, compared with 45% in 2024), however consumption of veal meat is relatively low.

STEC

- In 2025, only genotypic AMR markers were assessed in **human** STEC/EPEC isolates. Markers associated with resistance to **ampicillin**, **ciprofloxacin**, **sulfamethoxazole** and **trimethoprim** were significantly more frequent in non-O157:H7 isolates (10–19%) than in O157:H7 isolates (0–6%), as were markers for **multiple antimicrobial classes** (16% vs. 3%), most often in O103:H2 and O26:H11.
- Markers associated with resistance to **third-generation cephalosporins** were uncommon (3% in both groups), and no **carbapenem** resistance markers were detected.
- Although, therapeutic treatment of STEC infections with antimicrobials is not advised, monitoring AMR in STEC from symptomatic human cases is useful in assessing the risk of transmission of resistant bacteria (especially other *E. coli*).

Yersinia enterocolitica

- In **humans**, the levels of resistance to **amoxicillin/ampicillin** in *Y. enterocolitica* have been very high (98%) over the past five years. In that same time period, resistance levels against **ciprofloxacin** for this species decreased from 7% in 2021 to 2% in 2025, while the proportions of resistance to **third generation cephalosporins**, **cotrimoxazole**, and **gentamicin** have remained stable at levels below 2% in the same period.

2.5 Most important trends in antimicrobial resistance in commensal bacteria from farm-animals and food

2.5.1 General AMR surveillance – using indicator bacteria

E. coli

- An indicator *E. coli* for the surveillance of antimicrobial resistance (AMR) in animals is a non-pathogenic, commensal strain of *E. coli* that is commonly found in the intestinal tract of healthy animals. These indicator *E. coli* strains are used as a representative organism to monitor and track trends in antimicrobial resistance within animal populations and on food products, as they can acquire and transfer resistance genes in Gram-negative bacteria.
- The highest resistance levels in indicator *E. coli* were observed in broilers, turkeys, slaughter pigs, and veal calves, whereas resistance levels in isolates from dairy cattle were historically low.
- Over the period **2021-2025**, levels of resistance in *E. coli* stabilised in broilers, pigs and veal calves for most antibiotics.
- In **turkeys**, resistance levels of indicator *E. coli* from faecal samples substantially decreased compared to 2011, probably reflecting the effect of the considerable reduction in use of antibiotics in this sector.
- In 2025, resistance to ampicillin, chloramphenicol, tetracycline, sulfamethoxazole and trimethoprim was frequently observed (>10%) amongst indicator *E. coli* in broilers (except for chloramphenicol), pigs, and veal calves.
- Resistance to **fluoroquinolones** was common among indicator *E. coli* from caecal samples of broiler chickens (24.0%) and faecal samples of turkeys (13.8%), in contrast to the prevalence (<5%) observed in pigs, veal calves, and dairy cattle.
- Overall, levels of resistance in *E. coli* from retail beef was low ranging, from 0 – 7.9% across the different antimicrobials tested. Notably, resistance in *E. coli* from imported beef was even lower.
- For retail pork, *E. coli* resistance levels were higher than in retail beef for almost all antibiotic classes. The highest levels of resistance were observed in ampicillin, tetracycline, sulfamethoxazole and trimethoprim ranging from 12.6% to 14.5%.

Enterococci

- Enterococci are used as a representative organism to monitor and track trends in antimicrobial resistance within animal populations and on food products, as they can acquire and transfer resistance genes in Gram-positive bacteria. For this purpose non-pathogenic, commensal strains of *E. faecalis* or *E. faecium* that are commonly found in the intestinal tract of healthy animals are used.
- In 2025, resistance to **erythromycin** and **tetracycline** was frequently observed in enterococci (*E. faecium* and *E. faecalis*) isolated from caecal samples of slaughtered pigs: for *E. faecium*, the rates were 13.3% and 39.3%, respectively, while the highest

percentages were recorded for *E. faecalis*, at 32.1% and 60.4%, respectively.
- Resistance to **ampicillin** was only detected in *E. faecium*. Resistance to **ciprofloxacin**, **daptomycin**, **gentamicin**, **linezolid**, **tigecycline**, **teicoplanin**, and **vancomycin** was absent or present at low levels (<4%).

2.5.2 Specific AMR surveillance

- The prevalence of Extended Spectrum Cephalosporins (ESC)-resistant *E. coli* in farm animals and food are specifically monitored as they are considered one of the highest priority critically important antimicrobials for human medicine.
- In 2025, resistance to ESC was rarely detected (1.1%) amongst **randomly selected** *E. coli* on a non-selective plate from samples collected at slaughter houses and retail meat.
- The prevalence of ESC-resistant *E. coli* in **broiler chickens**, determined through **selective isolation** from caecal samples, fell back to the 2020 level -namely 10.4%- in 2025 with the presence of *bla*$_{\text{CTX-M-1}}$ beta-lactamase gene being the primary cause.
- Selective isolation of ESC-resistant *E. coli* revealed that veal calves had the highest prevalence of ESC-resistant *E. coli* among all farm animal sectors. With difference in prevalence among white veal calves (39.9%) and rosé veal calves (24.6%). The prevalence of the *bla*$_{\text{CTX-M-32}}$ gene remained high in white calves, consistent with the reported expansion of this lineage in 2024.
- The prevalence of ESC-resistant *E. coli* in **dairy cattle** showed a slight decrease from 22.9% in 2024 to 18.3% in 2025 after an increasing trend between 2014 - in 2024, *bla*$_{\text{CTX-M-15}}$ was the dominant beta lactamase gene.
- In meat, ESC-resistant *E. coli* prevalence in 2025 was broadly stable relative to 2024 in beef, veal, pork, and chicken, all remaining within the range of fluctuation seen since 2014; chicken remains the food category with the highest prevalence (18.3%).
- In 2025, a carbapenemase-producing *E. coli* carrying a *bla*$_{\text{OXA-181}}$ gene was detected in a fresh fecal floor sample from a dairy cow, collected on the farm. In 2025, an *Enterobacter cloacae* complex isolate carrying a *bla*$_{\text{IMI-3}}$ gene was identified in a fresh herb sample from Spain. In 2025, *E. coli* carrying *bla*$_{\text{OXA-48}}$ was found in a faecal sample from a dog. These findings in farm animals, food and companion animals demonstrate the value of ongoing CPE surveillance.
- The prevalence of *mcr*-positive *E. coli* in farm animals was low in 2025; *mcr-1* positive *E. coli* was detected in two samples from broilers (0.6%), two from pigs (0.7%) and one veal calf sample (0.3%).This probably reflects the low use of colistin.
- In 2025, samples were collected from pig farms for the second year in row. Conventional pig farms and organic pigs farms were compared, and conventional farms were shown to have a significantly higher LA-MRSA prevalence (78% in conventional pig farms and 12% in organic pig farms). In general, pig farms have a higher MRSA prevalence (67.6% in 2025) than other farm

types that were studied in previous years. MRSA prevalence among persons living or working on organic farms (8.7%) is lower than among persons working or living on conventional pig farms (41.2%).
- Isolates derived from the pig farms were compared to isolates collected in the national human MRSA-surveillance (Typened). In two cases, MRSA isolates from a human infection were genetically related to pig isolates from 2024-2025, including one isolate from pig meat.
- MRSA is found on pork, veal and beef. Imported pork is more contaminated than pork obtained from retail.

2.6 Implications for public health and health policy

Antimicrobial resistance is not only a clinical problem, but a major public health threat as it undermines the effectiveness of essential medicines, leading to harder-to-control infections, increased transmission, and greater risk of outbreaks. It also imposes a substantial societal burden through higher healthcare costs and widening global health inequalities.

For carbapenem-resistant Enterobacterales, the resistance percentage among diagnostic isolates has clearly increased from 0% to 0.04% in *E. coli* and from 0.09% to 0.3% in *K. pneumoniae* between 2021 and 2025. Moreover, the number of carbapenemase-producing Enterobacterales isolates submitted to the RIVM (n=812) was again considerably higher than in previous years and surpassed the numbers in pre- and post-COVID years. At the same the use of third-generation cephalosporins and carbapanems has increased with 45% and 20%, respectively, compared to 2019. These trends in both antibiotic resistance and antibiotic use are possibly related to shifts in patient related risk factors and/or changes in exposure. As in previous years the most frequently reported risk factor for CPE carriage is recent hospitalization abroad. In 2025 most patients with a diagnostic isolate had no known risk factor or it was unknown whether the person had a risk factor (63%). Moreover, in 14% of the CPE positive persons, no known risk factor and no invasive medical procedure or invasive medical device within twelve months prior to sampling was reported, leaving the origin or acquisition of the CPE unexplained.

In addition, ESBL-positive Enterobacterales also showed increases in the Netherlands in 2025 compared to the previous years. From 2021-2025, there has been a significant increase in ESBL-producing *E. coli* in general practice (GP) and intensive care units and an increase in ESBL-producing *K. pneumoniae* overall and specifically in outpatient and inpatient department populations. ESBL-producing *K. pneumoniae* percentages showed continuing percentages above 10% in the inpatient department population. In the 10-year-trends, the percentages of ESBL-producing *E. coli* and *K. pneumoniae* in 2025 in all healthcare departments are up or above the levels in the pre-COVID-years, which is worrisome. In June 2026, an expert meeting was organized by RIVM with relevant stakeholders to discuss the epidemiology and potential impact of the (inter)national rise in third-generation cephalosporin-resistant Enterobacterales (3GCR-E). The expert meeting concluded that this increase is worrisome, and considers it necessary to maintain, and

possibly strengthen, the current focus on controlling 3GCR-E in the curative care. It sees opportunities to optimize the implementation of antibiotic and infection prevention policies, which will require more detailed insight into the epidemiology of and the risk groups for 3GCR-E carriage and infection; together with the involved stakeholders, priority actions will be identified and elaborated that should contribute to delay the observed increase in 3GCR-E.
The overall proportion *S. aureus* isolates that were MRSA positive in 2025 remained at a low level of 3%, although the absolute number of MRSA isolates submitted for the enhanced MRSA surveillance is increasing each year and is higher compared to pre-COVID-19 pandemic levels. In addition, a continued significant increase was observed in phenotypic fusidic acid resistance among diagnostic *S. aureus* isolates including MRSA. Furthermore, resistance to other antimicrobials among some Gram-positive micro-organisms remains high, such as clindamycin resistance (including inducible resistance) among *S. aureus*, which warrants special attention for antibiotic stewardship programs and surveillance of these pathogens as well.

Besides these increasing trends, in 2025, an international genetic cluster with a sudden emergence of infections and colonisations with *E. hormaechei* ST1344 carrying *bla*$_{\text{NDM-5}}$ on an IncX3-plasmid was observed.[1] Up to May 2026, 57 cases were confirmed to be part of the outbreak, affecting seven countries, with the earliest case observed in March 2025. Sixteen of the cases were identified in the Netherlands. The outbreak investigation, including exposure questionnaires, revealed that many patients were hospitalized at the time of sampling (n=45). In addition, in the group of patients detected in the Netherlands, the majority had been exposed to prior medical treatment, including most of the patients who were not hospitalized at the moment of sampling. Only three cases reported recent traveling abroad. Up until now, a source has not been identified.

Worldwide and in Europe, antibiotic resistance continues to be a serious threat to public health, leading to increased healthcare costs, prolonged hospital stays, treatment failures and sometimes death.
In June 2023, the Council of the EU adopted a Council Recommendation[2] on stepping up EU actions to combat AMR using a One Health approach, which recommends targets to be achieved by the EU by 2030. These include three AMR targets to reduce the total EU incidence of bloodstream infections with MRSA, third-generation cephalosporin-resistant (3GCR) *E. coli* and carbapenem-resistant *K. pneumoniae*, by 15%, 10% and 5%, respectively, by 2030 compared to baseline year 2019.
The EU incidence of bloodstream infections with MRSA indicated that the EU target has been reached in 2025 with a statistically significant decreasing trend between 2019 and 2025, although the estimated incidence has been increasing in the last two years.[3] The results for the other two EU targets were not pointing in the right direction. The estimated EU incidence of 3GCR *E. coli* bloodstream infections with a 10% reduction target, increased with 16% compared to 2019. The estimated EU incidence of carbapenem-resistant *K. pneumoniae* increased by over 72% compared to 2019, which differs substantially

from the target of a 5% reduction by 2030. Increases were also observed for many other bacteria and antimicrobial groups under surveillance during the period 2021-2025 without an EU target, such as carbapenem-resistant *E. coli*, all estimated resistance incidences for *Streptococcus pneumoniae*, and vancomycin-resistant *Enterococcus faecium*.
Based on EARS-net, the estimated EU/EEA incidences of *E. coli* bloodstream infections with AMR increased compared to 2021 and there was a significantly increasing trend for aminopenicillin resistance, fluoroquinolone resistance, third-generation cephalosporin resistance, carbapenem resistance and aminoglycoside resistance. The same accounted for resistance to all antimicrobial groups in *K. pneumoniae*, and the incidence of combined resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides was also at the rise.
Compared to 2021, the 2025 estimated EU/EEA incidences of bloodstream infections with penicillin non-wild-type *S. pneumoniae* more than doubled and there was an increasing trend for all incidences. Combined resistance for macrolides and penicillin non-wild-type had also more than doubled compared to 2021.
Wide variations in the occurrence of antimicrobial resistance across the EU/EEA exist.[3] Higher AMR was generally reported by countries in southern, central and eastern Europe. In the absence of stronger public health action, it is unlikely that the EU will reach all its AMR targets by 2030.

Conclusions and discussion
The data presented in NethMap One Health 2026 demonstrate that ongoing attention is needed to combat antibiotic resistance and optimize antimicrobial use in humans and animals in the Netherlands but also in international context.
Although in general, the resistance percentages in the Netherlands are still low compared to other countries, for some clinically important bacterial species, antimicrobial resistance is increasing. Especially the gradual increase of 3GCR-E, in addition to increased third generation cephalosporine use, is worrisome, because this complicates treatment of common infections. It could lead to increased use of carbapenems for empirical and targeted treatment which could eventually drive the increase of carbapenem-resistant Enterobacterales. Actions will be taken to further investigate and adjust empirical treatment policies and to strengthen infection prevention and control measures.
When comparing farm animals in the Netherlands to other countries, the resistance percentages have declined in the last decade and are generally also below the average, but vigilance is prudent as the first detection of CPE in farm animals occurred in 2024 and was again found in 2025.
Current AMR control measures, including antimicrobial stewardship, surveillance and infection prevention, will be maintained. To control the spread and increase of HRMO, antimicrobial stewardship programs and infection prevention measures have been implemented universally in Dutch healthcare. The Antimicrobial Stewardship Monitor was developed by SWAB to evaluate and further improve antimicrobial stewardship programs. The usage of antimicrobials in farm animals has been greatly

reduced, benchmarks are implemented per sector and preparations are made for the future inclusion of currently unmonitored sectors. Finally adequate surveillance systems monitor the impact of measures to control the spread of antimicrobial resistance in human healthcare as well as the open population, the environment, food-producing animals and the food chain. In 2024 a new National Action Plan (NAP) on Antimicrobial Resistance 2024-2030[4] was launched, in which the Netherlands proposes numerous actions. The Netherlands plays the role of a proactive connector and partner in this effort, not only within its own borders but also internationally.

2.7 References

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3 Antimicrobial consumption in humans

3.1 Antimicrobial consumption in humans

3.1.1 Outpatient antibiotic use

Introduction

Most antibiotics for human use in the Netherlands are used outside hospitals. Trends in outpatient use therefore largely determine total antibiotic use and the selection pressure. Dispensing data show the volume and type of antibiotics used, but not the indication for which they were prescribed. Prescribing quality in general practice is addressed separately (see Antibiotic prescribing quality indicators in primary care).

Methods

Data on outpatient antibiotic use were obtained from the Foundation for Pharmaceutical Statistics (SFK). SFK collects dispensing data from community pharmacies, including hospital-based outpatient pharmacies, and extrapolates these data to all community pharmacies in the Netherlands. The data therefore include prescriptions by general practitioners, medical specialists and other prescribers such as dentists. Use was measured in Defined Daily Doses (DDD) per ATC code and route of administration. It is expressed as DDD per 1,000 inhabitants per day (DID). The denominator is the number of residents served by community pharmacies (16,737,238 in 2025, about 93% of the Dutch population). Residents supplied by a dispensing general practitioner are not included. This section is limited to antibiotics for systemic use (J01). Changes and percentages were calculated from unrounded values.

Results

Total systemic antibiotic use decreased by 4.2%, from 9.02 DID in 2024 to 8.64 in 2025 (Table 3.1.1.1, Figure 3.1.1.1). In absolute terms the largest decreases were seen for tetracyclines (−0.14 DID), penicillins with extended spectrum (−0.10), nitrofuran derivatives (−0.07) and combinations of penicillins with beta-lactamase inhibitors (−0.04). These four groups accounted for about 90% of the total decrease. The largest relative decreases were observed for beta-lactamase sensitive penicillins (−9.4%), penicillins with extended spectrum (−7.7%) and tetracyclines (−7.5%). Use of fosfomycin (+7.8%), sulfonamides with trimethoprim (+2.4%), lincosamides (+0.8%) and macrolides (+0.6%) increased. Use of beta-lactamase resistant penicillins remained stable at 0.60 DID. Compared with 2019, use of lincosamides increased by 27.7%, beta-lactamase resistant penicillins by 24.5% and sulfonamides with trimethoprim by 18.1%. Over the same period, use of nitrofuran derivatives decreased by 12.9% and trimethoprim by 10.5%.
At agent level, use of amoxicillin decreased by 7.7% and use of doxycycline by 7.4% (Figure 3.1.1.2). Within the macrolides, use of azithromycin decreased by 2.2%, whereas use of clarithromycin increased by 7.7%. Within the fluoroquinolones, the share of levofloxacin. Use of ciprofloxacin decreased by 5.2%, whereas use of

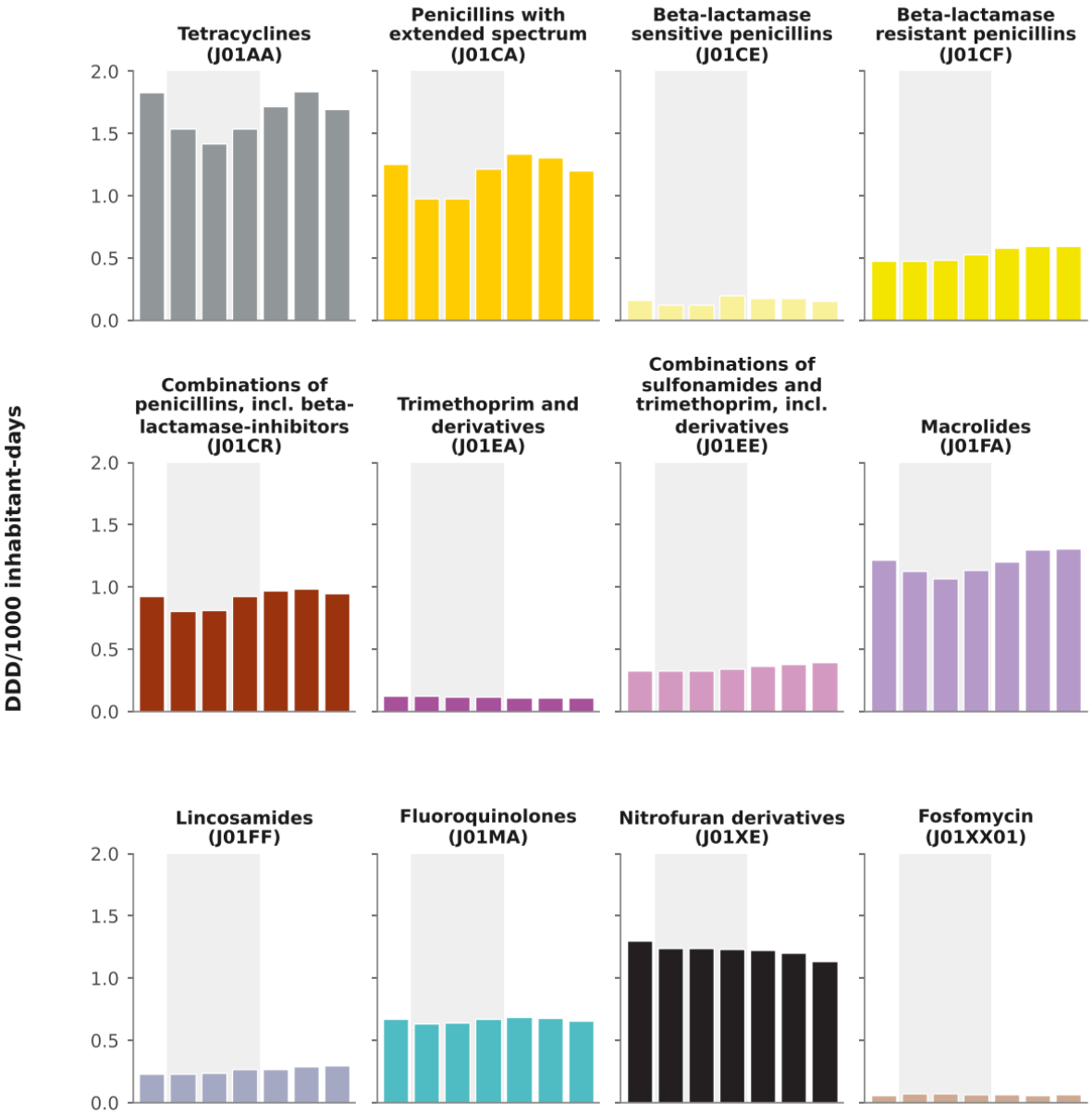
levofloxacin increased by 20.6% and its share in fluoroquinolone use rose from 9% in 2019 to 16% in 2025. Expressed in DDD, doxycycline had the largest volume of use in 2025 (1.58 DID), followed by amoxicillin (1.20), nitrofurantoin (1.14), azithromycin (0.98) and co-amoxiclav (0.94).

Table 3.1.1.1 *Use of antibiotics for systemic use (J01) in outpatients, by year and therapeutic group, 2019-2025, presented as DDD/1000 inhabitant-days (source: SFK)*

ATC group	Therapeutic group	2019	2020	2021	2022	2023	2024	2025
J01AA	Tetracyclines	1.83	1.54	1.42	1.54	1.72	1.84	1.70
J01CA	Penicillins with extended spectrum	1.26	0.98	0.98	1.22	1.34	1.30	1.20
J01CE	Beta-lactamase sensitive penicillins	0.16	0.12	0.13	0.20	0.18	0.17	0.16
J01CF	Beta-lactamase resistant penicillins	0.48	0.47	0.48	0.53	0.58	0.60	0.60
J01CR	Combinations of penicillins, incl. beta-lactamase-inhibitors	0.93	0.81	0.81	0.92	0.97	0.99	0.95
J01D	Cephalosporins, monobactams and carbapenems	0.03	0.03	0.03	0.03	0.03	0.03	0.03
J01EA	Trimethoprim and derivatives	0.12	0.12	0.12	0.12	0.11	0.11	0.11
J01EE	Combinations of sulfonamides and trimethoprim, incl. derivatives	0.33	0.33	0.33	0.35	0.37	0.38	0.39
J01FA	Macrolides	1.22	1.13	1.07	1.14	1.20	1.30	1.31
J01FF	Lincosamides	0.23	0.23	0.24	0.27	0.27	0.29	0.30
J01GB	Aminoglycosides	0.02	0.02	0.02	0.02	0.02	0.02	0.02
J01MA	Fluoroquinolones	0.67	0.64	0.64	0.67	0.69	0.68	0.66
J01XE	Nitrofuran derivatives	1.30	1.24	1.24	1.23	1.22	1.20	1.14
J01XX01	Fosfomycin	0.06	0.07	0.07	0.07	0.07	0.06	0.07
	Others [1]	0.03	0.03	0.03	0.03	0.03	0.03	0.02
J01	**Antibiotics for systemic use (total)**	**8.68**	**7.77**	**7.61**	**8.32**	**8.80**	**9.02**	**8.64**

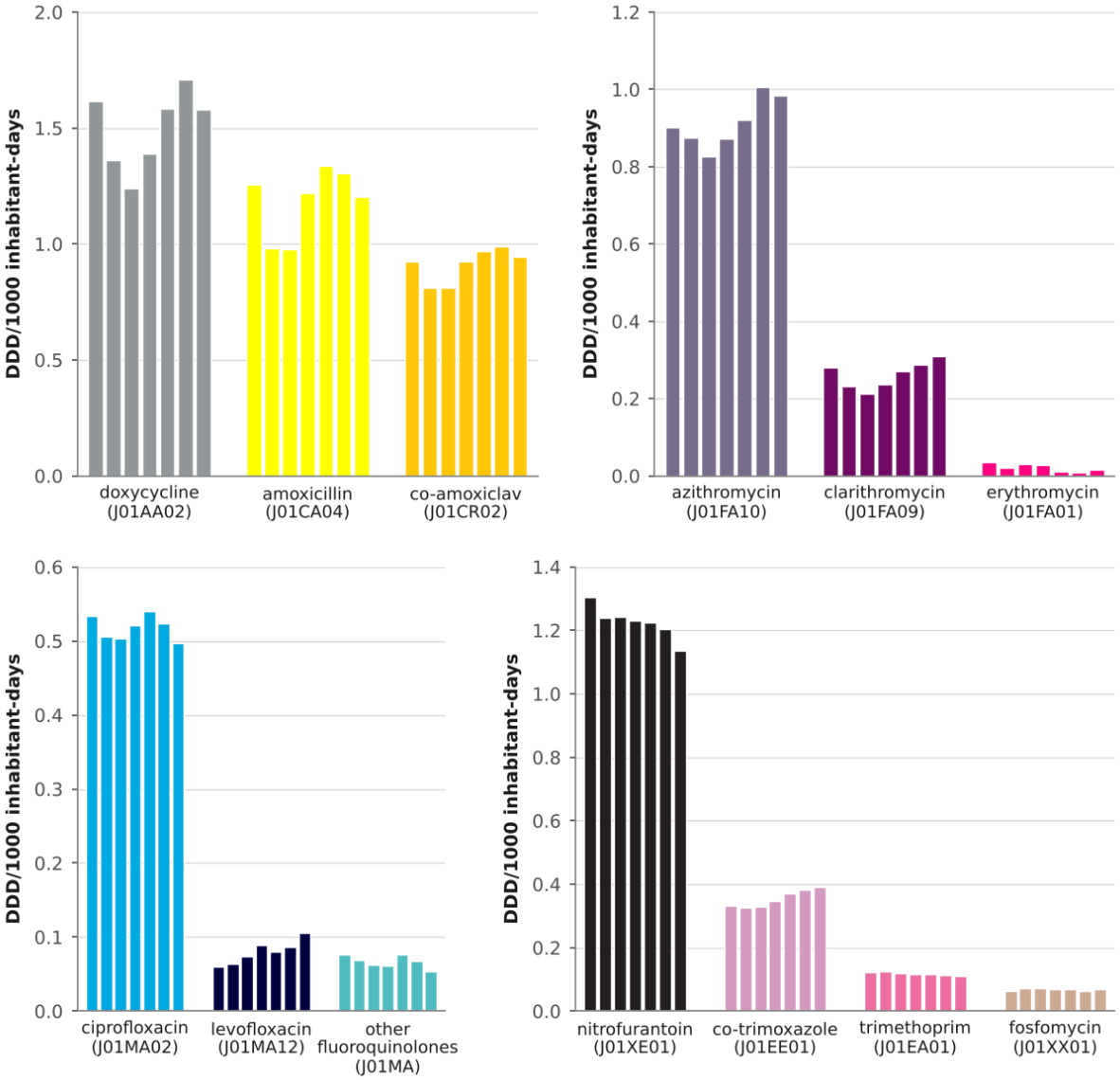
[1] Others: J01EC (intermediate-acting sulfonamides), J01XA (glycopeptides), J01XB (polymyxins), J01XC (steroid antibacterials), J01XD (imidazole derivatives), J01XX (other antibacterials, excluding fosfomycin)

Figure 3.1.1.1 *Use of antibiotics for systemic use (J01) in outpatients, by therapeutic group, 2019-2025, presented as DDD/1000 inhabitant-days (source: SFK)*



Bars denote 2019-2025. The grey areas highlight the years of the COVID-19 pandemic (2020-2022).

Figure 3.1.1.2 *Use of selected antibiotics in outpatients, by therapeutic agent, 2019-2025, presented as DDD/1000 inhabitant-days (source: SFK)*



Bars denote 2019-2025. Other fluoroquinolones: ofloxacin (J01MA01), norfloxacin (J01MA06) and moxifloxacin (J01MA14).

Discussion

In 2025, antibiotic use decreased for the first time since 2021, to a level slightly below that of 2019. Use had increased in 2022-2024 after a low during the COVID-19 pandemic. The decrease was mainly seen for doxycycline, amoxicillin and nitrofurantoin, whereas use of macrolides, lincosamides and sulfonamides with trimethoprim continued to increase modestly. DDD reflect the volume of use and not the number of prescriptions or treated patients.

SFK data include prescriptions by medical specialists and other prescribers, and antibiotics dispensed to residents of long-term care facilities supplied by a community pharmacy. They therefore partly overlap with the data presented under Long-term care facilities.

Conclusions

- Antibiotic use in outpatients decreased by 4.2% in 2025 to 8.64 DDD per 1,000 inhabitants per day. This marks the first decrease since 2021, resulting in use that is even slightly below that of 2019.
- The decrease was mainly seen for doxycycline, amoxicillin and nitrofurantoin.
- Use of macrolides, lincosamides and sulfonamides with trimethoprim continued to increase slightly.

3.1.2 Antibiotic prescribing quality indicators in primary care

Introduction
Antibiotic prescribing quality at general practitioner (GP) practice level is evaluated using the SABEL (Spiegelinformatie AntiBiotica EersteLijn) quality indicators (QIs)[1,2]. These QIs link antibiotic prescribing to clinical indications via illness episodes derived from International Classification of Primary Care (ICPC)-coded consultations from practices' electronic medical records.

Web-based feedback reports of these QI outcomes are made available to GPs and discussed during pharmacotherapy audit meetings (FTOs) organised by the regional antimicrobial resistance care networks, and via the VIPLive and Mijn INSZO (Instituut voor Zorgoptimalisatie) dashboards.

Methods
Each year, the RIVM receives the QI outcomes from GP practices that have given consent via Stichting Informatievoorziening voor Zorg en Onderzoek (STIZON) and from practices that collaborate with VIPLive. Data are available from 2018 to 2025.

For all analyses, GP practices with <500 registered patients and/or with <100 or >750 oral antibiotic prescriptions per 1000 registered patients are considered outliers and therefore excluded.

The fourteen QIs for primary care are described in Table 3.1.2.1. The median score for each QI outcome was calculated with its interquartile range (IQR, 25th–75th percentile).

Results
In 2025, data were available from 1663 GP practices in total (751 STIZON and 912 VIPLive), covering approximately 35% of the Dutch general population/GP practices. At least 13% of the included GP practices have participated in a SABEL FTO organised by the regional antimicrobial resistance care networks.

The median number of antibiotic prescriptions per 1000 registered patients was 251 (IQR: 213–305) (Table 3.1.2.1) in 2025, a decrease of 10% compared with 2024. Most QI outcomes show considerable between-practice variation.

Trend analyses from 2018 to 2025 are shown in Figure 3.1.2.1. After a sharp decline in overall antibiotic prescribing (QI1) during the COVID-19 pandemic, and an increase afterwards, QI1 in 2025 returned to a level similar to that during the pandemic (Figure 3.1.2.1 A).

The median percentages of co-amoxiclav, macrolide, and quinolone prescriptions were quite stable from 2018 to 2025 (Figure 3.1.2.1 B). Given the decrease in total antibiotic prescriptions, this implies a decrease in the absolute number of prescribed second-choice antibiotics. The overall decrease from 2024 to 2025 coincided with slightly lower antibiotic prescribing percentages for otitis media, upper respiratory

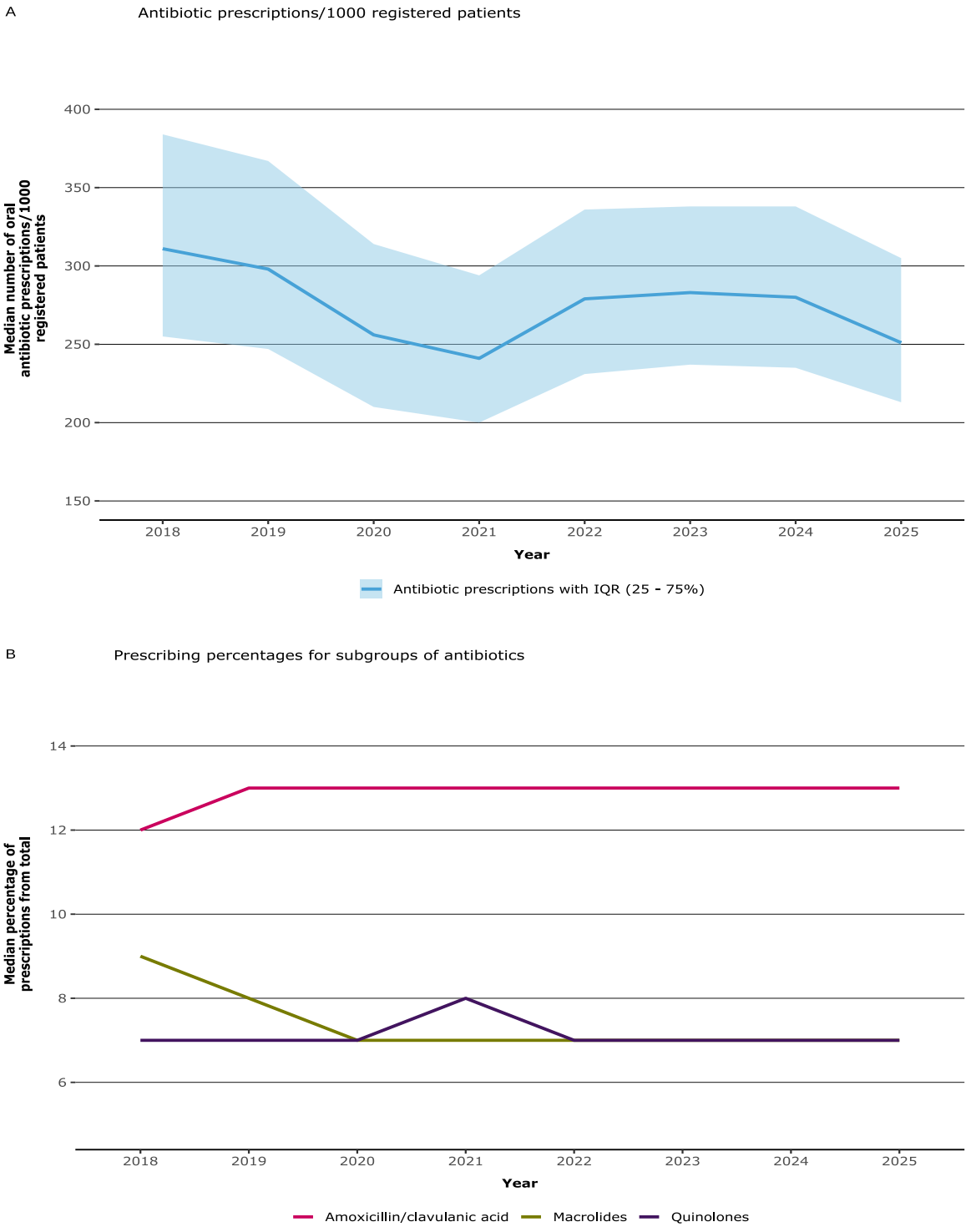
tract infections (URTI), lower respiratory tract infections (LRTI) and impetigo (Figure 3.1.2.1 C).

The QIs of first-choice antibiotic prescribing were stable for otitis media, cystitis in women and tonsillitis from 2019 to 2025 (Figure 3.1.2.1 D). The lowest percentage of first-choice prescribing was observed for tonsillitis. A small increase in first-choice antibiotic prescribing was seen for pneumonia, while impetigo showed the largest increase, from 50% in 2019 to 77% in 2025.

Table 3.1.2.1 *Outcomes of the antibiotic prescribing QIs for GP practices (n=1663) in 2025 (source: STIZON and VIPLive)*

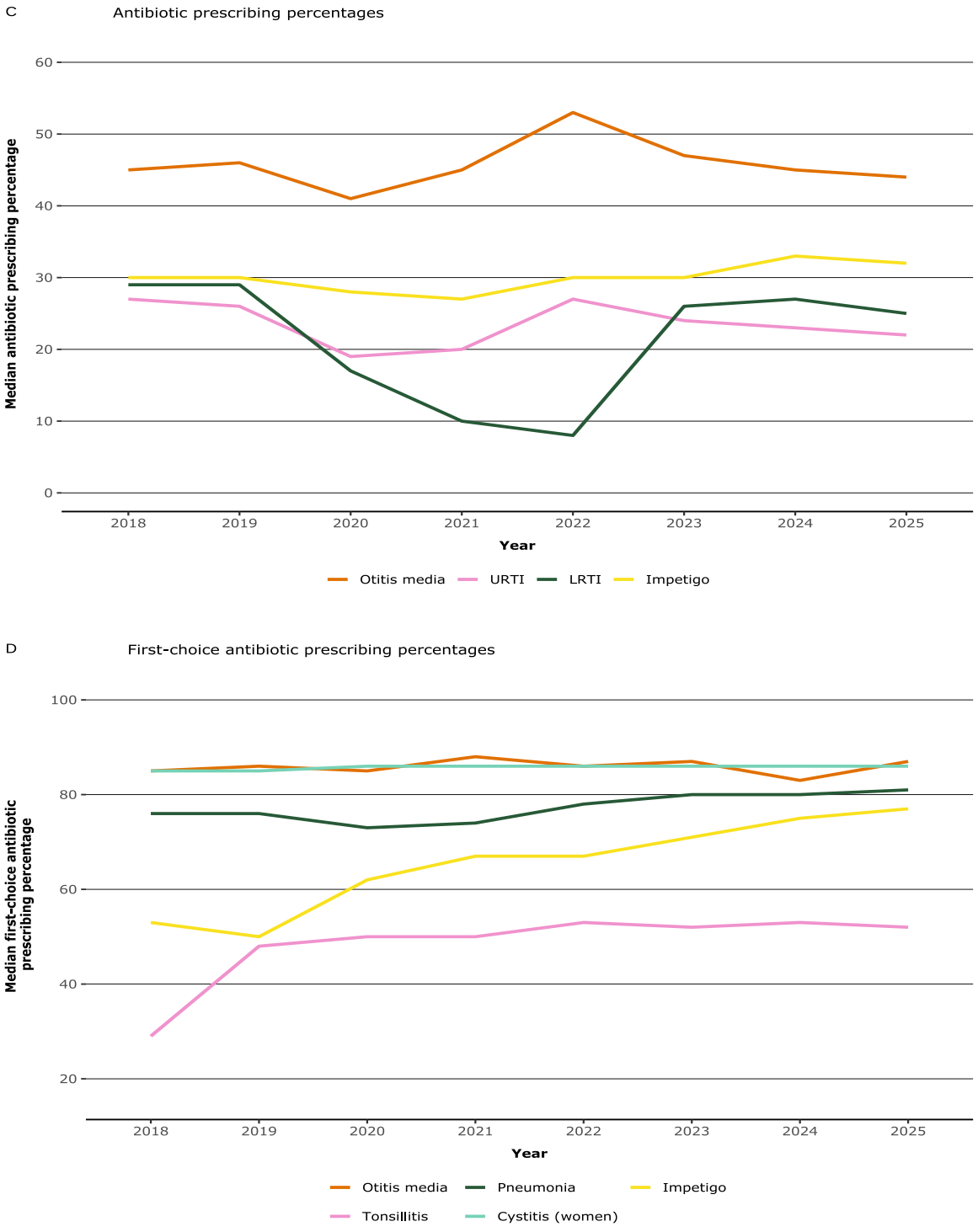
Quality indicator (QI)	Median	IQR (25%–75%)
General (excluding prescriptions for prophylaxis and/or chronic use)		
1. Antibiotic prescriptions/1000 patients (n)	251	213 - 305
2. Co-amoxiclav (%)	13	11 - 16
3. Macrolides (%)	7	5 - 9
4. Quinolones (%)	7	6 - 8
5. Co-amoxiclav + Macrolides + Quinolones (%)	28	25 - 31
Antibiotic prescribing % (percentages of episodes treated with antibiotics)		
6. Otitis media	44	36 - 52
7. Upper respiratory tract infection	22	17 - 27
8. Lower respiratory tract infection	25	20 - 31
9. Impetigo	32	26 - 40
First-choice antibiotic prescribing % (percentages of antibiotic-treated episodes treated with the first-choice antibiotic)[3]		
10. Otitis media (amoxicillin)	87	80 - 92
11. Tonsillitis (pheneticillin or phenoxymethylpenicillin)	52	38 - 64
12. Pneumonia (amoxicillin or doxycycline)	81	73 - 87
13. Cystitis (women, nitrofurantoin or fosfomycin)	86	83 - 89
14. Impetigo (flucloxacillin)	77	63 - 88

Figure 3.1.2.1 *Trends in antibiotic prescribing QI outcomes in primary care, 2018-2025, presented as medians (source: STIZON and VIPLive)*



(A) QI1, (B) QIs 2–4, (C) QIs 6–9, (D) QIs 10–14. See Table 3.1.2.1 for the definitions of the QIs. The y-axis has different ranges in panels B, C and D.

Figure 3.1.2.1 (continued) *Trends in antibiotic prescribing QI outcomes in primary care, 2018-2025 (source: STIZON and VIPLive)*



(A) QI1, (B) QIs 2–4, (C) QIs 6–9, (D) QIs 10–14. See Table 3.1.2.1 for the definitions of the QIs. The y-axis has different ranges in panels B, C and D.

Discussion

These QI outcomes provide insight into trends and variation in antibiotic prescribing quantity and quality by GPs in the Netherlands. Data are available at GP practice level which enables benchmarking of prescribing behaviour against other practices in the FTO group and against national data.

In 2025, a 10% decrease in overall antibiotic prescribing was observed compared with 2024. This coincided with decreases in antibiotic prescribing percentages. First-choice antibiotic prescribing for impetigo has increased from 2019 to 2025, which may be related to either an increase in the incidence of impetigo needing antibiotic treatment and/or with increased availability of flucloxacillin. A lower first-choice prescribing percentage for tonsillitis is probably related to lower availability of the first-choice antibiotics for tonsillitis.

Dispensing data from community pharmacies showed a smaller decrease of 4.2% compared with 2024 (see 3.1.1. Outpatient antibiotic use). The two data sources differ. The QIs are based on oral antibiotic prescriptions recorded in the electronic medical records of participating GP practices and are presented as the median of the practice scores. Overall prescribing (QI1) excludes prophylactic and chronic use. The dispensing data cover all systemic antibiotics dispensed by community pharmacies and are expressed in DDD. They also include prescriptions by medical specialists and other prescribers that are dispensed by community pharmacies, as well as prophylactic and chronic use. The two measures are therefore not directly comparable but are consistent. The slightly lower prescribing percentages for respiratory tract infections and otitis media are in line with the lower use of amoxicillin and doxycycline in the dispensing data. Both are first-choice antibiotics for respiratory tract infections, and amoxicillin is also the first choice for otitis media when an antibiotic is indicated (Table 3.1.2.1).

Conclusions

- In 2025, there was a median of 251 antibiotic prescriptions per 1000 registered patients by GP practices.
- There is wide variation in prescribing habits between GP practices, showing room for improvement in the higher-prescribing practices.
- The decrease in overall antibiotic prescribing in 2025 is encouraging.
- The QIs are based on GP practice records and not on pharmacy dispensing data, but both sources showed a decrease in 2025 (see 3.1.1 Outpatient antibiotic use).

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3.1.3 Inpatient antibiotic use

Introduction
Antibiotic use in hospitals is concentrated in a relatively small population receiving intensive treatment. Shifts in use therefore translate rapidly into selection pressure. Surveillance of the volume and type of antibiotics used is a prerequisite for evaluating stewardship and for interpreting the resistance data presented elsewhere in this report.

Methods
Data on antimicrobial use, admissions and bed-days in Dutch hospitals were collected via questionnaires distributed to all Dutch hospital pharmacies. Defined Daily Doses (DDD) were extracted from the Dutch drug database 'Z-index' per ATC code with route of administration. In 2025, data were obtained from 51 hospital pharmacies, covering 72 of the 105 hospital locations in the Netherlands (68.6%). In contrast to the previous publication, data for all years were calculated using the same method and the DDD definitions valid in July 2026. Therefore, results for 2019-2024 differ from those published previously.

Antimicrobial use is expressed as DDD per 100 patient-days. Total use is also expressed as DDD per 100 admissions (Table 3.1.3.1). The number of patient-days was estimated by subtracting admissions from bed-days, because bed-day statistics count both the day of admission and the day of discharge as full days. Missing denominator data were imputed with the mean of the preceding three years. Extrapolated data are expressed as DDD per 1,000 inhabitants per day (DID), as used in international surveillance by the European Centre for Disease Prevention and Control (ECDC) (Table 3.1.3.2). Population data were obtained from Statistics Netherlands (CBS). This chapter focuses mainly on antibiotics (J01), and briefly on antimycotics for systemic use (J02). To assess whether changes compared with 2024 can be attributed to the smaller and different group of participating hospitals, a separate sensitivity analysis compared hospital-level use (the unweighted mean of DDD per 100 patient-days over hospitals) between all reporting hospitals and the hospitals that reported in both years (see Sensitivity analysis). The results presented below are based on all reporting hospitals.

Results
Total systemic antibiotic use in hospitals decreased by 6.4%, from 90.3 DDD per 100 patient-days in 2024 to 84.5 in 2025 (Table 3.1.3.1). Expressed per 100 admissions, use decreased by 2.3%, from 324 to 317. Expressed as DID, use decreased by 10.3%, from 0.777 to 0.697 (Table 3.1.3.2).

Table 3.1.3.1 *Use of antibiotics for systemic use (J01) in hospitals, by year and therapeutic group, 2019-2025, presented as DDD/100 patient-days (source: SWAB, RIVM)*

ATC group	Therapeutic group	2019	2020	2021	2022	2023	2024	2025
J01AA	Tetracyclines	2.06	2.00	1.91	2.80	3.34	3.32	2.35
J01CA	Penicillins with extended spectrum	5.12	5.02	4.87	5.93	6.03	5.64	5.47
J01CE	Beta-lactamase sensitive penicillins	2.36	2.54	2.39	2.88	3.01	2.79	2.65
J01CF	Beta-lactamase resistant penicillins	10.37	11.74	11.25	12.47	13.00	12.90	11.88
J01CR	Combinations of penicillins, incl. beta-lactamase-inhibitors	10.04	10.37	8.90	9.94	10.10	8.54	8.33
J01DB	First-generation cephalosporins	6.61	6.46	7.15	7.51	7.49	8.54	7.81
J01DC	Second-generation cephalosporins	7.78	8.29	7.05	7.69	8.37	8.57	8.55
J01DD	Third-generation cephalosporins	7.53	10.03	11.41	10.50	10.79	11.57	10.95
J01DH	Carbapenems	1.39	1.49	1.63	1.66	1.66	1.81	1.67
J01EA	Trimethoprim and derivatives	0.20	0.23	0.17	0.20	0.14	0.14	0.12
J01EE	Combinations of sulfonamides and trimethoprim, incl. derivatives	2.41	2.92	2.59	2.91	3.28	2.83	2.71
J01FA	Macrolides	2.71	3.22	2.50	2.69	2.82	2.80	2.38
J01FF	Lincosamides	2.32	2.32	2.08	2.64	3.20	2.30	2.23
J01GB	Aminoglycosides	3.26	2.96	2.82	2.81	2.76	2.88	2.63
J01MA	Fluoroquinolones	6.87	7.28	6.57	7.60	7.66	6.95	6.37
J01XA	Glycopeptides	1.95	2.31	2.49	2.47	2.45	2.45	2.29
J01XB	Polymyxins	0.14	0.13	0.16	0.18	0.14	0.11	0.09
J01XD	Imidazole derivatives	3.11	3.23	3.49	3.75	3.79	4.04	3.93
J01XE	Nitrofuran derivatives	1.38	1.76	1.70	2.04	1.77	1.58	1.54
J01XX	Other antibacterials [1]	0.27	0.31	0.31	0.29	0.35	0.34	0.29
	Others [2]	0.12	0.10	0.12	0.15	0.16	0.21	0.22
J01	Antibiotics for systemic use (total)	77.99	84.72	81.55	89.11	92.33	90.29	84.48
	expressed in DDD/100 admissions:							
J01	**Antibiotics for systemic use (total)**	**312.44**	**329.36**	**305.00**	**327.40**	**347.00**	**324.41**	**316.80**

[1] Other antibacterials: fosfomycin (J01XX01), methenamine (J01XX05), linezolid (J01XX08), daptomycin (J01XX09)

[2] Others: J01DE (fourth-generation cephalosporins), J01DF (monobactams), J01DI (other cephalosporins and penems), J01EC (intermediate-acting sulfonamides), J01XC (steroid antibacterials)

Table 3.1.3.2 *Use of antibiotics for systemic use (J01) in hospitals, by year and therapeutic group, 2019-2025, presented as DDD/1000 inhabitant-days (source: SWAB, RIVM)*

ATC group	Therapeutic group	2019	2020	2021	2022	2023	2024	2025
J01AA	Tetracyclines	0.021	0.019	0.018	0.024	0.030	0.029	0.019
J01CA	Penicillins with extended spectrum	0.053	0.047	0.045	0.051	0.054	0.048	0.045
J01CE	Beta-lactamase sensitive penicillins	0.024	0.024	0.022	0.025	0.027	0.024	0.022
J01CF	Beta-lactamase resistant penicillins	0.107	0.110	0.103	0.107	0.116	0.111	0.098
J01CR	Combinations of penicillins, incl. beta-lactamase-inhibitors	0.104	0.097	0.082	0.085	0.090	0.073	0.069
J01DB	First-generation cephalosporins	0.068	0.060	0.066	0.064	0.067	0.073	0.064
J01DC	Second-generation cephalosporins	0.080	0.078	0.065	0.066	0.075	0.074	0.071
J01DD	Third-generation cephalosporins	0.078	0.094	0.105	0.090	0.096	0.099	0.090
J01DH	Carbapenems	0.014	0.014	0.015	0.014	0.015	0.016	0.014
J01EA	Trimethoprim and derivatives	0.002	0.002	0.002	0.002	0.001	0.001	0.001
J01EE	Combinations of sulfonamides and trimethoprim, incl. derivatives	0.025	0.027	0.024	0.025	0.029	0.024	0.022
J01FA	Macrolides	0.028	0.030	0.023	0.023	0.025	0.024	0.020
J01FF	Lincosamides	0.024	0.022	0.019	0.023	0.029	0.020	0.018
J01GB	Aminoglycosides	0.034	0.028	0.026	0.024	0.025	0.025	0.022
J01MA	Fluoroquinolones	0.071	0.068	0.060	0.065	0.068	0.060	0.053
J01XA	Glycopeptides	0.020	0.022	0.023	0.021	0.022	0.021	0.019
J01XB	Polymyxins	0.001	0.001	0.001	0.002	0.001	0.001	0.001
J01XD	Imidazole derivatives	0.032	0.030	0.032	0.032	0.034	0.035	0.032
J01XE	Nitrofuran derivatives	0.014	0.016	0.016	0.017	0.016	0.014	0.013
J01XX	Other antibacterials [1]	0.003	0.003	0.003	0.002	0.003	0.003	0.002
	Others [2]	0.001	0.001	0.001	0.001	0.001	0.002	0.002
J01	**Antibiotics for systemic use (total)**	**0.804**	**0.793**	**0.751**	**0.763**	**0.824**	**0.777**	**0.697**

[1] Other antibacterials: fosfomycin (J01XX01), methenamine (J01XX05), linezolid (J01XX08), daptomycin (J01XX09)

[2] Others: J01DE (fourth-generation cephalosporins), J01DF (monobactams), J01DI (other cephalosporins and penems), J01EC (intermediate-acting sulfonamides), J01XC (steroid antibacterials)

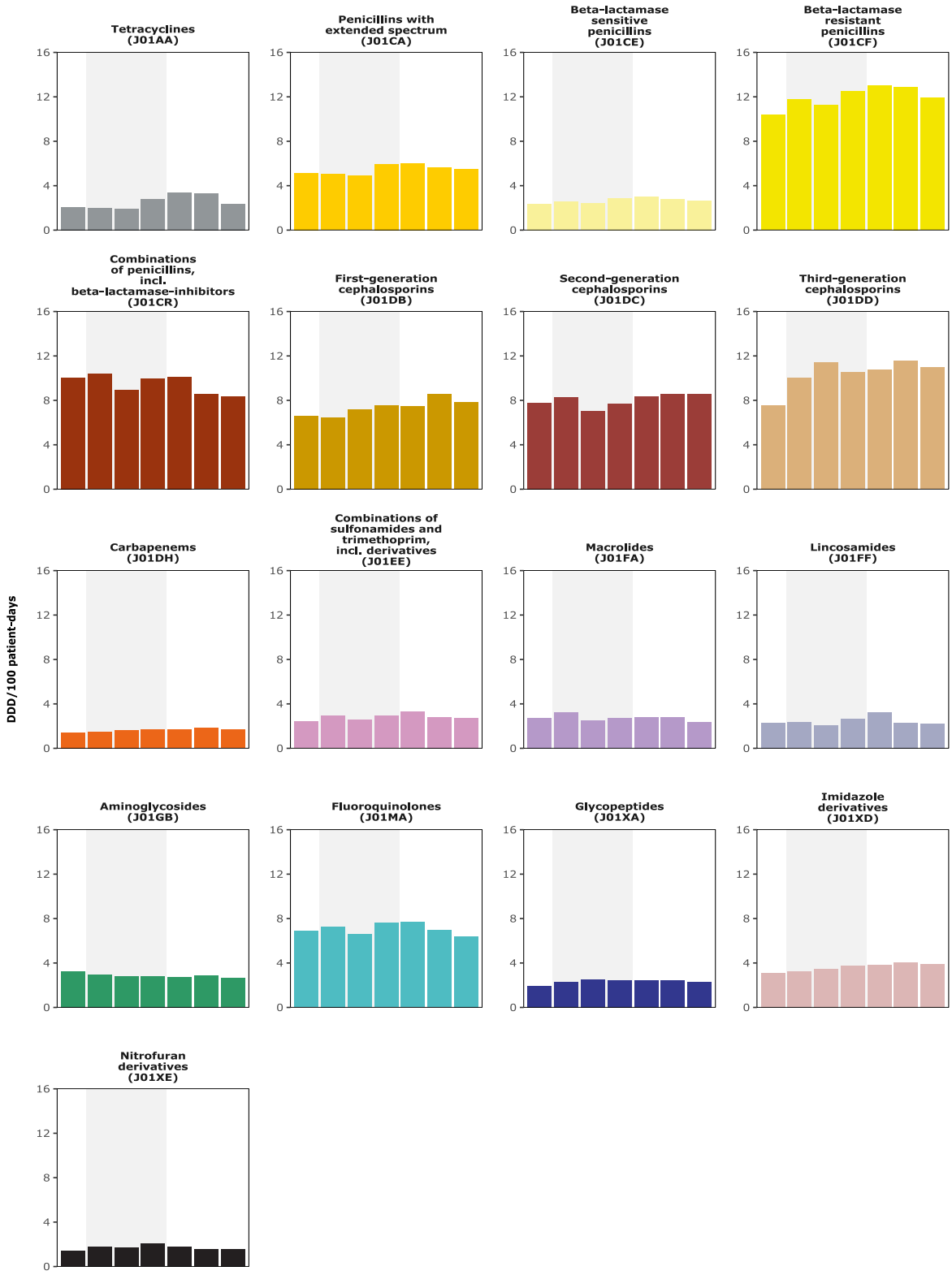
Data from the 72 participating hospital locations were extrapolated to all 105 hospital locations in the Netherlands (extrapolation factor 1.458).

The decrease from 2024 to 2025 was distributed across nearly all therapeutic groups. The only exceptions were second-generation cephalosporins, which remained stable at 8.6 DDD per 100 patient-days, and the residual category 'Others', which increased (Table 3.1.3.1, Figure 3.1.3.1). The largest relative decreases were observed for tetracyclines (−29.3%), macrolides (−14.8%) and other antibacterials (−14.4%), followed by first-generation cephalosporins, aminoglycosides and fluoroquinolones (−8.6%, −8.5% and −8.2%). In absolute terms the largest decreases were seen for beta-lactamase resistant penicillins and tetracyclines (both −1.0 DDD per 100 patient-days), for first-

generation cephalosporins (−0.7) and for third-generation cephalosporins and fluoroquinolones (both −0.6). Carbapenem use decreased by 7.9%, from 1.81 to 1.67, the first decrease since 2018 (data before 2019 not shown). Over the whole period, use of third-generation cephalosporins rose from 7.5 DDD per 100 patient-days in 2019 to 10.0–11.6 from 2020 onwards, and use of first-generation cephalosporins from 6.6 to 7.8 (8.5 in 2024). Expressed in DDD, flucloxacillin was the single agent with the largest volume of use, about 12 DDD per 100 patient-days in 2025 (Figure 3.1.3.2), followed by ceftriaxone, cefuroxime and cefazolin (Figure 3.1.3.5). This ranking reflects the number of DDD rather than the number of patients or treatment days: the WHO DDD for flucloxacillin (2 g) is well below the actual daily doses used in clinical practice (4–12 g).

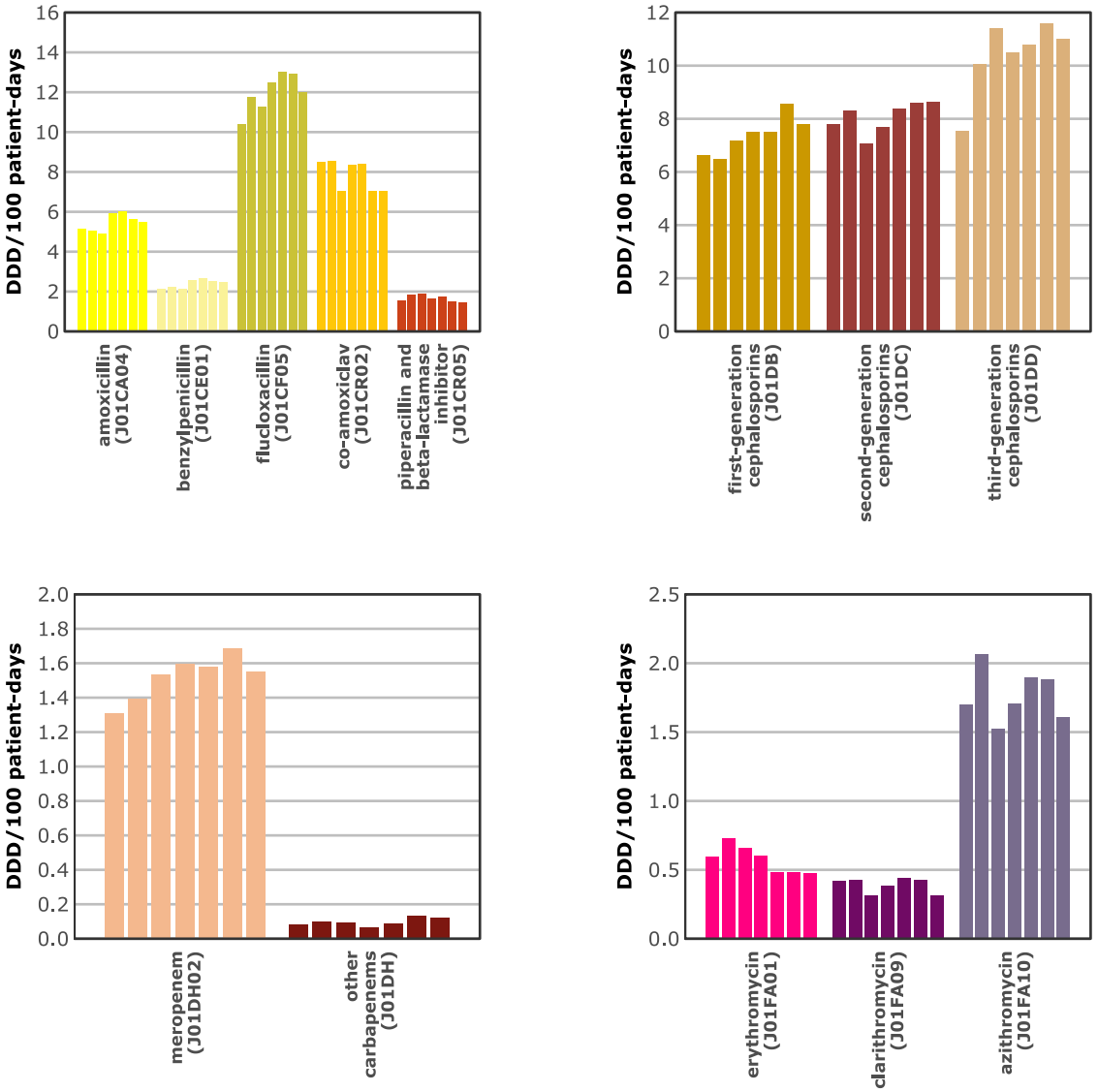
As in previous years, total use varied substantially between individual hospitals (Figure 3.1.3.3). On average, university hospitals reported the highest use and general hospitals the lowest. The types of antibiotics used also differed by hospital type, with a larger proportion of glycopeptides and carbapenems in university hospitals (Figure 3.1.3.4). Ceftriaxone predominated in university and large teaching hospitals, and cefuroxime in general hospitals (Figure 3.1.3.5). Carbapenem use was highest in university hospitals (Figure 3.1.3.6), as was antimycotic use, mostly triazole derivatives (Figure 3.1.3.7).

Figure 3.1.3.1 *Use of antibiotics for systemic use (J01) in hospitals, by therapeutic group, 2019-2025 presented as DDD/100 patient-days (Source: SWAB, RIVM)*



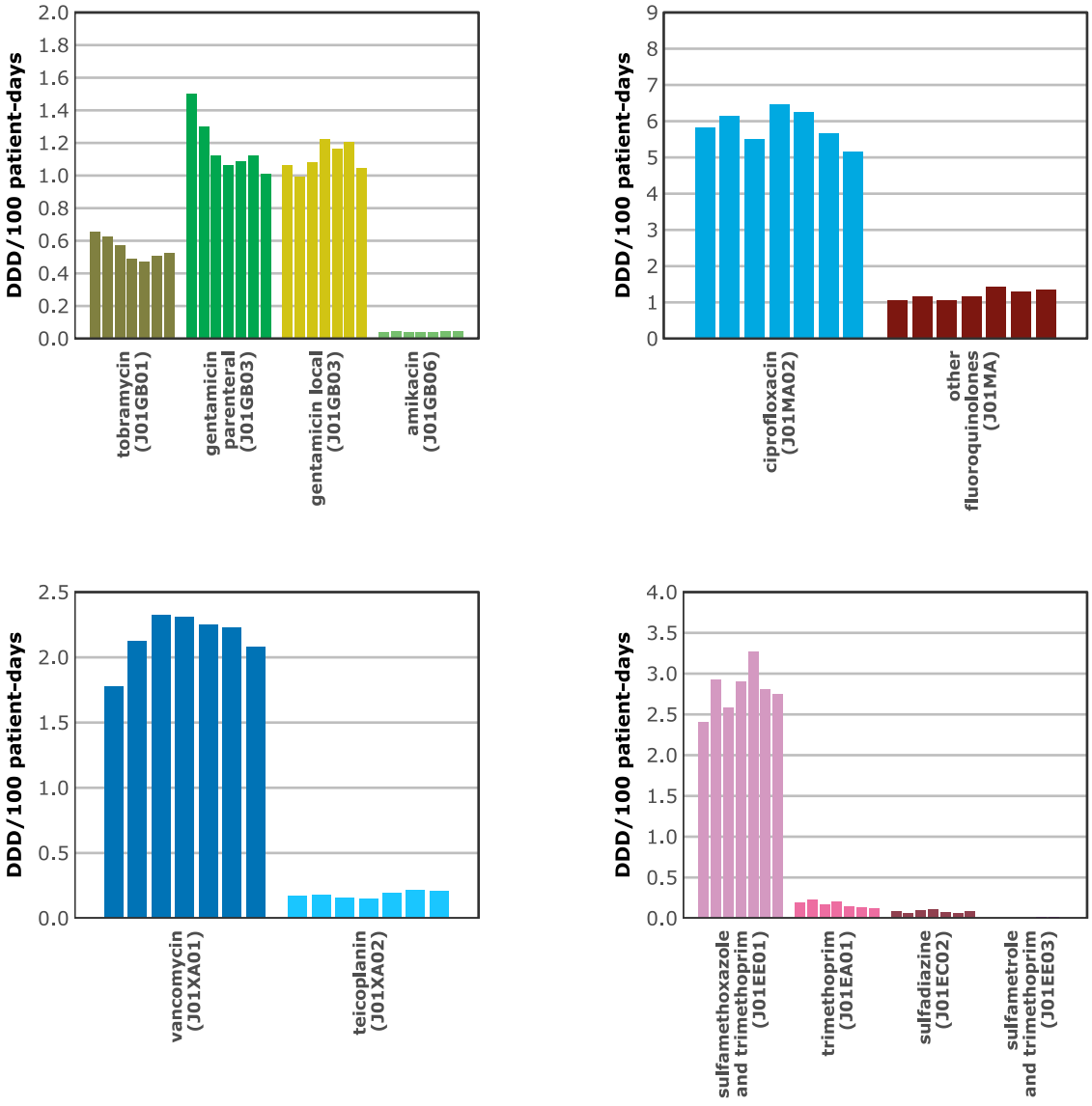
* Bars denote 2019-2025. The grey squares highlight the years of the COVID-19 pandemic (2020-2022).

Figure 3.1.3.2 *Use of beta-lactams, macrolides, aminoglycosides, fluoroquinolones, glycopeptides and other antibiotics in hospitals, by therapeutic agent, 2019-2025*, presented as DDD/100 patient-days (source: SWAB, RIVM)*



* Bars denote 2019-2025.

Figure 3.1.3.2 (continued) *Use of beta-lactams, macrolides, aminoglycosides, fluoroquinolones, glycopeptides and other antibiotics in hospitals, by therapeutic agent, 2019-2025*, presented as DDD/100 patient-days (source: SWAB, RIVM)*



* Bars denote 2019-2025.

Figure 3.1.3.3 *Use of antibiotics for systemic use (J01) in hospitals, by therapeutic group and individual hospital in 2025, presented as DDD/100 patient-days and in descending order of total use by type of hospital (source: SWAB, RIVM)*

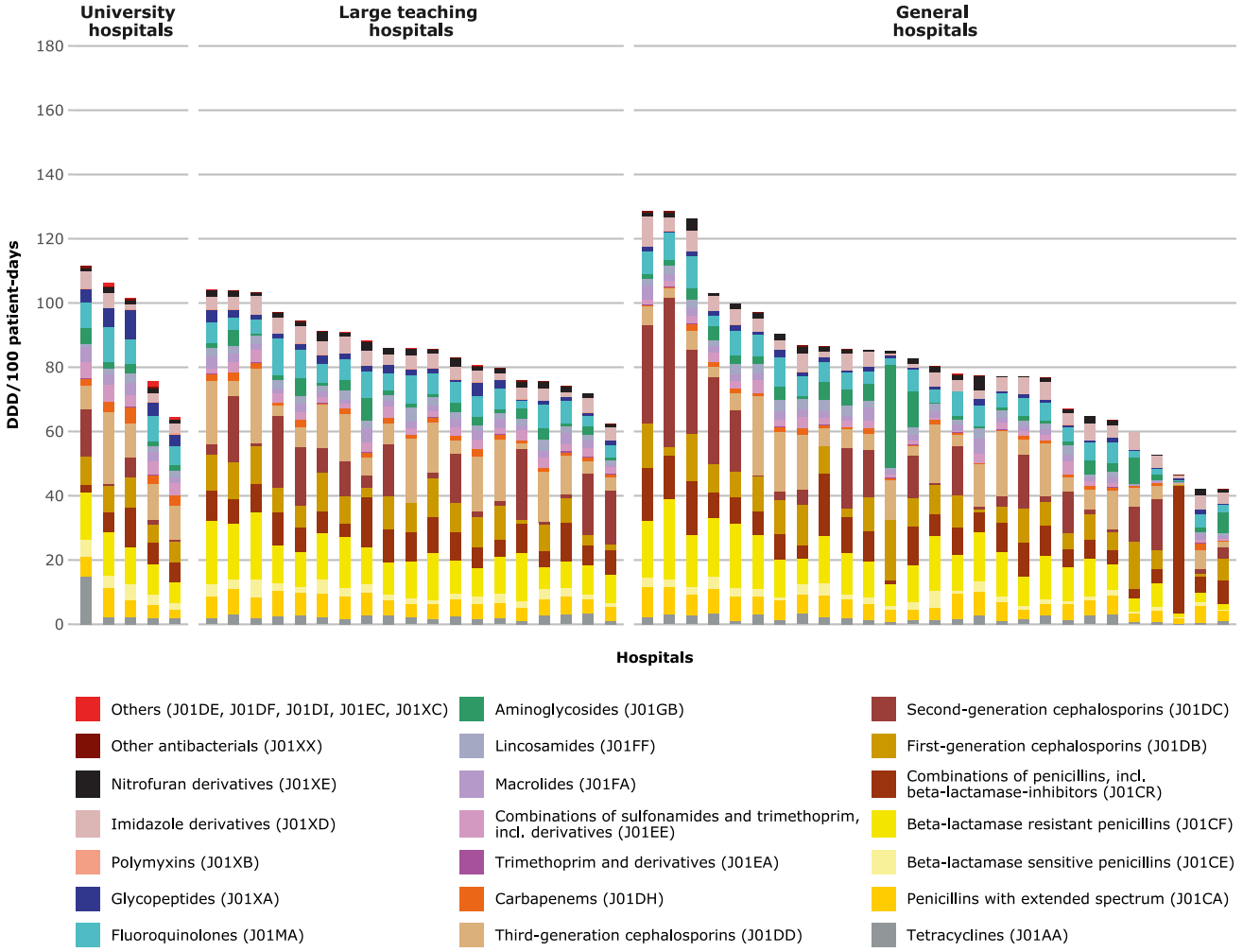


Figure 3.1.3.4 *Distribution (%) of therapeutic groups among total use of antibiotics for systemic use (J01) in hospitals, by type of hospital in 2025 (source: SWAB, RIVM)*

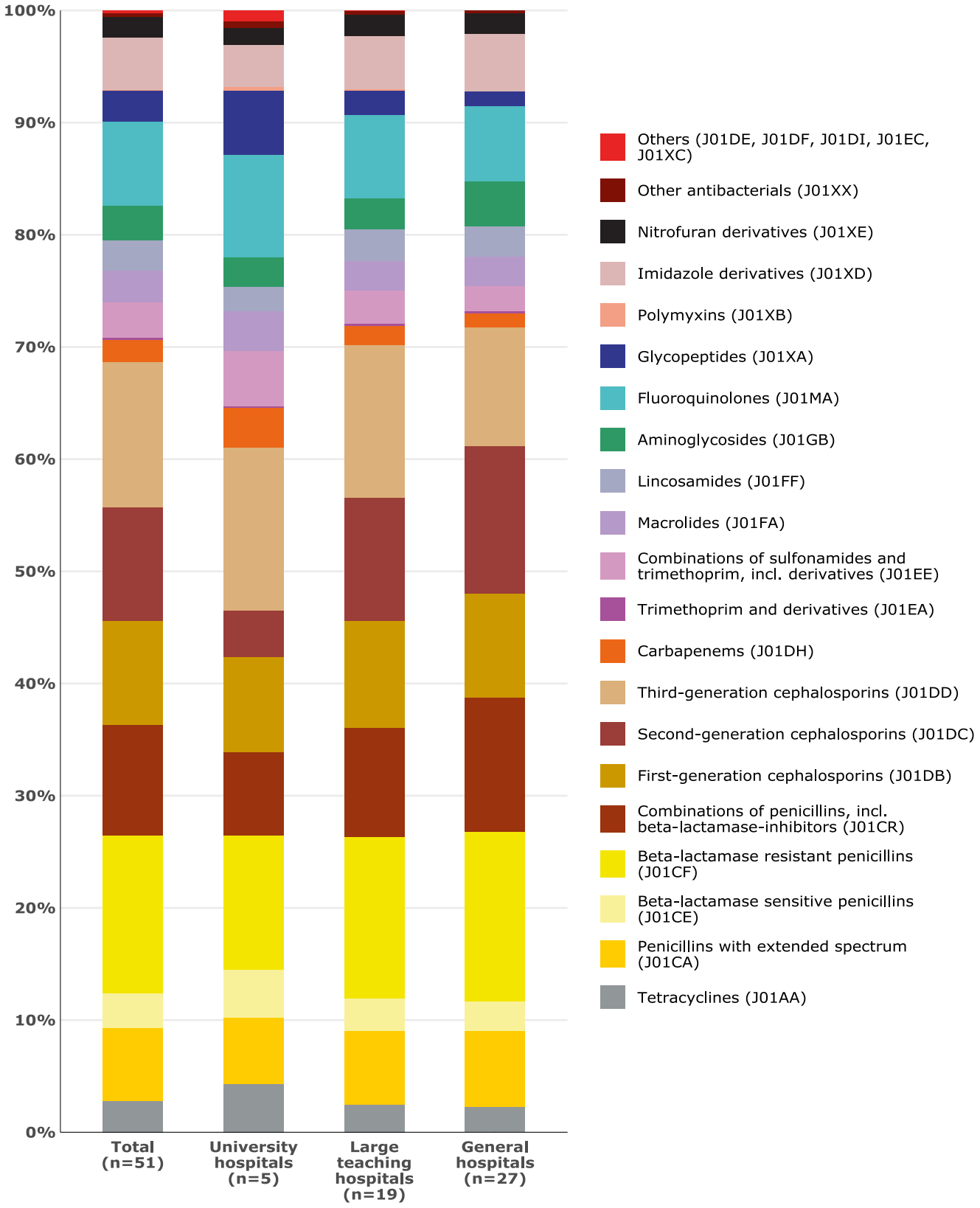
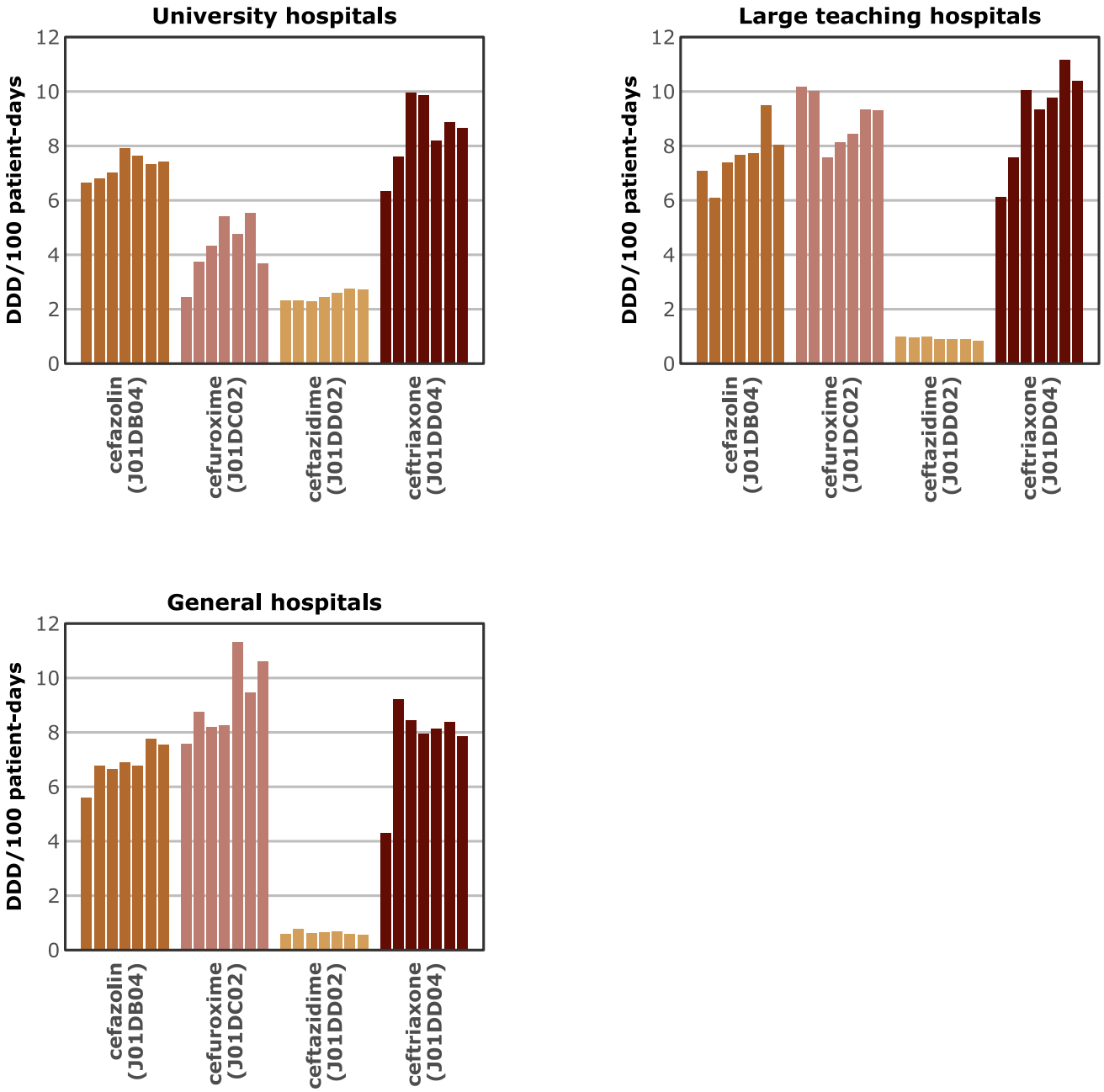
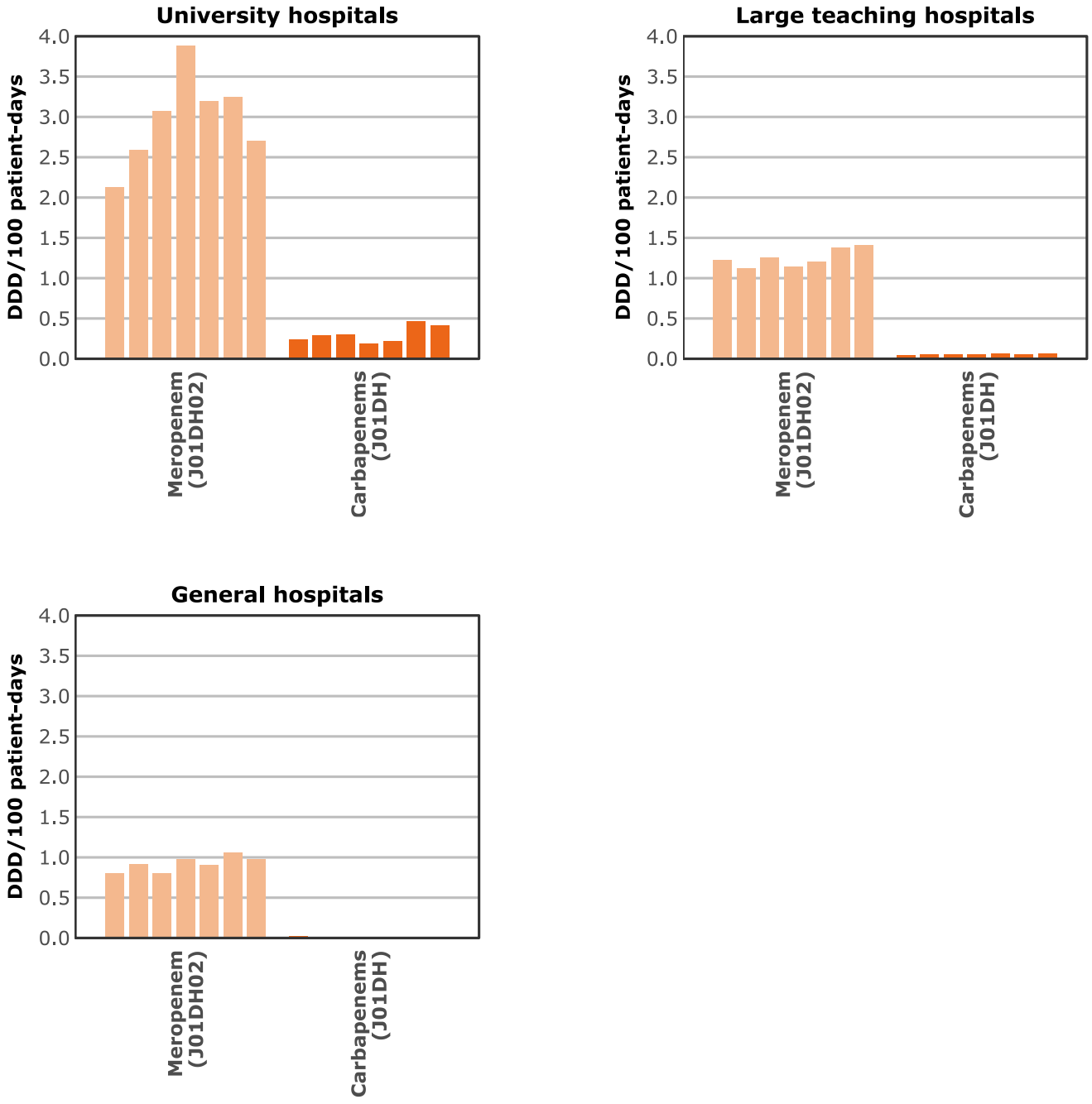


Figure 3.1.3.5 *Use of first, second and third generation cephalosporins in hospitals, by type of hospital, 2019-2025*, presented as DDD/100 patient-days (source: SWAB, RIVM)*



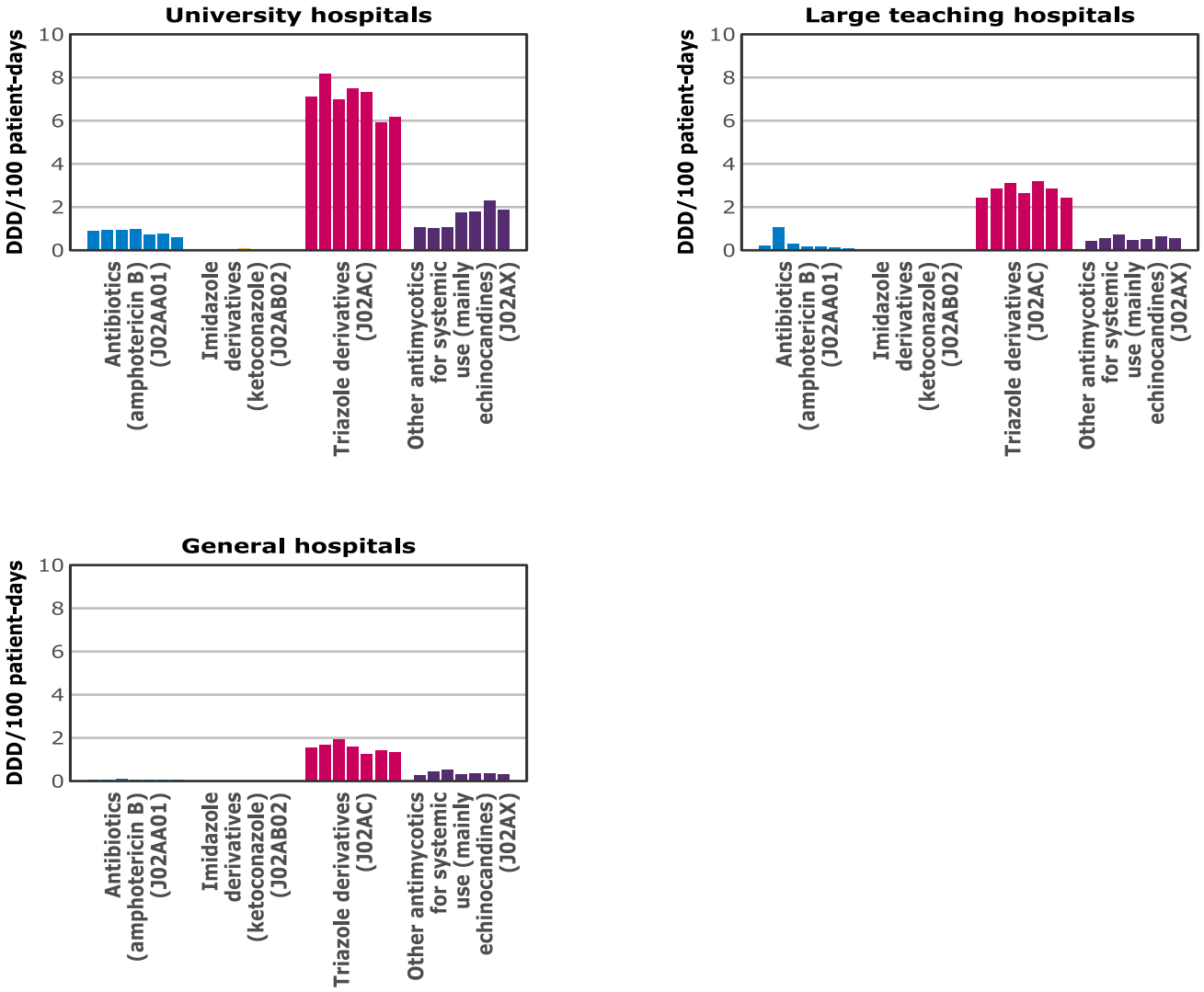
* Bars denote 2019-2025.

Figure 3.1.3.6 *Use of meropenem and other carbapenems in hospitals, by type of hospital, 2019-2025*, presented as DDD/100 patient-days (source: SWAB, RIVM)*



* Bars denote 2019-2025.

Figure 3.1.3.7 *Use of antimycotics (J02) in hospitals, by type of hospital and therapeutic group, 2019-2025*, presented as DDD/100 patient-days (source: SWAB, RIVM)*



* Bars denote 2019-2025.

Sensitivity analysis: change in participating hospitals in 2025 vs 2024
The results above are based on all hospitals reporting in each year. To assess whether the change compared with 2024 can be attributed to the change in participation, a separate analysis compared hospital-level use (the unweighted mean of DDD per 100 patient-days over hospitals) between all reporting hospitals and the hospitals reporting in both years. Data were analysed for the 56 hospitals for which a 2024 feedback report was available and the 51 hospitals that reported for 2025. Of these, 43 reported in both years (Table 3.1.3.3). Percentages were calculated from unrounded means. This analysis serves only to interpret the change reported above. Because it uses unweighted hospital means, its figures are not comparable with, and do not replace, the national figures in Table 3.1.3.1.

For all reporting hospitals, mean total use decreased by 8.2%, compared with 6.4% within the 43 hospitals reporting in both years

(Table 3.1.3.3). About one fifth of the observed decrease (1.7 DDD per 100 patient-days) is therefore attributable to the change in participation: the hospitals that did not report in 2025 had a slightly higher mean use in 2024 than all hospitals, and the newly reporting hospitals a lower mean use in 2025. Neither group deviated more from the overall mean than expected for a random selection of hospitals (permutation test, p = 0.72 and p = 0.38). Had the hospitals that did not report in 2025 remained at their 2024 level, mean use among the 56 hospitals reporting in 2024 would still have decreased by 4.9%. The decrease in total use is thus only to a small extent attributable to the change in participation.

The ranking of therapeutic groups by volume was not affected by the change in participation (Spearman rank correlation between all hospitals and the 43 hospitals ≥ 0.99). For three therapeutic groups, however, the change compared with 2024 is largely attributable to it (Table 3.1.3.3). Combinations of penicillins with beta-lactamase inhibitors increased for all hospitals but decreased within the 43 hospitals, because the newly reporting hospitals were high users of this group. Third-generation cephalosporins and fluoroquinolones decreased much less within the 43 hospitals than for all hospitals, because several hospitals that did not report in 2025 were high users of these groups. Among university hospitals (seven in 2024, five in 2025), the decrease of 9.8% for all reporting university hospitals was largely attributable to the absence of one hospital with high use. Within those reporting in both years the decrease was 3.8%.

The decrease in carbapenem use is also largely attributable to the change in participation. For all reporting hospitals, mean carbapenem use decreased by 8.4%, but within the 43 hospitals reporting in both years by only 0.7%, with about as many hospitals increasing as decreasing (Table 3.1.3.3). Several hospitals that did not report in 2025 were high users of carbapenems, including the hospital with the highest use in 2024, whereas the newly reporting hospitals used less. Had the hospitals that did not report in 2025 reported at their 2024 level, mean carbapenem use would have decreased by 0.5%.

Table 3.1.3.3 *Sensitivity analysis: use of antibiotics for systemic use (J01) and of selected therapeutic groups per hospital in 2024 and 2025, presented as the unweighted mean of DDD/100 patient-days over hospitals. All = all reporting hospitals, Both = the 43 hospitals reporting in both years, Left = hospitals that did not report in 2025 (mean of 2024), New = newly reporting hospitals (mean of 2025) (source: SWAB)*

ATC group	Therapeutic group	All 2024	All 2025	Change (%)	Both 2024	Both 2025	Change (%)	Left (2024)	New (2025)
J01	Antibiotics for systemic use (total)	91.6	84.0	−8.2	90.9	85.0	−6.4	93.8	78.5
J01CR	Combinations of penicillins, incl. beta-lactamase-inhibitors	8.6	9.0	+4.0	8.7	8.3	−4.7	8.3	12.4
J01DD	Third-generation cephalosporins	11.0	9.9	−10.1	10.4	10.1	−2.2	13.3	8.9
J01MA	Fluoroquinolones	6.8	6.0	−11.7	6.5	6.2	−4.4	7.8	4.9
J01DH	Carbapenems	1.50	1.37	−8.4	1.42	1.41	−0.7	1.75	1.16

Discussion
In 2025, total use decreased for the second consecutive year since the peak of 92.3 DDD per 100 patient-days in 2023, although it remains above the 2019 level of 78.0. Interpretation of the 2025 data requires caution, however. The number of participating hospitals decreased from 56 in 2024 to 51 in 2025, and some hospitals with above-average use did not provide data, so the observed decrease might partly reflect the changed composition of the reporting hospitals rather than prescribing behaviour. The sensitivity analysis indicates that about one fifth of the decrease in total use is attributable to the change in participating hospitals, but use also decreased within the hospitals that reported in both years. A decrease was also observed in outpatient antibiotic use in 2025 (see Outpatient antibiotic use).

Subject to the same reservation, carbapenem use decreased for the first time since 2018, from 1.81 to 1.67 DDD per 100 patient-days (Table 3.1.3.1). The sensitivity analysis indicates that this decrease is largely attributable to the change in participating hospitals: several hospitals with high carbapenem use in 2024 did not report in 2025, and within the hospitals reporting in both years carbapenem use was essentially unchanged. A second reservation concerns the meropenem shortage. Meropenem was unavailable for more than a month in 2025. Imported alternatives carry local article numbers, and although most of these are mapped to Z-index codes in the analysis, it cannot be excluded that some use during the shortage was not captured. The decrease therefore cannot be attributed to carbapenem-sparing stewardship, and next year's data are needed before a trend can be considered established.

Conclusions
- Reported antibiotic use in Dutch hospitals decreased by 6.4% in 2025, to 84.5 DDD per 100 patient-days, a second consecutive decrease, but remains above the 2019 level.
- Fewer hospitals participated than in preceding years. A sensitivity analysis indicates that about one fifth of the decrease in use is attributable to the changed composition of the reporting group.
- Carbapenem use decreased for the first time since 2018, but this decrease is largely attributable to the change in participating hospitals.
- Meropenem was unavailable for more than a month in 2025, which may also have affected the reported use.
- Variation in use between individual hospitals remains substantial.

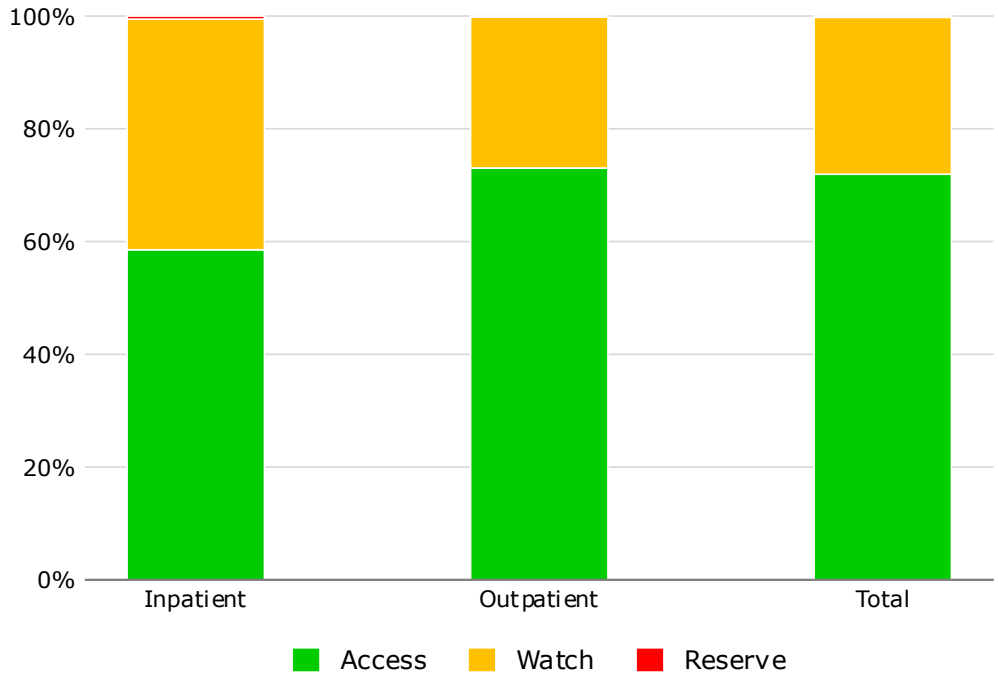
3.1.4 *AWaRe classification*

The AWaRe classification categorises antibiotics into Access, Watch and Reserve to support the monitoring of antibiotic use and the evaluation of stewardship policies aimed at containing antimicrobial resistance. The European Union has set a target for 2030 stipulating that at least 65% of total antibiotic consumption should be from the Access group. Applying this classification to 2025 data, 73.0% of antibiotics used by outpatients were from the Access, 26.8% from the Watch and 0.2% from the Reserve category (Figure 3.1.4.1). For inpatient use these percentages were 58.6%, 40.9% and 0.5%. Taken together, 72.0% of the antibiotics used in the Netherlands were from the Access category, so the European target continues to be met. The Reserve antibiotics used in hospitals were linezolid, colistin, daptomycin and ceftazidime/avibactam. In the community, Reserve use was mainly inhaled colistin, with smaller contributions from oral linezolid and inhaled aztreonam.

Two comments should be made. Minocycline is classified as Watch when administered orally and as Reserve when administered intravenously. Because the hospital data are not split by route for minocycline, its use was counted as oral. Methenamine is not part of the AWaRe classification and was excluded from both the numerator and the denominator.

The community pharmacy data cover about 93% of the population, as residents supplied by a dispensing general practitioner are not included. The combined percentage assumes that the AWaRe distribution among the remaining 7% is similar to that among the covered population.

Figure 3.1.4.1 *Antimicrobial consumption in 2025 according to the 2025 WHO AWaRe classification (source: SWAB, RIVM, SFK)*



3.1.5 Long-term care facilities

Introduction
Residents of long-term care facilities are frequently exposed to antibiotics, often for urinary and respiratory tract infections, while diagnostic possibilities in this setting are more limited than in hospitals. Surveillance of antibiotic use in these facilities complements the hospital and outpatient data and covers a population at appreciable risk of colonisation with resistant microorganisms.

Methods
Data on antibiotic use were collected from all long-term care facilities (LTCFs) participating in the antimicrobial surveillance programme of the Dutch Surveillance Network of Infectious Diseases in Nursing Homes (SNIV). Data were obtained either from the electronic prescribing system or from the dispensing pharmacist. Since 2024, facilities have been able to export these data automatically from the electronic prescribing system, using extracts developed with the system suppliers, which has increased the number of participating facilities. Because the number of dispenses cannot always be derived reliably from the prescribing system, corrections agreed with the system suppliers and SWAB were applied to estimate the medication dispensed. To account for differences in facility size, use was standardised as DDD per 1,000 resident-days for each facility.

Results
Data were obtained from 345 LTCFs from 37 organisations, serving 20,196 residents (2024: 18,964 residents). Facilities had a mean of 59 residents (SD: 45.5). Total antibiotic use in LTCFs decreased by 4.8%, from 53.1 DDD per 1,000 resident-days in 2024 to 50.6 in 2025 (Table 3.1.5.1). The groups with the highest use were combinations of penicillins including beta-lactamase inhibitors (10.9 DDD per 1,000 resident-days), nitrofuran derivatives (7.8) and fluoroquinolones (6.7). The largest decrease was seen for macrolides, from 8.4 to 6.2 DDD per 1,000 resident-days, and the largest increase for combinations of penicillins including beta-lactamase inhibitors, from 9.9 to 10.9. Use varied widely between facilities, from 4.3 to 404.3 DDD per 1,000 resident-days.

Discussion
The decrease in total use follows an increase reported for 2024, which was attributed in part to a change in data collection described in the Methods: automatic export from the prescribing system increased the number of included facilities and may have altered the study population. Improvements in the method to calculate medication dispenses may have resulted in the decrease in macrolide use compared with 2024. The wide range in use between facilities is a persistent feature of this surveillance system. It largely reflects differences in the type of care provided. Use is considerably higher in geriatric rehabilitation facilities, where residents have recently been discharged from hospital and often continue antibiotic treatment started there, than in psychogeriatric and somatic long-stay care.

Conclusions

- Total antibiotic use in long-term care facilities decreased by 4.8% in 2025, to 50.6 DDD per 1,000 resident-days.
- The largest decrease was observed for macrolides, partly reversing the increase reported for 2024.
- Use continues to vary widely between facilities, largely related to the type of care provided.

Table 3.1.5.1 *Use of antibiotics for systemic use (J01) in long-term care facilities, by year and therapeutic group, 2019-2025, presented as DDD/1000 resident-days*

ATC group	Therapeutic group	2019	2020	2021	2022	2023	2024	2025
J01AA	Tetracyclines	3.71	2.85	2.60	2.32	2.44	3.13	3.62
J01CA	Penicillins with extended spectrum	2.64	4.83	2.40	2.88	3.58	2.08	2.19
J01CE	Beta-lactamase sensitive penicillins	0.53	0.37	0.30	0.28	0.48	0.55	0.53
J01CF	Beta-lactamase resistant penicillins	3.02	2.54	2.40	2.90	3.04	2.59	2.58
J01CR	Combinations of penicillins, incl. beta-lactamase-inhibitors	12.02	10.16	7.70	10.72	10.93	9.89	10.89
J01DB	First-generation cephalosporins	0.02	0.15	0.30	0.11	0.09	0.26	0.15
J01DC	Second-generation cephalosporins	0.18	0.99	0.10	0.12	0.09	0.09	0.03
J01DD	Third-generation cephalosporins	0.43	0.53	0.40	0.62	0.42	0.44	0.59
J01DH	Carbapenems	0.28	0.06	0.00	0.11	0.13	0.05	0.07
J01EA	Trimethoprim and derivatives	0.84	1.19	1.00	0.74	0.86	1.03	1.34
J01EE	Combinations of sulfonamides and trimethoprim, including derivatives	2.96	2.64	1.90	1.72	2.01	3.20	3.05
J01FA	Macrolides	2.68	2.95	2.30	3.29	3.72	8.42	6.17
J01FF	Lincosamides	2.94	2.21	1.80	2.24	2.83	3.93	3.62
J01GB	Aminoglycosides	0.04	0.00	0.00	0.11	0.07	0.20	0.09
J01MA	Fluoroquinolones	7.26	9.11	5.50	6.73	7.80	6.99	6.67
J01XA	Glycopeptides	0.37	0.09	0.20	0.14	0.13	0.05	0.06
J01XB	Polymyxins	0.01	0.07	0.00	0.06	0.03	0.09	0.16
J01XD	Imidazole derivatives	0.02	0.02	0.10	0.02	0.02	0.00	0.03
J01XE	Nitrofuran derivatives	9.50	8.17	8.10	7.97	7.60	8.15	7.83
J01XX	Other antibacterials	0.92	1.42	0.80	0.81	0.85	1.93	0.86
Others	Others*	0.03	0.03	0.20	0.00	0.00	0.04	0.05
J01	**Antibiotics for systemic use (total)**	**50.40**	**50.38**	**38.10**	**43.89**	**47.12**	**53.12**	**50.60**

* Others: J01BA (amphenicols), J01CG (beta-lactamase inhibitors), J01DE (fourth-generation cephalosporins), J01DF (monobactams), J01DI (other cephalosporins and penems), J01EB (short-acting sulfonamides), J01EC (intermediate-acting sulfonamides), J01ED (long-acting sulfonamides), J01FG (streptogramins), J01GA (streptomycins), J01MB (other quinolones), J01RA (combinations of antibacterials), J01XC (steroid antibacterials).

3.2 Antimicrobial stewardship in hospitals

Introduction

Antimicrobial stewardship (AMS) has been formally promoted in the Netherlands since at least 2014, when the Dutch Health Care Inspectorate (IGZ, now IGJ) and the Ministry of Health (VWS) recommended that every hospital establish an AMS team (A-team) to optimize antibiotic use and combat antimicrobial resistance. The SWAB Practice Guide Antimicrobial Stewardship in the Netherlands was published in 2015. Since then, the SWAB has played a key role in promoting AMS by developing guidelines and supporting A-teams to measure and improve antibiotic use in Dutch hospitals.

To improve antibiotic use, A-teams need information on prescribing practices. Before 2020, data on the quality of antibiotic use were collected through point prevalence surveys (PPS). A PPS provides a cross-sectional assessment of quantity and quality of antibiotic prescribing in a healthcare facility at a defined point in time. To enable ongoing monitoring, SWAB developed the Antimicrobial Stewardship Monitor (AMSM). The AMSM provides Dutch hospitals with benchmarked feedback on the quantity and quality of their antibiotic use, enabling A-teams to compare their prescribing practices with other participating hospitals, identify areas for improvement and monitor changes after interventions. It also helps SWAB to identify national priorities for improving antibiotic use.

This chapter describes the AMSM, explains how hospitals can participate and benefit, summarizes its development over the past five years, and outlines the future plans as a national quality registry.

What is the AMSM?

The AMSM is a national monitoring system that gives hospitals insight into both the quantity and the quality of their antibiotic use, benchmarked against data from participating hospitals across the Netherlands. It supports A-teams in identifying whether interventions work.

The objectives of the AMSM are:

- to provide hospitals with benchmarked feedback on their antimicrobial use;
- to share this information with participating hospitals and their A-teams;
- to identify national priorities for improving antimicrobial use and the treatment of infectious diseases.

The AMSM is built on the principle of keeping the registration burden low. Routinely recorded data are extracted automatically from the hospital's electronic medical record (EMR). The following types of data are combined:

- Prescription data. Patient-level data on all antimicrobial prescriptions form the core of the AMSM. These data are extracted automatically from the hospital's electronic medical record.

- Hospital admission data. Patient-level data including date of admission, discharge, surgery and survival.
- Volume indicators**.** Including: number of unique patients in the calendar year, number of clinical admissions and number of patient days.
- Disease-specific data. Data on specific disease diagnoses, including standardized (billing and clinical) diagnosis codes offering deeper insight into the management of specific conditions, such as community-acquired pneumonia (CAP).

These data are used to calculate 'proxy indicators', that provide insight in the appropriateness of several aspects of antibiotic use. The indicators cover the choice and duration of empiric antibiotic treatment, intravenous-to-oral switch (IV-oral switch) of antibiotics, escalation of antimicrobial therapy, use of restricted antimicrobials and duration of surgical prophylaxis.

How can a hospital participate, and what are the benefits?
Hospitals interested in joining the AMSM can contact the AMSM coordination team at SWAB to obtain more information and to initiate the process of contracting and data sharing (https://swab.nl/nl/antimicrobial-stewardshipmonitor). SWAB and the hospital then sign confidentiality and data processing agreements. Next, the hospital's IT department and A-team work together to extract the data from the EMR. SWAB can provide assistance with data extraction and conversion to a batch file for export. Data is extracted at least once but preferably multiple times per year. The data are subsequently processed and analyzed by Medical Research Data Management (MRDM), the data processor. Further information is available on the MRDM support site (https://support.mrdm.nl/registraties/amsm/).

Participating hospitals receive feedback in several ways:

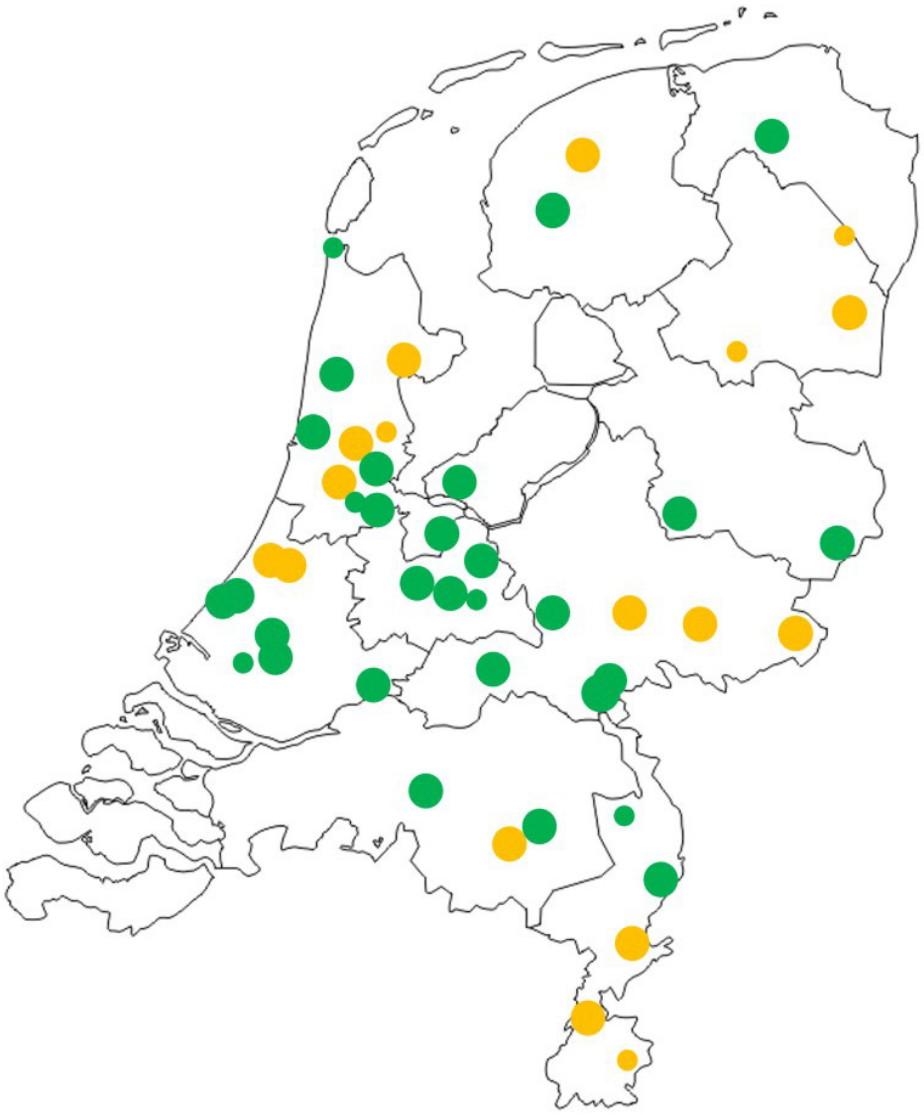
- **Feedback.** The AMSM dashboard shows each hospital's results at any time and compares them with other hospitals.
- **Annual report.** Aggregated national results are normally published in NethMap One Health, and each participating hospital receives an individual report.
- **Peer discussion.** Results are discussed in the national and regional A-team meetings, allowing hospitals to learn from each other and identify priorities for improvement.

The main benefit is that A-teams can use routinely collected data to identify areas for improvement monitor the effect of interventions over time, and justify their priorities to hospital boards and the inspectorate. Setting up data extraction for AMSM requires time and effort, but automated monitoring may reduce the need for labor-intensive PPS.

Development and findings over the past five years
The AMSM was established in 2020 and has expanded considerably since then. In the pilot phase, five hospitals delivered data for 2019. Since 2020, the number of hospitals connected to the AMSM has increased from 10 to 38, while the number of hospitals delivering data has grown from 5 to 25 (Figure 3.2.1). Of approximately 70 acute care hospitals in the Netherlands, the AMSM now covers more than half of them as

contracted sites. All but one of the university medical centers have joined; the remaining center is finalizing its contract. This growth makes national benchmarking increasingly meaningful, although full national coverage has not yet been achieved.

Figure 3.2.1 *Map of the Netherlands showing hospitals contracted to the AMSM and hospitals providing data*



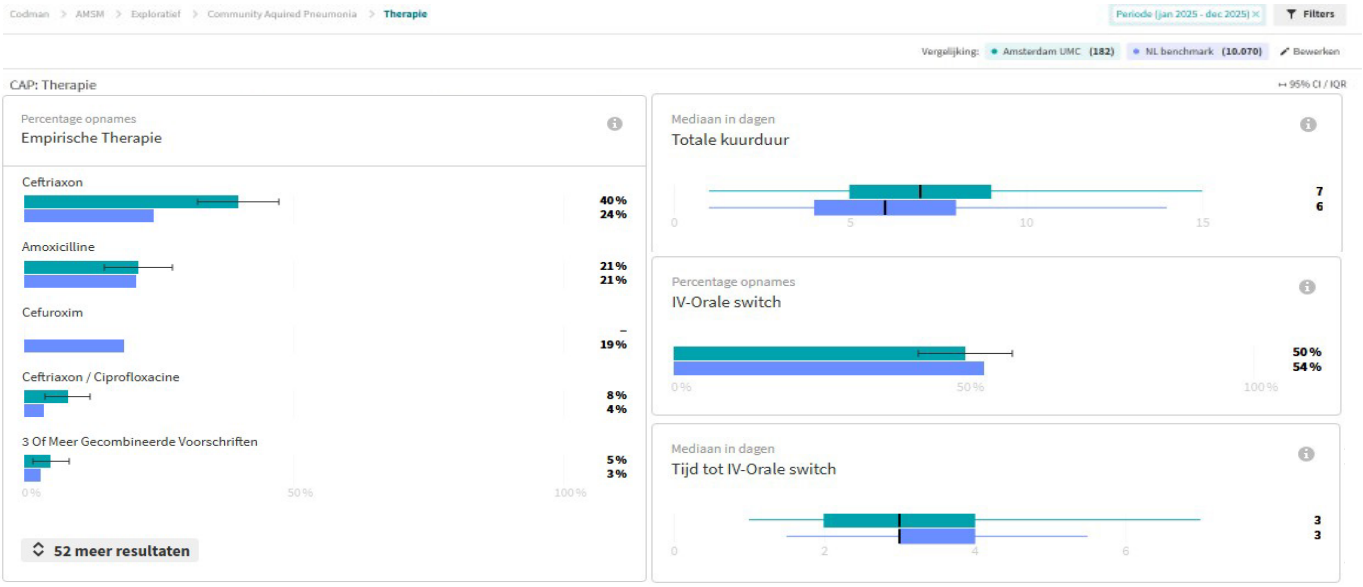
Green circles represent hospitals providing data to AMSM. Orange circles represent hospitals which are contracted but have not yet provided data. Smaller circles indicate affiliated hospital locations submitting data under the same hospital network.

What has the AMSM brought so far?
The main finding of the AMSM is that antibiotic prescribing and the quality of antibiotic use varies considerably between hospitals. This variation shows that benchmarking is useful: hospitals can compare their results, and the differences identify potential areas for improvement. One example is the timing of IV to oral switch, which varies considerably between hospitals, as shown in previous NethMap reports. Differences should be interpreted in the context of case mix and data quality.

As quality indicators or 'proxy indicators' are further developed, guideline adherence of antibiotic therapy can be assessed. The CAP module is an example. The National Health Care Institute (Zorginstituut Nederland, ZiN) has indicated in its improvement report on lower respiratory tract infections, that care for these patients can be improved (ZinnigeZorg-Verbetersignalement Onderste luchtweginfecties (1).pdf). Targets have been set for the choice of empirical antibiotic treatment for CAP, for the switch from intravenous (IV) to oral therapy, and for the total duration of treatment. The AMSM dashboard of the CAP module shows that these targets are not yet being met (Figure 3.2.2).

Transition to a quality registry in 2026
The next step for the AMSM is the recognition as a quality registry by ZiN (the National Health Care Institute, Zorginstituut Nederland, Het Register voor kwaliteitsregistraties). Inclusion would make participation mandatory for hospitals and facilitate comprehensive national coverage of the AMSM. This would strengthen national benchmarking and stewardship in Dutch hospital care. As a quality registry, the AMSM will focus on specific diagnoses, i.e. CAP, urinary tract infections and skin and soft tissue infections, with quality indicators refined specifically for these conditions.
In 2026, aggregated results of the AMSM indicators are not presented in NethMap One Health, due to the application process for admission to the register of quality registries by ZiN. Hospitals continue to receive their own results through the dashboard. Reporting of aggregated indicator results in Nethmap One Health is intended to resume after ZiN has completed its assessment, potentially in 2027.

Figure 3.2.2 *Community-acquired pneumonia (CAP) module within the AMSM dashboard (screenshot)*



This screenshot shows the indicators for community-acquired pneumonia (CAP): from left to right, empirical therapy, total duration of therapy, percentage and timing of intravenous (IV) to oral switch. In this example, the results of Amsterdam UMC in 2025 are shown (in green) compared to the national benchmark (in blue).

4 Usage of antibiotics in animal husbandry in the Netherlands

Sales and use of antimicrobial veterinary medicinal products (AVMPs) are monitored by the Netherlands Veterinary Medicines Institute (SDa, Diergeneesmiddelenautoriteit). The information described in this part of the NethMAP One Health report is presented in more detail in the annual reports of the SDa.[1]

4.1 Total sales of veterinary antibiotics in the Netherlands 2025

4.1.1 Analysis of sales data

FIDIN, the federation of the Dutch veterinary pharmaceutical industry, provided sales data for all Antimicrobial Veterinary Medicinal Products (AVMPs) on package level sold in 2025 in the Netherlands, as extracted from the Vetindex and supplemented with AVMPs data of non-FIDIN members. These data are estimated to cover approximately 98% of all sales in the Netherlands, according to FIDIN. 2.4% (in mass) of the sold AVMPs (including all administration forms like tablets and injectables) is exclusively authorized for companion animals not including (in contrast to previous years) horses. AVMPs that are marketed in accordance with legal exemptions such as products that are imported from other EU member states in accordance with cascade legislation, are not included in sales figures, but are revealed in usage. For 2025 0.8% of used mass consisted of AVMPs from other EU member states prescribed under EU 2019/6 Article 113/1(a) (cascade use) due to Dutch veterinary medicinal products shortages. Most frequently (86.9%) due to shortages in AVMPs for lactating cow (mastitis injectors) but main contribution in mass is neomycin (73.7%), since AVMPs with neomycin were not authorized anymore in the Netherlands and treatment was deemed necessary in veal calves. Other important sectors with cascade use due to absence of authorized AVMPs are the goat sector (13.7% of mass of cascade use) and the rabbit sector (11.3%). In 2024 the total cascade use comprised 2.3%.

AVMPs are reported as active base substance mass (excluding mass of salts and esters), including oral products, injectables, intramammary injectors and topical applications like ointments, eye drops and sprays. The sales data in this report involves total sales for all animals, not stratified by animal species. Detailed information about antibiotic usage by animal species in the Netherlands is reported in chapter 4.2.
Actual use in animal husbandries can be somewhat different from the quantities sold due to stock piling and cross border use, and sales include AVMPs for topical administration, while AMU monitoring is limited to systemically applied AVMPs, intramammary and intra-uterine AVMPs. Monitored mass used in the major livestock farming sectors (pigs, broilers, turkey, other poultry, veal calves, dairy- and other cattle, meat rabbits and goats) covered 88.4% of total sales in 2025. This coverage fluctuates over the years, due to not yet monitored sectors (e.g. sheep, horses, companion animals) and stockage differences between the years.

4.1.2 Trends in total sales

Table 4.1.1 shows the trends in the total sales of antibiotics licensed for therapeutic use in animals in the Netherlands. In 2025 in total 113 tonnes of AVMPs were sold, representing a decrease of 6.8% in comparison with 2024. A decrease in sales by 77.2 % over the years 2009-2025 is attained (with 2009 considered the reference year by the Dutch Government).

Figure 4.1.1 shows the trends in sales (mass, black line) in relation to the dynamics of liveweight of Dutch livestock (dashed line) and the total use on farms (mass, bars) in the livestock sectors monitored, from 2009 to 2025. Antimicrobial use (in kg) in livestock sectors is presented as bars in which the use in different animal species can be distinguished. Figure 4.1.1 shows a slightly decreasing trend in liveweight of Dutch livestock. Compared to 2009 the liveweight of Dutch livestock has decreased by 17.2%. The decrease in antimicrobial use is much greater, demonstrating that decreasing trends in total mass sold and used cannot be explained by a drop in the liveweight of Dutch livestock. Veal calves (light blue) and pigs (green) used 69% of the total mass of all AVMPs used. Animals treated in these two sectors are relatively large and therefore need more active substance per treatment than small animals like broiler chickens. This illustrates that sales data provide limited information about exposure of animals at risk. Use data based on mass applied per sector may result in the suggestion that exposure of broiler chickens to AVMPs is limited based on the small proportion of total mass used in these animals.

The discrepancy in mass in 2025 between total sales and usage in monitored sectors was 11.6% as previously mentioned and depicted in Figure 4.1.1. The difference between sales and use data fluctuates as visualized by the difference between the solid black line (mass sold) and bars (mass used in monitored sectors).

As demonstrated in Figure 4.1.2, antimicrobial sales depicted by antibiotic class shows a fluctuating pattern over the years, with an overall decreasing tendency in most antibiotic classes, and minor variation from year to year.

Antimicrobial classes most sold

Penicillins, tetracyclines, trimethoprim/ sulphonamides, macrolides & lincosamides represent over 90% of sold AVMPs.
First place in mass, sales of penicillins (including aminopenicillins) remained stable in 2025 compared to 2024. The distribution of broad and narrow spectrum penicillins (in mass sold) is comparable to previous years with 70.0% aminopenicillins.

Tetracyclines and penicillins changed places for first and second place again when expressed in mass; in 2025 the sales of tetracyclines have decreased with 23.8% compared to 2024. The fraction of doxycycline (not specified in Figure 4.1.2) was in 2025 67.2% of the total sales of tetracyclines (65.9% in 2024, comparable fractions since 2019).

Table 4.1.1 *Antimicrobial veterinary medicinal product sales from 2005-2025 in kg (thousands) (FIDIN, 2026)*

Year	'05	'06	'07	'08	'09	'10	'11	'12	'13	'14	'15	'16	'17	'18	'19	'20	'21	'22	'23	'24	'25
beta lactam antibiotics	51	57	61	70	73	71	66	54	45	48	45	39	42	43	36	40	34	29	30	31	31
tetracyclines	292	301	321	257	251	217	157	102	80	69	82	62	68	65	51	49	47	31	32	36	28
macrolides & lincosamides	28	42	55	52	46	39	34	26	25	28	23	23	25	25	23	24	21	19	21	20	22
aminoglycosides	11	11	12	11	10	8.6	7.3	5.8	3.4	1.8	2.7	2.1	1.9	2.0	1.8	1.7	1.8	1.5	1.5	1.8	1.7
(fluoro) quinolones	8.0	7.0	9.0	8.0	7.8	6.6	5.1	3.1	2.8	3.8	4.2	3.4	3.4	3.9	2.7	2.6	2.1	2.4	2.3	1.9	1.8
trimethoprim/ sulfonamides	91	93	99	100	92	78	58	48	53	49	42	39	34	33	29	30	32	22	24	24	24
other antibacterials	6.0	8.0	8.0	7.0	15	13	10	10	8.1	7.8	7.5	7.4	7.2	7.5	7.4	7.2	6.9	6.3	5.6	6.2	5.5
Total sales	487	519	565	506	495	433	338	249	217	207	206	176	181	179	150	154	145	112	117	121	113

Figure 4.1.1 *Mass balance of AVMPs sales data (black line, left y-axis) and use data (colored bars, left x-axis) (kg x 1000), combined with total live weight of the food animal population (dotted line, right y-axis, kg x 10^6) from 2009-2025*

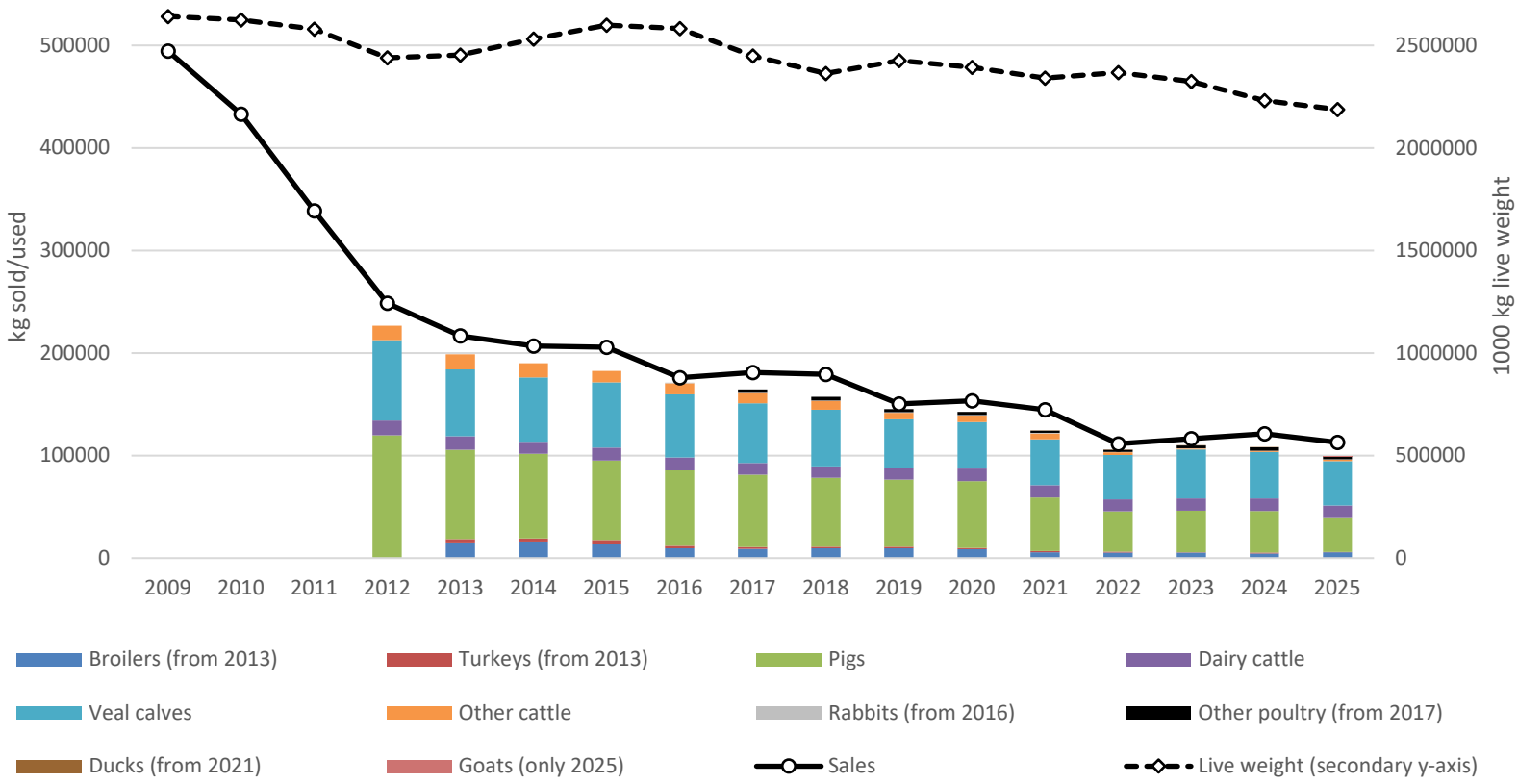
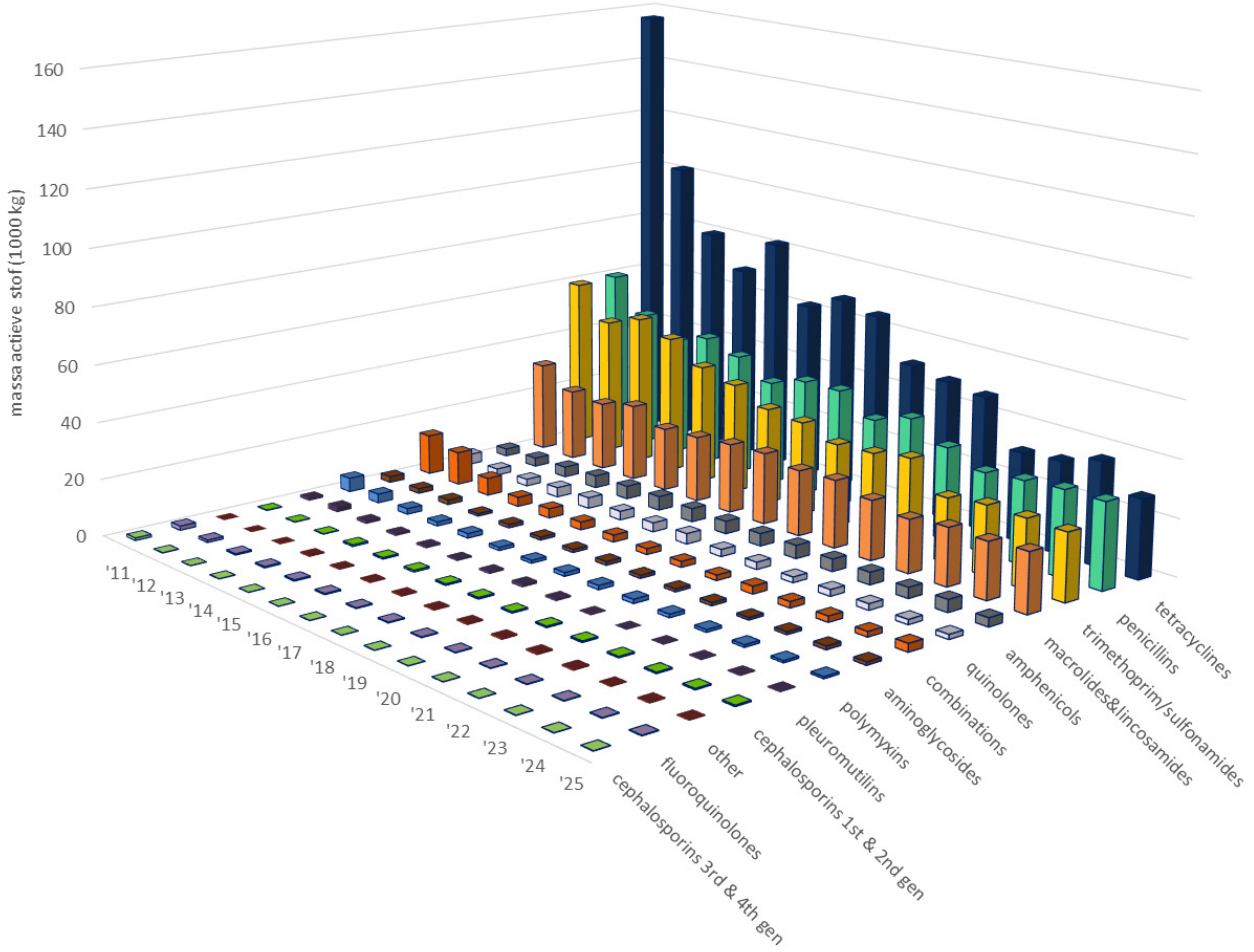


Figure 4.1.2 *Antimicrobial Veterinary Medicinal Product sales by antibiotic class from 2011-2025 in kg (thousands); antibiotic class "other" comprises bacitracin, fusidic acid and nitro-imidazole's*



Critically important antimicrobial classes

(Fluoro)quinolones
The sales of fluoroquinolones increased with 3kg (+2.3% compared to 2024). Still, an overall reduction of 91.4% was realized since 2011. In 2025, 48.8% of the sold fluoroquinolones were applied in the monitored sectors. Extending monitoring to other animal species (as is regulated with EU 2019/6) is warranted. The sales of quinolones (flumequine) decreased with 4.9% in 2025 when compared to 2024; these AVMPs are exclusively applied in food producing animals and partly substitute the use of colistin. Although the EMA Antimicrobial Advice ad hoc Expert Group (AMEG) decided not to differentiate between quinolones and fluoroquinolones (both category B), in the Netherlands quinolones were in 2025 still classified at a level of lower importance (2nd line, comparable with category C) than fluoroquinolones (3rd line, comparable with category B). The revised Netherlands working party for veterinary antibiotic policy (NWVAB) has published the new categorization in 2026, quinolones are now categorized at the same high importance level as fluoroquinolones (NWVAB.nl).

Cephalosporins 3rd/4th generation
Sales of these AVMPs were relatively stable at a low level since 2016, fluctuating in kg range. In 2025 0.6 kg active substance in authorized AVMPs was sold.
A reduction of 99.93% of cephalosporins 3rd/4th generation sales has been achieved since 2011.

Polymyxins
Colistin sales decreased in 2025 compared to 2024 with 7.6%. The reduction since 2011 is 87.3%. Based on the classification of polymyxins as *Highest Priority Critically Important Antimicrobials* (HP-CIAs) in the 6th revision of the WHO CIA list (2019)*,* the *Expert Panel of the* Netherlands Veterinary Medicines Institute considers polymyxins as third choice antibiotics, and this antibiotic class is reported as such. This implies that similar as for fluoroquinolones and 3rd/4th generation cephalosporins the Dutch target for use since 2020 is 0 $DDDA_F$. The ESVAC group introduced in 2016 the colistin desirable-level-benchmark for EU member states. This benchmark is below 1 mg/PCU for sales data, irrespective of the sectors in which colistin is used. Netherlands is below that unified benchmark. However, in weaned piglets and laying hens room for improvement can still be recognized. Colistin use in weaned piglets dropped for the fifth consecutive year. Colistin use in laying hens was reduced substantially, reaching the level of 2022 after two consecutive years of increased use. In veal calves and other poultry a remarkable increase was noted compared to previous years, in the other livestock sectors virtually no colistin is used.

4.2 Usage in pigs, veal calves, cattle, broilers, turkeys and rabbits in the Netherlands

In figure 4.2.1, antimicrobial use (AMU) based on annual prescription data is presented for each livestock sector. Important reductions in AMU have been achieved in all sectors (Figure 4.2.1) since monitoring of AMU was established.

Figure 4.2.2 shows that in most sectors first line antimicrobials (green and blue bars) are dominant. In most sectors, except for pigs, broilers and turkeys, this proportion of first choice AVMPs has attained a stable level, at over 80%. Figure 4.2.2 also illustrates that use of fluoroquinolones (red bar) is low in all livestock sectors, use is the highest in turkeys. Fluctuations from year to year in turkeys and rabbits can be attributed to the small number of farms (30-40). Veal calves is a large sector using 84% first choice AVMPs.

Expressing antimicrobial use as the number of Defined Daily Doses Animal (DDDA), as shown in Figures 4.2.1 and 4.2.2, allows for AMU comparisons between sectors. AMU decreased by 9.7% in pigs, while AMU in broilers increased by 24.7% compared with 2024; the causes of this increase are still under investigation. AMU in veal calves remained stable at a relatively high level. Use in the (dairy) cattle sector is consistently low. The antimicrobial classes used also differed substantially between these sectors.

For more details about all animal sectors, annual reports of the SDa should be consulted.[1]

EU regulation 2019/6 (VMP-reg)
EU Regulations about, amongst others, monitoring of veterinary antimicrobial *use* are implemented in national legislation for all EU member states. Sales data are reported to EMA, as has been done by most EU member states in the ESVAC project until 2022. Additionally, use data have been reported for pigs, cattle, turkeys and broilers in 2025 concerning 2024 use data. Monitoring of sales and use data may be expanded from anti*bacterial* substances for systemic use (obligatory scope) to all anti*microbial* substances including topical use and antimycotic, antifungal, antiviral and anticoccidial substances (voluntary scope). Cascade use of products imported from other EU countries will have to be incorporated in sales (and use) data. For the Netherlands sales data of antibacterial VMPs, including topical use, are collected and reported.

In 2026, monitoring of use of AVMPs will be extended to rabbits, sheep, goats, ducks, geese, finfish and horses. Most of these sectors (rabbits, goats and ducks) are already included in the Dutch AMU monitoring, AMU data for sheep and horses will be collected in 2026 as a pilot. In 2029 the use of these products will also be monitored in cats and dogs. For horses and companion animals cascade use of antimicrobial medicinal products for human use will have to be included as well in the *use* monitoring.

Figure 4.2.1 *Number of animal-defined daily dosages per animal-year for rabbits (grey), turkeys (purple), veal calves (blue), broilers (orange), pigs (light green) and dairy cattle (dark green) farms as reported by LEI WUR-MARAN (years 2007-2010 as DD/AY) and by SDa (years 2011-2025 as $DDDA_{NAT}$) depicting point estimates (dots), 95% confidence limits (error bars), smoothed trend line (penalized spline) and 95% confidence limits for the spline (shaded area)*

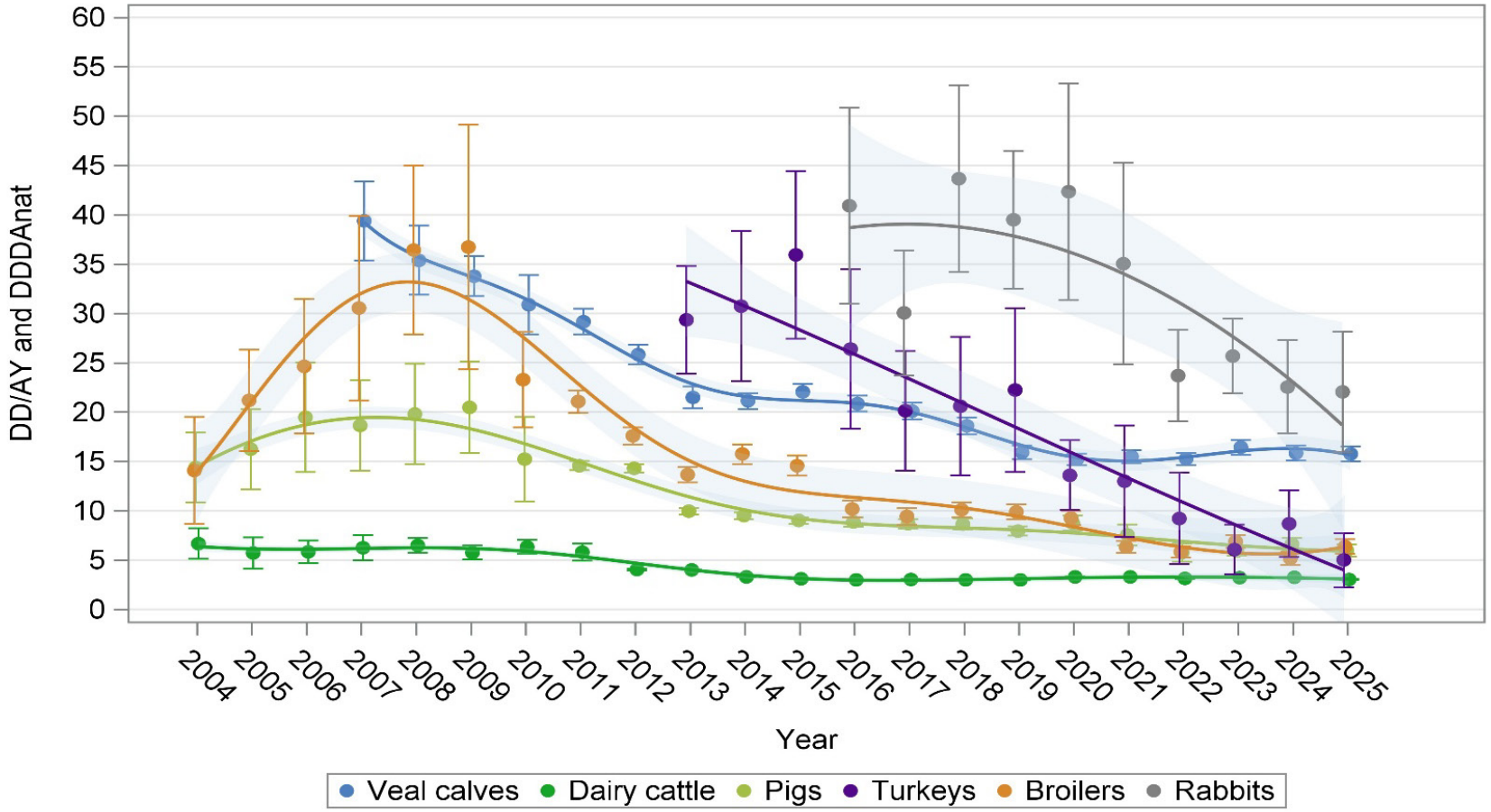
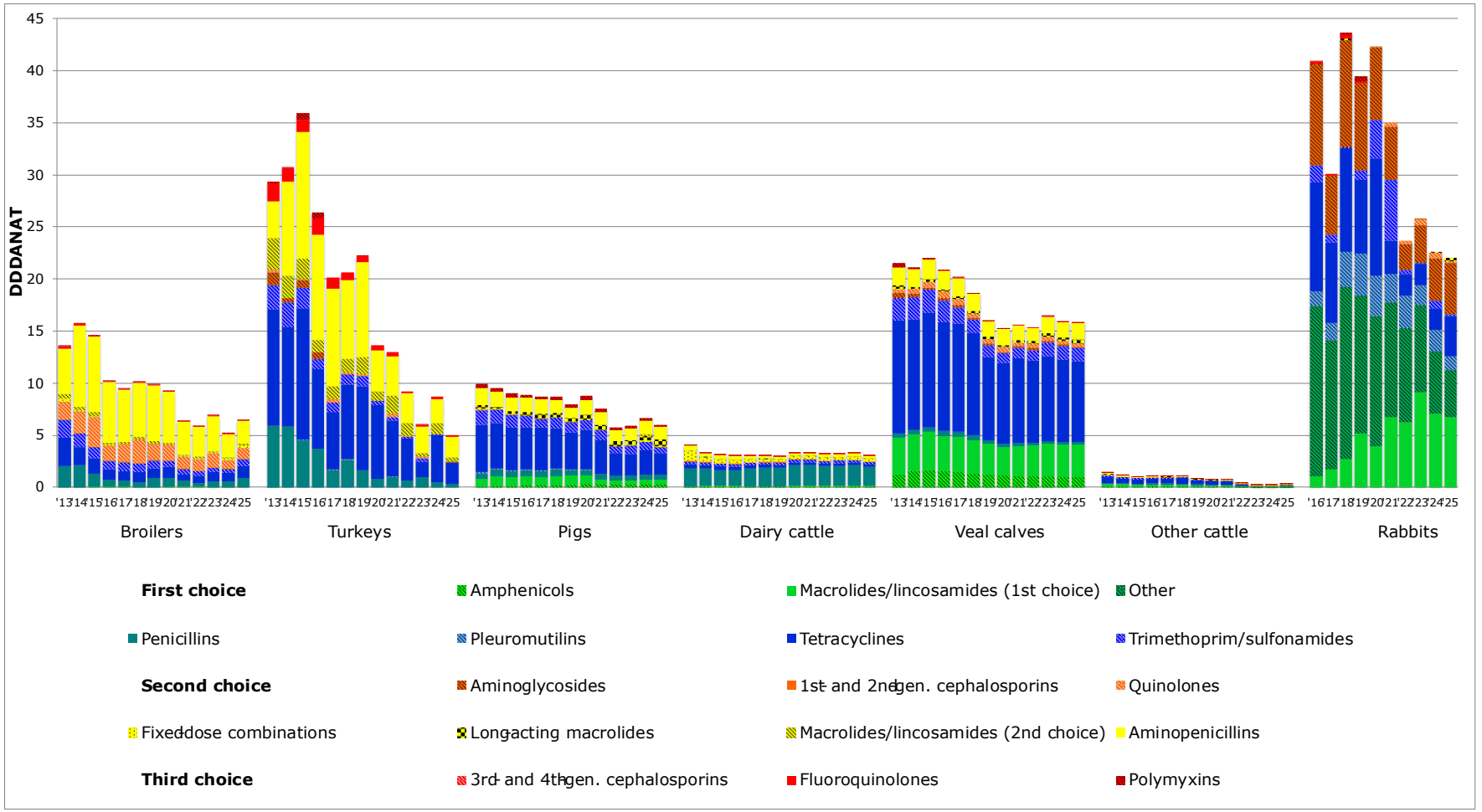


Figure 4.2.2 *Number of $DDDA_{NAT}$ per animal-year of antimicrobial veterinary medicinal products specified by antibiotic class per animal sector over the years 2013-2025*



Conclusions

Maximal transparency has been created since 2011 through monitoring antibiotic use by veterinarians and farmers. Total mass of active substances sold and used both decreased in 2025 compared to 2024, compared to reference year 2009 sales were reduced 77.2%. The calculation of consumption, based on national conversion factors (DDDAs) of authorized veterinary medicinal products, shows that use has stabilized in most sectors.

The use of antibiotics of critically important for human health care (especially cephalosporins of 3rd and 4th generation) is low, even in the unmonitored sectors. Use and sales of polymyxins decreased again in 2025, overall decrease since 2011 is 87.3% in sales. Of the fluoroquinolones, 51.2% is applied is sectors not yet monitored; an overall decrease of 91.4% since 2011 is observed.

References

1. SDa annual reports: https://www.autoriteitdiergeneesmiddelen.nl/en/publications/general-reports

5 AMR in human pathogens

5.1 General AMR surveillance

5.1.1 Methods and description of data from the Infectious Diseases Surveillance Information System for Antimicrobial resistance (ISIS-AR)

5.1.1.1 Methods

Since 2008, routinely available antimicrobial susceptibility data of all isolates from medical microbiology laboratories in the Netherlands, including minimal inhibitory concentration (MIC) values and disk zone diameters, are collected in the Infectious Diseases Surveillance Information System for Antimicrobial Resistance (ISIS-AR). This surveillance system is a combined initiative of the Ministry of Health, Welfare and Sport and the Dutch Society of Medical Microbiology (NVMM), and is coordinated by the Centre for Infectious Disease Control at the National Institute for Public Health and the Environment (RIVM) in Bilthoven.

In 2025, 46 laboratories were connected to ISIS-AR, all performing antimicrobial susceptibility testing (AST) according to EUCAST guidelines. Out of these 46 laboratories, 36 provided complete data on the last five years (2021 to 2025). Six of these 36 laboratories exclusively served university hospitals; 28 laboratories served non-university hospitals, general practices, and long-term care facilities; and two laboratories exclusively served general practices and long-term care facilities. We selected only data from these 36 laboratories to avoid bias in time trends due to incomplete data. Due to laboratory merges in 2024 and 2025, the total number of laboratories could change over time, and for this report the merged entities are counted as single laboratories. For all laboratories that merged during the years covered in this edition of NethMap One Health, each individual laboratory involved also had complete data for those years. Additionally, the set of laboratories that provides complete data over the last 5 years fluctuates per edition of NethMap One Health, due to technical issues, or because of differences in starting date. As a result, the number of participating laboratories is not directly comparable between different editions of NethMap One Health. For this edition, time trends were calculated based on the current selection of included laboratories.

All data provided to ISIS-AR are carefully validated[1]. Data with confirmed or probable technical errors are, after consultation with the laboratory that provided the data, corrected or excluded from the analyses in this report.

Selection of isolates

We calculated resistance levels and, if applicable, time trends by setting of care, i.e., general practices, outpatient departments, inpatient departments (excl. intensive care units, incl. emergency departments), intensive care units, urology departments (inpatient and outpatient separately), and long-term care facilities. For general practices (section 5.1.2) and long-term care facilities (section 5.1.4), we selected urine

isolates for analysis of resistance in Enterobacterales and *Pseudomonas aeruginosa*; wound or pus isolates for analysis of resistance in the *Staphylococcus aureus* complex; wound or pus, respiratory, and genital isolates for analysis of resistance in β-haemolytic *Streptococcus* group A; and urinary and genital isolates for analysis of resistance in β-haemolytic *Streptococcus* group B. In accordance with age categories used in the guidelines of the Dutch College of General Practitioners (NHG) for urinary tract infections, resistance levels and five-year trends for Enterobacterales and *P. aeruginosa* isolates from urine of general practice patients were calculated separately for patients aged ≤12 years and patients aged >12 years. For analyses on data from outpatient departments (section 5.1.3.1), inpatient departments (excl. intensive care units, section 5.1.3.2), and intensive care units (section 5.1.3.3), we selected isolates from blood, cerebrospinal fluid, urine, lower respiratory tract, and wound or pus. Additionally, we conducted a separate analysis for blood isolates from inpatients (incl. patients from intensive care units, section 5.1.3.4). For urology departments (section 5.1.3.5), we selected only urine isolates. In section 5.1.5, we show resistance levels for respiratory pathogens (S*treptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*) in general practitioners' patients and hospital patients. For the analysis on general practitioners' patients, we selected isolates from the upper and lower respiratory tract. For the analysis on hospital patients, we additionally selected isolates from blood and cerebrospinal fluid.

The category 'wound or pus isolates' comprises isolates from deep and superficial wounds, pus (including pus from abscesses), but also skin (excluding perineal swabs), normally sterile sites or cultures taken using a sterile procedure (i.e., biopsy, aspiration), synovial fluid, peritoneal cavity fluid and fluid for continuous ambulatory peritoneal dialysis (CAPD), eyes (both normally sterile and non-sterile sites), amniotic fluid, and samples from or related to medical implants. The category 'lower respiratory isolates' comprises respiratory isolates from below the glottis, whereas 'upper respiratory tract isolates' originate from respiratory samples that were taken above the glottis.

In each of these subsections, distribution of microorganisms within the materials selected for that chapter was calculated, including only isolates from organisms that were under active surveillance in ISIS-AR.

Since the number of *Staphylococcus argenteus* and *Staphylococcus schweitzeri* isolates was too small for separate analyses, the data for *S. aureus*, *S. argenteus* and *S. schweitzeri,* all belonging to the *S. aureus* complex, were analysed together and further referred to as *S. aureus*. In all sections 5.1.2 through 5.1.4, *S. argenteus* comprised 0 to 0.07% of the isolates from this complex. *S. schweitzeri* was found only once in a patient from an outpatient department, and once in a patient from a non-ICU hospital department.

For each analysis, we selected the first isolate per species per patient per year to avoid repeated sampling causing bias in the calculation of resistance levels and time trends. We included only data on diagnostic (=infection related) samples, and only calculated resistance levels for pathogens for which at least 100 isolates in each year were available for

analysis. Furthermore, to avoid bias due to selective testing of agents, for each pathogen-agent combination, we included only data from laboratories that tested at least 50% of isolates for that specific agent in each year. Finally, for sufficient representativeness of the results, we only calculated the resistance level and time trend of a pathogen-agent combination if the data from at least 50% of the selected laboratories could be included, with a minimum of 15 laboratories.

Calculation of resistance levels
We calculated the percentage of resistant isolates ('R'). To avoid bias due to differences in (versions of) breakpoint guidelines and expert rules used in the participating laboratories, we first reinterpreted all crude test values (minimum inhibitory concentrations (MICs) and diameters) according to EUCAST breakpoints version 15.0 (2025). We included data from all laboratories for which at least 80% of test values could be reinterpreted each year. Where reinterpretation was not possible, this was due to missing crude data or test values that were not compatible with EUCAST breakpoints.

For several pathogen-agent combinations EUCAST has specified breakpoints that apply only to a specific diagnosis or treatment strategy, for example, separate breakpoints for meningitis and other indications than meningitis. For each of those pathogen-agent combinations resistance percentages are shown for the diagnosis or treatment strategy that is most common. When we refer to an 'uncomplicated urinary tract infection (UTI)', we mean a UTI that presents without evidence of tissue invasion or systemic symptoms according to the SWAB guidelines[2]. For Enterobacterales, the co-amoxiclav MIC breakpoint for uncomplicated UTIs is the diagnosis that is most common in general practices and long-term care facilities. However, up until 2024, this breakpoint could not be used to reinterpret MIC values because the maximum test value of >16 mg/L that could be measured by the VITEK2 system did not reach the breakpoint of 32 mg/L. From 2025 onwards, a new test panel has been introduced for the VITEK2 system, with a testing range that includes the test value of 32 mg/L for co-amoxiclav. Therefore, data from 2025 onwards can be re-interpreted according to the breakpoint for uncomplicated UTIs, but a time trend calculation between 2021-2025 is not yet possible. Therefore, in sections 5.1.2 (Primary care) and 5.1.4 (Long-term care facilities), for Enterobacterales, we present resistance to co-amoxiclav and all combinations of agents that include co-amoxiclav according to two breakpoints: (1) the breakpoint for intravenous administration, for which the time trend between 2021-2025 is calculated, and (2) the breakpoint for oral treatment of uncomplicated UTIs, for which only the resistance percentage in 2025 is calculated. Likewise, in *Escherichia coli*, the fosfomycin MIC breakpoint for oral administration in uncomplicated UTI could not be used to reinterpret MIC values, because the minimum test value of ≤16 as measured by both the VITEK2 system and the Phoenix system do not reach the breakpoint of 8 mg/L. To approximate resistance percentages for oral administration as close as possible, we reinterpreted MIC-values according to the lowest cut-off that was possible; which was 16 mg/L, whereas we reinterpreted diameters according to the EUCAST breakpoint for oral administration (24 mm). As a consequence, isolates with an MIC between 8-16 mg/L were

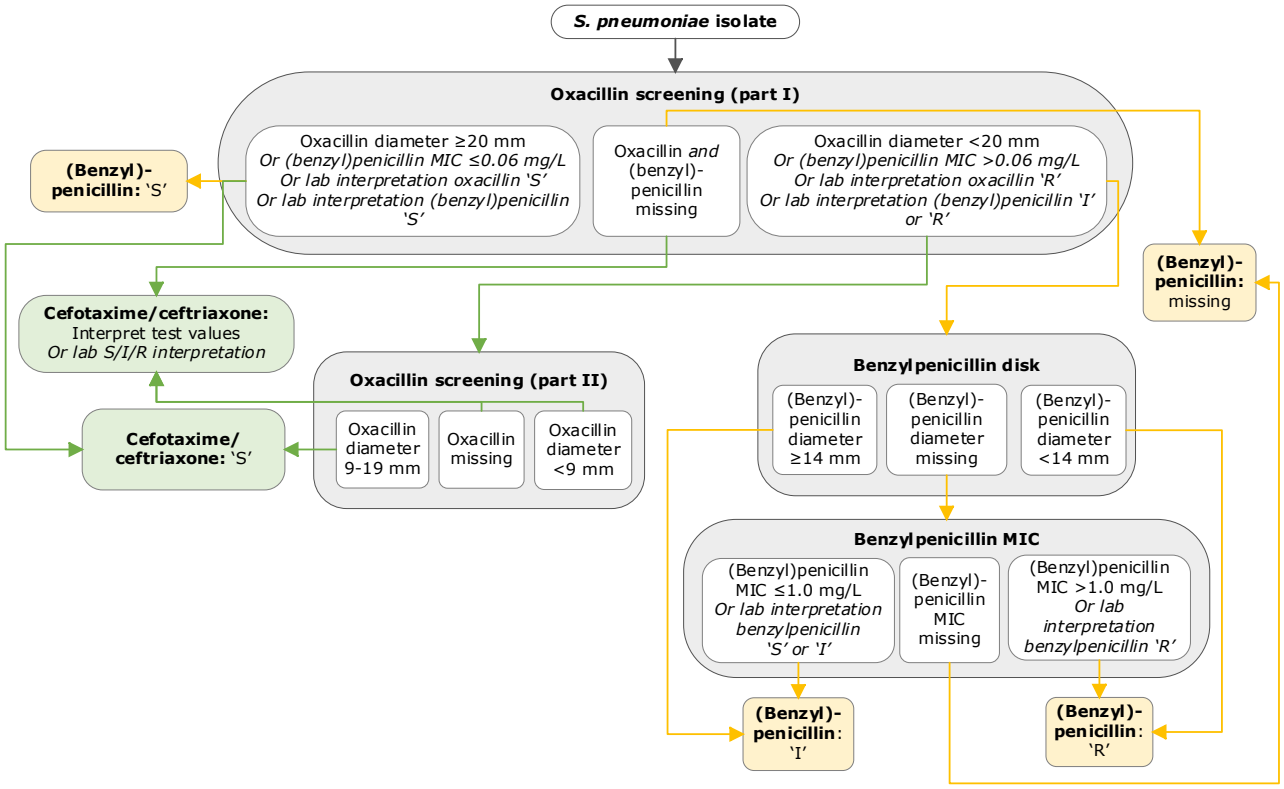
interpreted as sensitive ('S') instead of resistant ('R'). Even though these MIC values do not occur often, this could have led to a slight underestimation of the resistance percentage.

For *Staphylococcus* spp. and *Streptococcus* spp. we present both resistance to clindamycin as measured, as well as the percentage of isolates resistant to clindamycin including inducible resistance. Because data on tests for inducible clindamycin were often not available in ISIS-AR, we calculated resistance levels for clindamycin including inducible resistance based on re-interpretation of raw test values for clindamycin resistance, unless there was a positive test on inducible clindamycin resistance. In that case we counted the isolate as resistant to clindamycin. If no data on a test for inducible clindamycin test were available, but the laboratory reported the isolate being resistant to clindamycin we assumed that results of the test for inducible resistance was taken into account and counted the isolate as resistant.

We approximated the percentage MRSA among *S. aureus* based on positivity of MRSA confirmation tests (presence of *mecA* or *mecC* gene or *pbp2*), whereas if these tests were lacking, prevalence was based on reinterpretation of crude test values for cefoxitin or, if no data on a cefoxitin test was available, for flucloxacillin/oxacillin, according to EUCAST breakpoints version 15.0. However, interpretations based on phenotypic results in absence of MRSA confirmation tests may introduce bias, as 'borderline oxacillin-resistant *S. aureus* (BORSA)' isolates may be misclassified as MRSA. This can potentially lead to an overestimation of MRSA frequency.

To test resistance of *S. pneumoniae* to β-lactam antibiotics EUCAST has specified a flowchart with testing steps based on test values for oxacillin, (benzyl)penicillin, and the β-lactam antibiotic of interest. To resemble this flowchart we used an algorithm to estimate resistance to (benzyl)penicillin and cefotaxime/ceftriaxone as depicted in figure 5.1.1.1.1. However, available gradient tests (ETEST™ and MTS™) for (benzyl)penicillin systematically underestimate MIC-values in *S. pneumoniae*[3]. Therefore, resistance percentages for (benzyl)penicillin in *S. pneumoniae* may be biased towards a lower level.
Similarly, for *H. influenzae* EUCAST has specified a flowchart to estimate resistance for β-lactam antibiotics, with testing steps based on test values for (benzyl)penicillin, β-lactamase production, co-amoxiclav, and the β-lactam antibiotic of interest. To resemble this flowchart we used an algorithm to estimate resistance to amoxicillin/ampicillin, co-amoxiclav, and cefuroxime as depicted in figure 5.1.1.1.2.

Figure 5.1.1.1.1 *Flowchart depicting the algorithm used to calculate resistance to β-lactam antibiotics in S. pneumoniae*



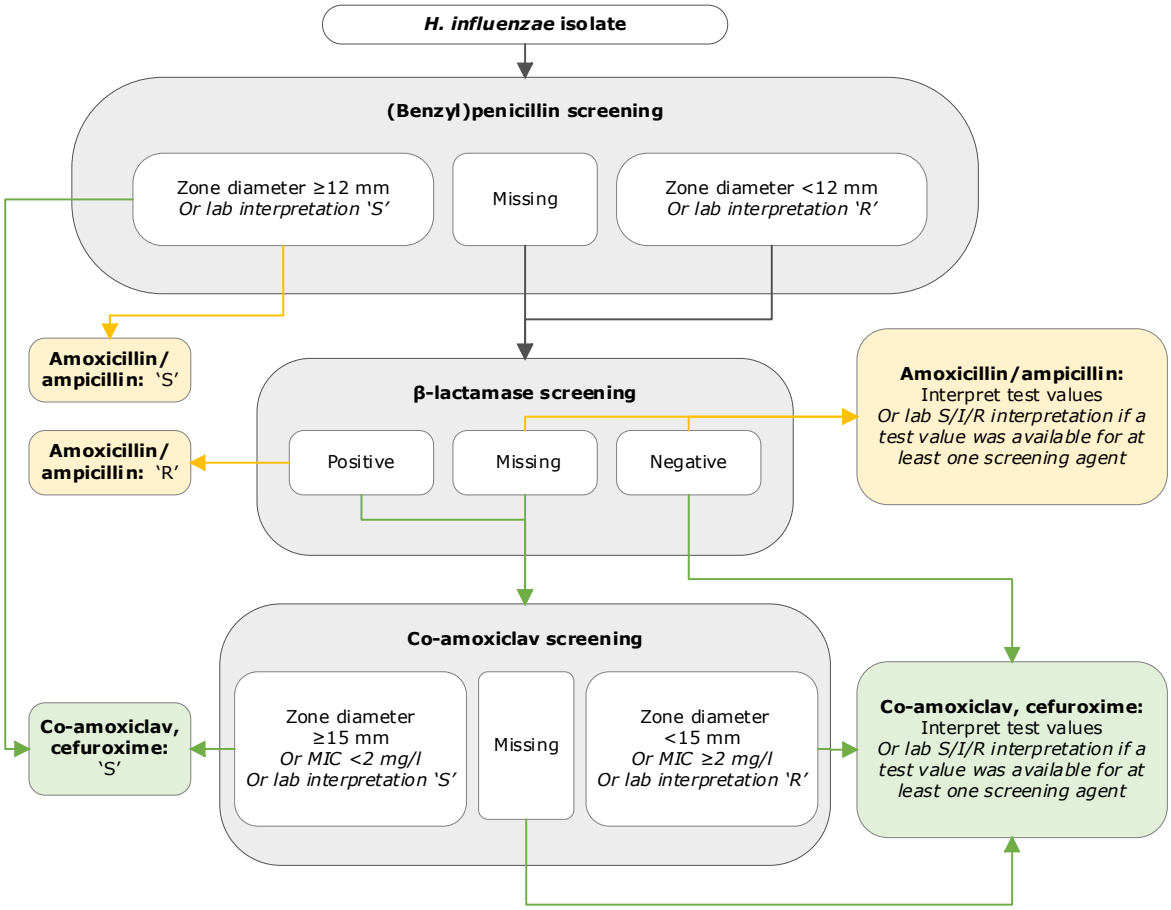
Note: The breakpoint for indications other than endocarditis and meningitis was applied for (benzyl)penicillin and cefotaxime/ceftriaxone.

'Or' indicates that if the primary option was not available, the concurrent option was used.

Color Legend: (1) Yellow arrows and boxes: Specific to (benzyl)penicillin. (2) Green arrows and boxes: Specific to cefotaxime/ceftriaxone.

We considered *S. pneumoniae* susceptible to levofloxacin/moxifloxacin if the isolate was susceptible to norfloxacin according to the screening breakpoint. Otherwise susceptibility was based on reinterpretation of test values of levofloxacin/moxifloxacin, or, if no test values were available and the isolate was resistant to norfloxacin, on laboratory interpretation of susceptibility. Likewise, we considered the viridans streptococci as being susceptible to amoxicillin/ampicillin if the isolate was susceptible to (benzyl)penicillin according to the screening breakpoint. Otherwise susceptibility was based on reinterpretation of test values of amoxicillin/ampicillin, or, if no test values were available and the isolate was resistant to (benzyl)penicillin, on laboratory interpretation of susceptibility.

Figure 5.1.1.1.2 *Flowchart depicting the algorithm used to calculate resistance to β-lactam antibiotics in H. influenzae*



Note: The IV and non-meningitis breakpoint was applied for amoxicillin/ampicillin, co-amoxiclav and cefuroxime.

'Or' indicates that if the primary option was not available, the concurrent option was used.

Color Legend: (1) Yellow arrows and boxes: Specific to amoxicillin/ampicillin. (2) Green arrows and boxes: Specific to co-amoxiclav and cefuroxime.

For some antimicrobial agents presented in this report, mutual comparable resistance mechanisms exist, namely benzylpenicillin/penicillin, amoxicillin/ampicillin, cefotaxime/ceftriaxone, meropenem/imipenem (except for *P. aeruginosa* and *Proteus mirabilis*), and doxycycline/tetracycline (except for *H. pylori*), and often the laboratories report results for either one. For these combinations, we calculated the percentage of isolates that was resistant to at least one of both agents. However, it should be mentioned that *S. aureus* can be susceptible for doxycycline while being resistant to tetracycline. Therefore, the resistance to doxycycline/tetracycline cannot be used as a proxy for the resistance to doxycycline, since that might be an overestimation.

For *H. pylori* and all Gram-negative bacteria except *Enterobacter cloacae* complex and *Acinetobacter baumannii/calcoaceticus* complex, we calculated resistance to specific combinations of agents that are

frequently used for empiric therapy (for Enterobacterales: cefuroxime + gentamicin, cefuroxime + ciprofloxacin, cefotaxime/ceftriaxone + gentamicin, and cefotaxime/ceftriaxone + ciprofloxacin; for *P. aeruginosa*: ceftazidime + tobramycin; for *H. pylori* amoxicillin/ampicillin + clarithromycin, and amoxicillin/ampicillin + metronidazole, clarithromycin + metronidazole, and tetracycline + metronidazole). For these combinations, we defined resistance as resistance to both agents.

For *S. aureus*, no data on levofloxacin were available for a large part of laboratories. Often, susceptibility to levofloxacin is only tested when the *S. aureus* isolate is resistant to ciprofloxacin. Resistance percentages of levofloxacin may, consequently, be biased toward a higher level. Therefore, we also calculated resistance to ciprofloxacin as a class indicator for resistance to fluoroquinolones.

For Enterobacterales isolates, we calculated the percentage of isolates that was multidrug resistant to oral therapy (MDOT), which we defined as resistance to the oral agents co-amoxiclav (according to breakpoint for intravenous administration), ciprofloxacin (according to breakpoint for indications other than meningitis), and co-trimoxazole combined.

Calculation of time trends
In addition to resistance levels in 2025, for sections 5.1.2 to 5.1.5 we calculated time trends over the last five years (2021 to 2025) using logistic regression models, except when data in one or more years before 2025 did not meet criteria for calculation of resistance levels. Because adoption of new guidelines or changes in breakpoints can have a substantial effect on resistance levels, we only analysed trends for resistance levels that were based on reinterpretation of crude test values from all five years according to EUCAST breakpoint guidelines version 15.0. We made an exception for trends in resistance to clindamycin including inducible resistance in *S. aureus* and resistance to β-lactam antibiotics in *S. pneumoniae* and *H. influenzae* (figures 5.1.1.1.1 and 5.1.1.1.2), which we partly based on laboratory S/I/R interpretation, as described above. However, we do not expect spurious time trends in resistance for these pathogen-agent combinations, because for *H. influenzae* the EUCAST breakpoints for these agents were not changed between 2021 and 2025, and for *S. pneumoniae*, the first screening step (oxacillin and (benzyl)penicillin screening breakpoints) also did not change between 2021 and 2025. However, the R breakpoint for (benzyl)penicillin did change between 2024 and 2025, and therefore, using laboratory interpretations in the years before 2025 might lead to a slight underestimation of resistance percentages.

We considered two-sided p-values for trend <0.05 to be statistically significant. When the absolute difference in predicted resistance from the logistic regression model between 2021 and 2025 was larger than the square root of the predicted resistance in 2021, we considered the trend to be microbiologically relevant. In the tables, statistically significant increasing trends that were considered to be microbiologically relevant are indicated in a red font, together with an up arrow, whereas decreasing trends that meet the same criteria are indicated in green, together with a down arrow. In addition, for each pathogen-agent combination, the resistance levels from 2021 to 2025 are shown in bar

charts. Trends that meet the criteria for significant and microbiologically relevant are indicated with an asterisk.

References

1. Altorf-van der Kuil W, Schoffelen AF, de Greeff SC, et al. (2017) National laboratory-based surveillance system for antimicrobial resistance: a successful tool to support the control of antimicrobial resistance in the Netherlands. Euro Surveill 22(46).
2. SWAB Urinary Tract Infections Guidelines Committee. Optimization of the antibiotic policy in the Netherlands: SWAB guidelines for antimicrobial therapy of urinary tract infections in adults. SWAB; 2020. Available from: https://swab.nl/nl/exec/file/download/148
3. EUCAST 2019, *Warning against the use of gradient tests for benzylpenicillin MIC in Streptococcus pneumoniae*, accessed August 6. 2025, http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Warnings/Warnings_docs/Warning_-_gradient_for_benzyl_and_pnc_21nov2019.pdf

5.1.1.2 Descriptive characteristics of ISIS-AR data

In this section, several descriptive characteristics of the data from the ISIS-AR antimicrobial resistance surveillance system are presented. In figure 5.1.1.2.1, the smoothed distribution of isolates over the country, based on the percentage of inhabitants for whom at least one isolate was included in the analyses in sections 5.1.2 through 5.1.5, is shown by 4-digit postal code area. Furthermore, in the same figure the geographical distribution of laboratories is presented by status of connection to ISIS-AR and inclusion in the analyses in sections 5.1.2 through 5.1.5 (see section 5.1.1.1 for inclusion criteria). In table 5.1.1.2.1, characteristics of included isolates are listed by pathogen.

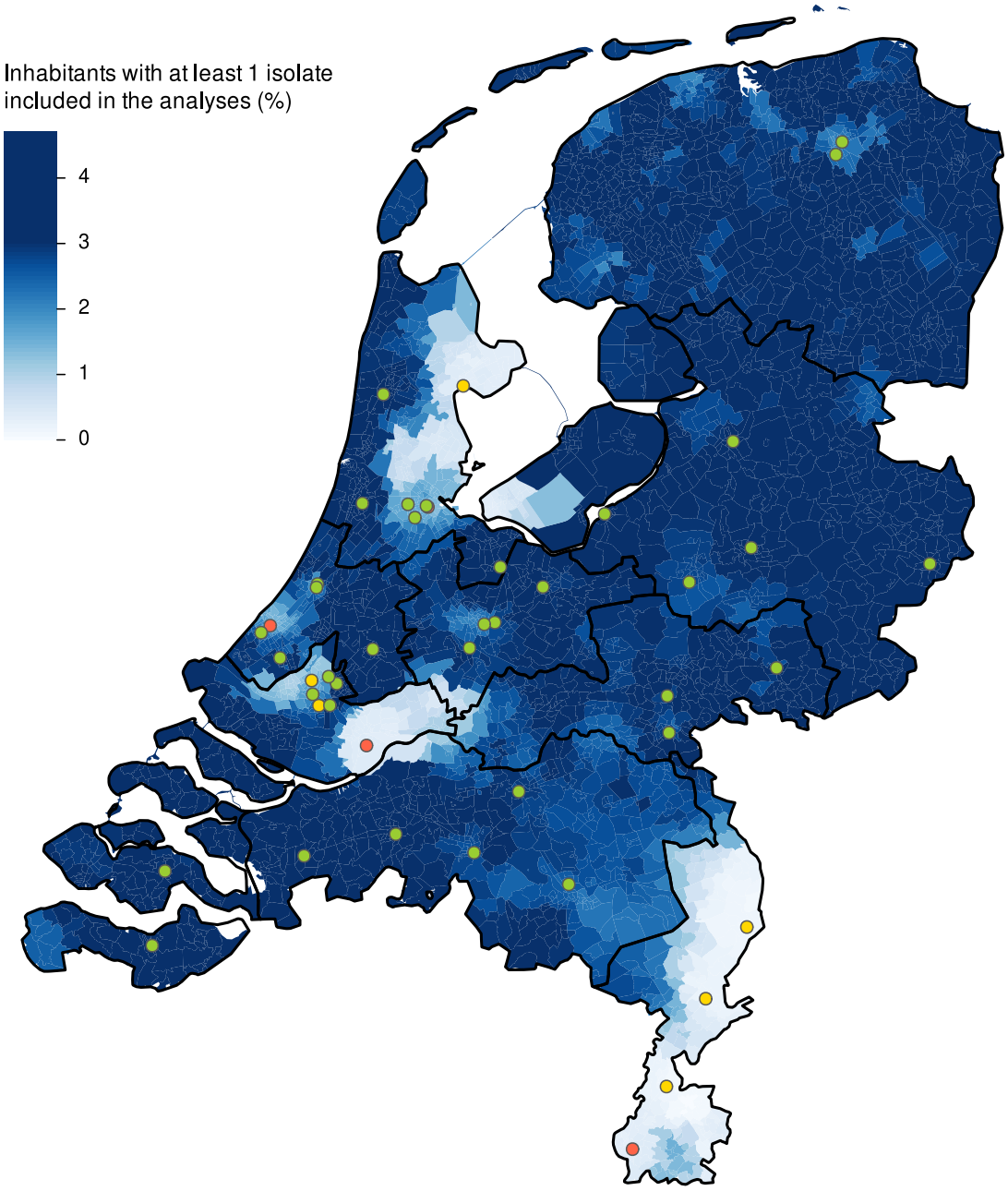
In each edition of NethMap One Health, all laboratories are included that have continuously sent data during at least the last five years to ISIS-AR. This results in variation in the mixture of included laboratories through the years, and data from this chapter cannot be compared to data from NethMap One Health 2025.

Key findings

Descriptive characteristics of ISIS-AR data

- For the 2025 analyses, data of 36 laboratories could be used, resulting in inclusion of data on 518,929 isolates.
- The distribution of laboratories that have provided antimicrobial resistance data over the past five years was considerably more balanced across the Netherlands compared to earlier editions of NethMap
- The number of laboratories from which data could be included in the analyses was relatively low in the regions ‘Noord-Holland Oost’, ‘Zuidwest-Nederland’ and ‘Limburg’. The distribution of included laboratories was reflected in the geographical distribution of isolates.

Figure 5.1.1.2.1 *Geographical distribution of laboratories, by status of connection to ISIS-AR and inclusion in the analyses in sections 5.1.2 through 5.1.5, together with smoothed geographical distribution of isolates, based on the percentage of inhabitants for whom at least one isolate was included in those analyses, by 4-digit postal code area and with regional cooperative network borders, ISIS-AR 2025*



- Laboratories with incomplete data in 2025
- Laboratories with complete data in 2025, but not included in the analyses because of incomplete data between 2021 and 2024
- Laboratories included in the analyses

Table 5.1.1.2.1 *Characteristics of 518,929 isolates, sampled in 2025, included in the analyses in sections 5.1.2 through 5.1.5, by pathogen*

	E. coli	*K. pneumoniae*	*P. mirabilis*	*E. cloacae* complex	*P. aeruginosa*	*A. baumannii / calcoaceticus* complex	*E. faecalis*	*E. faecium*	*S. aureus*
Total number of isolates	224,132	39,822	24,688	12,630	28,351	1,596	33,273	6,244	77,604
Sex of patient (%)									
Male	27	34	42	56	54	59	54	54	54
Female	73	66	58	44	46	41	45	46	46
Setting of care (%)									
General practices	65	54	52	38	37	34	49	10	37
Outpatient departments	12	17	17	24	29	27	19	11	34
Inpatient departments (excl. Intensive Care Units)	17	21	20	31	26	30	26	62	24
Intensive Care Units	1	1	1	3	2	5	2	14	3
Long-term care facilities	5	6	10	4	6	3	5	4	3
Age category of patient in years (%)									
0-4	3	1	3	3	2	5	3	0	6
5-18	4	1	2	2	5	4	2	1	9
19-64	33	25	21	28	30	37	28	32	44
>65	60	72	74	67	63	54	66	67	41
Isolate source (%)									
Blood	3	3	2	4	2	3	3	14	4
Respiratory tract	1	3	2	6	14	9	0	1	12
Urine	91	88	84	62	42	51	86	49	12
Wound or Pus	3	4	9	21	33	28	10	30	53
Genital	1	0	1	0	1	0	0	0	3
Other	1	2	3	7	8	8	1	6	16
Type of hospital (hospital isolates only, %)									
General	36	34	37	32	31	31	32	24	33
Top clinical	47	47	46	46	45	41	50	48	46
University hospital	17	19	18	22	24	28	18	29	21

The first isolate per patient, per pathogen, per setting of care was selected.

Table 5.1.1.2.1 (continued) *Characteristics of 518,929 isolates, sampled in 2025, included in the analyses in sections 5.1.2 through 5.1.5, by pathogen*

	ß-haemolytic *Streptococcus* spp. group A	ß-haemolytic *Streptococcus* spp. group B	ß-haemolytic *Streptococcus* spp. groups C and G	*S. anginosus* group	*S. mitis* group	*B. fragilis* complex	*C. perfringens*	*S. pneumoniae*	*H. influenzae*	*M. catarrhalis*
Total number of isolates	5,953	26,354	8,985	5,048	1,996	1,434	341	5,346	11,518	3,562
Sex of patient (%)										
Male	44	23	54	56	58	57	62	53	51	50
Female	56	77	46	44	42	43	38	47	49	50
Setting of care (%)										
General practices	52	58	32	5	7	3	4	7	12	12
Outpatient departments	24	21	31	29	18	22	18	29	47	46
Inpatient departments (excl. Intensive Care Units)	22	18	33	61	71	69	73	58	37	36
Intensive Care Units	1	1	2	4	4	5	5	6	3	4
Long-term care facilities	1	2	2	1	0	1	0	0	1	2
Age category of patient in years (%)										
0-4	13	1	1	1	5	1	0	7	10	10
5-18	14	3	3	5	4	5	2	4	4	3
19-64	55	66	50	54	40	39	31	37	33	27
>65	17	31	45	39	52	54	67	53	54	60
Isolate source (%)										
Blood	5	2	10	11	45	26	33	31	2	1
Respiratory tract	8	1	3	3	1	0	0	54	85	90
Urine	7	52	12	7	13	1	2	1	0	0
Wound or Pus	46	10	46	69	37	65	56	12	11	9
Genital	22	31	15	3	0	1	2	0	2	0
Other	13	5	14	6	4	7	7	2	0	0
Type of hospital (hospital isolates only, %)										
General	33	36	38	30	30	38	28	35	30	33
Top clinical	49	50	50	48	41	45	51	49	49	52
University hospital	17	14	12	22	29	17	21	16	20	16

The first isolate per patient, per pathogen, per setting of care was selected.

5.1.2 Primary care

The distribution of pathogens in diagnostic urine, wound or pus, respiratory, and genital samples from general practitioners' (GP) patients in 2025 is presented in table 5.1.2.1. The resistance levels in 2025 for *E. coli*, *K. pneumoniae*, *P. mirabilis*, and *P. aeruginosa* isolates from urine samples are presented in table 5.1.2.2. In accordance with age categories used in the Dutch College of General Practitioners (NHG) guidelines for urinary tract infections, resistance levels and five-year trends for urine isolates are calculated separately for patients aged ≤12 years and patients aged >12 years. For *S. aureus* isolates from wound or pus samples resistance levels in 2025 are presented in table 5.1.2.3. For β-haemolytic *Streptococcus* spp. group A isolates from wound/pus, respiratory, or genital samples as well as for β-haemolytic *Streptococcus* spp. group B isolates from urine or genital samples resistance levels in 2025 are shown in table 5.1.2.4. Five-year trends in resistance are shown in figure 5.1.2.1 (*E. coli*, *K. pneumoniae*, *P. mirabilis*, and *P. aeruginosa*), figure 5.1.2.2 (*S. aureus*) and figure 5.1.2.3 (β-haemolytic *Streptococcus* spp. group A and group B).

In accordance with the NHG guidelines, GPs typically initiate empirical antibiotic treatment before sending urine, wound, or pus samples for culture and susceptibility testing. Diagnostic samples are usually taken only in cases of therapy failure or, in the case of urine samples, suspected complicated urinary tract infections. Therefore, many of the pathogens isolated in primary care are likely to have been exposed to prior antibiotic treatment, introducing antibiotic selective pressure. As a result, the presented resistance levels are likely to be higher than those for all patients with urinary tract infections caused by Enterobacterales or *P. aeruginosa,* or wound infections or pus caused by *S. aureus* or β-haemolytic *Streptococcus* spp. group A presenting at the GP. Bias due to selective sampling of patients is expected to be limited for β-haemolytic *Streptococcus* spp. group B, because initial therapy of urinary tract infections is not expected to affect resistance to most antibiotics presented for *Streptococcus* spp. and genital samples are taken as part of routine diagnostics.

Because of the potential bias in results for Enterobacterales, *P. aeruginosa*, *S. aureus* and β-haemolytic *Streptococcus* spp. group A, the patients from whom samples were taken are hereafter referred to as 'selected general practitioners' patients'.

Table 5.1.2.1 *Distribution of isolated pathogens in diagnostic urine samples (by patient age category) and diagnostic wound or pus, respiratory, and genital samples from selected general practitioners' patients, ISIS-AR 2025*

	Urine		Wound or pus	Respiratory tract	Genital
	Age≤12	Age>12			
Pathogen	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**
E. coli	9,628 (71)	133,605 (55)	859 (2)	78 (2)	617 (7)
K. pneumoniae	272 (2)	20,601 (8)	281 (1)	69 (2)	82 (1)
P. mirabilis	725 (5)	11,462 (5)	616 (2)	31 (1)	51 (1)
Other Enterobacterales[1]	656 (5)	25,925 (11)	2,741 (8)	268 (6)	164 (2)
P. aeruginosa	213 (2)	5,356 (2)	4,470 (12)	236 (5)	111 (1)
Other non-fermenters[2]	107 (1)	1,733 (1)	773 (2)	381 (8)	14 (0)
Other Gram-negatives[3]	4 (0)	15 (0)	443 (1)	867 (19)	139 (2)
S. aureus	165 (1)	4,683 (2)	20,436 (56)	2,126 (47)	1,296 (14)
ß-haemolytic *Streptococcus* spp. group A	153 (1)	170 (0)	1,573 (4)	189 (4)	1,040 (11)
ß-haemolytic *Streptococcus* spp. group B	167 (1)	9,621 (4)	910 (3)	31 (1)	4,700 (51)
Other Gram-positives[4]	1,485 (11)	29,402 (12)	3,090 (9)	283 (6)	918 (10)
Anaerobes[5]	0 (0)	4 (0)	45 (0)	0 (0)	1 (0)

[1] In order of frequency: *Klebsiella* spp. (non-*pneumoniae*), *Citrobacter* spp., *Enterobacter* spp., *Morganella* spp., *Serratia* spp., *Raoultella* spp., *Proteus* spp. (non-*mirabilis*), *Providencia* spp., *Pantoea* spp., *Escherichia* spp. (non-*coli*), *Salmonella* spp., *Hafnia* spp., *Mixta* spp., *Cronobacter* spp.

[2] In order of frequency: *Acinetobacter* spp., *Pseudomonas* spp. (non-*aeruginosa*), *S. maltophilia*, *M. catarrhalis*.

[3] In order of frequency: *H. influenzae*, *H. parainfluenzae*, *N. meningitidis*, *H. pylori*.

[4] In order of frequency: *Enterococcus* spp., *Staphylococcus* spp. (non-*aureus*), *A. urinae*, *S. mitis*, *S. canis*, *S. gordonii*, *S. equi*, *S. dysgalactiae* subsp. *equisimilis*, *ß-haemolytic Streptococci* group C not further defined, *S. intermedius*, *S. constellatus*, *S. oralis*, *S. mitis* group not further defined, *S. dysgalactiae* subsp. *dysgalactiae*, *S. mitis/oralis* not further defined, *S. anginosus*, *ß-haemolytic Streptococci* group G not further defined, *S. anginosus* group not further defined, *S. dysgalactiae* not further defined, *S. pneumoniae*, *L. monocytogenes*.

[5] In order of frequency: *B. fragilis*, *C. perfringens*.

Table 5.1.2.2 *Resistance levels (%) among diagnostic urine isolates of E. coli, K. pneumoniae, P. mirabilis, and P. aeruginosa from selected general practitioners' patients, by age category, ISIS-AR 2025*

	E. coli		***K. pneumoniae***		***P. mirabilis***		***P. aeruginosa***	
	Age ≤12	**Age >12**	**Age ≤12**	**Age >12**	**Age ≤12**	**Age >12**	**Age ≤12**	**Age >12**
median age	5	69	5	74	3	76	3	79
Antibiotic								
amoxicillin/ampicillin	35	36	-	-	15	18	-	-
co-amoxiclav[a]	9°	8°	7°	5°	1.9°	3°	-	-
co-amoxiclav[b]	26	26	18 ↓	15	5	7	-	-
piperacillin-tazobactam	-	-	-	-	-	-	3	4
cefuroxime	7 ↑	9	8	11	1.7	0.9	-	-
cefotaxime/ceftriaxone[c]	5 ↑	5 ↑	4	5 ↑	1.2	0.5	-	-
ceftazidime	4 ↑	4	3	4 ↑	0.4	0.1	0.5	1.7
meropenem[c]	-	-	-	-	-	-	0.0	0.4
imipenem	-	-	-	-	-	-	1.6	4
ciprofloxacin[c]	7	10	5	10	4	8	1.4	8
gentamicin	5	4	0.7	1.8	3	4	-	-
tobramycin	5	4	0.4	2	2	3	0.0	0.5
fosfomycin[1]	1.1	2	-	-	-	-	-	-
trimethoprim	21	22	9	17	20 ↓	26	-	-
co-trimoxazole	18	19	6	8	15 ↓	20	-	-
nitrofurantoin	0.2	1.9	-	-	-	-	-	-
Multidrug resistance								
MDOT[2]	1.7	3	1.4	2	1.0	1.5	-	-

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

[1] Resistance percentage calculated using an MIC cut-off of 16 mg/L and a diameter cut-off of 24 mm. For more details see section 5.1.1.1.

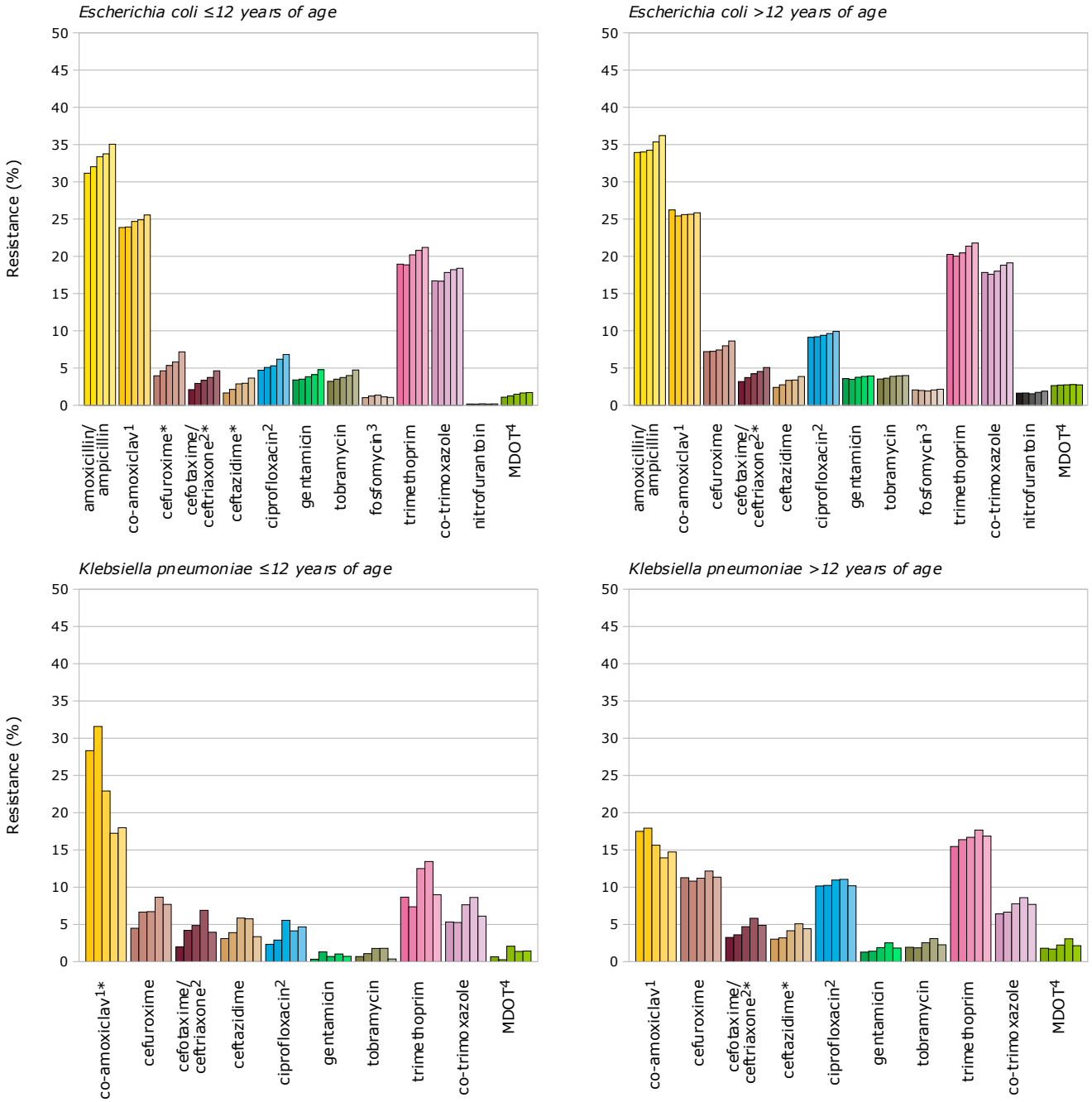
[2] MDOT = multidrug resistance to oral therapy, defined as resistance to all of the following oral agents: co-amoxiclav (according to breakpoint for intravenous administration), ciprofloxacin (according to breakpoint for indications other than meningitis), and co-trimoxazole.

[a] According to breakpoint for oral treatment of uncomplicated urinary tract infections. For more details see section 5.1.1.1.

[b] According to breakpoint for intravenous administration. For more details see section 5.1.1.1.

[c] According to breakpoint for indications other than meningitis (for ciprofloxacin this only applies to *E. coli*, *K. pneumoniae*, and *P. mirabilis*). For more details see section 5.1.1.1.

Figure 5.1.2.1 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic urine isolates of E. coli, K. pneumoniae, P. mirabilis, and P. aeruginosa from selected general practitioners' patients in ISIS-AR, by age category*



* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

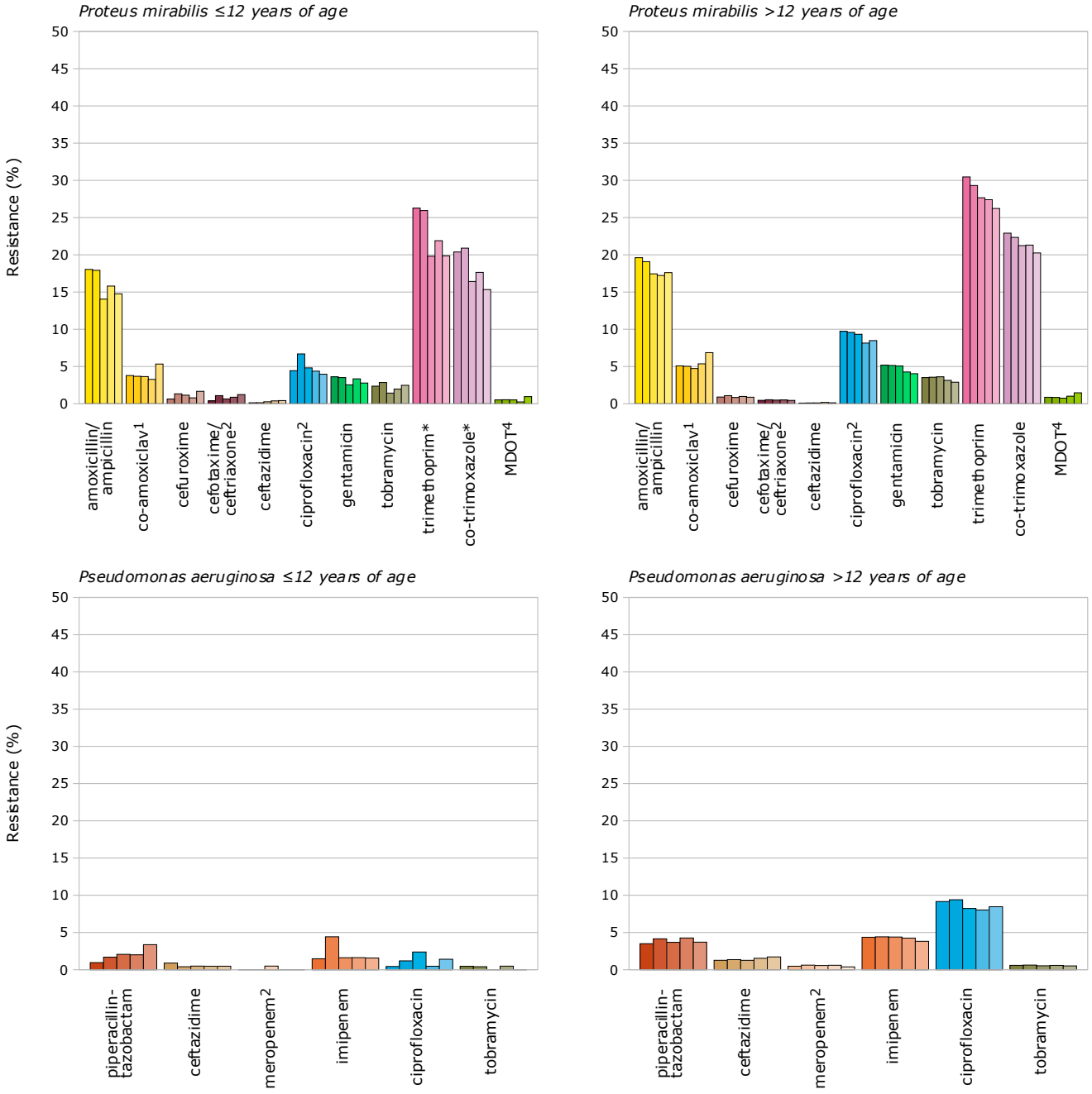
[1] According to breakpoint for intravenous administration. For more details see section 5.1.1.1.

[2] According to breakpoint for indications other than meningitis. For more details see section 5.1.1.1.

[3] Resistance percentage calculated using an MIC cut-off of 16 mg/L and a diameter cut-off of 24 mm. For more details see section 5.1.1.1.

[4] MDOT = multidrug resistance to oral therapy, defined as resistance to all of the following oral agents: co-amoxiclav (according to breakpoint for intravenous administration), ciprofloxacin (according to breakpoint for indications other than meningitis), and co-trimoxazole.

Figure 5.1.2.1 (continued) *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic urine isolates of E. coli, K. pneumoniae, P. mirabilis, and P. aeruginosa from selected general practitioners' patients in ISIS-AR, by age category*



* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

[1] According to breakpoint for intravenous administration. For more details see section 5.1.1.1.

[2] According to breakpoint for indications other than meningitis. For more details see section 5.1.1.1.

[3] Resistance percentage calculated using an MIC cut-off of 16 mg/L and a diameter cut-off of 24 mm. For more details see section 5.1.1.1.

[4] MDOT = multidrug resistance to oral therapy, defined as resistance to all of the following oral agents: co-amoxiclav (according to breakpoint for intravenous administration), ciprofloxacin (according to breakpoint for indications other than meningitis), and co-trimoxazole.

Table 5.1.2.3 *Resistance levels (%) among diagnostic wound or pus isolates of S. aureus from selected general practitioners' patients, ISIS-AR 2025*

	S. aureus
Antibiotic	
MRSA[1]	3
ciprofloxacin[2]	1.9
levofloxacin[3]	1.8
erythromycin	15
clindamycin	1.7
clindamycin (including inducible resistance)[4]	14
doxycycline/tetracycline	3
fusidic acid[a]	30 ↑
co-trimoxazole	2
mupirocin	3 ↑
Multidrug resistance	
fusidic acid + mupirocin[a]	3 ↑

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

[1] MRSA = Methicillin resistant *S. aureus*. For the estimation method of MRSA see section 5.1.1.1.; Within the *S. aureus* complex 0 out of 14 *S. argenteus* and 0 out of 0 *S. schweitzeri* were methicillin resistant.

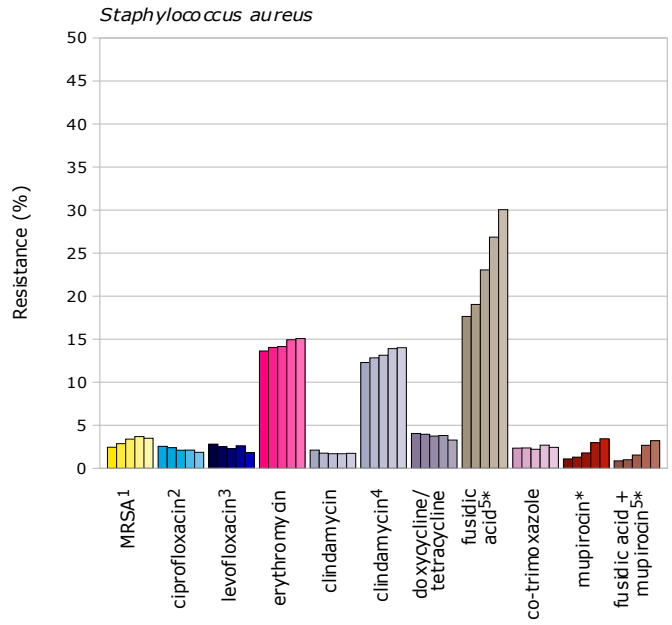
[2] Resistance to ciprofloxacin is intended to be a class indicator for resistance to fluoroquinolones.

[3] Often, susceptibility to levofloxacin is only tested when resistant to ciprofloxacin. Resistance percentages may, therefore, be biased toward a higher level. For details see section 5.1.1.1.

[4] For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

[a] According to breakpoint for topical use. For more details see section 5.1.1.1.

Figure 5.1.2.2 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic wound or pus isolates of S. aureus from selected general practitioners' patients in ISIS-AR*



* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

[1] MRSA = Methicillin resistant *S. aureus*. For the estimation method of MRSA see section 5.1.1.1.

[2] Resistance to ciprofloxacin is intended to be a class indicator for resistance to fluoroquinolones.

[3] Often, susceptibility to levofloxacin is only tested when resistant to ciprofloxacin. Resistance percentages may, therefore, be biased toward a higher level. For details see section 5.1.1.1.

[4] Including inducible resistance. For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

[5] According to breakpoint for topical use. For more details see section 5.1.1.1.

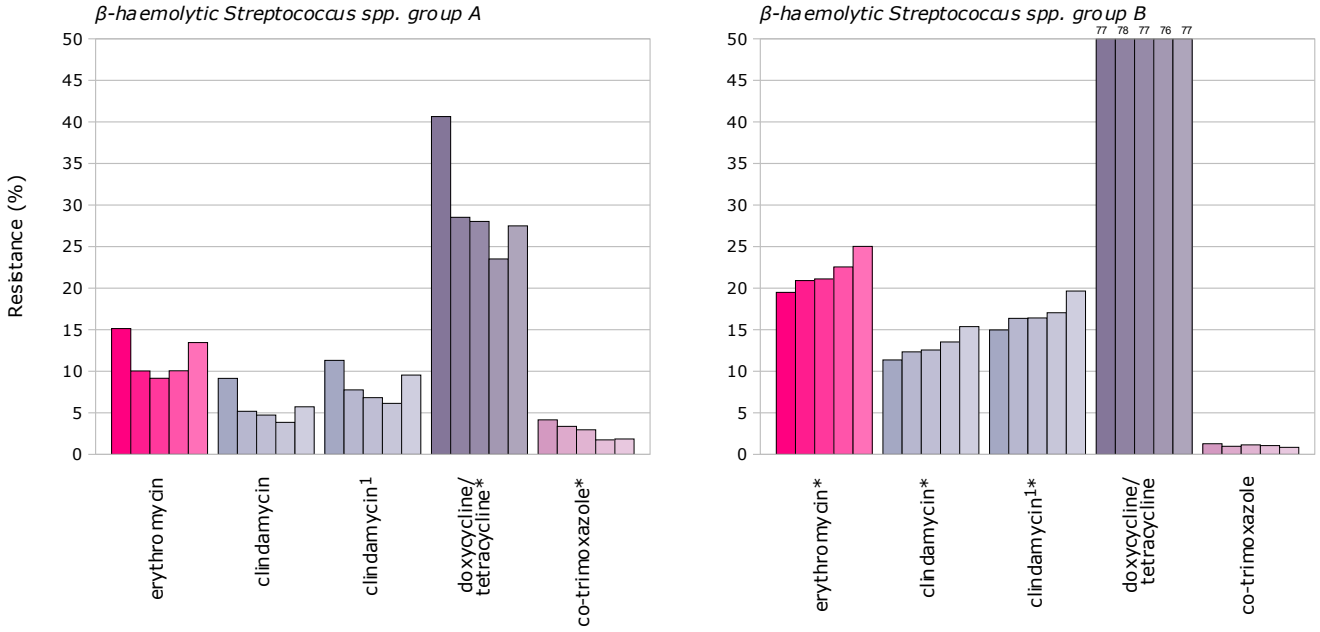
Table 5.1.2.4 *Resistance levels (%) among diagnostic wound/pus, respiratory, or genital isolates of β-haemolytic Streptococcus spp. group A and diagnostic urine or genital isolates of β-haemolytic Streptococcus spp. group B from selected general practitioners' patients, ISIS-AR 2025*

	ß-haemolytic *Streptococcus* spp. group A	**ß-haemolytic *Streptococcus* spp. group B**
Antibiotic		
erythromycin	13	25 ↑
clindamycin	6	15 ↑
clindamycin (including inducible resistance)[1]	10	20 ↑
doxycycline/tetracycline	27 ↓	77
co-trimoxazole	1.9 ↓	0.8

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

[1] For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

Figure 5.1.2.3 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic wound/pus, respiratory or genital isolates of β-haemolytic Streptococcus spp. group A and diagnostic urine or genital isolates of β-haemolytic Streptococcus spp. group B from selected general practitioners' patients in ISIS-AR*



* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

[1] Including inducible resistance. For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

Key findings
Primary care

Urine: Enterobacterales and P. aeruginosa

Uncomplicated urinary tract infections (UTI) (age >12)

- Resistance to **nitrofurantoin** and **fosfomycin** in *E. coli* remained stable and low (≤2%), consistent with 2024 and before. These agents therefore remain reliable first- and second-choice empirical options for uncomplicated UTI in adults. **Trimethoprim** resistance in *E. coli* was 21–22%, unchanged from 2024 (21%). **Co-amoxiclav** resistance levels were 8% in *E. coli* (using the breakpoint for uncomplicated UTI).

Complicated UTI (age >12)

- **Ciprofloxacin** resistance remained stable at 10% for both *E. coli* and *K. pneumoniae*, in line with the previous 5 years. Resistance to **co-amoxiclav** was 26% in *E. coli* (breakpoint for complicated UTI) and 15% in *K. pneumoniae,* essentially unchanged compared to previous years. **Co-trimoxazole** resistance was high but stable in both *E. coli* (19%) and *K. pneumoniae* (8%). Multidrug resistance to oral therapy (MDOT) remained low across all Enterobacterales (≤3%).

Wound or pus: S. aureus

- Overall resistance levels in *S. aureus* remained relatively low in 2025, with most antibiotics below 5%. **MRSA** prevalence was 3% in 2025 and stable over the past five years.
- The most notable finding was the continued significant increase in resistance to **fusidic acid**: 30% in 2025 (up from 18% in 2021) — a continuing and worrisome upward trend. Also, resistance to **mupirocin** (3% in 2025) showed an increasing trend over five years.
- Rising topical resistance remains a concern, although the figures may be somewhat inflated due to selective sampling (as cultures are usually taken after treatment failure). Despite this, the trend is considered real.

Wound/pus, respiratory or genital: β-haemolytic Streptococcus spp. groups A and B

- *Group A (Streptococcus pyogenes)*: Continuing the favourable trends observed in 2024, resistance to both **doxycycline/tetracycline** (27%) and **co-trimoxazole** (1.9%) showed a significant decreasing trend over five years.

- *Group B (Streptococcus agalactiae):* In contrast to group A, group B showed significant increasing trends for **erythromycin** (25%), **clindamycin** (15%), and **clindamycin including inducible resistance** (20%) in 2025. The percentages of resistant isolates in 2025 are notably higher than 2024 levels. Resistance to **doxycycline/tetracycline** remained very high at 77%.

5.1.3 Hospital departments

In this section, resistance levels among isolates from patients in outpatient departments (section 5.1.3.1), inpatient departments (excluding intensive care units, section 5.1.3.2), and intensive care units (section 5.1.3.3) are presented. Additionally, resistance levels are shown separately for blood isolates from patients admitted to inpatient hospital departments (including intensive care units) in section 5.1.3.4 and for urine isolates from patients in urology departments (outpatient and inpatient departments) in section 5.1.3.5.

5.1.3.1 Outpatient departments

The distribution of pathogens isolated from diagnostic samples (lower and upper respiratory tract, urine, wound or pus and other materials) from patients attending outpatient departments in 2025 is presented in table 5.1.3.1.1. The resistance levels for a selection of pathogens isolated from these patients in 2025 are presented in tables 5.1.3.1.2 (*E. coli*, *K. pneumoniae*, *P. mirabilis*, and *P. aeruginosa*), 5.1.3.1.3 (*S. aureus*) and 5.1.3.1.4 (β-haemolytic *Streptococcus* spp. group A and B). Five-year trends in resistance are shown in figures 5.1.3.1.1 (*E. coli*, *K. pneumoniae*, *P. mirabilis*, and *P. aeruginosa*), 5.1.3.1.2 (*S. aureus*), and 5.1.3.1.3 (β-haemolytic *Streptococcus* spp. group A and B).

In outpatient departments in the Netherlands, a sample is taken from the majority of patients presenting with infections and susceptibility testing is performed as part of routine diagnostics. Therefore, bias due to selective sampling will be lower than in GP patients and resistance percentages in this section are considered representative of resistance in outpatient departments.

Table 5.1.3.1.1 *Distribution of isolated pathogens in diagnostic samples from patients attending outpatient departments, ISIS-AR 2025*

	Lower respiratory tract	Upper respiratory tract	Urine	Wound or pus	Other
Pathogen	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**
E. coli	397 (3)	72 (2)	23,004 (41)	2,266 (5)	414 (12)
K. pneumoniae	229 (2)	34 (1)	5,393 (10)	499 (1)	44 (1)
P. mirabilis	115 (1)	28 (1)	2,536 (4)	1,126 (3)	41 (1)
Other Enterobacterales[1]	932 (8)	321 (7)	8,709 (15)	4,068 (10)	62 (2)
P. aeruginosa	1,528 (13)	144 (3)	2,146 (4)	3,754 (9)	39 (1)
Other non-fermenters[2]	1,816 (15)	245 (6)	711 (1)	860 (2)	1 (0)
Other Gram-negatives[3]	4,226 (35)	598 (14)	13 (0)	796 (2)	77 (2)
S. aureus	1,645 (14)	2,371 (55)	2,056 (4)	18,244 (43)	418 (12)
ß-haemolytic *Streptococcus* spp. group A	48 (0)	109 (3)	23 (0)	1,046 (2)	139 (4)
ß-haemolytic *Streptococcus* spp. group B	60 (0)	18 (0)	1,973 (3)	1,345 (3)	1,752 (51)
Other Gram-positives[4]	1,029 (9)	363 (8)	10,111 (18)	7,837 (19)	448 (13)
Anaerobes[5]	0 (0)	2 (0)	9 (0)	328 (1)	5 (0)

[1] In order of frequency*: Klebsiella* spp. *(*non-*pneumoniae), Enterobacter* spp.*, Citrobacter* spp.*, Serratia* spp.*, Morganella* spp.*, Proteus* spp. *(*non-*mirabilis), Raoultella* spp.*, Providencia* spp.*, Pantoea* spp.*, Hafnia* spp.*, Escherichia* spp. *(*non-*coli), Salmonella* spp.*, Mixta* spp.

[2] In order of frequency*: M. catarrhalis, Acinetobacter* spp.*, S. maltophilia, Pseudomonas* spp. *(*non-*aeruginosa), B. cepacia.*

[3] In order of frequency*: H. influenzae, H. parainfluenzae, N. meningitidis, H. pylori.*

[4] In order of frequency*: Enterococcus* spp.*, S. sanguinis* group not further defined*, S. dysgalactiae subsp. equisimilis, S. gordonii, S. pneumoniae, S. dysgalactiae* not further defined*, S. mitis* group not further defined*, S. australis, ß-haemolytic Streptococci* group *G* not further defined*, S. canis, S. infantis, S. oralis, S. cristatus, S. peroris, S. anginosus, S. anginosus* group not further defined*, S. dysgalactiae subsp. dysgalactiae, S. mitis/oralis* not further defined*, S. equi, ß-haemolytic Streptococci* group C not further defined*, S. mitis, S. constellatus, S. intermedius, Staphylococcus* spp. *(*non-*aureus), A. urinae, L. monocytogenes.*

[5] In order of frequency*: B. fragilis, Bacteroides fragilis* complex not further defined*, C. perfringens.*

Table 5.1.3.1.2 *Resistance levels (%) among diagnostic isolates of E. coli, K. pneumoniae, P. mirabilis, and P. aeruginosa from patients attending outpatient departments, ISIS-AR 2025*

	E. coli	*K. pneumoniae*	*P. mirabilis*	*P. aeruginosa*
Antibiotic				
amoxicillin/ampicillin	42	-	21	-
co-amoxiclav[a]	30	17	8	-
piperacillin-tazobactam	4	12	0.3	5
cefuroxime	12	14	1.7	-
cefotaxime/ceftriaxone[b]	7	10 ↑	1.3	-
ceftazidime	6	9 ↑	0.4	3
meropenem/imipenem[b]	0.0	0.2	-	-
meropenem[b]	-	-	0.0	0.9
imipenem	-	-	-	5
ciprofloxacin[b]	16	14	12	10
gentamicin	5	4	6	-
tobramycin	5	5	5	1.7
fosfomycin[1]	3	-	-	-
trimethoprim	27	21	30	-
co-trimoxazole	24	13	24	-
nitrofurantoin	3	-	-	-
Empiric therapy combinations				
cefuroxime + gentamicin	1.8	3	0.8 ↑	-
cefuroxime + ciprofloxacin[b]	6	8	0.9	-
cefotaxime/ceftriaxone + gentamicin[b]	1.6	3	0.7 ↑	-
cefotaxime/ceftriaxone + ciprofloxacin[b]	5	6 ↑	0.8 ↑	-
Multidrug resistance				
MDOT[2]	5	5	3 ↑	-

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

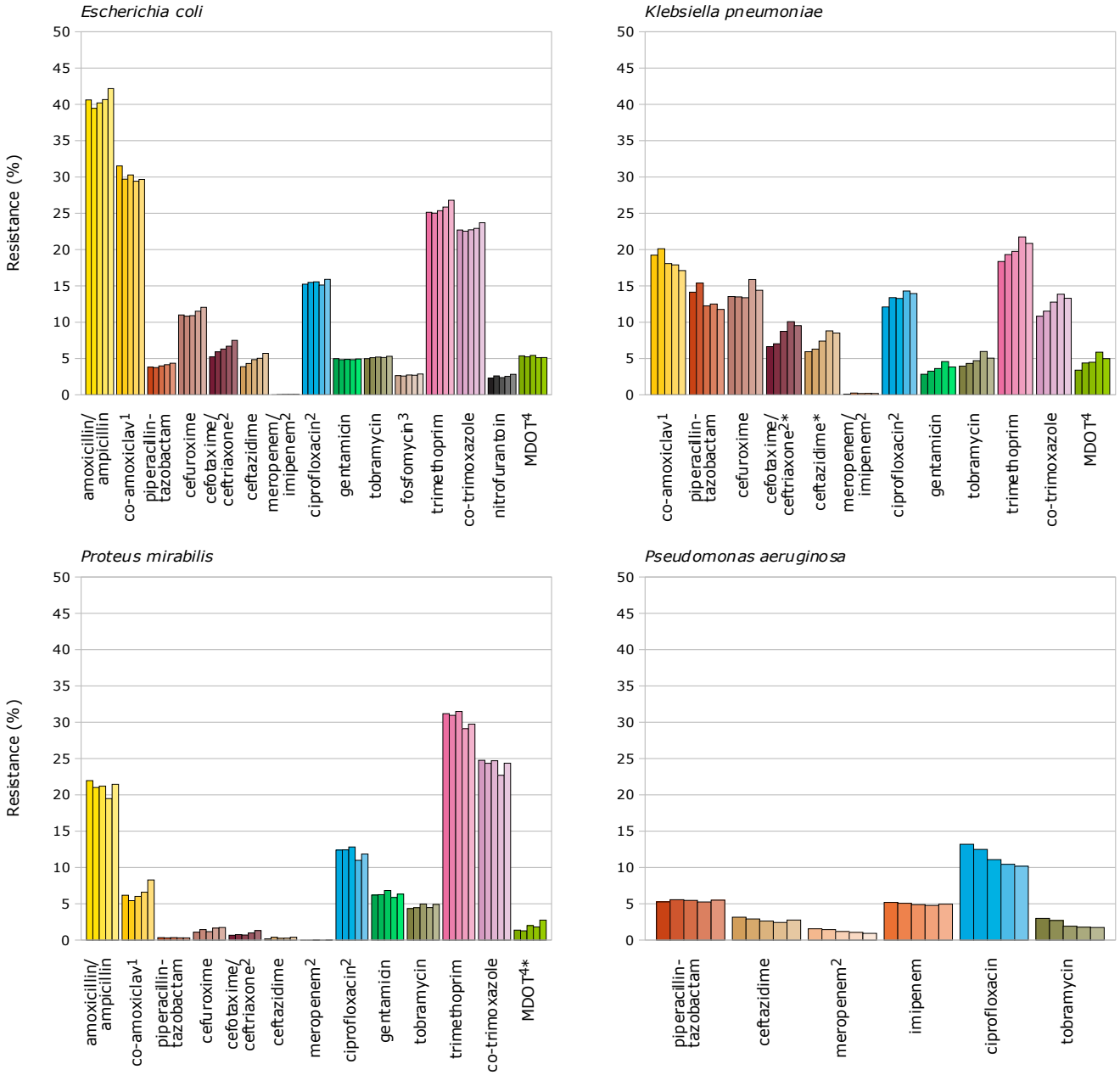
[1] Resistance percentage calculated using an MIC cut-off of 16 mg/L and a diameter cut-off of 24 mm. For more details see section 5.1.1.1.

[2] MDOT = multidrug resistance to oral therapy, defined as resistance to all of the following oral agents: co-amoxiclav (according to breakpoint for intravenous administration), ciprofloxacin (according to breakpoint for indications other than meningitis), and co-trimoxazole.

[a] According to breakpoint for intravenous administration. For more details see section 5.1.1.1.

[b] According to breakpoint for indications other than meningitis (for ciprofloxacin this only applies to *E. coli*, *K. pneumoniae*, and *P. mirabilis*). For more details see section 5.1.1.1.

Figure 5.1.3.1.1 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic isolates of E. coli, K. pneumoniae, P. mirabilis, and P. aeruginosa from patients attending outpatient departments in ISIS-AR*



* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

[1] According to breakpoint for intravenous administration. For more details see section 5.1.1.1.

[2] According to breakpoint for indications other than meningitis. For more details see section 5.1.1.1.

[3] Resistance percentage calculated using an MIC cut-off of 16 mg/L and a diameter cut-off of 24 mm. For more details see section 5.1.1.1.

[4] MDOT = multidrug resistance to oral therapy, defined as resistance to all of the following oral agents: co-amoxiclav (according to breakpoint for intravenous administration), ciprofloxacin (according to breakpoint for indications other than meningitis), and co-trimoxazole.

Table 5.1.3.1.3 *Resistance levels (%) among diagnostic isolates of S. aureus from patients attending outpatient departments, ISIS-AR 2025*

	S. aureus
Antibiotic	
MRSA[1]	3
ciprofloxacin[2]	3
levofloxacin[3]	3
gentamicin	1.3
erythromycin	20
clindamycin	3
clindamycin (including inducible resistance)[4]	19 ↑
doxycycline/tetracycline	4
fusidic acid[a]	10
linezolid	0.1
co-trimoxazole	1.9
rifampicin	0.2
mupirocin	0.9
Multidrug resistance	
fusidic acid + mupirocin[a]	0.5

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

[1] MRSA = Methicillin resistant *S. aureus*. For the estimation method of MRSA see section 5.1.1.1.; Within the *S. aureus* complex 1 out of 19 *S. argenteus* and 0 out of 0 *S. schweitzeri* were methicillin resistant.

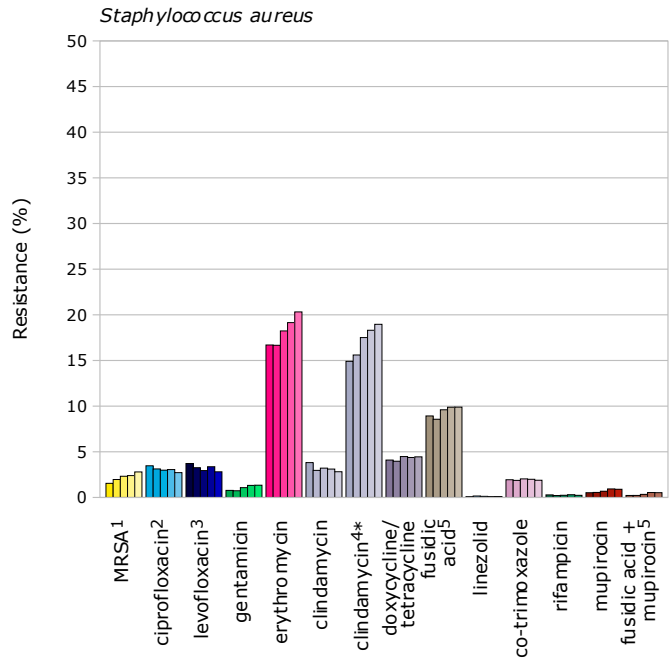
[2] Resistance to ciprofloxacin is intended to be a class indicator for resistance to fluoroquinolones.

[3] Often, susceptibility to levofloxacin is only tested when resistant to ciprofloxacin. Resistance percentages may, therefore, be biased toward a higher level. For details see section 5.1.1.1.

[4] For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

[a] According to breakpoint for topical use. For more details see section 5.1.1.1.

Figure 5.1.3.1.2 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic isolates of S. aureus from patients attending outpatient departments in ISIS-AR*



* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

[1] MRSA = Methicillin resistant *S. aureus*. For the estimation method of MRSA see section 5.1.1.1.

[2] Resistance to ciprofloxacin is intended to be a class indicator for resistance to fluoroquinolones.

[3] Often, susceptibility to levofloxacin is only tested when resistant to ciprofloxacin. Resistance percentages may, therefore, be biased toward a higher level. For details see section 5.1.1.1.

[4] Including inducible resistance. For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

[5] According to breakpoint for topical use. For more details see section 5.1.1.1.

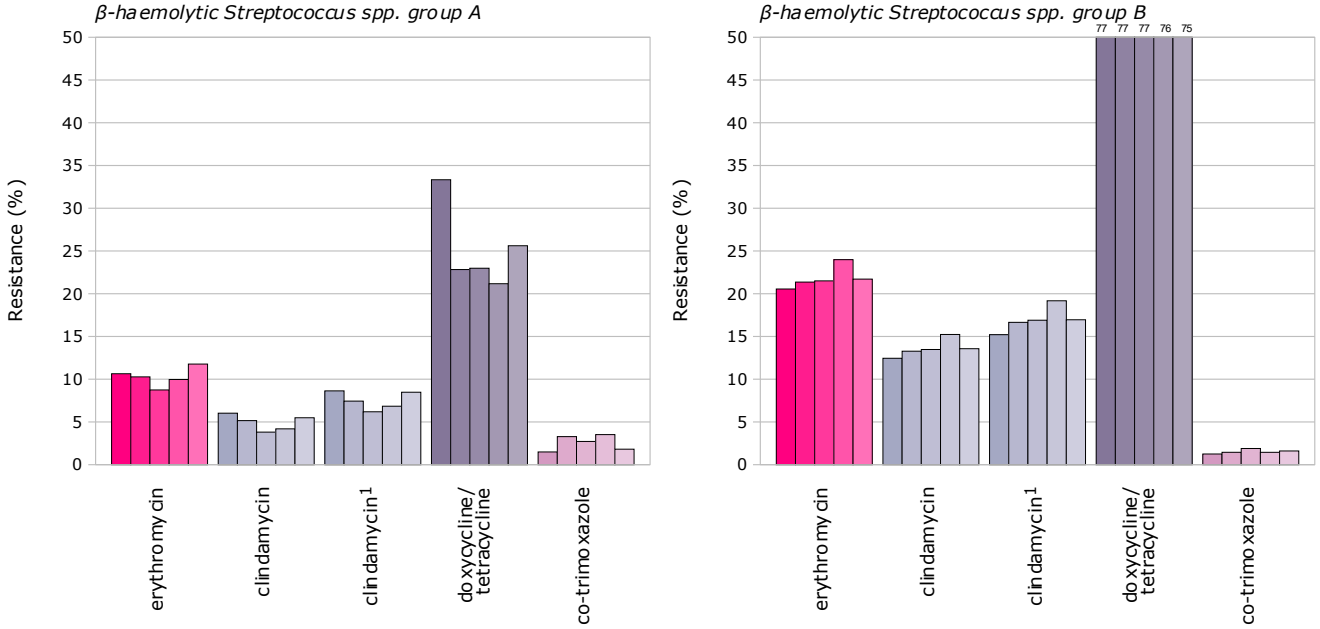
Table 5.1.3.1.4 *Resistance levels (%) among diagnostic wound/pus, respiratory, or genital isolates of ß-haemolytic Streptococcus spp. group A and diagnostic urine or genital isolates of ß-haemolytic Streptococcus spp. group B from patients attending outpatient departments, ISIS-AR 2025*

	ß-haemolytic *Streptococcus* spp. group A	**ß-haemolytic *Streptococcus* spp. group B**
Antibiotic		
erythromycin	12	22
clindamycin	5	14
clindamycin (including inducible resistance)[1]	8	17
doxycycline/tetracycline	26	75
co-trimoxazole	1.8	1.6

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

[1] For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

Figure 5.1.3.1.3 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic wound/pus, respiratory or genital isolates of β-haemolytic Streptococcus spp. group A and diagnostic urine or genital isolates of β-haemolytic Streptococcus spp. group B from patients attending outpatient departments in ISIS-AR*



Note: None of the trends were statistically significant and microbiologically relevant (for details see section 5.1.1.1).

[1] Including inducible resistance. For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

Key findings

Outpatient departments (OPD)

Urine, wound/pus and respiratory: E. coli, K. pneumoniae, and P. aeruginosa

- Resistance levels for Enterobacterales and *P. aeruginosa* in OPD patients remained higher than those in primary care patients, consistent with previous years.
- For the three main oral antibiotics used empirically in OPD practice, resistance levels were essentially unchanged over the past 5 years: **Co-amoxiclav**: 30% in *E. coli*, 17% in *K. pneumoniae*; **ciprofloxacin**: 16% in *E. coli*, 14% in *K. pneumoniae*, 10% in *P. aeruginosa*; **co-trimoxazole**: 24% in *E. coli*, 13% in *K. pneumoniae*.
- Combined resistance to all three oral agents (MDOT) was 5% in both *E. coli* and *K. pneumoniae*, indicating that in the majority of cases at least one oral treatment option remains available.
- In *K. pneumoniae*, resistance levels to **third-generation cephalosporins** in 2025 were more or less similar to those in 2024; however, resistance increased significantly over the 2020–2025 period.

Urine, wound/pus and respiratory: S. aureus

- Resistance levels in OPD *S. aureus* isolates were generally low and comparable to 2024, with a few notable exceptions:
- **MRSA**: 3% in 2025, still low but worth monitoring.
- **Clindamycin** (including inducible resistance): 19% in 2025, showing a newly significant increasing trend over the last five years.
- We also report **clindamycin** resistance without considering inducible resistance which is much lower (3%). According to EUCAST, clindamycin may still be used for short-term therapy in less severe skin and soft tissue infections if tested susceptible, even in the presence of an inducible resistance mechanism.

Wound/pus and respiratory: β-haemolytic Streptococcus spp. group A

- No significant trends — increasing or decreasing — were identified in OPD group A streptococci in 2025. Resistance levels were comparable to 2024: **clindamycin including inducible resistance** 8%, **doxycycline/tetracycline** 26%, and **co-trimoxazole** 1.8%.

Urine and genital: β-haemolytic Streptococcus spp. group B

- Similarly, no significant trends were identified for group B streptococci in the OPD setting in 2025. **Doxycycline/tetracycline** resistance remained very high at 75%, **clindamycin including inducible resistance** (17%) were also elevated, with the same clinical implication as in primary care: these levels complicate empirical treatment in patients with beta-lactam allergy.

5.1.3.2 Inpatient hospital departments (excl. ICU)

The distribution of pathogens from diagnostic samples (blood, cerebrospinal fluid, lower respiratory tract, urine, wound or pus and other materials) from patients admitted to inpatient hospital departments (excl. ICU) in 2025 is presented in table 5.1.3.2.1. The resistance levels for a selection of pathogens isolated from these patients in 2025 are presented in tables 5.1.3.2.2 (*E. coli*, *K. pneumoniae*, *P. mirabilis*, *E. cloacae* complex, *P. aeruginosa*, and *A. baumannii/calcoaceticus* complex), 5.1.3.2.3 (*E. faecalis* and *E. faecium*), 5.1.3.2.4 (*S. aureus*), 5.1.3.2.5 (β-haemolytic *Streptococcus* spp. groups A, B, C and G, *S. anginosus* group, and *S. mitis* group), and 5.1.3.2.6 (*B. fragilis* complex and *C. perfringens*). Five-year trends in resistance are shown in figures 5.1.3.2.1 (*E. coli*, *K. pneumoniae*, *P. mirabilis*, *E. cloacae* complex, *P. aeruginosa*, and *A. baumannii/calcoaceticus* complex) 5.1.3.2.2 (*E. faecalis* and *E. faecium*), 5.1.3.2.3 (*S. aureus*), 5.1.3.2.4 (β-haemolytic *Streptococcus* spp. groups A, B, C and G, *S. anginosus* group and *S. mitis* group), and 5.1.3.2.5 (*B. fragilis* complex and *C. perfringens*).

In inpatient hospital departments in the Netherlands, a sample is taken from the majority of patients presenting with infections and susceptibility testing is performed as part of routine diagnostics. Therefore, bias due to selective sampling of patients is expected to be limited.

Table 5.1.3.2.1 *Distribution of isolated pathogens in diagnostic samples from patients admitted to inpatient departments (excl. intensive care units), ISIS-AR 2025*

	Blood	Cerebro-spinal fluid	Lower respiratory tract	Urine	Wound or pus	Other
Pathogen	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**
E. coli	6,034 (21)	8 (2)	961 (6)	24,718 (43)	3,979 (10)	20 (41)
K. pneumoniae	1,190 (4)	7 (1)	543 (3)	5,044 (9)	953 (2)	1 (2)
P. mirabilis	408 (1)	2 (0)	168 (1)	3,248 (6)	832 (2)	1 (2)
E. cloacae complex	439 (2)	6 (1)	444 (3)	1,529 (3)	1,511 (4)	0 (0)
Other Enterobacterales[1]	1,705 (6)	12 (2)	1,790 (11)	6,281 (11)	3,517 (9)	0 (0)
P. aeruginosa	616 (2)	2 (0)	1,661 (10)	2,807 (5)	2,189 (5)	0 (0)
A. baumannii-calcoaceticus complex	50 (0)	9 (2)	80 (1)	158 (0)	204 (1)	0 (0)
Other non-fermenters[2]	327 (1)	8 (2)	1,938 (12)	347 (1)	598 (1)	0 (0)
Other Gram-negatives[3]	318 (1)	28 (6)	4,254 (27)	7 (0)	288 (1)	0 (0)
E. faecalis	987 (3)	10 (2)	24 (0)	5,410 (9)	2,230 (6)	0 (0)
E. faecium	746 (3)	8 (2)	27 (0)	1,679 (3)	1,506 (4)	0 (0)
S. aureus	3,222 (11)	45 (9)	2,410 (15)	1,717 (3)	10,689 (27)	3 (6)
ß-haemolytic *Streptococcus* spp. group A	292 (1)	2 (0)	57 (0)	71 (0)	701 (2)	0 (0)
ß-haemolytic *Streptococcus* spp. group B	438 (2)	8 (2)	127 (1)	1,421 (2)	844 (2)	22 (45)
ß-haemolytic *Streptococcus* spp. groups C and G	864 (3)	1 (0)	55 (0)	197 (0)	1,442 (4)	1 (2)
S. anginosus group	564 (2)	6 (1)	38 (0)	97 (0)	2,288 (6)	1 (2)
S. mitis group	873 (3)	15 (3)	12 (0)	48 (0)	469 (1)	0 (0)
Other Gram-positives[4]	9,004 (32)	304 (63)	1,370 (9)	2,934 (5)	4,971 (12)	0 (0)
B. fragilis complex	355 (1)	0 (0)	2 (0)	8 (0)	621 (2)	0 (0)
C. perfringens	104 (0)	0 (0)	0 (0)	2 (0)	142 (0)	0 (0)

[1] In order of frequency: *Klebsiella* spp. (non-*pneumoniae*), *Citrobacter* spp., *Serratia* spp., *Morganella* spp., *Proteus* spp. (non-*mirabilis*), *Raoultella* spp., *Providencia* spp., *Salmonella* spp., *Hafnia* spp., *Pantoea* spp., *Enterobacter* spp. (non-*cloacae* complex), *Escherichia* spp. (non-*coli*), *Mixta* spp., *Cronobacter* spp., *Yersinia* spp., *Shigella* spp.

[2] In order of frequency: *M. catarrhalis*, *S. maltophilia*, *Acinetobacter* spp., *Pseudomonas* spp. (non-*aeruginosa*), *B. cepacia*.

[3] In order of frequency: *H. parainfluenzae*, *H. influenzae*, *N. meningitidis*, *C. coli*, *C. lari*, *C. jejuni*, *H. pylori*.

[4] In order of frequency: *Staphylococcus* spp. (non-*aureus*), *S. pneumoniae*, *A. urinae*, *Enterococcus* spp. (non-*faecalis*, non-*faecium*), *L. monocytogenes*.

Table 5.1.3.2.2 *Resistance levels (%) among diagnostic isolates of E. coli, K. pneumoniae, P. mirabilis, E. cloacae complex, P. aeruginosa, and A. baumannii/calcoaceticus complex from patients admitted to inpatient departments (excl. intensive care units), ISIS-AR 2025*

	E. coli	*K. pneumoniae*	*P. mirabilis*	*E. cloacae* complex	*P. aeruginosa*	*A. baumannii / calcoaceticus* complex
Antibiotic						
amoxicillin/ampicillin	41	-	20	-	-	-
co-amoxiclav[a]	29	17	8	-	-	-
piperacillin-tazobactam	4	13	0.3	-	6	-
cefuroxime	12	15	1.8	-	-	-
cefotaxime/ceftriaxone[b]	7	10 ↑	1.3	-	-	-
ceftazidime	6	9 ↑	0.4	-	4	-
meropenem/imipenem[b]	0.0	0.5	-	0.3	-	3
meropenem[b]	-	-	0.0	-	1.0	-
imipenem	-	-	-	-	5	-
ciprofloxacin[b]	13	13	10	3	9	7
gentamicin	5	4	6	2	-	5
tobramycin	5	5	4	3	1.5	4 ↑
fosfomycin[1]	3	-	-	-	-	-
trimethoprim	25	19	27	8	-	-
co-trimoxazole	22	12 ↑	22	7	-	4
nitrofurantoin	2	-	-	-	-	-
Empiric therapy combinations						
cefuroxime + gentamicin	1.7	3	0.8	-	-	-
cefuroxime + ciprofloxacin[b]	6	8	0.9	-	-	-
cefotaxime/ceftriaxone + gentamicin[b]	1.5	3	0.7	-	-	-
cefotaxime/ceftriaxone + ciprofloxacin[b]	5	6 ↑	0.8	-	-	-
ceftazidime + tobramycin	-	-	-	-	0.6	-
Multidrug resistance						
MDOT[2]	4	5	2	-	-	-

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

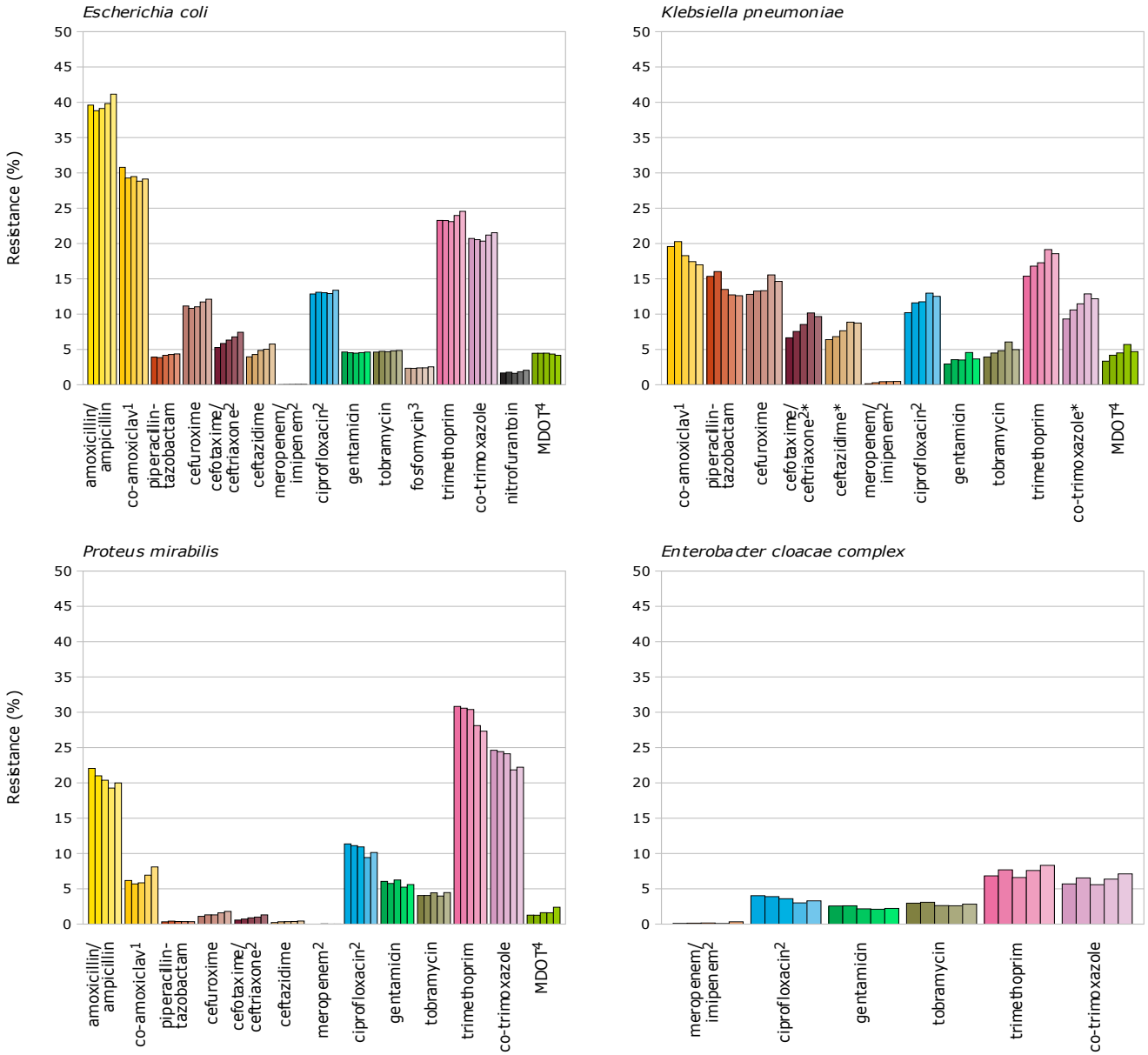
[1] Resistance percentage calculated using an MIC cut-off of 16 mg/L and a diameter cut-off of 24 mm. For more details see section 5.1.1.1.

[2] MDOT = multidrug resistance to oral therapy, defined as resistance to all of the following oral agents: co-amoxiclav (according to breakpoint for intravenous administration), ciprofloxacin (according to breakpoint for indications other than meningitis), and co-trimoxazole.

[a] According to breakpoint for intravenous administration. For more details see section 5.1.1.1.

[b] According to breakpoint for indications other than meningitis (for ciprofloxacin this only applies to *E. coli*, *K. pneumoniae*, *P. mirabilis*, and *E. cloacae* complex). For more details see section 5.1.1.1.

Figure 5.1.3.2.1 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic isolates of E. coli, K. pneumoniae, P. mirabilis, E. cloacae complex, P. aeruginosa, and A. baumannii/calcoaceticus complex from patients admitted to inpatient departments (excl. intensive care units) in ISIS-AR*



* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

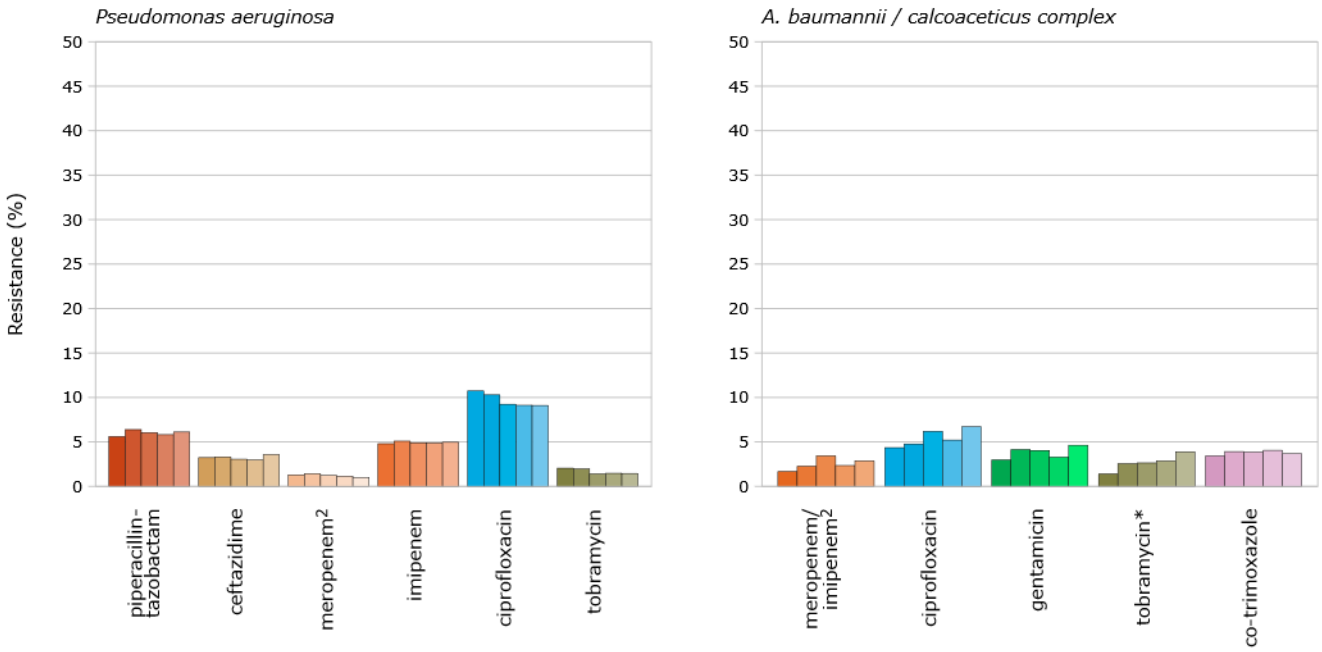
[1] According to breakpoint for intravenous administration. For more details see section 5.1.1.1.

[2] According to breakpoint for indications other than meningitis. For more details see section 5.1.1.1.

[3] Resistance percentage calculated using an MIC cut-off of 16 mg/L and a diameter cut-off of 24 mm. For more details see section 5.1.1.1.

[4] MDOT = multidrug resistance to oral therapy, defined as resistance to all of the following oral agents: co-amoxiclav (according to breakpoint for intravenous administration), ciprofloxacin (according to breakpoint for indications other than meningitis), and co-trimoxazole.

Figure 5.1.3.2.1 (continued) *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic isolates of E. coli, K. pneumoniae, P. mirabilis, E. cloacae complex, P. aeruginosa, and A. baumannii/calcoaceticus complex from patients admitted to inpatient departments (excl. intensive care units) in ISIS-AR*



* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

[1] According to breakpoint for intravenous administration. For more details see section 5.1.1.1.

[2] According to breakpoint for indications other than meningitis. For more details see section 5.1.1.1.

[3] Resistance percentage calculated using an MIC cut-off of 16 mg/L and a diameter cut-off of 24 mm. For more details see section 5.1.1.1.

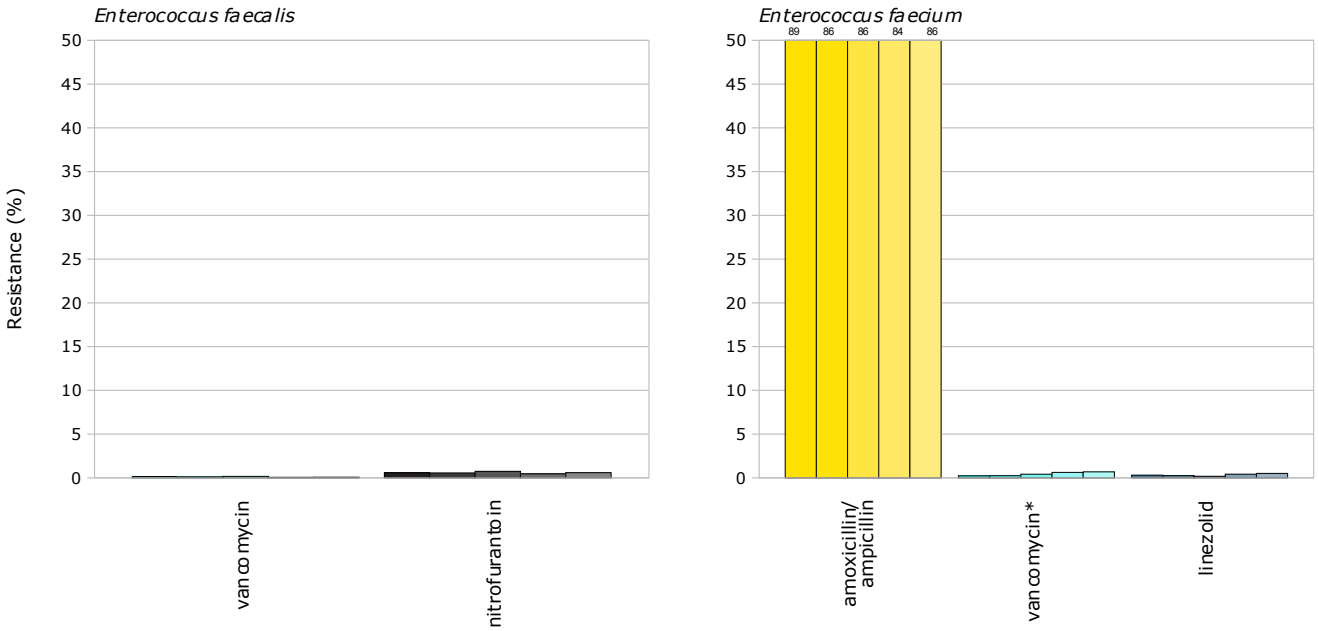
[4] MDOT = multidrug resistance to oral therapy, defined as resistance to all of the following oral agents: co-amoxiclav (according to breakpoint for intravenous administration), ciprofloxacin (according to breakpoint for indications other than meningitis), and co-trimoxazole.

Table 5.1.3.2.3 *Resistance levels (%) among diagnostic isolates of E. faecalis and E. faecium from patients admitted to inpatient departments (excl. intensive care units), ISIS-AR 2025*

	E. faecalis	***E. faecium***
Antibiotic		
amoxicillin/ampicillin	-	86
vancomycin	0.1	0.7 ↑
linezolid	-	0.5
nitrofurantoin	0.6	-

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

Figure 5.1.3.2.2 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic isolates of E. faecalis and E. faecium from patients admitted to inpatient departments (excl. intensive care units) in ISIS-AR*



* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

Table 5.1.3.2.4 *Resistance levels (%) among diagnostic isolates of S. aureus from patients admitted to inpatient departments (excl. intensive care units), ISIS-AR 2025*

	S. aureus
Antibiotic	
MRSA[1]	3
ciprofloxacin[2]	3
levofloxacin[3]	3
gentamicin	1.3
Erythromycin	20
clindamycin	3
clindamycin (including inducible resistance)[4]	18 ↑
doxycycline/tetracycline	4
fusidic acid[a]	9
linezolid	0.1
co-trimoxazole	1.8
rifampicin	0.3
mupirocin	0.8
Multidrug resistance	
fusidic acid + mupirocin[a]	0.4

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

[1] MRSA = Methicillin resistant *S. aureus*. For the estimation method of MRSA see section 5.1.1.1.; Within the *S. aureus* complex 3 out of 31 *S. argenteus* and 0 out of 0 *S. schweitzeri* were methicillin resistant.

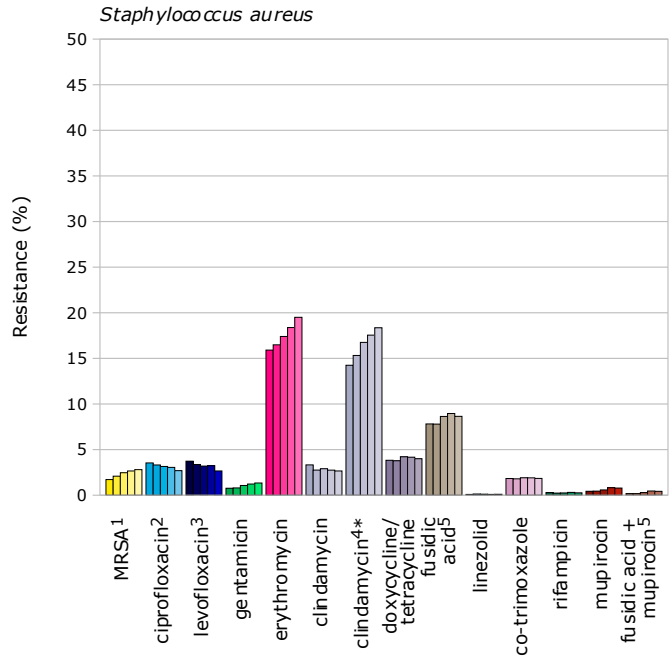
[2] Resistance to ciprofloxacin is intended to be a class indicator for resistance to fluoroquinolones.

[3] Often, susceptibility to levofloxacin is only tested when resistant to ciprofloxacin. Resistance percentages may, therefore, be biased toward a higher level. For details see section 5.1.1.1.

[4] For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

[a] According to breakpoint for topical use. For more details see section 5.1.1.1.

Figure 5.1.3.2.3 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic isolates of S. aureus from patients admitted to inpatient departments (excl. intensive care units) in ISIS-AR*



* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

[1] MRSA = Methicillin resistant *S. aureus*. For the estimation method of MRSA see section 5.1.1.1.

[2] Resistance to ciprofloxacin is intended to be a class indicator for resistance to fluoroquinolones.

[3] Often, susceptibility to levofloxacin is only tested when resistant to ciprofloxacin. Resistance percentages may, therefore, be biased toward a higher level. For details see section 5.1.1.1.

[4] Including inducible resistance. For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

[5] According to breakpoint for topical use. For more details see section 5.1.1.1.

Table 5.1.3.2.5 *Resistance levels (%) among diagnostic isolates of β-haemolytic Streptococcus spp. groups A, B, C and G, S. anginosus group, and S. mitis group from patients admitted to inpatient departments (excl. intensive care units), ISIS-AR 2025*

	ß-haemolytic *Streptococcus* spp. group A	**ß-haemolytic *Streptococcus* spp. group B**	**ß-haemolytic *Streptococcus* spp. groups C and G**	***S. anginosus* group**	***S. mitis* group**
Antibiotic					
(benzyl)penicillin[a]	-	-	-	0.2	5
amoxicillin/ampicillin[1,a]	-	-	-	0.1	3
erythromycin	14 ↑	23	15	-	-
clindamycin	6	14	6	8	7
clindamycin (including inducible resistance)[2]	10	18	12	9	8
doxycycline/tetracycline	34	74	28	-	-
co-trimoxazole	2	1.1	0.4	-	-

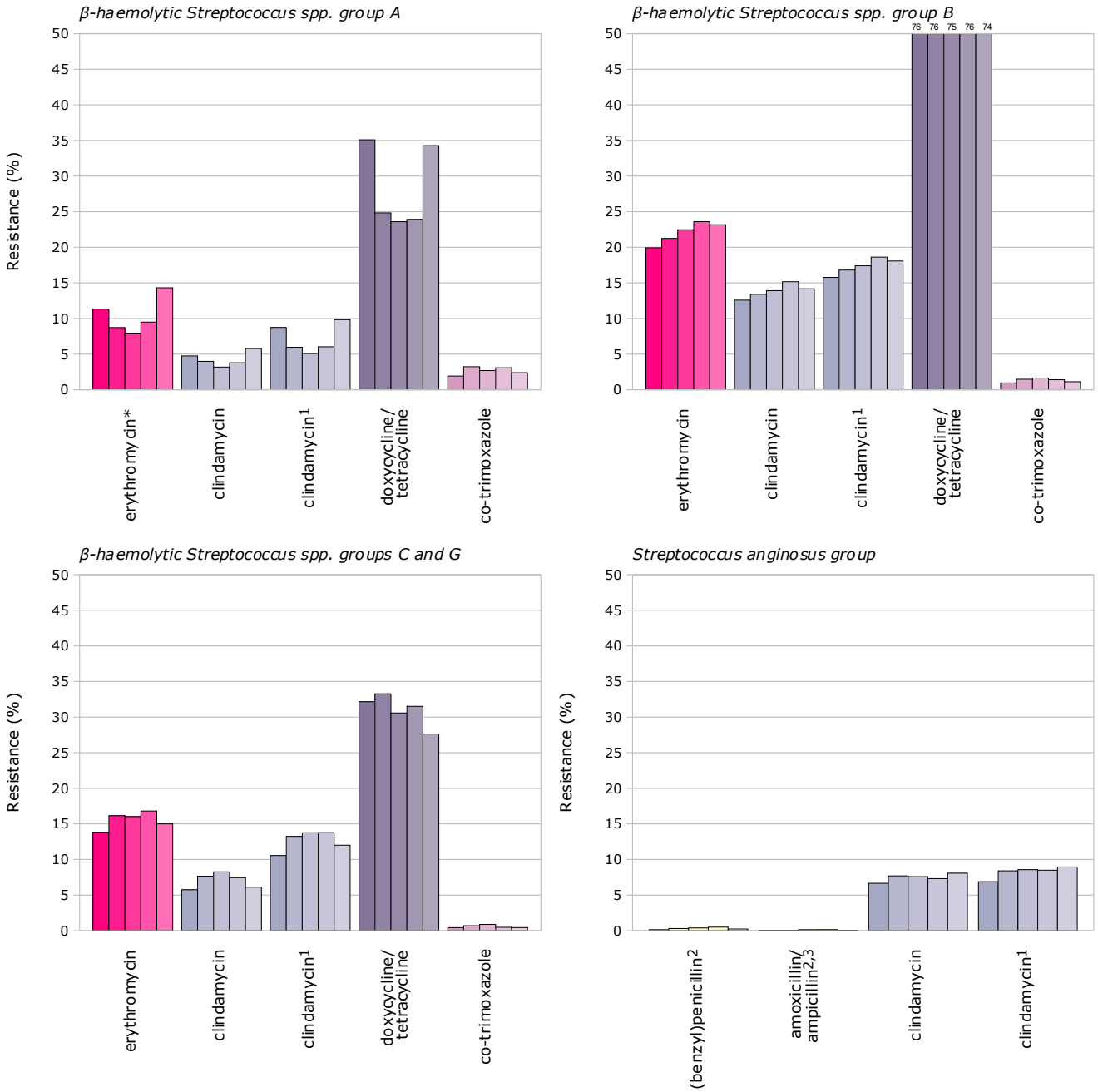
10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

[1] Resistance to amoxicillin/ampicillin in *S. anginosus* group and *S. mitis* group was calculated based on (benzyl)penicillin and amoxicillin/ampicillin according to directions in the EUCAST guidelines. For details see section 5.1.1.1.

[2] For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

[a] According to breakpoint for other indications than endocarditis. For more details see section 5.1.1.1.

Figure 5.1.3.2.4 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic isolates of β-haemolytic Streptococcus spp. groups A, B, C and G, S. anginosus group and S. mitis group from patients admitted to inpatient departments (excl. intensive care units) in ISIS-AR*



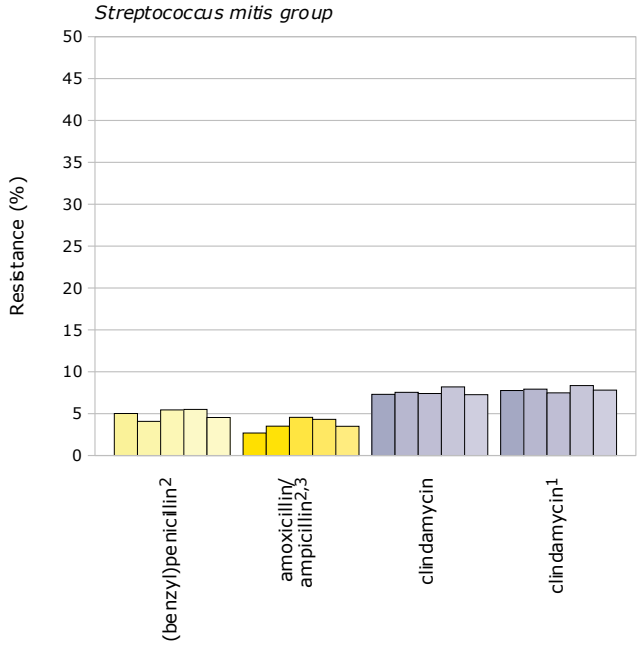
* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

[1] Including inducible resistance. For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

[2] According to breakpoint for other indications than endocarditis. For more details see section 5.1.1.1.

[3] Resistance to amoxicillin/ampicillin in *S. anginosus* group and *S. mitis* group was calculated based on (benzyl)penicillin and amoxicillin/ampicillin according to directions in the EUCAST guidelines. For details see section 5.1.1.1.

Figure 5.1.3.2.4 (continued) *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic isolates of β-haemolytic Streptococcus spp. groups A, B, C and G, S. anginosus group and S. mitis group from patients admitted to inpatient departments (excl. intensive care units) in ISIS-AR*



* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

[1] Including inducible resistance. For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

[2] According to breakpoint for other indications than endocarditis. For more details see section 5.1.1.1.

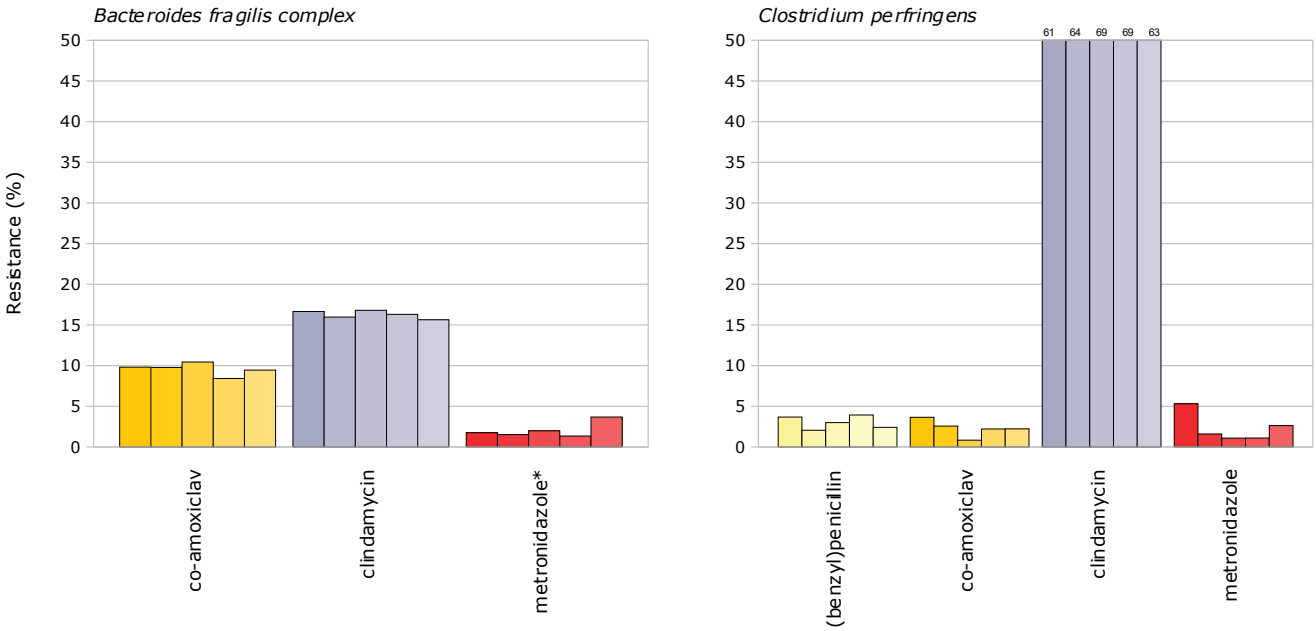
[3] Resistance to amoxicillin/ampicillin in *S. anginosus* group and *S. mitis* group was calculated based on (benzyl)penicillin and amoxicillin/ampicillin according to directions in the EUCAST guidelines. For details see section 5.1.1.1.

Table 5.1.3.2.6 *Resistance levels (%) among diagnostic isolates of B. fragilis complex and C. perfringens from patients admitted to inpatient departments (excl. intensive care units), ISIS-AR 2025*

	***B. fragilis* complex**	***C. perfringens***
Antibiotic		
(benzyl)penicillin	-	2
co-amoxiclav	9	2
clindamycin	16	63
metronidazole	4 ↑	3

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

Figure 5.1.3.2.5 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic isolates of B. fragilis complex and C. perfringens from patients admitted to inpatient departments (excl. intensive care units) in ISIS-AR*



* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

Key findings

Inpatient hospital departments (excl. ICU)

Blood, urine, wound/pus and respiratory: E. coli, K. pneumoniae, P. aeruginosa, and Acinetobacter baumannii/calcoaceticus complex

- For *E. coli*, resistance levels in 2025 were largely stable compared to 2024: **cefuroxime** resistance was 12% and **cefotaxime/ceftriaxone** 7%.
- For *K. pneumoniae*, the prevalence of resistance to **third-generation cephalosporins** (10%) was more or less similar as in 2024. However, a significant increase was observed over the past five years. Resistance to **cefuroxime** was 15%. This means that patients that are infected with *K. pneumoniae* have a considerable risk of non-adequate empiric treatment with a **second or (to a lesser extent) third generation cephalosporin**. In case of severe infection, empiric combination therapy with aminoglycosides, reduced likelihood of resistance to 3%. **Meropenem/imipenem** resistance rose to 0.5% in 2025, continuing its gradual upward trajectory, though absolute levels remain low.
- For *P. aeruginosa*, resistance was relatively low and stable for all antibiotics over the last five years. Empirical treatment with **ceftazidime** when infections are potentially caused by *P. aeruginosa* remains therefore adequate.
- For *A. baumannii/calcoaceticus* complex, **tobramycin** resistance (4%) showed a new significant increasing trend in 2025, where previously increasing trends in this pathogen had been flagged for **meropenem/imipenem**, **ciprofloxacin**, and **tobramycin** collectively in 2024 compared to the previous 5 years. **Meropenem/imipenem** resistance was 3% and **ciprofloxacin** 7%, consistent with levels in the previous 5 years.

Blood, urine, wound/pus and respiratory: Enterococci

- **Vancomycin** resistance in *E. faecium* was 0.7% and now shows a newly significant increasing trend in 2025.

Blood, urine, wound/pus and respiratory: S. aureus

- Most resistance levels in inpatient *S. aureus* were stable and very similar to OPD findings but **clindamycin (including inducible resistance)**, as in OPD setting, showed a significant increasing trend in 2025 (18%). This indicates that culture and susceptibility testing are advised before starting treatment with this drug. We also analysed **clindamycin resistance without considering inducible resistance** (3%). According to EUCAST, clindamycin may still be used for short-term therapy in less severe skin and soft tissue infections if tested susceptible, even in the presence of an inducible resistance mechanism.
- Resistance to **levofloxacin, doxycycline**, and **co-trimoxazole** was 4% or less.
- **MRSA** was found in 3% of *S. aureus* isolates of hospitalised patients which remained stable over the previous 5 years.

Blood, urine, blood, wound/pus, and respiratory: β-haemolytic Streptococcus spp. groups A, B and C/G

- *Group A:* **Erythromycin** resistance rose to 14% and now shows a significant increasing trend — a new finding not flagged in 2024. **Clindamycin including inducible resistance** was 10% (stable). **Doxycycline/tetracycline** resistance increased to 34% though no significant trend was indicated.
- *Group B:* **Doxycycline/tetracycline** resistance remained very high at 74%. **Clindamycin including inducible resistance** was 18%. **Erythromycin** was stable at 23%.
- *Groups C and G:* **Clindamycin including inducible resistance** was 12%, **doxycycline/tetracycline** 28%, **erythromycin** 15%, all stable.

Blood, urine, blood, wound/pus, and respiratory: Anaerobes

- The previously stable picture for *B. fragilis* complex was disrupted in 2025: **metronidazole** resistance increased to 4% and now shows a significant increasing trend. This is a clinically important finding given that **metronidazole** is a cornerstone of anaerobic treatment. **Clindamycin** resistance in *B. fragilis* complex remained high at 16%. **Co-amoxiclav** resistance was stable at 9%.
- For *C. perfringens*, **clindamycin** resistance (63%) remained very high and stable. **Co-amoxiclav** resistance was 2% and **metronidazole** 3% with no trend flags.

5.1.3.3 Intensive Care Units

The distribution of pathogens from diagnostic samples (blood, cerebrospinal fluid, lower respiratory tract, urine, and wound or pus) from patients admitted to intensive care units in 2025 is presented in table 5.1.3.3.1. The resistance levels for a selection of pathogens isolated from these patients in 2025 are presented in tables 5.1.3.3.2 (*E. coli*, *K. pneumoniae*, *P. mirabilis*, *E. cloacae* complex and *P. aeruginosa*), 5.1.3.3.3 (*E. faecalis* and *E. faecium*), 5.1.3.3.4 (*S. aureus*) and 5.1.3.3.5 (β-haemolytic *Streptococcus* spp. group B and *S. anginosus* group). Five-year trends in resistance are shown in figures 5.1.3.3.1 (*E. coli*, *K. pneumoniae*, *P. mirabilis*, *E. cloacae* complex and *P. aeruginosa*), 5.1.3.3.2 (*E. faecalis* and *E. faecium)*, 5.1.3.3.3 (*S. aureus*) and 5.1.3.3.4 (β-haemolytic *Streptococcus* spp. group B and *S. anginosus* group). For *Acinetobacter calcoaceticus/baumannii* complex, β-haemolytic *Streptococcus* spp. groups A, C and G*, S. mitis* group, *B. fragilis* complex, and *C. perfringens*, resistance levels and trends were not calculated because data were available for less than 100 isolates each year. For β-haemolytic *Streptococcus* spp. group B, only 2025 data were used for the same reason (Figure 5.1.3.3.4).

In intensive care units in the Netherlands, diagnostic (infection related) samples are taken from almost all patients presenting with infections and susceptibility testing is performed as part of routine diagnostics. Bias due to selective sampling of patients is therefore expected to be very low.

Table 5.1.3.3.1 *Distribution of isolated pathogens in diagnostic samples from patients admitted to intensive care units, ISIS-AR 2025*

	Blood	Cerebro-spinal fluid	Lower respiratory tract	Urine	Wound or pus
Pathogen	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**
E. coli	191 (7)	3 (3)	337 (9)	516 (38)	353 (13)
K. pneumoniae	43 (2)	1 (1)	169 (4)	125 (9)	93 (3)
P. mirabilis	11 (0)	0 (0)	36 (1)	53 (4)	39 (1)
E. cloacae complex	31 (1)	0 (0)	153 (4)	41 (3)	105 (4)
Other Enterobacterales[1]	93 (3)	1 (1)	659 (17)	150 (11)	249 (9)
P. aeruginosa	44 (2)	1 (1)	280 (7)	81 (6)	166 (6)
Other non-fermenters[2]	26 (1)	5 (4)	435 (11)	10 (1)	68 (2)
Other Gram-negatives[3]	16 (1)	1 (1)	373 (10)	0 (0)	13 (0)
E. faecalis	106 (4)	2 (2)	13 (0)	151 (11)	237 (9)
E. faecium	262 (10)	2 (2)	19 (0)	112 (8)	315 (11)
S. aureus	290 (11)	6 (5)	976 (26)	49 (4)	364 (13)
ß-haemolytic *Streptococcus* spp. group B	16 (1)	3 (3)	59 (2)	23 (2)	27 (1)
S. anginosus group	19 (1)	3 (3)	15 (0)	1 (0)	165 (6)
Other Gram-positives[4]	1,568 (57)	89 (76)	276 (7)	56 (4)	502 (18)
Anaerobes[5]	28 (1)	0 (0)	2 (0)	1 (0)	56 (2)

[1] In order of frequency: *Klebsiella* spp. (non-*pneumoniae*), *Serratia* spp., *Citrobacter* spp., *Morganella* spp., *Proteus* spp. (non-*mirabilis*), *Hafnia* spp., *Raoultella* spp., *Providencia* spp., *Enterobacter* spp. (non-*cloacae* complex), *Pantoea* spp., *Salmonella* spp., *Cronobacter* spp., *Escherichia* spp. (non-*coli*).

[2] In order of frequency: *S. maltophilia*, *M. catarrhalis*, *Acinetobacter* spp., *Pseudomonas* spp. (non-*aeruginosa*), *B. cepacia*.

[3] In order of frequency: *H. parainfluenzae*, *H. influenzae*, *N. meningitidis*, *C. jejuni*.

[4] In order of frequency: *Staphylococcus* spp. (non-*aureus*), *S. oralis*, *S. dysgalactiae* not further defined, *S. pyogenes*, *ß-haemolytic Streptococcus* spp. group G not further defined, *S. infantis*, *S. mitis*, *S. cristatus*, *S. pneumoniae*, *S. dysgalactiae* subsp. *dysgalactiae*, *S. mitis* group not further defined, *ß-haemolytic Streptococcus* spp. group A not further defined, *S. gordonii*, *ß-haemolytic Streptococcus* spp. group C not further defined, *S. sanguinis* group not further defined, *S. dysgalactiae* subsp. *equisimilis*, *S. mitis/oralis* not further defined, *Enterococcus* spp. (non-*faecalis*, non-*faecium*), *A. urinae*, *L. monocytogenes*.

[5] In order of frequency: *B. fragilis*, *Bacteroides fragilis* complex not further defined, *C. perfringens*.

Table 5.1.3.3.2 *Resistance levels (%) among diagnostic isolates of E. coli, K. pneumoniae, P. mirabilis, E. cloacae complex and P. aeruginosa from patients admitted to intensive care units, ISIS-AR 2025*

	E. coli	*K. pneumoniae*	*P. mirabilis*	*E. cloacae* complex	*P. aeruginosa*
Antibiotic					
amoxicillin/ampicillin	46	-	26	-	-
co-amoxiclav[a]	33	24	11	-	-
piperacillin-tazobactam	6	17	0.7	-	11 ↓
cefuroxime	19	23	3	-	-
cefotaxime/ceftriaxone[b]	13	17	4 ↑	-	-
ceftazidime	10	15	1.5	-	10
meropenem/imipenem[b]	0.1	3 ↑	-	0.6	-
meropenem[b]	-	-	0.0	-	1.9
imipenem	-	-	-	-	6
ciprofloxacin[b]	15	12	11	3 ↓	9
gentamicin	6	4	8	3 ↓	-
tobramycin	6	9	7	3 ↓	1.4 ↓
co-trimoxazole	23	15	18 ↓	7 ↓	-
Empiric therapy combinations					
cefuroxime + gentamicin	3	4	1.8	-	-
cefuroxime + ciprofloxacin[b]	9	10	3	-	-
cefotaxime/ceftriaxone + gentamicin[b]	3	4	3	-	-
cefotaxime/ceftriaxone + ciprofloxacin[b]	8 ↑	10	4	-	-
ceftazidime + tobramycin	-	-	-	-	0.7
Multidrug resistance					
MDOT[1]	5	6	4	-	-

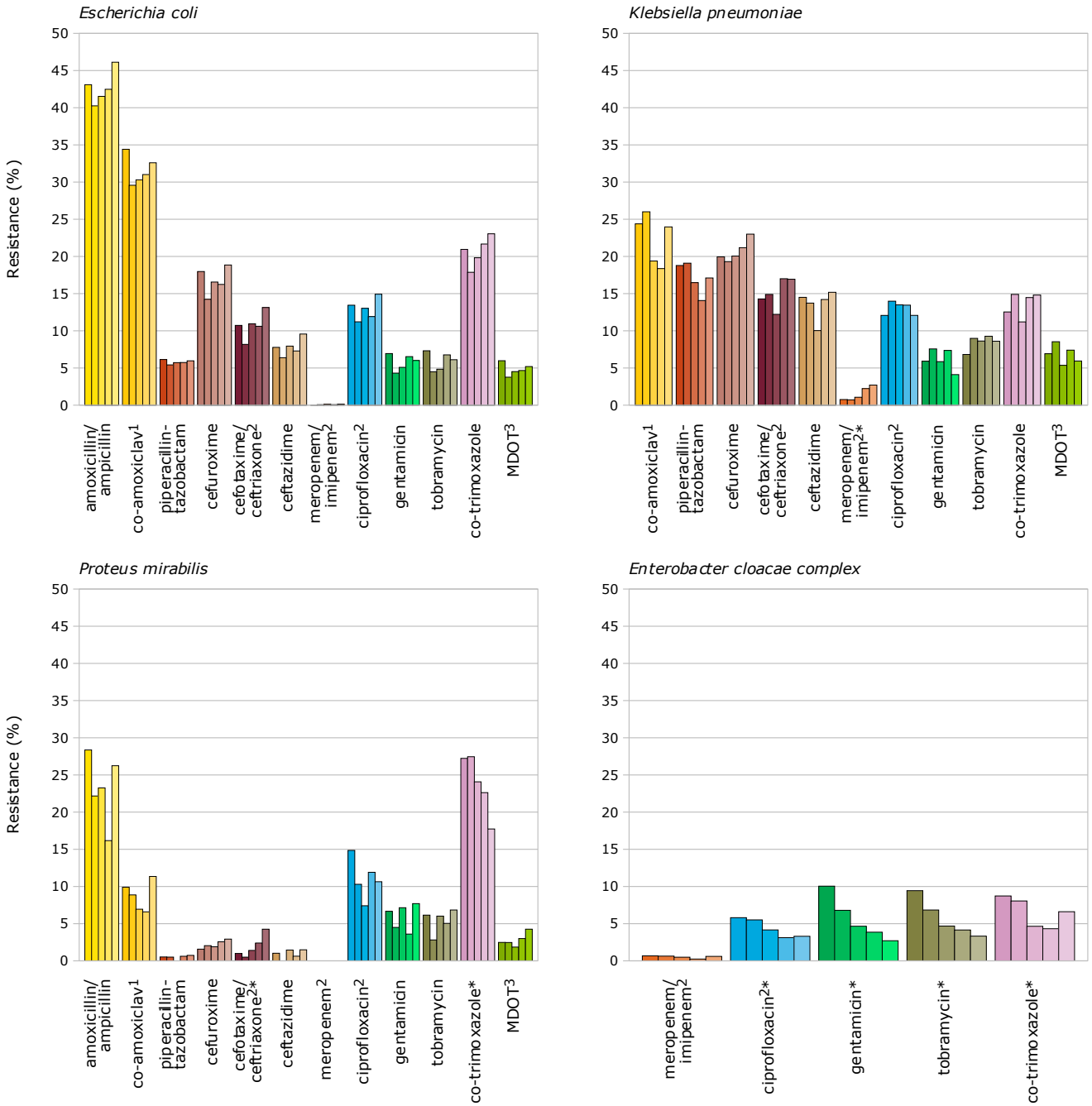
10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

[1] MDOT = multidrug resistance to oral therapy, defined as resistance to all of the following oral agents: co-amoxiclav (according to breakpoint for intravenous administration), ciprofloxacin (according to breakpoint for indications other than meningitis), and co-trimoxazole.

[a] According to breakpoint for intravenous administration. For more details see section 5.1.1.1.

[b] According to breakpoint for indications other than meningitis (for ciprofloxacin this only applies to *E. coli*, *K. pneumoniae*, *P. mirabilis*, and *E. cloacae* complex). For more details see section 5.1.1.1.

Figure 5.1.3.3.1 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic isolates of E. coli, K. pneumoniae, P. mirabilis, E. cloacae complex and P. aeruginosa from patients admitted to intensive care units in ISIS-AR*



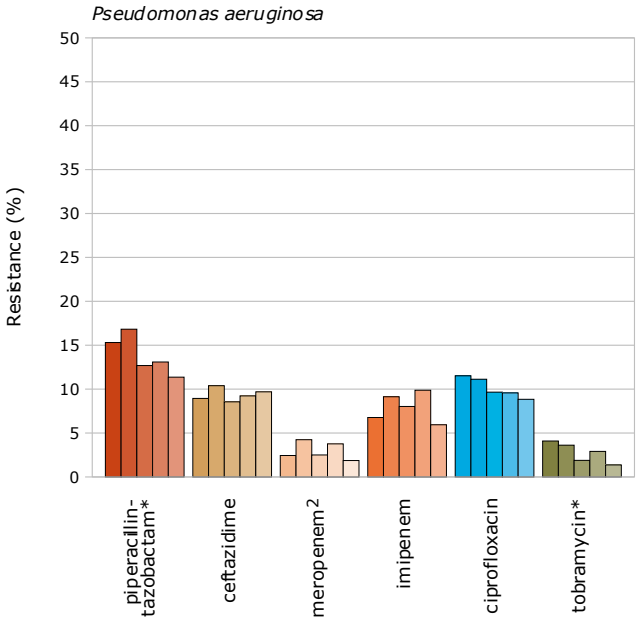
* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

[1] According to breakpoint for intravenous administration. For more details see section 5.1.1.1.

[2] According to breakpoint for indications other than meningitis. For more details see section 5.1.1.1.

[3] MDOT = multidrug resistance to oral therapy, defined as resistance to all of the following oral agents: co-amoxiclav (according to breakpoint for intravenous administration), ciprofloxacin (according to breakpoint for indications other than meningitis), and co-trimoxazole.

Figure 5.1.3.3.1 (continued) *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic isolates of E. coli, K. pneumoniae, P. mirabilis, E. cloacae complex and P. aeruginosa from patients admitted to intensive care units in ISIS-AR*



* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

[1] According to breakpoint for intravenous administration. For more details see section 5.1.1.1.

[2] According to breakpoint for indications other than meningitis. For more details see section 5.1.1.1.

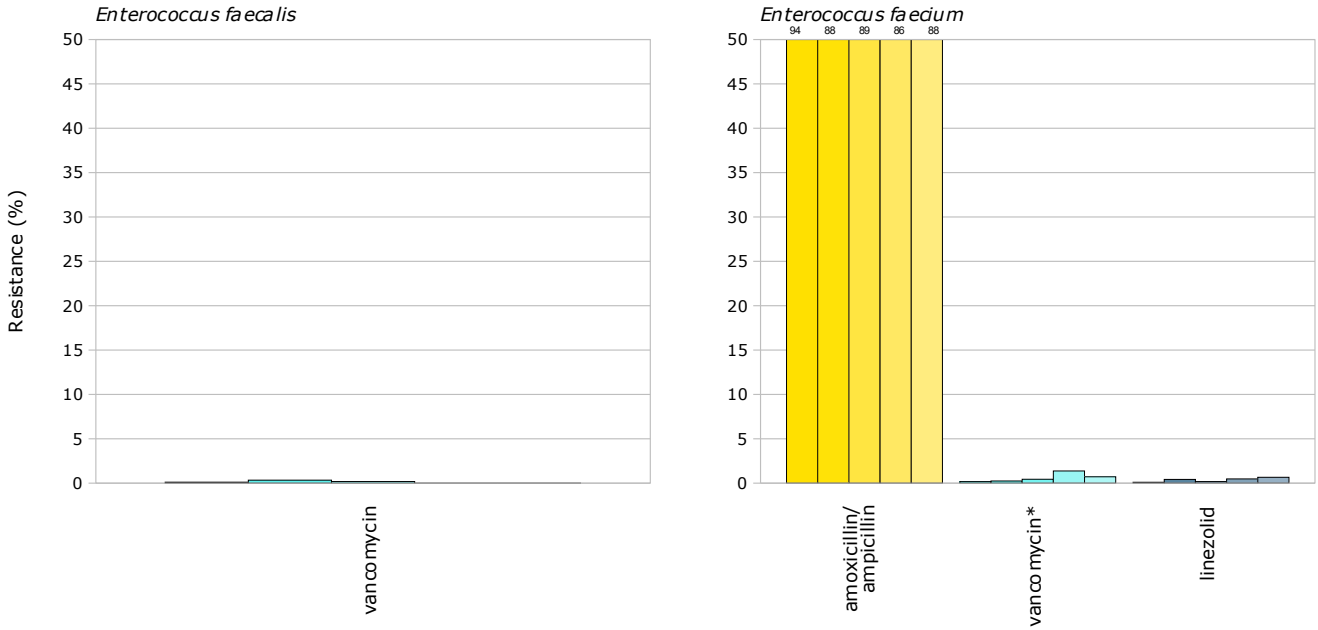
[3] MDOT = multidrug resistance to oral therapy, defined as resistance to all of the following oral agents: co-amoxiclav (according to breakpoint for intravenous administration), ciprofloxacin (according to breakpoint for indications other than meningitis), and co-trimoxazole.

Table 5.1.3.3.3 *Resistance levels (%) among diagnostic isolates of E. faecalis and E. faecium from patients admitted to intensive care units, ISIS-AR 2025*

	E. faecalis	***E. faecium***
Antibiotic		
amoxicillin/ampicillin	-	88
vancomycin	0.0	0.7 ↑
linezolid	-	0.7

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

Figure 5.1.3.3.2 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic isolates of E. faecalis and E. faecium from patients admitted to intensive care units in ISIS-AR*



* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

Table 5.1.3.3.4 *Resistance levels (%) among diagnostic isolates of S. aureus from patients admitted to intensive care units, ISIS-AR 2025*

	S. aureus
Antibiotic	
MRSA[1]	4
ciprofloxacin[2]	1.7
levofloxacin[3]	1.9
gentamicin	1.8
erythromycin	18
clindamycin	1.7
clindamycin (including inducible resistance)[4]	17
doxycycline/tetracycline	4
fusidic acid[a]	5
linezolid	0.4
co-trimoxazole	1.2
rifampicin	0.4
mupirocin	0.5
Multidrug resistance	
fusidic acid + mupirocin[a]	0.2

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

[1] MRSA = Methicillin resistant *S. aureus*. For the estimation method of MRSA see section 5.1.1.1.; Within the *S. aureus* complex 1 out of 1 *S. argenteus* and 0 out of 0 *S. schweitzeri* were methicillin resistant.

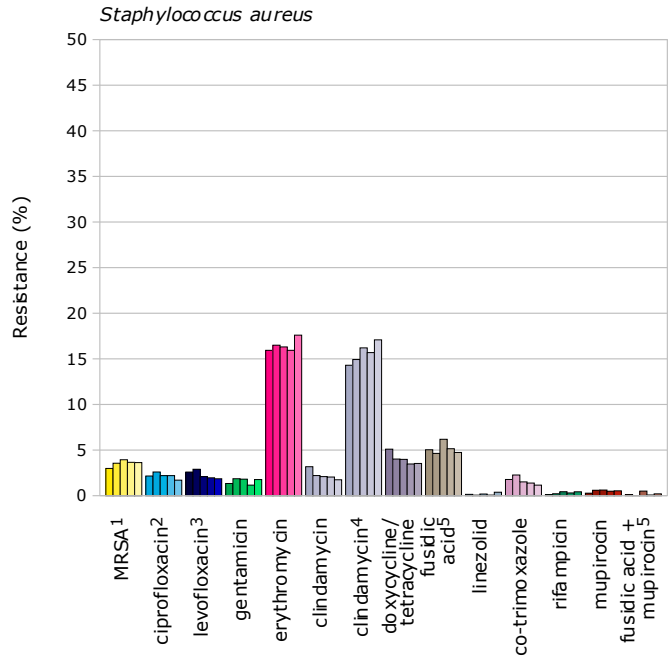
[2] Resistance to ciprofloxacin is intended to be a class indicator for resistance to fluoroquinolones.

[3] Often, susceptibility to levofloxacin is only tested when resistant to ciprofloxacin. Resistance percentages may, therefore, be biased toward a higher level. For details see section 5.1.1.1.

[4] For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

[a] According to breakpoint for topical use. For more details see section 5.1.1.1.

Figure 5.1.3.3.3 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic isolates of S. aureus from patients admitted to intensive care units in ISIS-AR*



Note: None of the trends were statistically significant and microbiologically relevant (for details see section 5.1.1.1).

[1] MRSA = Methicillin resistant *S. aureus*. For the estimation method of MRSA see section 5.1.1.1.

[2] Resistance to ciprofloxacin is intended to be a class indicator for resistance to fluoroquinolones.

[3] Often, susceptibility to levofloxacin is only tested when resistant to ciprofloxacin. Resistance percentages may, therefore, be biased toward a higher level. For details see section 5.1.1.1.

[4] Including inducible resistance. For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

[5] According to breakpoint for topical use. For more details see section 5.1.1.1.

Table 5.1.3.3.5 *Resistance levels (%) among diagnostic isolates of β-haemolytic Streptococcus spp. group B, and S. anginosus group from patients admitted to intensive care units, ISIS-AR 2025*

	ß-haemolytic *Streptococcus* spp. group B	***S. anginosus* group**
Antibiotic		
(benzyl)penicillin[a]	-	0.0
amoxicillin/ampicillin[1,a]	-	0.0
erythromycin	18°	-
clindamycin	9°	6
clindamycin (including inducible resistance)[2]	12°	6
co-trimoxazole	0.0°	-

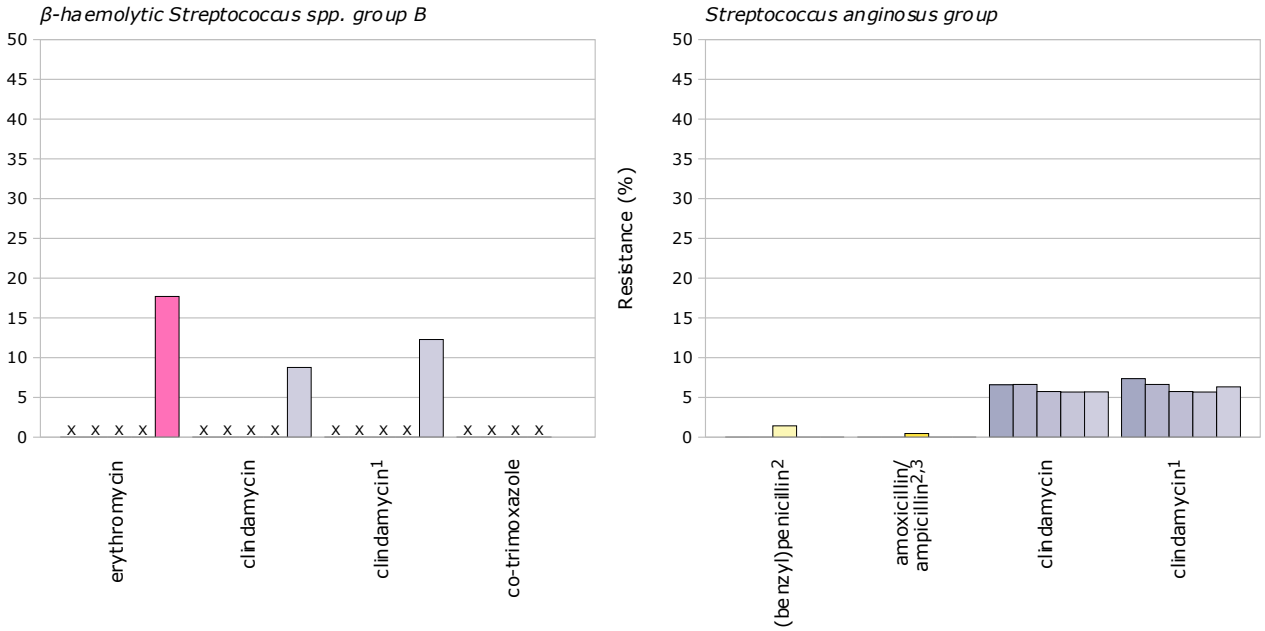
10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

[1] Resistance to amoxicillin/ampicillin in *S. anginosus* group and *S. mitis* group was calculated based on (benzyl)penicillin and amoxicillin/ampicillin according to directions in the EUCAST guidelines. For details see section 5.1.1.1.

[2] For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

[a] According to breakpoint for other indications than endocarditis. For more details see section 5.1.1.1.

Figure 5.1.3.3.4 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic isolates of β-haemolytic Streptococcus spp. group B and S. anginosus group from patients admitted to intensive care units in ISIS-AR*



Note: None of the trends were statistically significant and microbiologically relevant (for details see section 5.1.1.1).

[1] Including inducible resistance. For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

[2] According to breakpoint for other indications than endocarditis. For more details see section 5.1.1.1.

[3] Resistance to amoxicillin/ampicillin in *S. anginosus* group and *S. mitis* group was calculated based on (benzyl)penicillin and amoxicillin/ampicillin according to directions in the EUCAST guidelines. For details see section 5.1.1.1.

Key findings

Intensive Care Units

Blood, urine, blood, wound/pus, and respiratory: Enterobacterales and P. aeruginosa

- In *E. coli* **cefuroxime** resistance was 19% and **cefotaxime/ceftriaxone** 13%. In *K. pneumoniae*, **cefuroxime** resistance was 23% and **cefotaxime/ceftriaxone** was 17%. This indicates a continuing pattern of elevated **cephalosporin** resistance in the ICU compared to other settings and maintaining the high risk of inadequate empirical therapy with **second- and third-generation cephalosporins** for both *E. coli* and *K. pneumoniae*.
- Empiric **aminoglycoside combination therapy with cefuroxime or cefotaxime/ceftriaxone** reduced combined resistance to 3% for *E. coli* and 4% for *K. pneumoniae*. Combination treatment with **ciprofloxacin and cefuroxime or cefotaxime/ceftriaxone** is less successful with combined resistance levels of 9% and 10% for *E. coli* and *K. pneumoniae*, respectively.
- Most critically, **meropenem/imipenem** resistance in *K. pneumoniae* rose to 3% (2% in 2024) and now carries a significant and worrisome increasing trend over the past 5 years. This escalating **carbapenem** resistance in ICU for *K. pneumoniae* is the most clinically alarming finding in this setting.
- *P. aeruginosa*: **Piperacillin-tazobactam** resistance showed a newly significant decreasing trend over the past 5 years in 2025 and is now 11% (2024: 14% — previously this had been highlighted as a concern given its high level compared to other settings). **Tobramycin** resistance also showed a decreasing trend at 1.4%. **Ceftazidime** and **ciprofloxacin** resistance were stable at 10% and 9%, respectively.

Blood, urine, blood, wound/pus, and respiratory: S. aureus and E. faecium

- **MRSA** percentage in clinical *S. aureus* isolates of ICU patients remained stable at 4% over the last five years.
- The percentage of **vancomycin** resistance in clinical *E. faecium* isolates of ICU patients increased significantly to 0.7% over the last five years.

5.1.3.4 Blood isolates from inpatient departments (incl. intensive care units)

The distribution of pathogens isolated from blood of patients admitted to non-intensive care inpatient departments (non-ICU) and intensive care units (ICU) in 2025 is presented in table 5.1.3.4.1. Resistance levels for a selection of pathogens isolated from these patients in 2025 are presented in tables 5.1.3.4.2 (*E. coli*, *K. pneumoniae*, *P. mirabilis*, *E. cloacae* complex, and *P. aeruginosa*), 5.1.3.4.3 (*E. faecalis* and *E. faecium*), 5.1.3.4.4 (*S. aureus*), 5.1.3.4.5 (β-haemolytic *Streptococcus* spp. groups A, B, C and G, *S. anginosus* group, and *S. mitis* group), and 5.1.3.4.6 (*B. fragilis* complex). Five-year trends in resistance are presented in figures 5.1.3.4.1 (*E. coli, K. pneumoniae, P. mirabilis, E. cloacae* complex, and *P. aeruginosa*), 5.1.3.4.2 (*E. faecalis* and *E. faecium*), 5.1.3.4.3 (*S. aureus*), 5.1.3.4.4 (β-haemolytic *Streptococcus* spp. groups A, B, C and G, *S. anginosus* group, and *S. mitis* group), and 5.1.3.4.5 (*B. fragilis* complex).

In most hospitals, blood samples are taken from all patients suspected of having sepsis and susceptibility testing is performed as part of routine diagnostics. Bias due to selective sampling of patients is therefore unlikely.

Table 5.1.3.4.1 *Distribution of pathogens in diagnostic blood samples from patients admitted to non-intensive care inpatient departments (non-ICU) and intensive care units (ICU), ISIS-AR 2025*

	Non-ICU	ICU
Pathogen	**N (%)**	**N (%)**
E. coli	7,322 (25)	195 (7)
K. pneumoniae	1,479 (5)	44 (2)
P. mirabilis	528 (2)	14 (1)
E. cloacae complex	480 (2)	38 (1)
Other Enterobacterales[1]	1,874 (6)	117 (4)
P. aeruginosa	736 (2)	45 (2)
Other non-fermenters[2]	360 (1)	30 (1)
Other Gram-negatives[3]	322 (1)	18 (1)
E. faecalis	1,044 (4)	108 (4)
E. faecium	592 (2)	285 (10)
S. aureus	3,526 (12)	241 (9)
ß-haemolytic *Streptococcus* spp. group A	312 (1)	6 (0)
ß-haemolytic *Streptococcus* spp. group B	468 (2)	16 (1)
ß-haemolytic *Streptococcus* spp. groups C and G	896 (3)	10 (0)
S. anginosus group	561 (2)	22 (1)
S. mitis group	847 (3)	34 (1)
Other Gram-positives[4]	7,704 (26)	1,505 (55)
B. fragilis complex	343 (1)	22 (1)
Other anaerobes[5]	99 (0)	5 (0)

[1] In order of frequency: *Klebsiella* spp. (non-*pneumoniae*), *Serratia* spp., *Citrobacter* spp., *Salmonella* spp., *Morganella* spp., *Raoultella* spp., *Pantoea* spp., *Proteus* spp. (non-*mirabilis*), *Providencia* spp., *Hafnia* spp., *Enterobacter* spp. (non-*cloacae* complex), *Escherichia* spp. (non-*coli*), *Mixta* spp., *Shigella* spp., *Yersinia* spp., *Cronobacter* spp.

[2] In order of frequency: *Acinetobacter* spp., *Pseudomonas* spp. (non-*aeruginosa*), *S. maltophilia*, *M. catarrhalis*.

[3] In order of frequency: *H. parainfluenzae*, *H. influenzae*, *C. lari*, *C. coli*, *C. jejuni*, *N. meningitidis*.

[4] In order of frequency: *Staphylococcus* spp. (non-*aureus*), *S. pneumoniae*, *Enterococcus* spp. (non-*faecalis*, non-*faecium*), *A. urinae*, *L. monocytogenes*.

[5] In order of frequency: *C. perfringens*.

Table 5.1.3.4.2 *Resistance levels (%) among diagnostic blood isolates of E. coli, K. pneumoniae, P. mirabilis, E. cloacae complex, and P. aeruginosa from patients admitted to inpatient departments (incl. intensive care units), ISIS-AR 2025*

	E. coli	*K. pneumoniae*	*P. mirabilis*	*E. cloacae* complex	*P. aeruginosa*
Antibiotic					
amoxicillin/ampicillin	43	-	21	-	-
co-amoxiclav[a]	30	17	8 ↑	-	-
piperacillin-tazobactam	4	12	0.2	-	7
cefuroxime	13	15 ↑	1.3	-	-
cefotaxime/ceftriaxone[b]	9 ↑	12 ↑	0.9	-	-
ceftazidime	7	10 ↑	0.6	-	4
meropenem/imipenem[b]	0.1	0.9 ↑	-	0.4	-
meropenem[b]	-	-	0.0	-	2
imipenem	-	-	-	-	4
ciprofloxacin[b]	14	13 ↑	10	4	9
gentamicin	6	4	5	3	-
tobramycin	6	5	4	3	1.1 ↑
co-trimoxazole	23	13	19 ↓	7	-
Empiric therapy combinations					
cefuroxime + gentamicin	2	4	0.7	-	-
cefuroxime + ciprofloxacin[b]	7	9 ↑	1.0	-	-
cefotaxime/ceftriaxone + gentamicin[b]	2	4	0.6	-	-
cefotaxime/ceftriaxone + ciprofloxacin[b]	6	8 ↑	0.9	-	-
ceftazidime + tobramycin	-	-	-	-	0.9
Multidrug resistance					
MDOT[1]	5	5 ↑	2.0	-	-

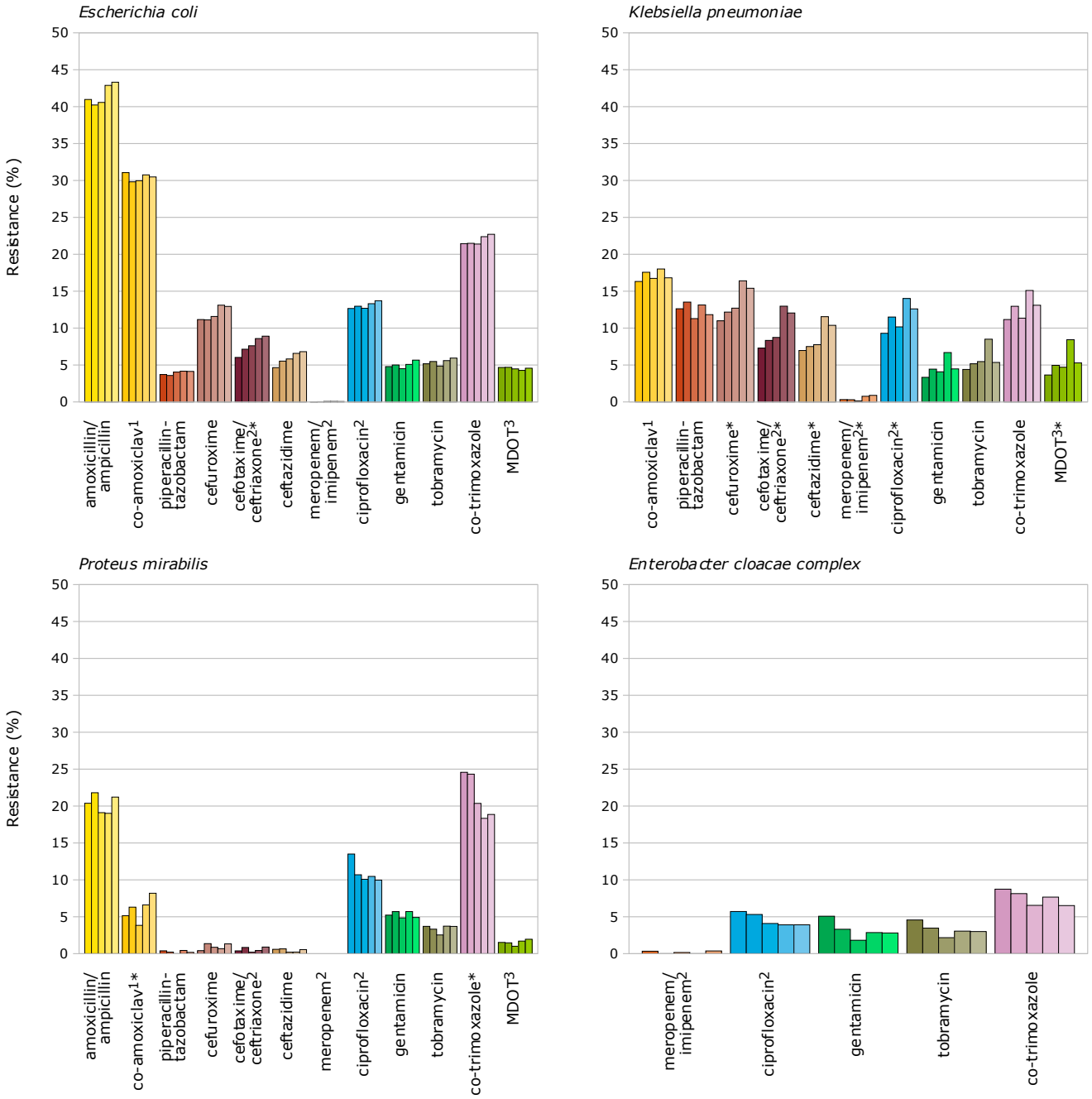
10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

[1] MDOT = multidrug resistance to oral therapy, defined as resistance to all of the following oral agents: co-amoxiclav (according to breakpoint for intravenous administration), ciprofloxacin (according to breakpoint for indications other than meningitis), and co-trimoxazole.

[a] According to breakpoint for intravenous administration. For more details see section 5.1.1.1.

[b] According to breakpoint for indications other than meningitis (for ciprofloxacin this only applies to *E. coli*, *K. pneumoniae*, *P. mirabilis*, and *E. cloacae* complex). For more details see section 5.1.1.1.

Figure 5.1.3.4.1 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic blood isolates of E. coli, K. pneumoniae, P. mirabilis, E. cloacae complex, and P. aeruginosa from patients admitted to inpatient departments (incl. intensive care units) in ISIS-AR*



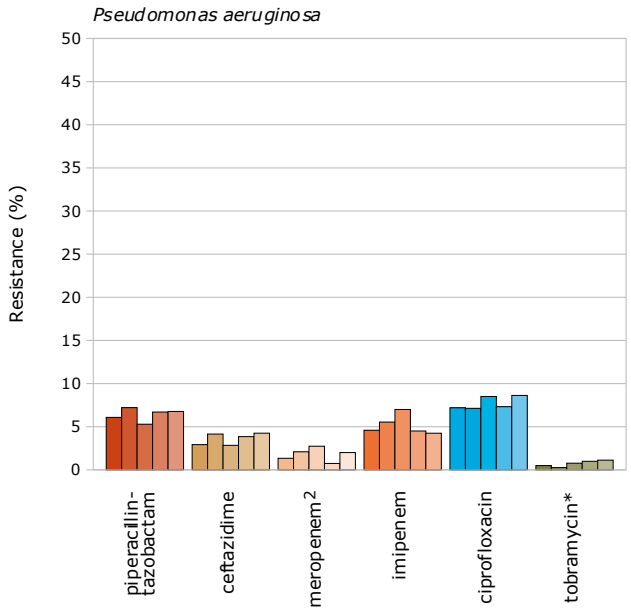
* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

[1] According to breakpoint for intravenous administration. For more details see section 5.1.1.1.

[2] According to breakpoint for indications other than meningitis. For more details see section 5.1.1.1.

[3] MDOT = multidrug resistance to oral therapy, defined as resistance to all of the following oral agents: co-amoxiclav (according to breakpoint for intravenous administration), ciprofloxacin (according to breakpoint for indications other than meningitis), and co-trimoxazole.

Figure 5.1.3.4.1 (continued) *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic blood isolates of E. coli, K. pneumoniae, P. mirabilis, E. cloacae complex, and P. aeruginosa from patients admitted to inpatient departments (incl. intensive care units) in ISIS-AR*



* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

[1] According to breakpoint for intravenous administration. For more details see section 5.1.1.1.

[2] According to breakpoint for indications other than meningitis. For more details see section 5.1.1.1.

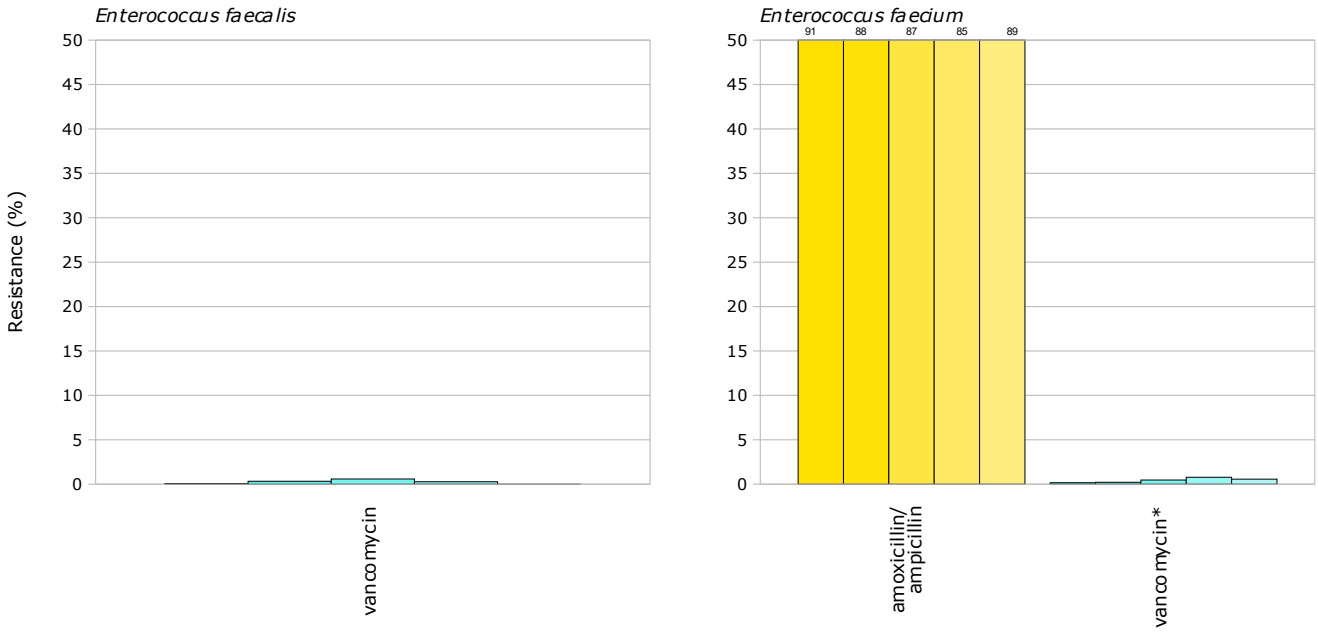
[3] MDOT = multidrug resistance to oral therapy, defined as resistance to all of the following oral agents: co-amoxiclav (according to breakpoint for intravenous administration), ciprofloxacin (according to breakpoint for indications other than meningitis), and co-trimoxazole.

Table 5.1.3.4.3 *Resistance levels (%) among diagnostic blood isolates of E. faecalis and E. faecium from patients admitted to inpatient departments (incl. intensive care units), ISIS-AR 2025*

	E. faecalis	***E. faecium***
Antibiotic		
amoxicillin/ampicillin	-	89
vancomycin	0.0	0.6 ↑

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

Figure 5.1.3.4.2 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic blood isolates of E. faecalis and E. faecium from patients admitted to inpatient departments (incl. intensive care units) in ISIS-AR*



* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

Table 5.1.3.4.4 *Resistance levels (%) among diagnostic blood isolates of S. aureus from patients admitted to inpatient departments (incl. intensive care units), ISIS-AR 2025*

	S. aureus
Antibiotic	
MRSA[1]	2.0
ciprofloxacin[2]	2
levofloxacin[3]	2
gentamicin	1.0
erythromycin	16
clindamycin	2
clindamycin (including inducible resistance)[4]	16
doxycycline/tetracycline	3
linezolid	0.1
co-trimoxazole	1.4
rifampicin	0.1

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

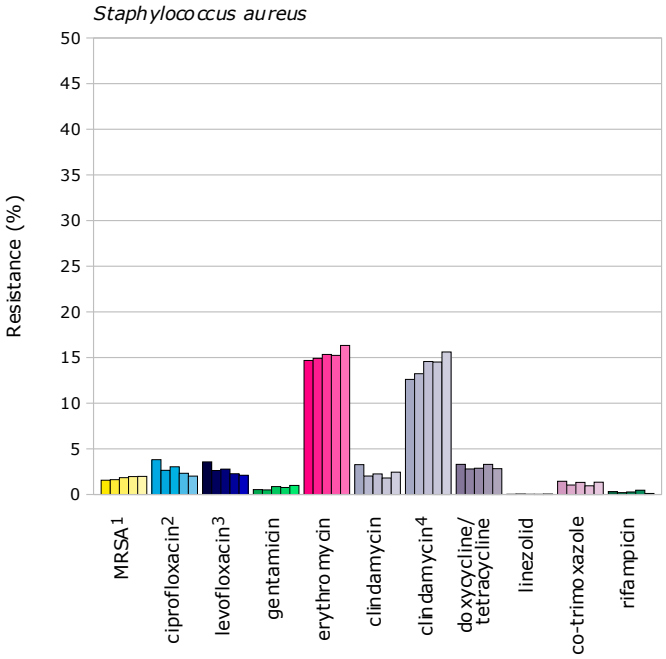
[1] MRSA = Methicillin resistant *S. aureus*. For the estimation method of MRSA see section 5.1.1.1.; Within the *S. aureus* complex 0 out of 0 *S. argenteus* and 0 out of 0 *S. schweitzeri* were methicillin resistant.

[2] Resistance to ciprofloxacin is intended to be a class indicator for resistance to fluoroquinolones.

[3] Often, susceptibility to levofloxacin is only tested when resistant to ciprofloxacin. Resistance percentages may, therefore, be biased toward a higher level. For details see section 5.1.1.1.

[4] For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

Figure 5.1.3.4.3 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic blood isolates of S. aureus from patients admitted to inpatient departments (incl. intensive care units) in ISIS-AR*



Note: None of the trends were statistically significant and microbiologically relevant (for details see section 5.1.1.1).

[1] MRSA = Methicillin resistant *S. aureus*. For the estimation method of MRSA see section 5.1.1.1.

[2] Resistance to ciprofloxacin is intended to be a class indicator for resistance to fluoroquinolones.

[3] Often, susceptibility to levofloxacin is only tested when resistant to ciprofloxacin. Resistance percentages may, therefore, be biased toward a higher level. For details see section 5.1.1.1.

[4] Including inducible resistance. For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

Table 5.1.3.4.5 *Resistance levels (%) among diagnostic blood isolates of β-haemolytic Streptococcus spp. groups A, B, C and G, S. anginosus group, and S. mitis group from patients admitted to inpatient departments (incl. intensive care units), ISIS-AR 2025*

	ß-haemolytic *Streptococcus* spp. group A	**ß-haemolytic *Streptococcus* spp. group B**	**ß-haemolytic *Streptococcus* spp. groups C and G**	***S. anginosus* group**	***S. mitis* group**
Antibiotic					
(benzyl)penicillin[a]	-	-	-	0.4	5
amoxicillin/ampicillin[1,a]	-	-	-	0.0	3
erythromycin	14 ↑	23	16	-	-
clindamycin	6 ↑	15	5	7	6
clindamycin (including inducible resistance)[2]	11 ↑	20	13 ↑	8	6
doxycycline/tetracycline	36°	78	24 ↓	-	-
co-trimoxazole	4°	1.1	1.1	-	-

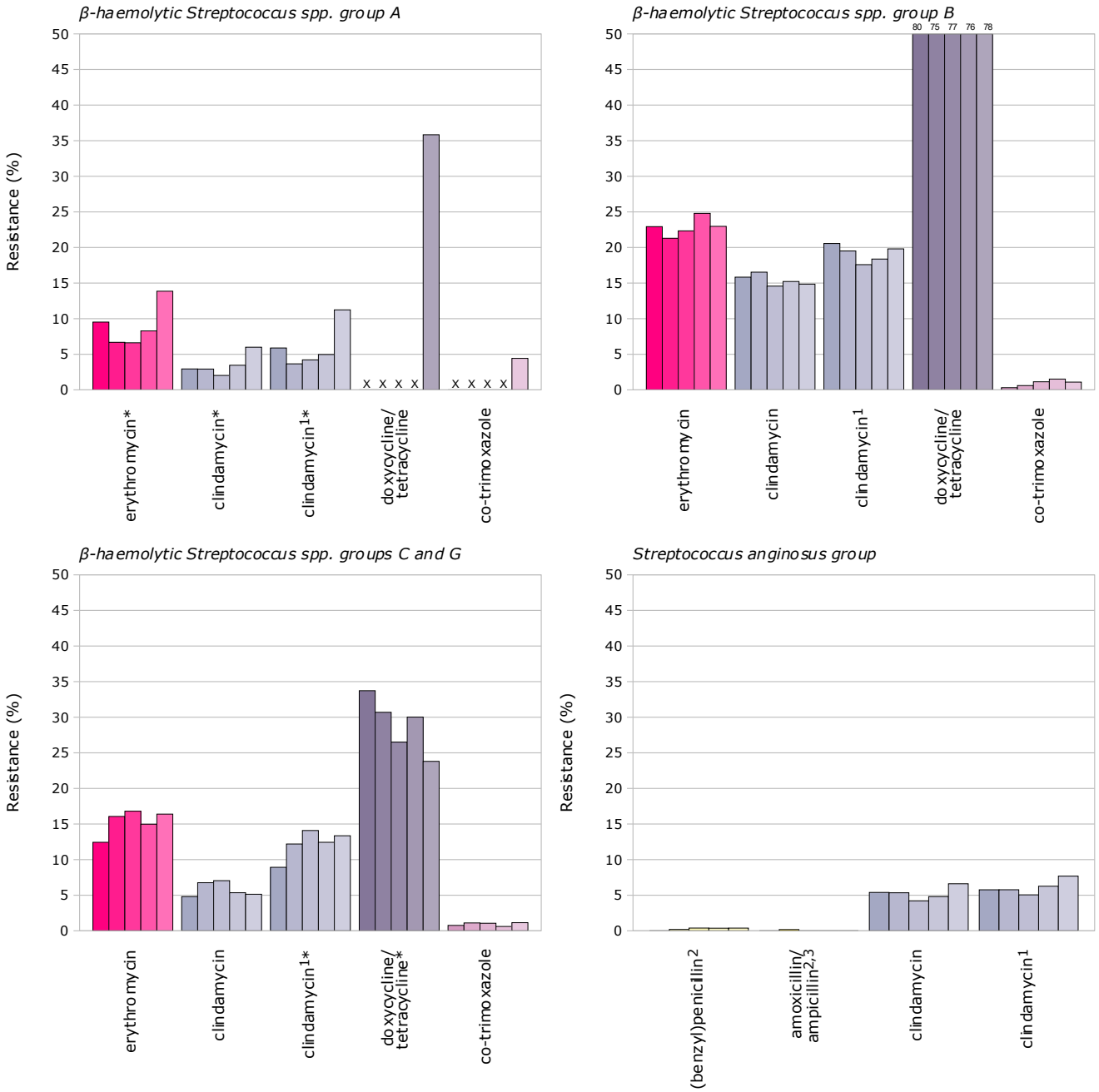
10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

[1] Resistance to amoxicillin/ampicillin in *S. anginosus* group and *S. mitis* group was calculated based on (benzyl)penicillin and amoxicillin/ampicillin according to directions in the EUCAST guidelines. For details see section 5.1.1.1.

[2] For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

[a] According to breakpoint for other indications than endocarditis. For more details see section 5.1.1.1.

Figure 5.1.3.4.4 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic blood isolates of β-haemolytic Streptococcus spp. groups A, B, C and G, S. anginosus group, and S. mitis group from patients admitted to inpatient departments (incl. intensive care units) in ISIS-AR*



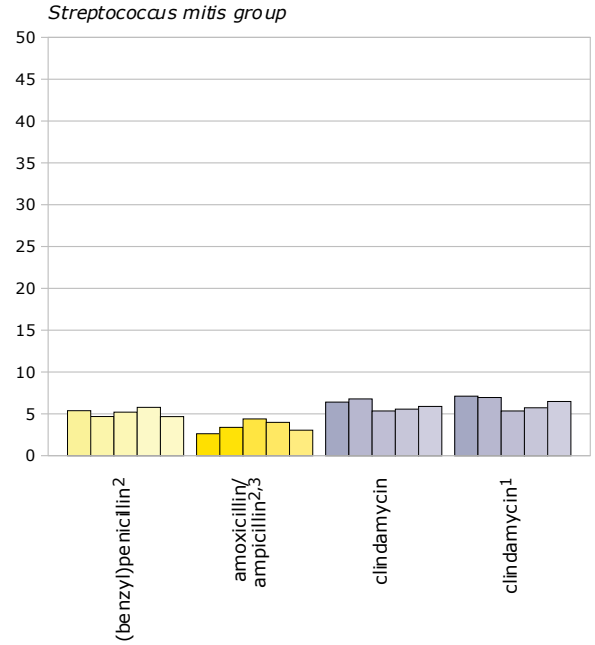
* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

[1] Including inducible resistance. For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

[2] According to breakpoint for other indications than endocarditis. For more details see section 5.1.1.1.

[3] Resistance to amoxicillin/ampicillin in *S. anginosus* group and *S. mitis* group was calculated based on (benzyl)penicillin and amoxicillin/ampicillin according to directions in the EUCAST guidelines. For details see section 5.1.1.1.

Figure 5.1.3.4.4 (continued) *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic blood isolates of β-haemolytic Streptococcus spp. groups A, B, C and G, S. anginosus group, and S. mitis group from patients admitted to inpatient departments (incl. intensive care units) in ISIS-AR*



* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

[1] Including inducible resistance. For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

[2] According to breakpoint for other indications than endocarditis. For more details see section 5.1.1.1.

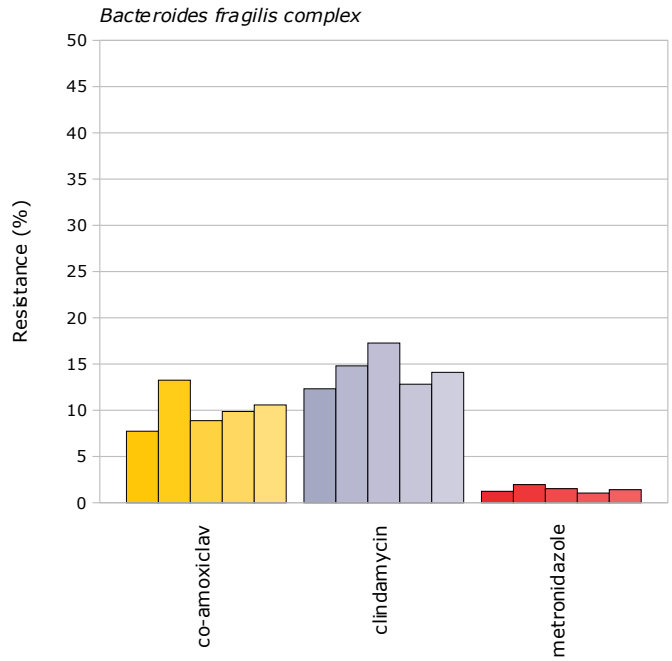
[3] Resistance to amoxicillin/ampicillin in *S. anginosus* group and *S. mitis* group was calculated based on (benzyl)penicillin and amoxicillin/ampicillin according to directions in the EUCAST guidelines. For details see section 5.1.1.1.

Table 5.1.3.4.6 *Resistance levels (%) among diagnostic blood isolates of B. fragilis complex from patients admitted to inpatient departments (incl. intensive care units), ISIS-AR 2025*

	***B. fragilis* complex**
Antibiotic	
co-amoxiclav	11
clindamycin	14
metronidazole	1.4

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

Figure 5.1.3.4.5 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic blood isolates of B. fragilis complex from patients admitted to inpatient departments (incl. intensive care units) in ISIS-AR*



Note: None of the trends were statistically significant and microbiologically relevant (for details see section 5.1.1.1).

Key findings

Blood isolates from inpatient departments (incl. intensive care units)

Enterobacterales and P. aeruginosa in blood cultures

- In *E. coli* from blood cultures, resistance levels to **cefuroxime** remained stable at 13% but resistance to **cefotaxime/ceftriaxone** increased significantly to 9% over the last five years. **Meropenem/imipenem** resistance remained low at 0.1%.
- In *K. pneumoniae* resistance **cefuroxime** and **cefotaxime/ceftriaxone** remained stable between 2024 and 2025. However, a worrisome increase was observed over the past five years to 15% and 12%, respectively. Also, a significant increase in resistance to **meropenem/imipenem** (0.9%) was found over the last 5 years.
- Patients with a bloodstream infection with *E. coli* or *K. pneumoniae* thus have a considerable risk of non-adequate empiric treatment with **a second or third generation cephalosporin**. In case of severe infection, empiric combination therapy with **cefuroxime or ceftriaxone/cefotaxime** and an **aminoglycoside**, reduced the likelihood of resistance to 2% in *E. coli* and 4% in *Klebsiella pneumoniae*. Empirical combination therapy with **cephalosporins and ciprofloxacin** appears to provide little additional benefit over treatment with a **second- or third-generation cephalosporin** alone (combined resistance 9%).

- After initial iv treatment, in patients with *E. coli* or *K. pneumoniae* bacteremia, a switch to either **ciprofloxacin, co-trimoxazole**, or **co-amoxiclav** was most often possible given the relatively low (≤5%) combined resistance rates for these oral agents.
- In *P. aeruginosa* isolates from blood cultures, resistance to **ceftazidime** (4%), **piperacillin-tazobactam** (7%) and **ciprofloxacin** (9%) remained stable over the past 5 years.

S. aureus and E. faecium in blood cultures

- **MRSA** was found in 2% of *S. aureus* isolates in blood cultures, the lowest MRSA rate across all care settings.
- **Vancomycin** resistance was found in 0.6% of *Enterococcus faecium* isolates in blood cultures which was still low but has increased significantly over the previous 5 years.

5.1.3.5 Urology services

The distribution of pathogens in urine samples from patients attending urology outpatient departments (OPD) and patients admitted to urology inpatient departments (IPD) in 2025 is presented in table 5.1.3.5.1. Resistance levels for a selection of pathogens isolated from these patients in 2025 are presented by type of department in tables 5.1.3.5.2 (*E. coli*, *K. pneumoniae*, *P. mirabilis*, and *P. aeruginosa*) and 5.1.3.5.3 (*E. faecalis* and *E. faecium*). Five-year trends in resistance are shown in figure 5.1.3.5.1 (*E. coli*, *K. pneumoniae*, *P. mirabilis*, and *P. aeruginosa*) and 5.1.3.5.2 (*E. faecalis* and *E. faecium*).

In urology departments of Dutch hospitals, a urine sample is routinely taken from patients presenting with complicated urinary tract infections and susceptibility testing is performed as part of routine diagnostics. However, guidelines do not indicate sampling in case of uncomplicated urinary tract infections. As a result, for those infections often only a sample is taken after therapy failure, and the presented resistance levels are likely to be higher than those for all patients with urinary tract infections at urology departments.

Table 5.1.3.5.1 *Distribution of isolated pathogens in diagnostic urine samples from patients attending urology outpatient departments (OPD) and patients admitted to urology inpatient departments (IPD), ISIS-AR 2025*

	OPD	IPD
Pathogen	**N (%)**	**N (%)**
E. coli	13,444 (36)	938 (28)
K. pneumoniae	3,497 (9)	344 (10)
P. mirabilis	1,629 (4)	157 (5)
Other Enterobacterales[1]	6,295 (17)	622 (18)
P. aeruginosa	1,432 (4)	243 (7)
Other non-fermenters[2]	559 (2)	64 (2)
Other Gram-negatives[3]	10 (0)	1 (0)
E. faecalis	3,710 (10)	440 (13)
E. faecium	227 (1)	127 (4)
Other Gram-positives[4]	6,063 (16)	427 (13)
Anaerobes[5]	6 (0)	1 (0)

[1] In order of frequency: *Klebsiella* spp. (non-*pneumoniae*), *Citrobacter* spp., *Enterobacter* spp., *Serratia* spp., *Morganella* spp., *Raoultella* spp., *Providencia* spp., *Proteus* spp. (non-*mirabilis*), *Pantoea* spp., *Escherichia* spp. (non-*coli*), *Hafnia* spp., *Salmonella* spp., *Mixta* spp., *Cronobacter* spp.

[2] In order of frequency: *Acinetobacter* spp., *S. maltophilia*, *Pseudomonas* spp. (non-*aeruginosa*).

[3] In order of frequency: *H. influenzae*, *H. parainfluenzae*.

[4] In order of frequency: *Staphylococcus* spp., *A. urinae*, *S. oralis*, *S. constellatus*, *S. pyogenes*, *S. gordonii*, *S. anginosus*, *S. mitis*, *S. pneumoniae*, *S. dysgalactiae* not further defined, *S. anginosus* group not further defined, *ß-haemolytic Streptococcus* spp. group C not further defined, *S. dysgalactiae* subsp. *equisimilis*, *ß-haemolytic Streptococcus* spp. group G not further defined, *S. mitis/oralis* not further defined, *S. agalactiae*, *S. dysgalactiae* subsp. *dysgalactiae*, *S. mitis* group not further defined, *Enterococcus* spp. (non-*faecalis*, non-*faecium*).

[5] In order of frequency: *B. fragilis*, *C. perfringens*.

Table 5.1.3.5.2 *Resistance levels (%) among diagnostic urine isolates of E. coli, K. pneumoniae, P. mirabilis, and P. aeruginosa from patients attending urology outpatient departments (OPD) and patients admitted to urology inpatient departments (IPD), ISIS-AR 2025*

	E. coli		***K. pneumoniae***		***P. mirabilis***		***P. aeruginosa***	
	OPD	**IPD**	**OPD**	**IPD**	**OPD**	**IPD**	**OPD**	**IPD**
Antibiotic								
amoxicillin/ampicillin	43	47	-	-	22	21	-	-
co-amoxiclav[a]	30	34	17	22	8 ↑	8 ↑	-	-
piperacillin-tazobactam	5	6	11	16	0.3	0.9	5	5
cefuroxime	13	17	14	20 ↑	1.6	1.5	-	-
cefotaxime/ceftriaxone[b]	8	12 ↑	9 ↑	16 ↑	1.4	0.9	-	-
ceftazidime	6	10 ↑	8 ↑	14 ↑	0.4	0.6	1.6	3
meropenem/imipenem[b]	0.0	0.0	0.1	0.0	-	-	-	-
meropenem[b]	-	-	-	-	0.0	0.0	0.4	0.5
imipenem	-	-	-	-	-	-	5	5
ciprofloxacin[b]	19	22	16	20 ↑	15	15	12	12
gentamicin	5	6	4 ↑	6	7	5 ↓	-	-
tobramycin	6	7	5	8 ↑	5	5	0.8	0.9
fosfomycin[1]	3	4	-	-	-	-	-	-
trimethoprim	29	32	22	26 ↑	33	31 ↓	-	-
co-trimoxazole	26	29	13	20 ↑	26	24 ↓	-	-
nitrofurantoin	4	3	-	-	-	-	-	-
Empiric therapy combinations								
cefuroxime + gentamicin	2.0	3	3 ↑	5 ↑	0.9	0.7	-	-
cefuroxime + ciprofloxacin[b]	7	11	9	14 ↑	0.9	0.9	-	-
cefotaxime/ceftriaxone + gentamicin[b]	1.8	3	3 ↑	5 ↑	0.7	0.7	-	-
cefotaxime/ceftriaxone + ciprofloxacin[b]	6	8	7 ↑	12 ↑	0.9	0.9	-	-
ceftazidime + tobramycin	-	-	-	-	-	-	0.3	0.7
Multidrug resistance								
MDOT[2]	6	9	5	9 ↑	3 ↑	3	-	-

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

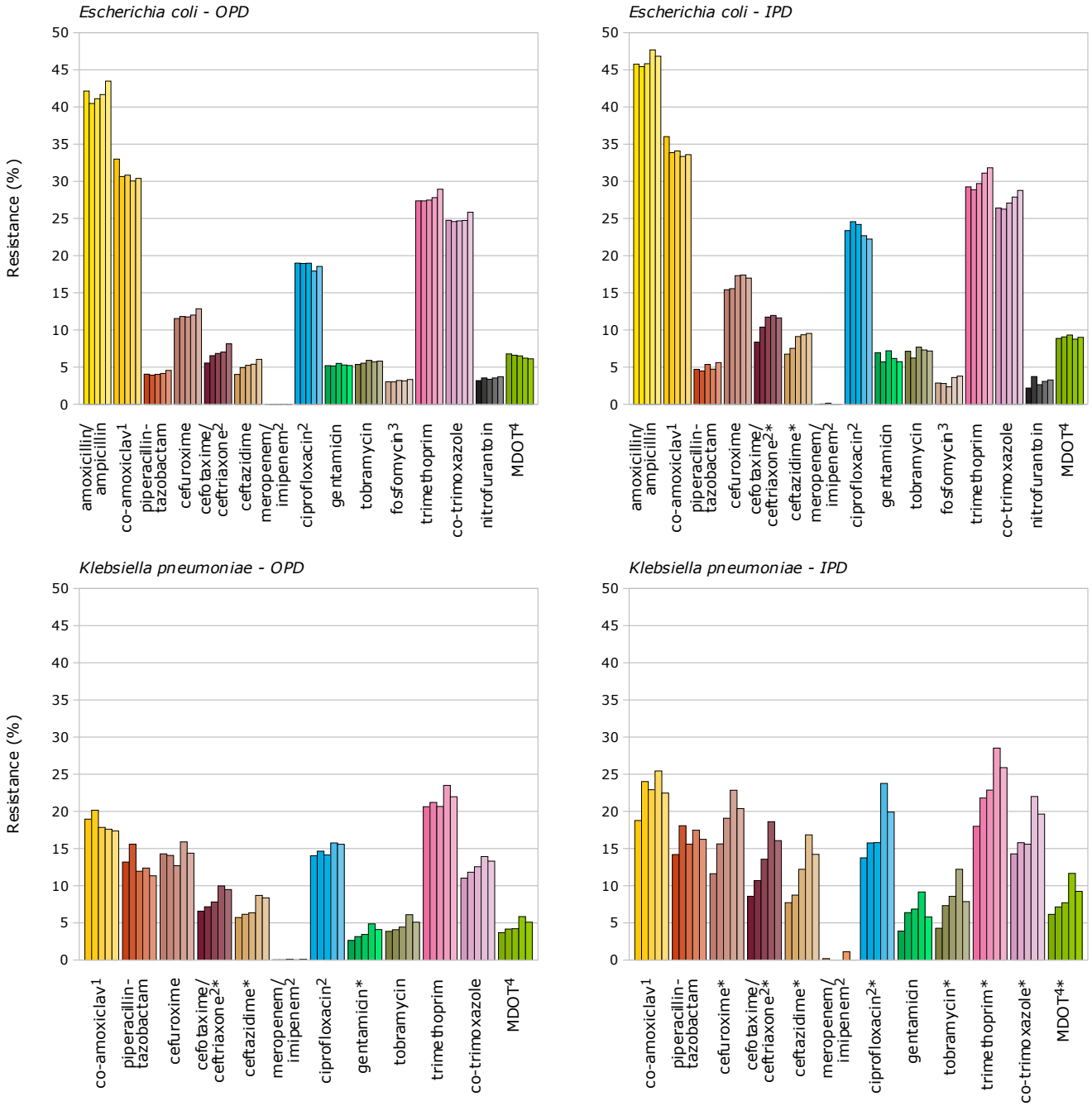
[1] Resistance percentage calculated using an MIC cut-off of 16 mg/L and a diameter cut-off of 24 mm. For more details see section 5.1.1.1.

[2] MDOT = multidrug resistance to oral therapy, defined as resistance to all of the following oral agents: co-amoxiclav (according to breakpoint for intravenous administration), ciprofloxacin (according to breakpoint for indications other than meningitis), and co-trimoxazole.

[a] According to breakpoint for intravenous administration. For more details see section 5.1.1.1.

[b] According to breakpoint for indications other than meningitis (for ciprofloxacin this only applies to *E. coli*, *K. pneumoniae*, and *P. mirabilis*). For more details see section 5.1.1.1.

Figure 5.1.3.5.1 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic urine isolates of E. coli, K. pneumoniae, P. mirabilis, and P. aeruginosa from patients attending urology outpatient departments (OPD) and patients admitted to urology inpatient departments (IPD) in ISIS-AR*



* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

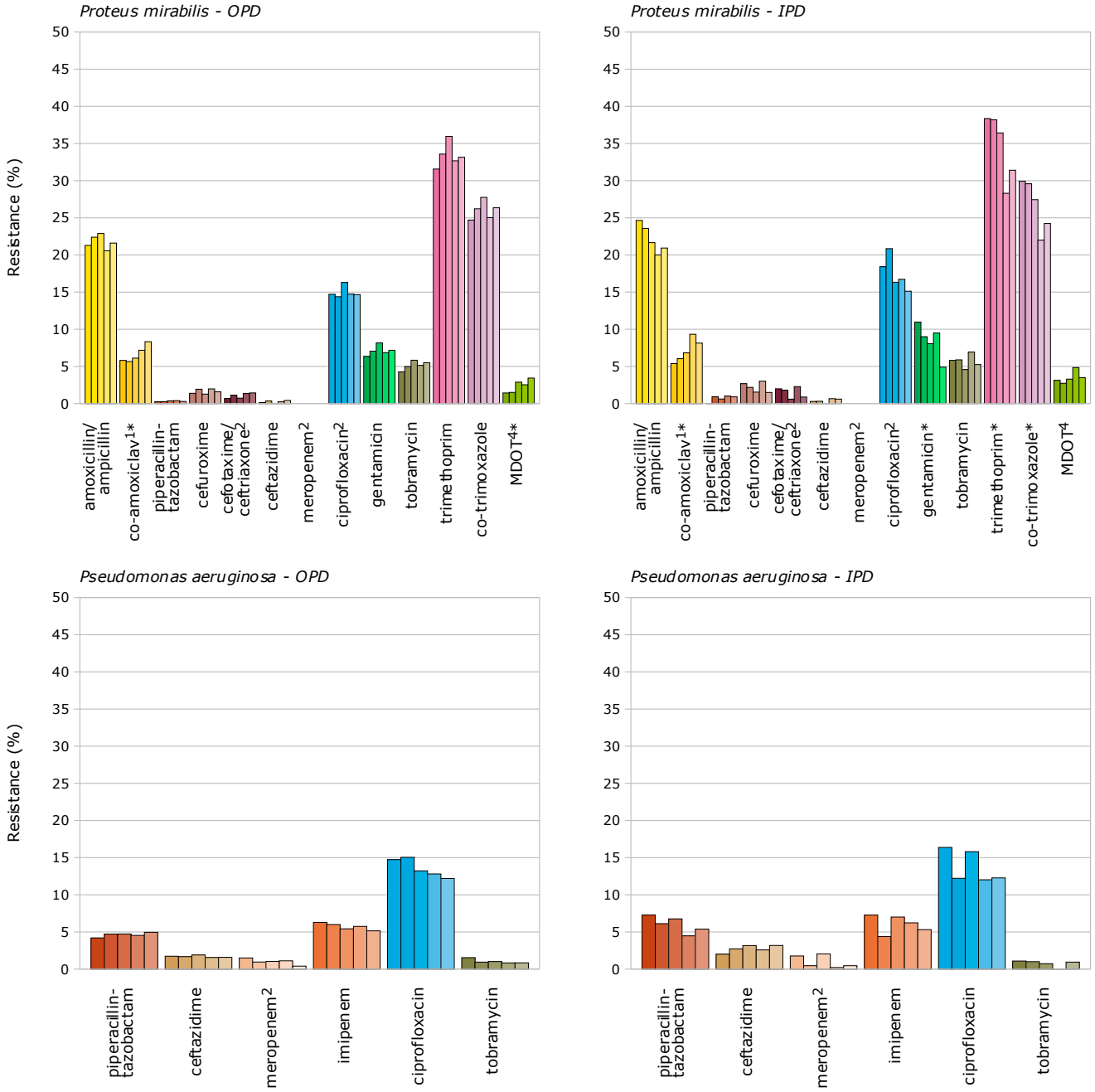
[1] According to breakpoint for intravenous administration. For more details see section 5.1.1.1.

[2] According to breakpoint for indications other than meningitis. For more details see section 5.1.1.1.

[3] Resistance percentage calculated using an MIC cut-off of 16 mg/L and a diameter cut-off of 24 mm. For more details see section 5.1.1.1.

[4] MDOT = multidrug resistance to oral therapy, defined as resistance to all of the following oral agents: co-amoxiclav (according to breakpoint for intravenous administration), ciprofloxacin (according to breakpoint for indications other than meningitis), and co-trimoxazole.

Figure 5.1.3.5.1 (continued) *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic urine isolates of E. coli, K. pneumoniae, P. mirabilis, and P. aeruginosa from patients attending urology outpatient departments (OPD) and patients admitted to urology inpatient departments (IPD) in ISIS-AR*



* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

[1] According to breakpoint for intravenous administration. For more details see section 5.1.1.1.

[2] According to breakpoint for indications other than meningitis. For more details see section 5.1.1.1.

[3] Resistance percentage calculated using an MIC cut-off of 16 mg/L and a diameter cut-off of 24 mm. For more details see section 5.1.1.1.

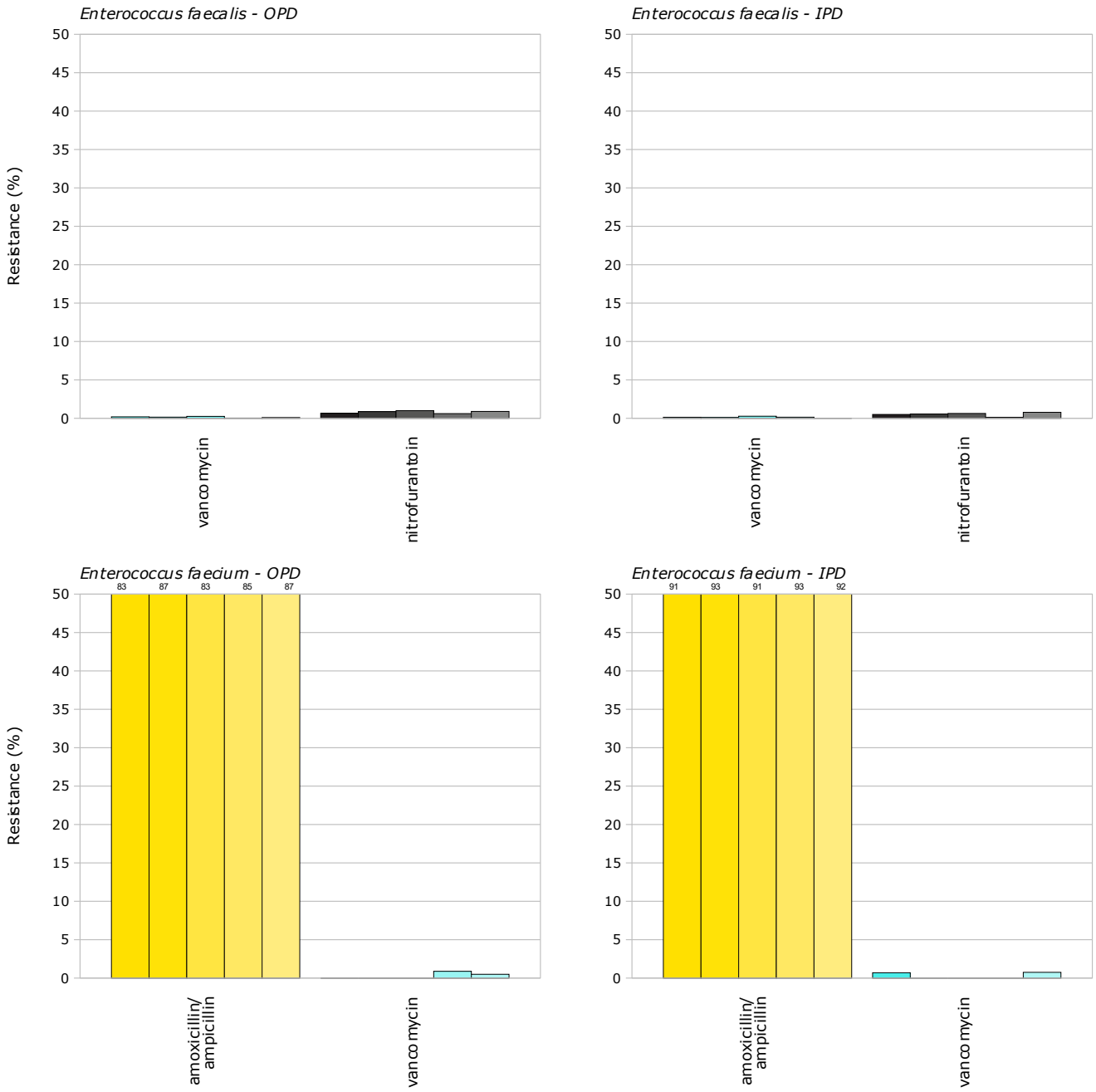
[4] MDOT = multidrug resistance to oral therapy, defined as resistance to all of the following oral agents: co-amoxiclav (according to breakpoint for intravenous administration), ciprofloxacin (according to breakpoint for indications other than meningitis), and co-trimoxazole.

Table 5.1.3.5.3 *Resistance levels (%) among diagnostic urine isolates of E. faecalis and E. faecium from patients attending urology outpatient departments (OPD) and patients admitted to urology inpatient departments (IPD), ISIS-AR 2025*

	E. faecalis		***E. faecium***	
	OPD	**IPD**	**OPD**	**IPD**
Antibiotic				
amoxicillin/ampicillin	-	-	87	92
vancomycin	0.1	0.0	0.5	0.8
nitrofurantoin	0.9	0.8	-	-

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

Figure 5.1.3.5.2 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic urine isolates of E. faecalis and E. faecium from patients attending urology outpatient departments (OPD) and patients admitted to urology inpatient departments (IPD), ISIS-AR 2025*



Note: None of the trends were statistically significant and microbiologically relevant (for details see section 5.1.1.1).

Key findings
Urology services

Urine: Enterobacterales and P. aeruginosa

- Resistance levels in Enterobacterales and *P. aeruginosa* from patients in urology services traditionally have been higher than in non-urology patients.
- Within urology services, resistance levels were higher in isolates from patients that were admitted compared to patients seen in OPD.
- For *E. coli*, resistance to **cefuroxime** was 13% (OPD) and 17% (IPD), and to **cefotaxime/ceftriaxone** 8% (OPD) and 12% (IPD). A new significant increasing trend was identified for **cefotaxime/ceftriaxone/ceftazidime** in *E. coli* from urology IPD patients in 2025. Resistance to **ciprofloxacin** was 19% and to **co-trimoxazole** 26% in OPD patients and 22% and 29% in IPD patients.
- Although more or less similar to 2024, a worrisome increase in resistance to almost all antibiotics was seen for *K. pneumoniae* from admitted patients over the last five years: resistance to **ciprofloxacin** and **co-trimoxazole** both significantly increased to 20%; resistance to **cefuroxime** increased to 20% and **cefotaxime/ceftriaxone** to 16%. The **meropenem/imipenem** increasing trend that had been a major concern in urology IPD patients in 2024 is no longer flagged in 2025, a notable and reassuring change.
- Empiric **aminoglycoside combination therapy — cefuroxime + gentamicin** (5%) and **cefotaxime/ceftriaxone + gentamicin** (5%) in *K. pneumoniae* IPD reduced the combined failure risk but both carried increasing trends, representing a substantial risk in the treatment of severe *K. pneumoniae* infections in admitted urology patients.
- For *P. aeruginosa* in urology patients, resistance levels were comparable to 2024. **Ciprofloxacin** resistance was 12% in both OPD and IPD. This is clinically important, as **ciprofloxacin** remains the only available oral treatment option for *P. aeruginosa* infections. **Piperacillin-tazobactam** resistance was 5% in both OPD and IPD, unchanged. **Ceftazidime** resistance was 3% in IPD patients.

5.1.4 Long-term care facilities

The distribution of pathogens in diagnostic urine and wound or pus samples from residents of long-term care facilities (LTCFs) in 2025 is presented in table 5.1.4.1. The resistance levels in 2025 for *E. coli*, *K. pneumoniae*, *P. mirabilis*, and *P. aeruginosa* isolates from urine samples are presented in table 5.1.4.2 and for *S. aureus* isolates from wound or pus samples in table 5.1.4.3. Five-year trends in resistance are shown in figures 5.1.4.1 (*E. coli*, *K. pneumoniae*, *P. mirabilis*, and *P. aeruginosa*), and 5.1.4.2 (*S. aureus*).

In 2018 a new sampling guideline for urinary tract infections was implemented in LTCFs, in which urinary culture and susceptibility testing is advised always when a urine dipstick test is positive. Although the indications to take a urine dipstick test were narrowed down, this may have resulted in lower resistance levels than before implementation of the guideline, when urine culture was only advised in case of treatment failure. Because it is not clear whether all LTCFs have adopted the new guideline fully and at the same time, resistance percentages may still be somewhat higher than those for all residents with urinary tract infections caused by Enterobacterales or *P. aeruginosa*, and falsely decreasing time trends may be found. Therefore, the trends in resistance for these infections should be interpreted with caution.

LTCFs usually send wound or pus samples for culture and susceptibility testing in case of antimicrobial therapy failure. As a result, the presented resistance levels are likely to be higher than those for all residents with wound infections or pus caused by *S. aureus* presenting in LTCFs.

Because the urinary, wound, or pus infections that were cultured may be a selection of all infections in LTCF residents, residents from whom samples were taken are hereafter referred to as ‘selected residents of long-term care facilities’.

Table 5.1.4.1 *Distribution of isolated pathogens in diagnostic urine and wound or pus samples from selected residents of long-term care facilities, ISIS-AR 2025*

	Urine	Wound or pus
Pathogen	**N (%)**	**N (%)**
E. coli	9,964 (43)	123 (5)
K. pneumoniae	2,465 (11)	49 (2)
P. mirabilis	2,340 (10)	163 (7)
Other Enterobacterales[1]	2,578 (11)	170 (8)
P. aeruginosa	1,173 (5)	318 (14)
Other non-fermenters[2]	86 (0)	26 (1)
Other Gram-negatives[3]	0 (0)	1 (0)
S. aureus	822 (4)	1,057 (47)
Other Gram-positives[4]	3,918 (17)	328 (15)
Anaerobes[5]	0 (0)	16 (1)

[1] In order of frequency: *Klebsiella* spp. (non-*pneumoniae*), *Citrobacter* spp., *Enterobacter* spp., *Morganella* spp., *Serratia* spp., *Proteus* spp. (non-*mirabilis*), *Providencia* spp., *Raoultella* spp., *Hafnia* spp., *Pantoea* spp., *Escherichia* spp. (non-*coli*), *Salmonella* spp., *Mixta* spp.

[2] In order of frequency: *Acinetobacter* spp., *Pseudomonas* spp. (non-*aeruginosa*), *S. maltophilia*, *B. cepacia*.

[3] In order of frequency: *H. influenzae*.

[4] In order of frequency: *Enterococcus* spp., *A. urinae*, *S. mitis*, *S. canis*, *S. pyogenes*, *S. dysgalactiae* subsp. *equisimilis*, *S. anginosus*, *S. intermedius*, *S. pneumoniae*, *S. constellatus*, *S. anginosus* group not further defined, *ß-haemolytic Streptococcus* spp. group C not further defined, *S. dysgalactiae* subsp. *dysgalactiae*, *ß-haemolytic Streptococcus* spp. group G not further defined, *ß-haemolytic Streptococcus* spp. group A not further defined, *S. agalactiae*, *S. dysgalactiae* not further defined, *S. mitis* group not further defined, *Staphylococcus* spp. (non-*aureus*).

[5] In order of frequency: *B. fragilis*, *C. perfringens*.

Table 5.1.4.2 *Resistance levels (%) among diagnostic urine isolates of E. coli, K. pneumoniae, P. mirabilis, and P. aeruginosa from selected residents of long-term care facilities, ISIS-AR 2025*

	E. coli	*K. pneumoniae*	*P. mirabilis*	*P. aeruginosa*
Antibiotic				
amoxicillin/ampicillin	40	-	17	-
co-amoxiclav[a]	11°	7°	3°	-
co-amoxiclav[b]	29	17 ↓	7	-
piperacillin-tazobactam	5	11 ↓	0.4	5
cefuroxime	12	13	0.9	-
cefotaxime/ceftriaxone[c]	6	8 ↑	0.6	-
ceftazidime	5	7	0.2	3
meropenem/imipenem[c]	0.0 ↑	0.1	-	-
meropenem[c]	-	-	0.0	0.5
imipenem	-	-	-	5
ciprofloxacin[c]	14	13	10 ↓	9
gentamicin	4	4	4	-
tobramycin	5	5	3	0.7
fosfomycin[1]	3	-	-	-
trimethoprim	22	18	28	-
co-trimoxazole	19	11	21	-
nitrofurantoin	3	-	-	-
Multidrug resistance				
MDOT[2]	4	5	1.7	-

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

[1] Resistance percentage calculated using an MIC cut-off of 16 mg/L and a diameter cut-off of 24 mm. For more details see section 5.1.1.1.

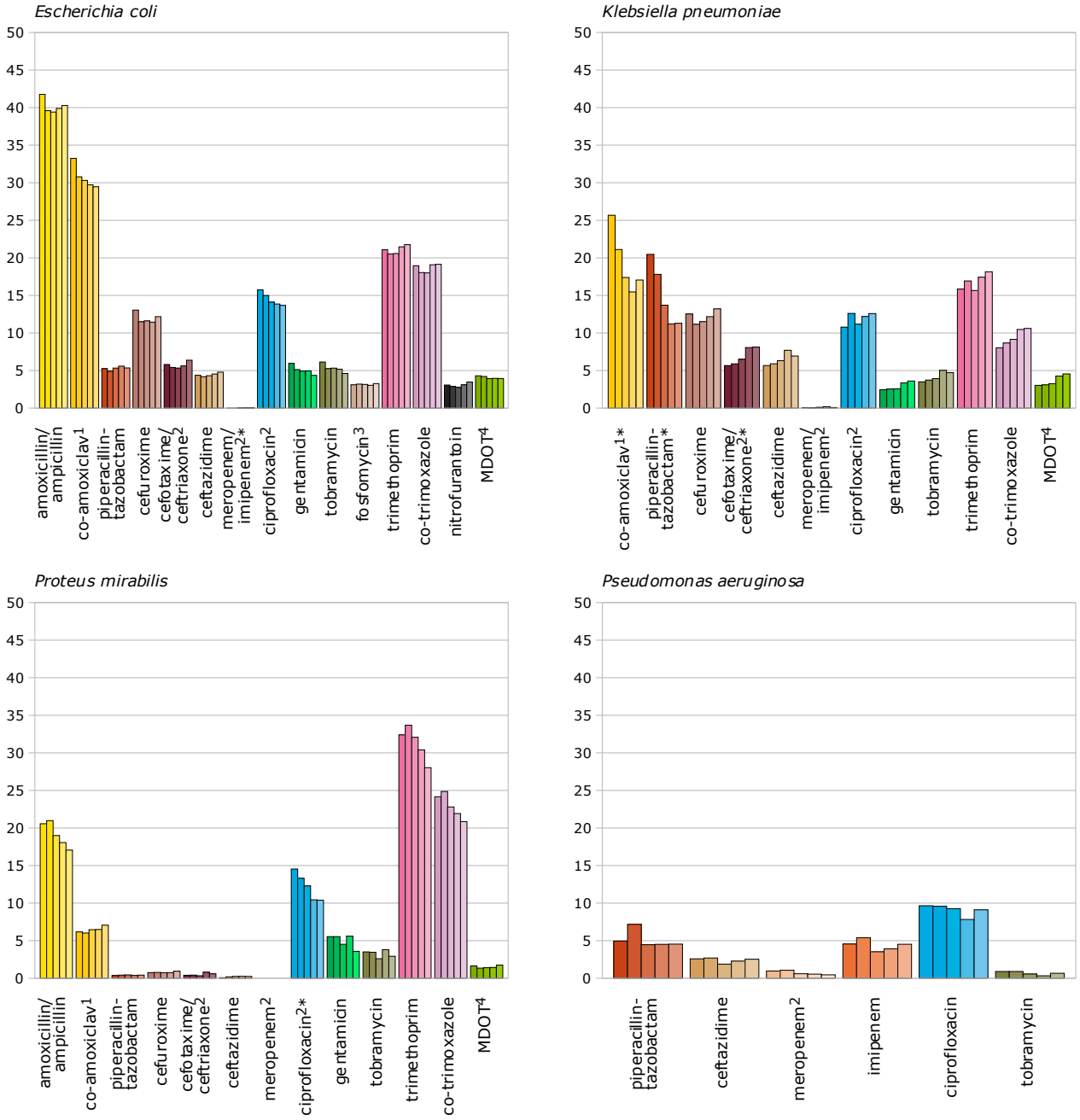
[2] MDOT = multidrug resistance to oral therapy, defined as resistance to all of the following oral agents: co-amoxiclav (according to breakpoint for intravenous administration), ciprofloxacin (according to breakpoint for indications other than meningitis), and co-trimoxazole.

[a] According to breakpoint for oral treatment of uncomplicated urinary tract infections. For more details see section 5.1.1.1.

[b] According to breakpoint for intravenous administration. For more details see section 5.1.1.1.

[c] According to breakpoint for indications other than meningitis (for ciprofloxacin this only applies to *E. coli*, *K. pneumoniae*, and *P. mirabilis*). For more details see section 5.1.1.1.

Figure 5.1.4.1 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic urine isolates of E. coli, K. pneumoniae, P. mirabilis, and P. aeruginosa from selected residents of long-term care facilities in ISIS-AR*



* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

[1] According to breakpoint for intravenous administration. For more details see section 5.1.1.1.

[2] According to breakpoint for indications other than meningitis. For more details see section 5.1.1.1.

[3] Resistance percentage calculated using an MIC cut-off of 16 mg/L and a diameter cut-off of 24 mm. For more details see section 5.1.1.1.

[4] MDOT = multidrug resistance to oral therapy, defined as resistance to all of the following oral agents: co-amoxiclav (according to breakpoint for intravenous administration), ciprofloxacin (according to breakpoint for indications other than meningitis), and co-trimoxazole.

Table 5.1.4.3 *Resistance levels (%) among diagnostic wound or pus isolates of S. aureus from selected residents of long-term care facilities, ISIS-AR 2025*

	S. aureus
Antibiotic	
MRSA[1]	3 ↑
ciprofloxacin[2]	12
levofloxacin[3]	14
erythromycin	21 ↑
clindamycin	4
clindamycin (including inducible resistance)[4]	20 ↑
doxycycline/tetracycline	4
fusidic acid[a]	10
co-trimoxazole	1.0
mupirocin	0.4
Multidrug resistance	
fusidic acid + mupirocin[a]	0.1

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

[1] MRSA = Methicillin resistant *S. aureus*. For the estimation method of MRSA see section 5.1.1.1.; Within the *S. aureus* complex 0 out of 0 *S. argenteus* and 0 out of 0 *S. schweitzeri* were methicillin resistant.

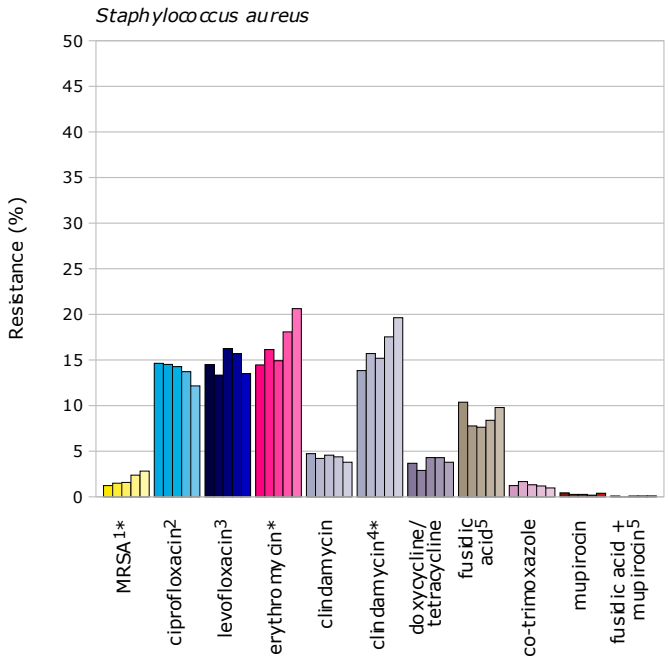
[2] Resistance to ciprofloxacin is intended to be a class indicator for resistance to fluoroquinolones.

[3] Often, susceptibility to levofloxacin is only tested when resistant to ciprofloxacin. Resistance percentages may, therefore, be biased toward a higher level. For details see section 5.1.1.1.

[4] For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

[a] According to breakpoint for topical use. For more details see section 5.1.1.1.

Figure 5.1.4.2 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic wound or pus isolates of S. aureus from selected residents of long-term care facilities in ISIS-AR*



* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

[1] MRSA = Methicillin resistant *S. aureus*. For the estimation method of MRSA see section 5.1.1.1.

[2] Resistance to ciprofloxacin is intended to be a class indicator for resistance to fluoroquinolones.

[3] Often, susceptibility to levofloxacin is only tested when resistant to ciprofloxacin. Resistance percentages may, therefore, be biased toward a higher level. For details see section 5.1.1.1.

[4] Including inducible resistance. For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

[5] According to breakpoint for topical use. For more details see section 5.1.1.1.

Key findings
Long-term care facilities

Urine: Enterobacterales and P. aeruginosa

- Resistance levels in *E. coli, K. pneumoniae* and *P. aeruginosa* urine isolates from selected LTCF residents were higher than resistance levels in selected GP patients and comparable to resistance levels in OPD and hospital patients, consistent with the pattern observed in previous years.
- Resistance levels for **nitrofurantoin** and **fosfomycin** in *E. coli*, first and second choice antibiotics for the treatment of uncomplicated UTI in adults, remained stable and low (both 3%).
- Resistance levels for **ciprofloxacin**, first choice antibiotic for the empiric oral treatment of complicated UTI in adults, remained stable in *E. coli* (14%) and *K. pneumoniae* (13%) and *P. aeruginosa* (9%) over the past 5 years. Resistance levels for **co-amoxiclav**, second choice antibiotic for the treatment of complicated UTI, remained stable in *E. coli* (29%) but significantly decreased to 17% in *K. pneumoniae* over the past 5 years. Resistance levels for **co-trimoxazole**, third choice antibiotic for this indication, was stable at 19% in *E. coli* and 11% in *K. pneumoniae*.

Wound/pus: S. aureus

- Resistance levels in *S. aureus* isolates from selected LTCF residents were higher than resistance levels in selected GP patients and comparable to resistance levels in OPD and hospital patients, with the exception of resistance to **levofloxacin** (14%), which was much higher in *S. aureus* from selected LTCF residents than in *S. aureus* from OPD (3%), hospital (3%) and ICU patients (2%), which might be the result of either selective sampling or intensive use of fluoroquinolones in this setting.
- **MRSA** was 3% and now carries a significant increasing trend — the first time an increasing MRSA trend has been identified in the LTCF setting.
- **Clindamycin resistance including inducible resistance** was 20% and also carries a significant increasing trend in 2025. **Clindamycin** resistance without inducible mechanisms was 4%, unchanged from 2024. According to EUCAST, **clindamycin** may still be used for short-term therapy in less severe skin and soft tissue infections if tested susceptible, even in the presence of an inducible resistance mechanism.

5.1.5 Respiratory pathogens

The distribution of pathogens isolated from diagnostic lower and upper respiratory tract samples from general practitioners' (GP) patients and from diagnostic blood or cerebrospinal fluid, and lower and upper respiratory tract samples from hospital patients (outpatients and inpatients, including intensive care patients) in 2025 is presented in table 5.1.5.1. Resistance levels for respiratory pathogens (*S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*) in 2025 are presented by patient group in table 5.1.5.2. Five-year trends in resistance are shown in figure 5.1.5.1.

Although patients from general practitioners are assumed to be representative of the community with respect to resistance levels of pathogens, in accordance with the NHG guidelines, general practitioners do not routinely take a sample when respiratory tract infection is suspected. Therefore, the results may be biased towards higher resistance levels due to overrepresentation of more severe or recurrent cases of respiratory tract infections.

In hospitals in the Netherlands, according to the newest clinical guidelines, a sample should be taken for routine diagnostic purposes only when a severe lower respiratory tract infection is suspected, which may lead to sampling bias. In addition, resistance levels in hospital patients may be higher than in the community, as patients with previous treatment failure, chronic obstructive pulmonary diseases, and cystic fibrosis may be overrepresented.

Table 5.1.5.1 *Distribution of isolated pathogens in diagnostic respiratory samples from general practitioners' patients (GP) and in diagnostic blood or cerebrospinal fluid and respiratory samples from hospital patients (outpatient and inpatient departments, incl. intensive care units), ISIS-AR 2025*

	GP		Hospital departments		
	Lower respiratory tract	**Upper respiratory tract**	**Blood or cerebrospinal fluid**	**Lower respiratory tract**	**Upper respiratory tract**
Pathogen	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**
S. pneumoniae	183 (9)	9 (0)	1,753 (5)	2,377 (8)	191 (3)
Other Gram-positives[1]	230 (11)	2,207 (87)	17,176 (51)	4,587 (16)	4,114 (62)
H. influenzae	775 (39)	56 (2)	211 (1)	7,928 (28)	611 (9)
M. catarrhalis	256 (13)	40 (2)	32 (0)	2,603 (9)	210 (3)
Other non-fermenters[2]	278 (14)	43 (2)	1,159 (3)	4,408 (16)	420 (6)
Enterobacterales[3]	264 (13)	182 (7)	12,616 (38)	5,772 (20)	1,009 (15)
Other Gram-negatives[4]	23 (1)	13 (1)	151 (0)	565 (2)	95 (1)
Anaerobes[5]	0 (0)	0 (0)	487 (1)	2 (0)	2 (0)

[1] In order of frequency: *Staphylococcus* spp.*, S. mitis/oralis* not further defined*, S. dysgalactiae subsp. dysgalactiae, ß-haemolytic Streptococcus* spp. group G not further defined*, S. peroris, S. cristatus, S. anginosus* group not further defined*, S. anginosus, ß-haemolytic Streptococcus* spp. group A not further defined*, S. equi, S. gordonii, S. mitis, S. constellatus, S. oralis, S. agalactiae, S. pyogenes, S. dysgalactiae* not further defined*, S. mitis* group not further defined*, S. australis, S. sanguinis* group not further defined*, S. dysgalactiae subsp. equisimilis, ß-haemolytic Streptococcus* spp. group C not further defined*, S. intermedius, S. canis, S. infantis, Enterococcus* spp.*, A. urinae, L. monocytogenes.*

[2] In order of frequency: *Pseudomonas* spp.*, S. maltophilia, Acinetobacter* spp.*, B. cepacia.*

[3] In order of frequency: *Escherichia* spp.*, Klebsiella* spp.*, Serratia* spp.*, Enterobacter* spp.*, Proteus* spp.*, Citrobacter* spp., *Morganella* spp.*, Raoultella* spp.*, Salmonella* spp.*, Pantoea* spp.*, Hafnia* spp., *Providencia* spp., *Mixta* spp., *Shigella* spp., *Yersinia* spp., *Cronobacter* spp.

[4] In order of frequency: *H. parainfluenzae, N. meningitidis, C. lari, C. coli, C. jejuni.*

[5] In order of frequency: *B. fragilis, Bacteroides fragilis* complex not further defined*, C. perfringens.*

Table 5.1.5.2 *Resistance levels (%) among diagnostic isolates of S. pneumoniae, H. influenzae, and M. catarrhalis from general practitioners' patients and hospital patients (outpatient and inpatient departments, incl. intensive care units), ISIS-AR 2025*

	S. pneumoniae		***H. influenzae***		***M. catarrhalis***	
	GP	**Hospital**	**GP**	**Hospital**	**GP**	**Hospital**
Antibiotic						
(benzyl)penicillin (R)[1,a]	0.5	1.2	-	-	-	-
(benzyl)penicillin (I)[1,a]	8	10 ↑	-	-	-	-
amoxicillin/ampicillin[1,b]	-	-	28	28	-	-
co-amoxiclav[1,b]	-	-	11	14	1.3	1.2
cefuroxime[1,b]	-	-	6 ↓	13 ↑	-	-
cefotaxime/ceftriaxone[1,a]	0	0.0	-	-	-	-
ciprofloxacin	-	-	10	8 ↓	2°	5
levofloxacin/moxifloxacin[2]	0.9°	0.5	-	-	-	-
erythromycin	11°	9	-	-	5°	7
doxycycline/tetracycline	9°	8	3	3	0	1.4
co-trimoxazole	7°	11	22	25	3	5

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

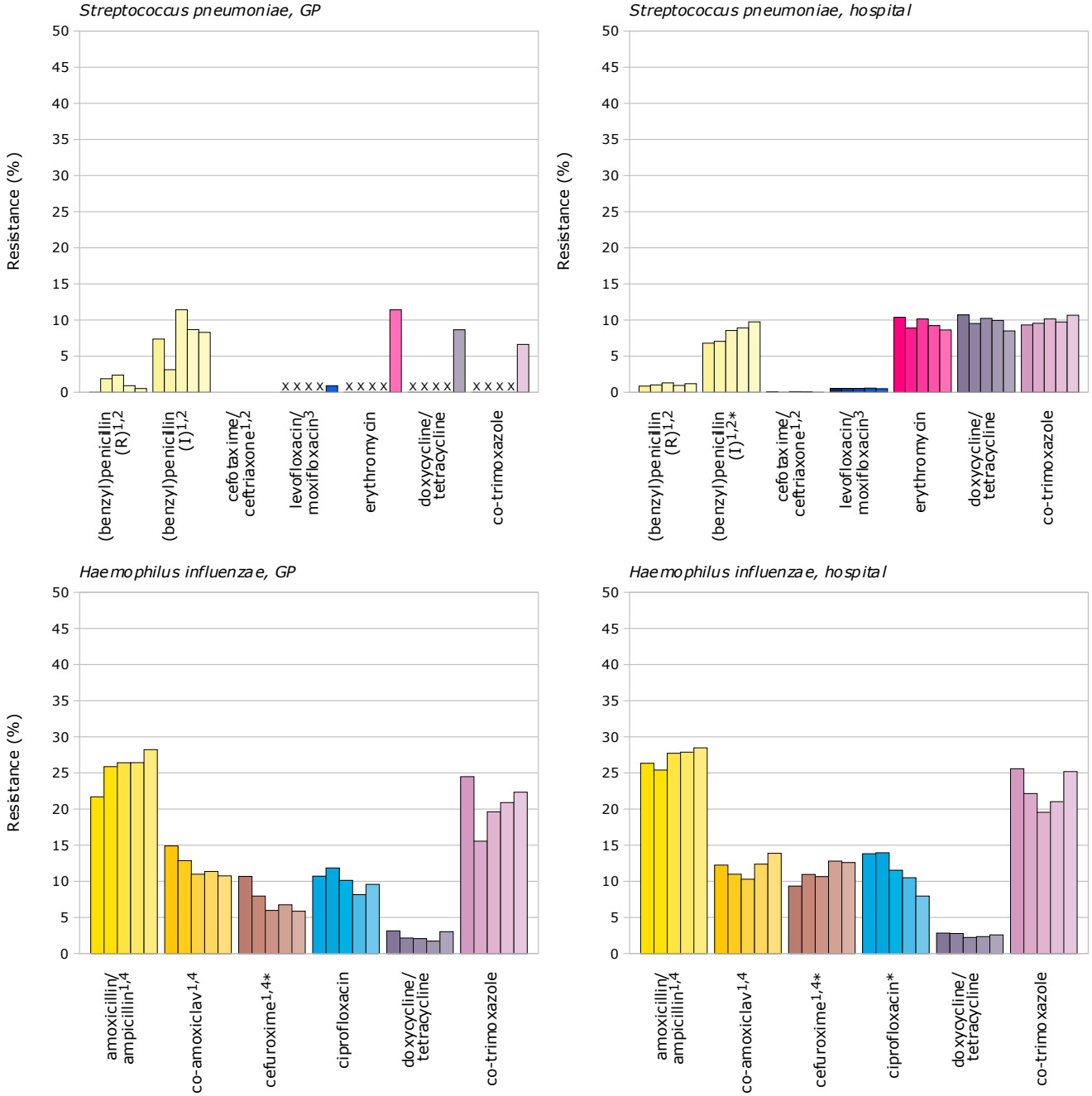
[1] Resistance to beta-lactam antibiotics in *S. pneumoniae* and *H. influenzae* was calculated based on a flow chart according to directions in the EUCAST guidelines (for details see section 5.1.1.1). Available gradient strip tests (Etest™ and MTS™) systematically underestimate (benzyl)penicillin MIC values in *S. pneumoniae* (for details see section 5.1.1.1). Resistance percentages may therefore be biased toward a lower level.

[2] Resistance to levofloxacin/moxifloxacin in *S. pneumoniae* was calculated based on norfloxacin and levofloxacin/moxifloxacin according to directions in the EUCAST guidelines. For details see section 5.1.1.1.

[a] According to breakpoint for indications other than endocarditis and meningitis. For more details see section 5.1.1.1.

[b] According to breakpoint for intravenous administrations (for co-amoxiclav this only applies to *H. influenzae*). For more details see section 5.1.1.1.

Figure 5.1.5.1 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic isolates of S. pneumoniae, H. influenzae, and M. catarrhalis from general practitioners' patients and hospital patients (outpatient and inpatient departments, incl. intensive care units) in ISIS-AR*



* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

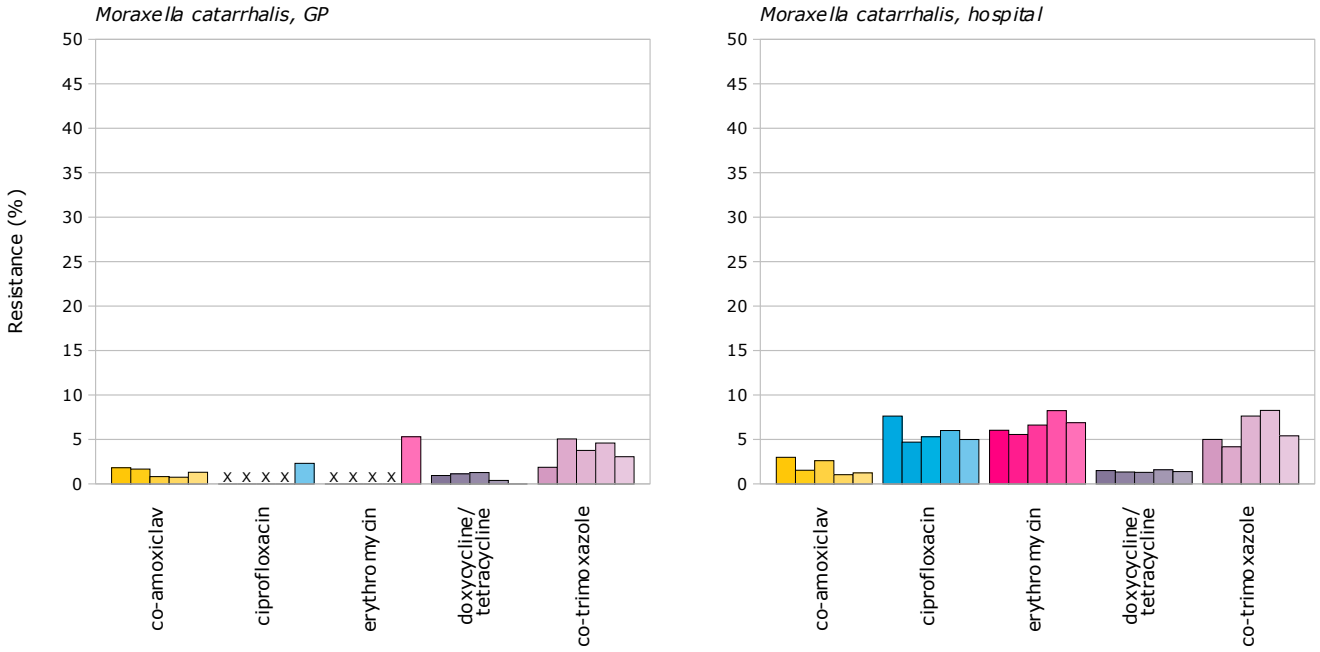
[1] Resistance to beta-lactam antibiotics in *S. pneumoniae* and *H. influenzae* was calculated based on a flow chart according to directions in the EUCAST guidelines for indications (for details see section 5.1.1.1). Available gradient strip tests (Etest™ and MTS™) systematically underestimate (benzyl)penicillin MIC values in *S. pneumoniae* (for details see section 5.1.1.1). Resistance percentages may therefore be biased toward a lower level.

[2] According to breakpoint for indications other than endocarditis and meningitis. For more details see section 5.1.1.1.

[3] Resistance to levofloxacin/moxifloxacin in *S. pneumoniae* was calculated based on norfloxacin and levofloxacin/moxifloxacin according to directions in the EUCAST guidelines. For details see section 5.1.1.1.

[4] According to breakpoint for intravenous administration. For more details see section 5.1.1.1.

Figure 5.1.5.1 (continued) *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic isolates of S. pneumoniae, H. influenzae, and M. catarrhalis from general practitioners' patients and hospital patients (outpatient and inpatient departments, incl. intensive care units) in ISIS-AR*



* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

[1] Resistance to beta-lactam antibiotics in *S. pneumoniae* and *H. influenzae* was calculated based on a flow chart according to directions in the EUCAST guidelines for indications (for details see section 5.1.1.1). Available gradient strip tests (Etest™ and MTS™) systematically underestimate (benzyl)penicillin MIC values in *S. pneumoniae* (for details see section 5.1.1.1). Resistance percentages may therefore be biased toward a lower level.

[2] According to breakpoint for indications other than endocarditis and meningitis. For more details see section 5.1.1.1.

[3] Resistance to levofloxacin/moxifloxacin in *S. pneumoniae* was calculated based on norfloxacin and levofloxacin/moxifloxacin according to directions in the EUCAST guidelines. For details see section 5.1.1.1.

[4] According to breakpoint for intravenous administration. For more details see section 5.1.1.1.

Key findings

Respiratory pathogens

S. pneumoniae

- The proportion of *S. pneumoniae* isolates in the I-category for **(benzyl)penicillin** was 8% in GP patients and 10% in hospital patients. The significant increasing trend over the previous 5 years for **(benzyl)penicillin** I-category resistance in hospital patients that was identified in 2024 was confirmed in 2025. Resistance to (benzyl)penicillin remained very low: 0.5% in GP and 1.2% in hospital patients, with no significant increasing trend for each group.
- Resistance to **doxycycline/tetracycline** in *S. pneumoniae* was 9% in GP and 8% in hospital patients.

H. influenzae

- In *Haemophilus influenzae* **co-amoxiclav** resistance was 11% in GP and 14% in hospital patients, which was stable over the years, confirming **co-amoxiclav** as a reliable treatment option in the majority of cases. **Cefuroxime** resistance in *H. influenzae* in IPD showed an significant increasing trend at 13%, already flagged last year and now confirmed.
- **Doxycycline/tetracycline** resistance was 3% in GP and 3% in hospital patients, low and stable. **Ciprofloxacin** resistance was 10% in GP and 8% in hospital patients.

M. catarrhalis

- Resistance levels for *M. catarrhalis* were generally low and stable in 2025. **Co-amoxiclav** resistance remained very low (≤1.3%) in both settings, supporting its continued empirical utility for *M. catarrhalis* respiratory infections.

5.2 Specific AMR surveillance

5.2.1 Extended spectrum β-lactamases

Introduction

Extended spectrum β-lactamase producing Enterobacterales (ESBL-E) have become a major concern worldwide. The prevalence of ESBL-E carriage has become quite widespread, also in the WHO European Region.[1] The percentage of ESBLs among clinical isolates of Enterobacterales in the Netherlands was estimated for the period 2021-2025 using the ISIS-AR database. Here we present data from ISIS-AR for *Escherichia coli* and *Klebsiella pneumoniae*.

Methods

Data were extracted from the ISIS-AR database. The percentages of ESBL-producing *E. coli* and *K. pneumoniae* were estimated based on positivity of confirmation tests (available >99% of the ESBL positive isolates), or, if data from these tests were lacking, inferred from the MICs for third generation cephalosporins (cefotaxime/ceftriaxone/ceftazidime) based on the EUCAST 2025 clinical resistance breakpoints.

Results

In table 5.2.1.1 and 5.2.1.2, the estimated percentages of ESBL-carrying *E. coli* and *K. pneumoniae* among all isolates of *E. coli* and *K. pneumoniae* are shown by healthcare setting or department, i.e. general practice (GP), outpatient departments, inpatient departments, and intensive care units (ICUs), in 2025. In figure 5.2.1.1, trends in ESBL percentages (from left to right 2021 to 2025) among all diagnostic isolates of *E. coli* and *K. pneumoniae* by healthcare setting are shown. Overall, the percentages of ESBL for *E. coli* and *K. pneumoniae* seem to increase during the previous five years, with a significant and microbiologically relevant increasing trend in ESBL *E. coli* in patients cultured at general practitioners or intensive care units, and in ESBL *K. pneumoniae* in patients cultured at outpatient and inpatient departments in hospitals. The ESBL percentages in both *E. coli* and *K. pneumoniae* from diagnostic ICU isolates remain high in the previous five years, up to 13% in *E. coli* and 16% in *K. pneumoniae* in 2025.

Table 5.2.1.1 *Extended spectrum β-lactamase (ESBL) producing E. coli in the Netherlands in 2025 in diagnostic isolates, based on ISIS-AR data*

Type of department	Tested isolates, N	ESBL, number (%)[1]
GP	138,791	6,710 (5) ↑
Outpatient departments	25,582	1,839 (7)
Inpatient departments excl. intensive care units	35,412	2,699 (8)
Intensive care units	1,400	179 (13) ↑
Total	**201,185**	**11,427 (6)**

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10	No significant and microbiologically relevant time trend.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

Numbers are based on a selection of 36 laboratories that continuously reported to the ISIS-AR database in the past five years. The first diagnostic *E. coli* isolate per patient was selected.

[1] The percentage of ESBL producing *E. coli* was estimated based on positivity of ESBL confirmatory tests, or, if no data on confirmatory tests were available, by resistance to cefotaxime/ceftriaxone (according to a cut-off of 2 mg/L for both cefotaxime and ceftriaxone or 17 mm for cefotaxime and 24 mm for ceftriaxone) and/or ceftazidime (according to a cut-off of 4 mg/L or 19 mm), based on re-interpretation of test values according to EUCAST 2025.

Table 5.2.1.2 *Extended spectrum β-lactamase (ESBL) producing K. pneumoniae in the Netherlands in 2025 in diagnostic isolates, based on ISIS-AR data*

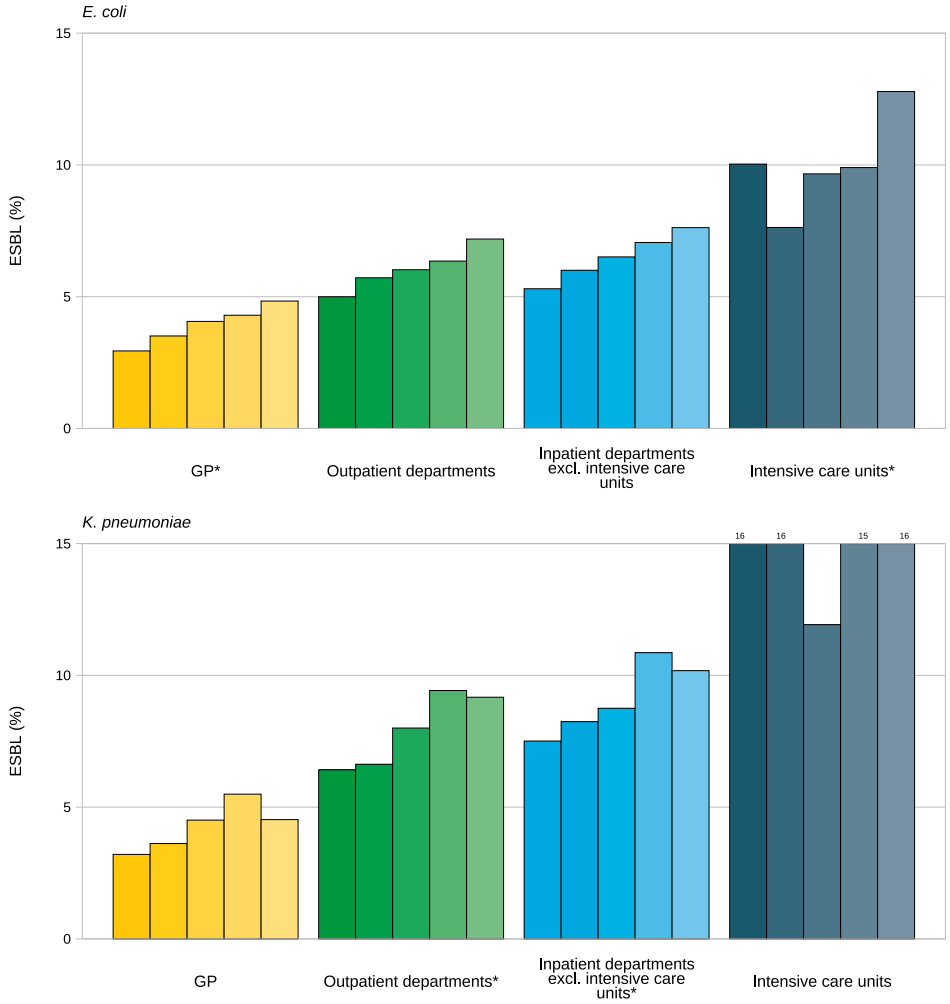
Type of department	Tested isolates, N	ESBL, number (%)[1]
GP	20,478	927 (5)
Outpatient departments	6,160	565 (9) ↑
Inpatient departments excl. intensive care units	7,594	773 (10) ↑
Intensive care units	414	66 (16)
Total	**34,646**	**2,331 (7) ↑**

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10	No significant and microbiologically relevant time trend.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

Numbers are based on a selection of 36 laboratories that continuously reported to the ISIS-AR database in the past five years. The first diagnostic *K. pneumoniae* isolate per patient was selected.

[1] The percentage of ESBL producing *K. pneumoniae* was estimated based on positivity of ESBL confirmatory tests, or, if no data on confirmatory tests were available, by resistance to cefotaxime/ceftriaxone (according to a cut-off of 2 mg/L for both cefotaxime and ceftriaxone or 17 mm for cefotaxime and 24 mm for ceftriaxone) and/or ceftazidime (according to a cut-off of 4 mg/L or 19 mm), based on re-interpretation of test values according to EUCAST 2025.

Figure 5.2.1.1 *Trends in extended spectrum β-lactamase (ESBL) producing E. coli and K. pneumoniae in the Netherlands (from left to right 2021 to 2025), based on ISIS-AR data*



Numbers are based on a selection of 36 laboratories that continuously reported to the ISIS-AR database in the past five years. The first diagnostic *E. coli* and *K. pneumoniae* isolate per patient per year was selected.
* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

The percentage of ESBL producing *E. coli* and *K. pneumoniae* was estimated based on positivity of ESBL confirmatory tests, or, if no data on confirmatory tests were available, by resistance to cefotaxime/ceftriaxone (according to a cut-off of 2 mg/L for both cefotaxime and ceftriaxone or 17 mm for cefotaxime and 24 mm for ceftriaxone) and/or ceftazidime (according to a cut-off of 4 mg/L or 19 mm), based on re-interpretation of test values according to EUCAST 2025.

Discussion

Over the past 5 years, ESBL-producing *E. coli* showed a significantly increasing trend in GP and intensive care units. ESBL-producing *K. pneumoniae* showed a significantly increasing trend overall particularly in outpatient and inpatient department populations. During the COVID-years (2020 and 2021), the proportions of both ESBL-producing *K. pneumoniae* and *E. coli* were lower, with resistance increasing again in all healthcare departments in the post-COVID period. When considering 10-year-trends (data not shown), however, the proportions of ESBL-positive *E. coli* and *K. pneumoniae* in 2025 exceed the proportions in the pre-COVID-years in most types of healthcare departments, especially in the inpatient departments and intensive care units, indicating a sustained rise in resistance rather than a temporary rebound.
Thus, resistance percentages above 10% in inpatient settings, and the overall increasing trend is alarming.
Similar trends are seen internationally in the EU/EEA region in the 2020-2024 data from the EARS-Net surveillance.[1]
In June 2026, an expert meeting was organized by RIVM with relevant stakeholders to discuss the epidemiology and potential impact of the (inter)national rise in ESBL-E. The expert meeting concluded that this increase is worrisome, and that optimal control requires better insight into the epidemiology and the risk groups for carriage and infection. Future research goals were defined and research projects will be set up to investigate epidemiological characteristics of populations having a higher risk of getting colonized or infected with ESBL-E. Adjustments in empirical treatment policies and infection prevention control measures potentially diminishing the spread of ESBL-E are going to be investigated as well.

Conclusions

- From 2021-2025, there has been a significant increase in ESBL-producing *E. coli* in GP and intensive care units and an increase in ESBL-producing *K. pneumoniae* overall and specifically in outpatient and inpatient department populations.
- ESBL-producing *K. pneumoniae* percentages showed continuing percentages above 10% in the inpatient department population.
- In the 10-year-trends, the percentages of ESBL-producing *E. coli* and *K. pneumoniae* in all healthcare departments are up or above the levels in the pre-COVID-years (data not shown), which is worrisome.

References

5. Surveillance of antimicrobial resistance in Europe https://www.ecdc.europa.eu/en/publications-data/antimicrobial-resistance-eueea-ears-net-annual-epidemiological-report-2024

5.2.2 Carbapenem-resistant and carbapenemase-producing Enterobacterales

Introduction
Carbapenem-resistant Enterobacterales (CRE) and carbapenemase-producing Enterobacterales (CPE) have been reported all over the world. Because carbapenems represent a group of antibiotics of last resort for treatment of many bacterial infections, resistance poses a significant challenge to clinicians and negatively impacts patient care.[1] In Europe, CRE were first described in the early 2000s and their prevalence has increased since then.[2] The current epidemiology in Europe varies from sporadic imported cases, to sporadic hospital outbreaks, to (inter-) regional spread between hospitals, to CRE being endemic in healthcare settings.[3] In the Netherlands, CRE are mainly found in hospitalised patients so far, but community-spread has been described.[4,5] CRE are therefore considered a growing public health threat.[6]
This chapter describes the prevalence of CRE/CPE, (molecular) epidemiology and outbreaks of CPE in the Netherlands.

Methods
Data on CRE/CPE were obtained from the ISIS-AR and the Type-Ned databases, mandatory notifications in OSIRIS, and outbreaks reported to the Early warning and response meeting of Healthcare associated Infections and AntiMicrobial Resistance (SO-ZI/AMR).[9,10]

Prevalence of carbapenem-resistant and carbapenemase-producing Enterobacterales based on ISIS-AR
These analyses focus on all Enterobacterales, divided into 4 categories: *Escherichia coli*, *Klebsiella pneumoniae, Enterobacter cloacae* complex and all other Enterobacterales species. The category *E. cloacae* complex in the ISIS-AR database contains the following species: *E. cloacae*, *E. hormaechei*, *E. asburiae*, *E. cancerogenus*, *E. kobei*, *E. roggenkampii*, and *E. cloacae* complex not further specified. We searched the ISIS-AR database (years 2021-2025) for diagnostic (infection-related) isolates that were tested for meropenem and/or imipenem by an automated system and/or gradient strip test. For *Proteus* spp., *Providencia* spp., *Serratia* spp. and *Morganella morganii*, only meropenem test results were included and analysed because of intrinsic low activity of imipenem against these species.[8] If results from an automated system and a gradient strip test were available then the result of the gradient strip was used.

Several breakpoints are used in this chapter: i) the screening breakpoint as defined by the Dutch national guideline[8] (which is >0.25 mg/L for meropenem and >1 mg/L for imipenem), and ii) the clinical breakpoints according to EUCAST v15.0, namely the clinical susceptible (S, which is ≤2 mg/L for both imipenem and meropenem) and the clinical resistant (R) breakpoint, which is >8 mg/L for meropenem and >4 mg/L for imipenem. Based on the crude automated and gradient strip test values, we categorized isolates as having either an:

i) MIC ≤ the screening breakpoint,
ii) MIC > the screening breakpoint and ≤ the EUCAST clinical S breakpoint,

iii) MIC > the clinical S breakpoint and ≤ the clinical R breakpoint (the clinical I category, i.e., susceptible with Increased dosing or exposure), or
iv) MIC > the clinical R breakpoint (also referred to as CRE).

Categories ii, iii and iv are together referred to as elevated MIC. If meropenem and imipenem were tested then the antibiotic with the highest category was used.

Subsequently, for 35 of the 36 laboratories that continuously submitted data to ISIS-AR from 2021 to 2025 (data from one laboratory were excluded due to incorrect test values) we searched the ISIS-AR and Type-Ned database for records on confirmatory tests (i.e., phenotypic tests for carbapenemase production or genotypic tests for carbapenemase genes). We included only one isolate per patient per bacterial species or complex per year. An isolate with data on confirmatory tests (further referred to as CPE determined by positive phenotypic and/or genotypic testing) was prioritized over an isolate of the same person with only an automated test and/or gradient strip test result. If multiple isolates per person were eligible for inclusion, we prioritized the most resistant isolate. To estimate resistance percentages, we counted the number of isolates with automated and/or gradient strip MIC test results in the respective categories in 2025, the number of isolates with available data on confirmatory tests and the number of isolates that were CPE confirmed per micro-organism species or complex. We calculated the annual percentage of isolates i) with an elevated MIC based on automated testing and/or gradient strip testing, and ii) categorized as CRE, and describe trends over time.

Molecular characteristics of carbapenemase-producing Enterobacterales and patient related characteristics based on Type-Ned
For the enhanced surveillance of CPE via Type-Ned, Dutch laboratories are requested to submit screening or diagnostic Enterobacterales isolates to the RIVM with a positive confirmatory test for carbapenemase production and/or a detected carbapenemase-encoding gene. A restriction is that the laboratory can only send the first species/carbapenemase gene combination per person per year. The RIVM allows consecutive isolates from the same person from the same lab if these are Enterobacterales species with other carbapenemase-encoding gene combinations when compared to the first isolate. The RIVM confirms the species by MALDI-ToF, determines the MIC for meropenem by Etest, and tests for carbapenemase production by the carbapenem inactivation method (CIM).[11] The presence of carbapenemase-encoding genes (carba-PCR on *bla*$_{NDM}$, *bla*$_{KPC}$, *bla*$_{IMP}$, bla$_{VIM}$, and *bla*$_{OXA-48}$-like) and mobile colistin resistance gene (*mcr*-1) are assessed by PCR. Next-generation sequencing (NGS) and Nanopore long-read sequencing is performed for all isolates that are CIM positive to describe trends in molecular epidemiology and to identify genetic clusters.[12] The data described in this chapter are based on the first unique CIM-positive Enterobacterales species/carbapenemase-encoding allele combination per person for the period 2021-2025.

Since 2022, due to the Russia-Ukraine war, a substantial number of CPE isolates were cultured from patients originating from Ukraine, who had

migrated or been evacuated to the Netherlands. Normally, these isolates would be excluded from further analysis because of the lack of a person ID (encrypted BSN). However, in the current analysis CPE from persons without a person ID were included for NGS and further molecular analysis if it represented a unique person, based on gender, age and postal code and when country of origin was Ukraine and/or if Ukrainian origin was confirmed by the MML. CPE from persons without a person ID not originating from Ukraine were not included in further analyses.

Whole-genome multi-locus sequence typing (wgMLST) was used to detect genetic clusters consisting of genetically highly related *E. coli*, *K. pneumoniae*, *E. cloacae* complex and *Citrobacter freundii* complex isolates and clusters are systematically assigned consecutive cluster numbers. A genetic cluster is defined per bacterial species and includes ≥2 highly related isolates of one species that differ typically ≤20 wgMLST alleles and ≤25 for *E. coli*.

Genetic clusters based on Type-Ned
Assigning genetic clusters started in 2018 and all sequenced isolates available from the national surveillance since 2014 were included in the wgMLST cluster analysis. Clusters solely consisting of multiple isolates from the same patient, included over different years and/or submitted by different laboratories, were not counted. Since the end of 2019, genetic clusters for CPE are reported to the submitting laboratories in Type-Ned in order to inform local infection prevention specialists and control further spread whenever possible.

Clinical/epidemiological characteristics of persons with carbapenemase-producing Enterobacterales based on mandatory notifications in OSIRIS
From 1 July 2019 onwards, CPE, either phenotypically or genotypically confirmed, is mandatorily notifiable on person level (not on isolate level). Accordingly, epidemiological patient data are reported by Municipal Health Services (MHS) via the national web-based system for notifiable diseases (OSIRIS).

Outbreaks based on SO-ZI/AMR
The SO-ZI/AMR database (see chapter 5.2.7 for more details) was interrogated for CPE outbreaks that were reported in 2025.[10]

Results

Prevalence of carbapenem-resistant and carbapenemase-producing Enterobacterales based on ISIS-AR

Absolute numbers of isolates and categorization according to automated and gradient strip MICs in 2025 are presented in Table 5.2.2.1. Of a total number of 287,165 isolates with an automated test or gradient strip test value for meropenem or imipenem (182,557 *E. coli,* 31,966 *K. pneumoniae,* 11,001 *E. cloacae* complex*,* and 61,641 other Enterobacterales species), an elevated MIC was found in 1.5% of isolates (4,303). Confirmed CPE among isolates with an elevated MIC were mostly found in *K. pneumoniae* (111/387, 28.7% of isolates with an elevated MIC), followed by *E. coli* (117/609, 19.2%), *E. cloacae* complex (27/395, 6.8%) and other Enterobacterales (33/2,912, 0.1%). Most CPE confirmation tests were performed for isolates in the category *E. cloacae* complex representing 1.5% of all isolates in the category, followed by other Enterobacterales (0.7%), *K. pneumoniae* (0.6%), and *E. coli* (0.1%).

Figure 5.2.2.1 shows the percentage of isolates with an elevated MIC and the percentage of isolates defined as CRE in the past 5 years. The overall prevalence of carbapenem resistant *E. coli* strains slightly increased between 2021 and 2025 from 0.00% to 0.04% (Figure 5.2.2.1a). For *K. pneumoniae*, the prevalence of carbapenem resistant strains increased between 2021 and 2025 from 0.09% to 0.30% (Figure 5.2.2.1a).

As for *E. cloacae* complex, the overall prevalence of carbapenem resistant strains increased between 2021 and 2025 from 0.05% to 0.23% (Figure 5.2.2.1b). For the other Enterobacterales species, the prevalence of carbapenem resistant strains increased between 2021 and 2025 from 0.02% to 0.04% (Figure 5.2.2.1b).

Molecular characteristics of carbapenemase-producing Enterobacterales and patient related characteristics based on Type-Ned

Carbapenemase-production was confirmed in 812 Enterobacterales isolates (unique species/carbapenemase allele combinations per person) obtained in 2025 from 689 patients with and 123 without an encrypted person ID. Forty-six (37%, 46/123) unique patients without a person ID were from Ukraine. The remainder 77 patients without person ID had unknown or variable countries of origin at time of submission and were not included, yielding 735 isolates in NGS analysis. The screening and diagnostic isolates were submitted to the RIVM by all Dutch medical microbiology laboratories.

The number of unique CPE isolates submitted to the RIVM was 245 in the COVID-19 year 2021, and continued to increase with 59.4% from 482 in 2022, 581 in 2023, and 699 in 2024, to 812 in 2025 (Figure 5.2.2.2a).

Table 5.2.2.1 *Results of MIC and confirmatory carbapenem susceptibility testing among diagnostic (infection-related) Enterobacterales isolates in 2025, in 35 laboratories participating in ISIS-AR*

	MIC*				
	MIC ≤ screening breakpoint **	**MIC > screening** and ≤ clinical S breakpoint *****	**MIC > clinical S and ≤ clinical R breakpoint *****	**MIC > clinical R breakpoint *****	**Total**
E. coli					
Total, N	181,948	474	34	101	182,557
CPE confirmatory test performed, N(% of total)	89 (0)	95 (20)	24 (71)	52 (52)	260 (0.1)
CPE confirmed, N(% of total)	22 (0)	55 (11.6)	16 (47)	46 (46)	139 (0.1)
K. pneumoniae					
Total, N	31,579	240	25	122	31,966
CPE confirmatory test performed, N(% of total)	22 (0.1)	56 (23.3)	22 (88)	96 (79)	196 (0.6)
CPE confirmed, N(% of total)	2 (0)	10 (4.2)	7 (28)	94 (77)	113 (0.4)
***E. cloacae* complex**					
Total, N	10,606	336	30	29	11,001
CPE confirmatory test performed, N(% of total)	36 (0.3)	83 (25)	21 (70)	22 (76)	162 (1.5)
CPE confirmed, N(% of total)	2 (0)	7 (2.1)	2 (7)	18 (62)	29 (0.3)
Other Enterobacterales****					
Total, N	58,729	2,829	52	31	61,641
CPE confirmatory test performed, N(% of total)	134 (0.2)	262 (9)	36 (69)	25 (81)	457 (0.7)
CPE confirmed, N(% of total)	1 (0)	9 (0.3)	8 (15)	16 (52)	34 (0.1)
All isolates					
Total, N	282,862	3,879	141	283	287,165

CPE confirmed = confirmation through phenotypical carbapenemase production test and/or genotypical carbapenemase gene test.
* Both automated and gradient strip MIC were used to define the 4 categories. If MICs of both test were available then the gradient strip MIC was used, even if the gradient strip MIC was lower than the automated MIC.
** Screening breakpoint according to NVMM guideline Laboratory detection of highly resistant microorganisms (MIC meropenem > 0.25 mg/L and/or MIC imipenem > 1 mg/L) (published November 2021).
*** Clinical breakpoints according to EUCAST guideline v.15.0 (i.e., clinical S (≤2 mg/L for both meropenem and imipenem and R (>8 mg/L for meropenem and >4 mg/L for imipenem).
**** All other Enterobacterales species present in the ISIS-AR database. For species within the *Proteus* spp., *Serratia* spp., *Providencia* spp. and *Morganella morganii* results of imipenem were excluded. Top 5 species are: *Proteus mirabilis*, *Klebsiella oxytoca*, *Citrobacter koseri*, *Serratia marcescens*, *Morganella morganii*.

Figure 5.2.2.1a *Proportion of isolates with elevated MIC and proportion of CRE isolates (%) in E. coli and K. pneumoniae by year, in 35 laboratories, ISIS-AR 2021-2025*

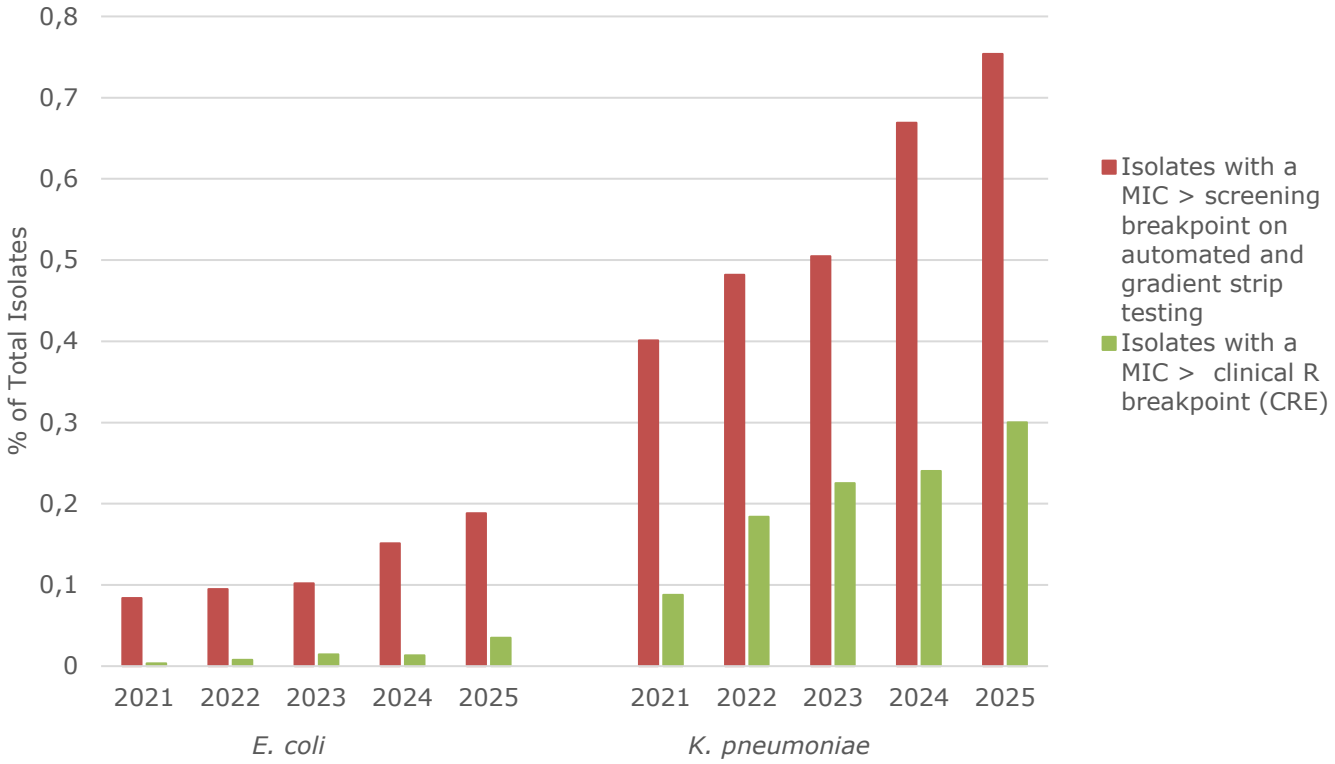
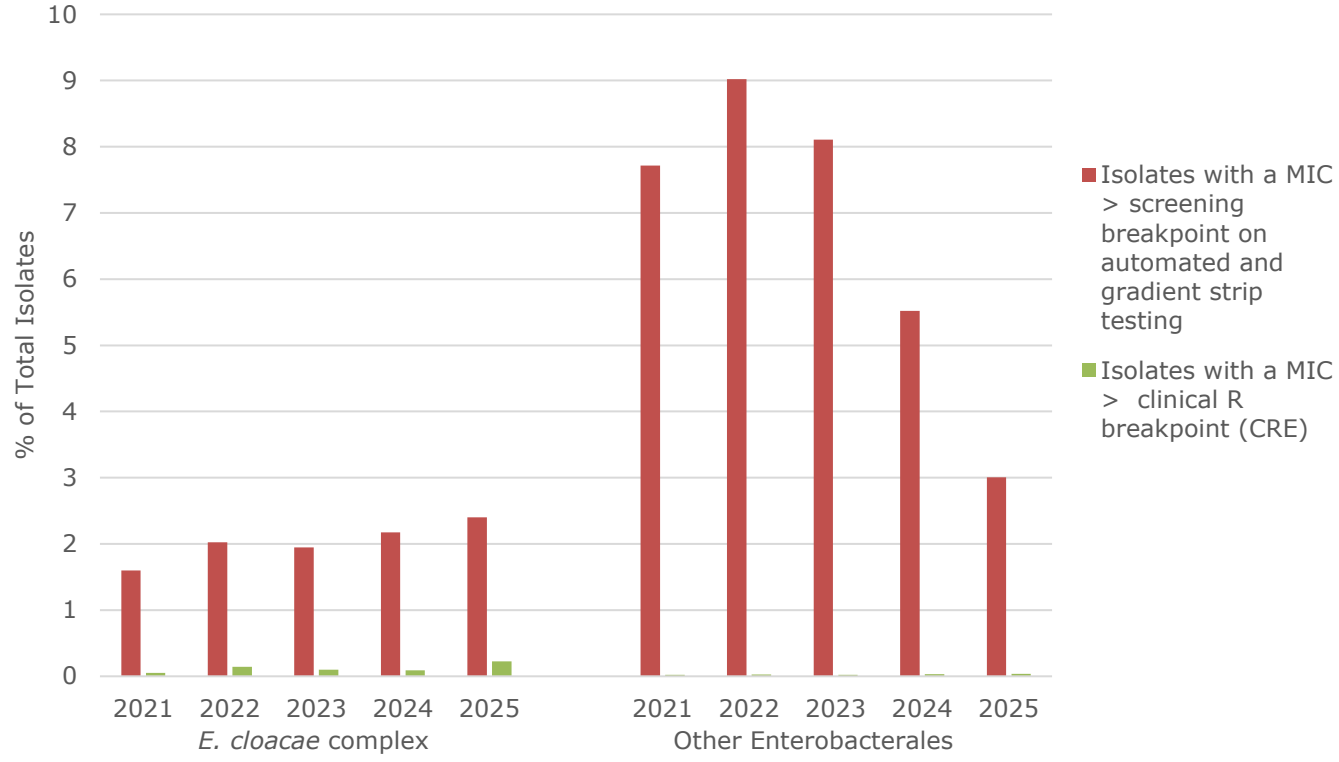


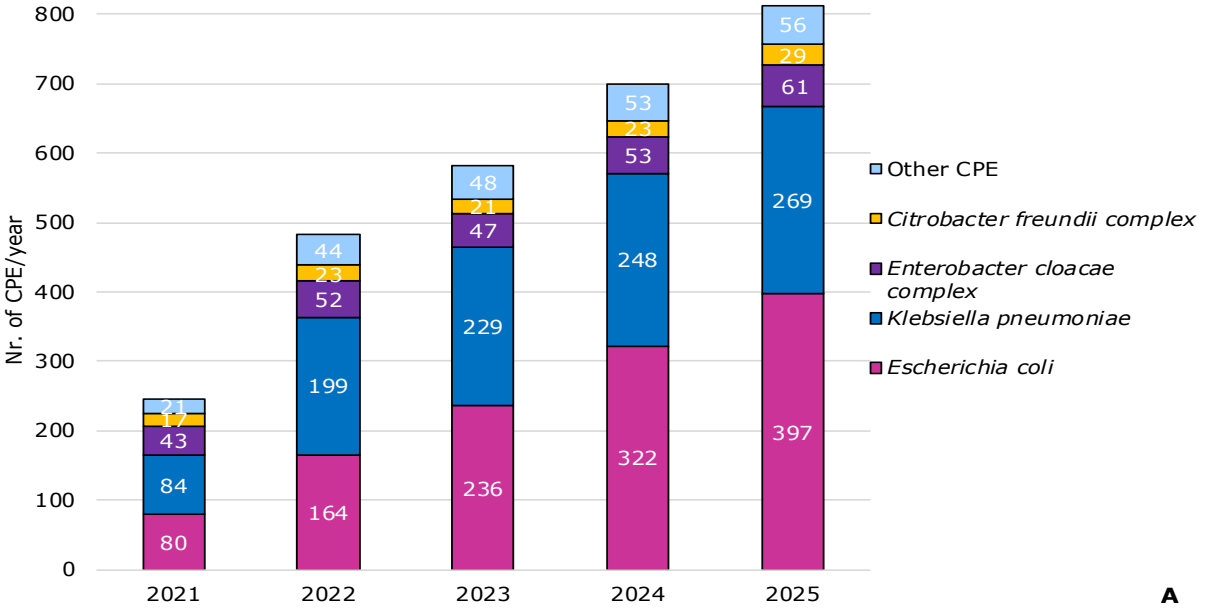
Figure 5.2.2.1b *Proportion of isolates with elevated MIC and proportion of CRE isolates (%) in E. cloacae complex and other Enterobacterales by year, in 35 laboratories, ISIS-AR 2021-2025*



Of the 812 CPE isolates in 2025, 397 (49%) were *E. coli*, 269 (33%) *K. pneumoniae*, 61 (8%) *E. cloacae* complex, 29 (3%) *C. freundii* complex, and the remaining 56 (7%) isolates belonged to other species (Figure 5.2.2.2a). Of the CPE analysed in 2025, 31% (226/735) carried a bla_{OXA-48}-like gene ($bla_{OXA-162}$, $bla_{OXA-181}$, $bla_{OXA-232}$, $bla_{OXA-244}$, $bla_{OXA-245}$, $bla_{OXA-484}$, $bla_{OXA-1205}$ or $bla_{OXA-1207}$). The bla_{NDM-5} gene ranked the second (22%, 164/735) carbapenemase-encoding gene in CPE isolates from 2025, while *bla*$_{OXA-48}$ ranked third with 16% (119/735) and *bla*$_{NDM-1}$ fourth (11%, 81/735) (Figure 5.2.2.2b). In 2025, the *bla*$_{OXA-48}$-like alleles were found in 45% (180/397) and 13% (34/269) of the *E. coli* and *K. pneumoniae* isolates, respectively. The *bla*$_{NDM-5}$ gene was found in 28% (112/397) and 10% (27/269) of the *E. coli* and *K. pneumoniae* isolates, respectively. Conversely, *bla*$_{NDM-1}$ was found predominantly in *K. pneumoniae* isolates (15%, 41/269) and only in 4% (14/397) of the *E. coli* isolates. The absolute number of OXA-48-producing CPE isolates remained relatively stable the past 5 years (Figure 5.2.2.2b). There was a proportional increase from 10% in 2021 to 28% in 2025 of other OXA-48-like-carrying CPE (Figure 5.2.2.2b).

When the EUCAST clinical breakpoints were applied, 393/812 (48%) of the CPE isolates were resistant (MIC >8 mg/L) to meropenem and 346/812 (43%) were susceptible for meropenem (MIC ≤2 mg/L). Nine percent (73/812) of the CPE were susceptible with increased exposure (MIC >2 and ≤8 mg/L). Notably, a considerable fraction of 142/812 (17%) of the CPE had a MIC for meropenem of ≤0.25 mg/L, as determined by E-test, questioning the lower limit of the MIC range for meropenem of semi-automated systems like Vitek (BioMérieux, i.e., ≤0.25 mg/L) and Phoenix (BD, i.e., ≤0.125 mg/L) for careful detection of all possible CPE's. In general, a larger proportion of the *K. pneumoniae* isolates (78%, 209/269) was meropenem resistant compared to the *E. coli* isolates (34%, 135/397), irrespective of the carbapenemase-encoding genes present. Sixty-three of the 144 (44%) *bla*$_{OXA-244}$ *E. coli* isolates submitted in 2025 and 10/17 (59%) of the *bla*$_{OXA-181}$ carrying *E. coli* had MICs for meropenem ≤0.25 mg/L. Only 28/119 (23%) of the CPE carrying *bla*$_{OXA-48}$ had a MIC above the clinical breakpoint for meropenem resistance (MIC >8 mg/L), while this was 135/164 (82%) for CPE carrying *bla*$_{NDM-5}$. Eight percent (66/812) of the CPE carried two carbapenemase-encoding genes, and in these cases 95% (63/66) of the isolates were resistant for meropenem. In 13/812 (2%) of the isolates no carbapenemase-encoding gene was detected. Of these isolates, 11 (73%) were Enterobacter spp. and 2 (38%) from other species. The nature of the apparent carbapenemase production in *Enterobacter* spp. is explained by the presence of Ambler class C-type (AmpC) of enzymes such as *bla*$_{ACT}$ or *bla*$_{MIR}$ in the absence of porins and/or AmpC-type regulatory genes.[13]

Figure 5.2.2.2 *Numbers of carbapenemase-producing Enterobacterales (CPE), per species (a), per carbapenemase allele (b), and relative contribution of detected carbapenemase genes (c), based on Type-Ned, unique species/carbapenemase allele combinations per person, 2021-2025*



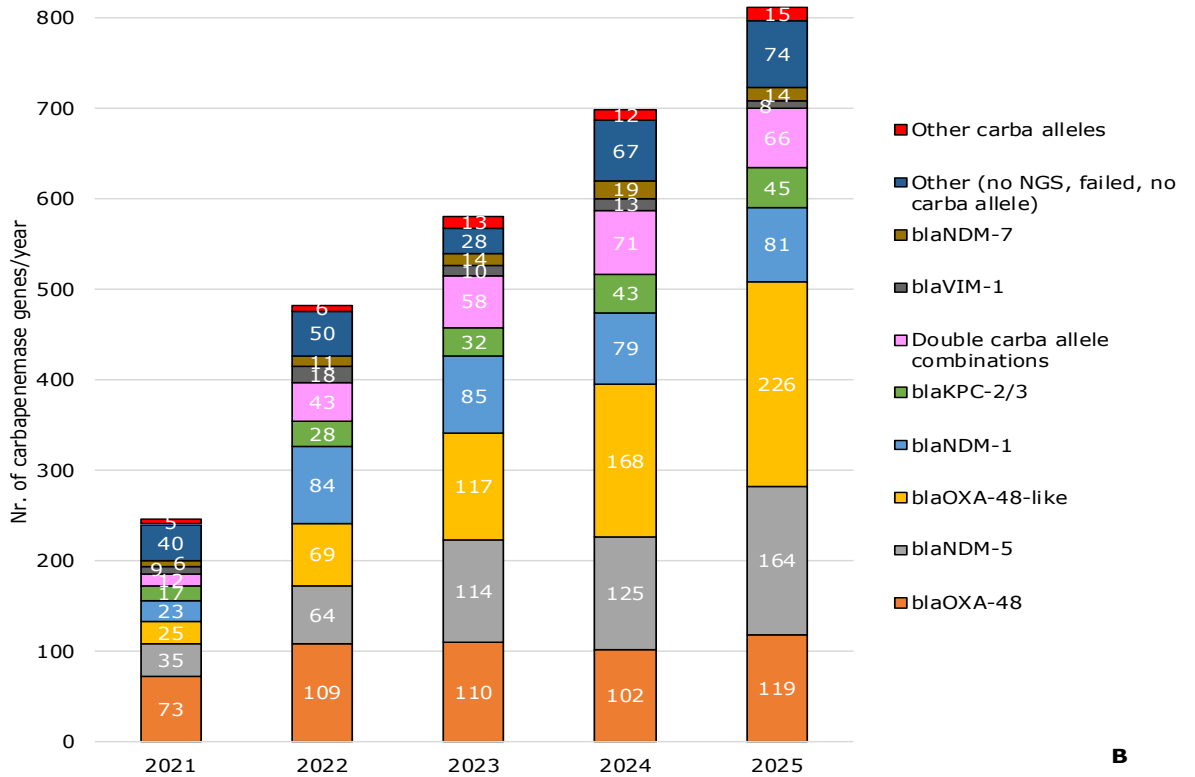
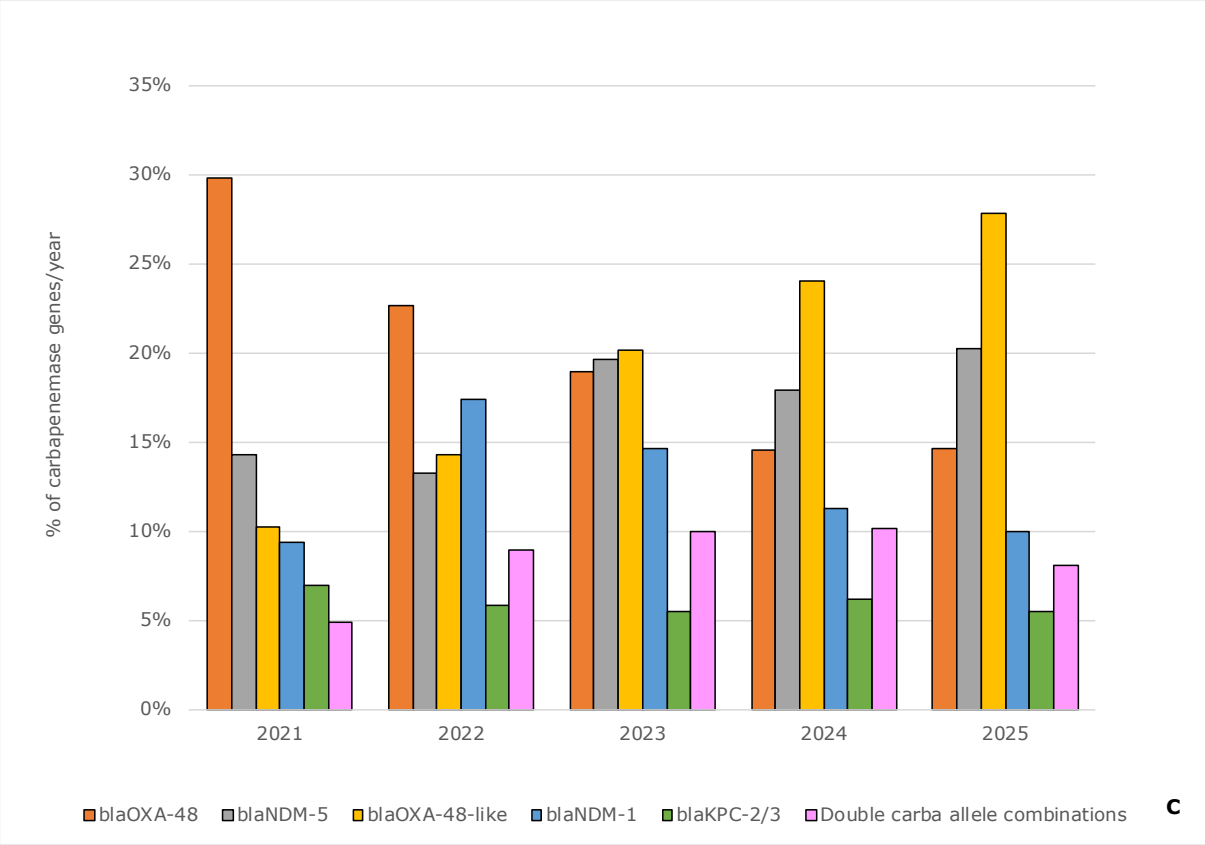


Figure 5.2.2.2 (continued) *Numbers of carbapenemase-producing Enterobacterales (CPE), per species (a), per carbapenemase allele (b), and relative contribution of detected carbapenemase genes (c), based on Type-Ned, unique species/carbapenemase allele combinations per person, 2021-2025*



Relatedness and genetic clusters among carbapenemase-producing Enterobacterales based on Type-Ned
Between 2021 and 2025, the CPE that could be typed by multilocus sequence typing (MLST) revealed a waxing and waning of the vast majority of distinct MLST sequence types through the years (not shown). However, there is persistence of globally epidemic and multidrug-resistant lineages in the top 15 of most commonly detected MLST sequence types, such as *K. pneumoniae* ST147, ST307, ST395 and *E. coli* ST38, ST167, and ST410 among other STs in the Netherlands (Table 5.2.2.2).

Based on species-specific whole-genome multilocus sequence typing (wgMLST), 1264 of the 2819 (45%) isolates from 2021-2025 fell in one of the detected 320 genetic clusters, including clusters partially containing older isolates (<2021). The species most involved were: *E. coli* (151 clusters), *K. pneumoniae* (123 clusters), *E. cloacae* complex (19 clusters), *C. freundii* complex (12 clusters) and *Proteus mirabilis* (6 clusters). The fifteen largest clusters are shown in Table 5.2.2.3.

In September 2025, a sudden emergence of infections/colonisations with *E. hormaechei* ST1344 carrying *bla*$_{\text{NDM-5}}$ on an IncX3-plasmid was observed, without epidemiological links between patients. This prompted a coordinated investigation for related cases in the European Union

(EU)/European Economic Area (EEA). Up to May 2026, 57 cases (29 female/28 male; median age: 73 years) were confirmed to be part of a cross-border outbreak affecting seven countries with the earliest case occurring in March 2025. Analysis using cgMLST revealed that isolates clustered with ≤ 4 allelic differences. The outbreak investigation, including exposure questionnaires, revealed that many of the patients (n = 45) were hospitalised at the time of sampling, some with extensive prior medical treatment, and only three reported travel abroad. A source could not be identified.[14]

Table 5.2.2.2 *Results of multilocus sequence typing (MLST) of 2819 CPE isolates from 2021-2025**

Species	MLST sequence type	2021	2022	2023	2024	2025	Total
K. pneumoniae	147	6	35	64	56	51	212
K. pneumoniae	307	10	32	27	28	29	126
E. coli	167	5	12	25	34	32	108
E. coli	38	8	13	20	22	36	99
K. pneumoniae	395	3	18	22	21	26	90
E. coli	410	2	14	17	20	24	77
E. coli	131	2	7	11	19	27	66
E. coli	10	3	9	14	17	16	59
E. coli	69	2	5	8	18	25	58
E. coli	361	1	8	16	13	19	57
E. coli	648	6	5	10	10	21	52
E. coli	405	2	5	16	11	17	51
E. clocacae complex	121	10	13	6	5	10	44
K. pneumoniae	11	7	8	10	14	5	44
K. pneumoniae	16	4	8	10	9	8	39
Not shown	Various	174	290	305	402	466	1637
Total		**245**	**482**	**581**	**699**	**812**	**2819**

** Red indicates high number of isolates with specific MLST sequence type, while blue indicates low number of isolates with MLST sequence type.*

Table 5.2.2.3 *The fifteen largest genetic clusters by wgMLST, based on the number of patients between 2021 and 2025*

Species	MLST	Carba-alleles	Year start	n (all years)	n 2021-2025	Meropenem MIC	Remarks
K. pneumoniae	ST147	bla_{NDM-1} a/o bla_{OXA-48}	2022	44	44	93% R	multi-institutional; Ukraine
E. cloacae complex	ST121	bla_{OXA-48}	2016	56	41	98% S	>80% 1 institute
E. coli	ST127	bla_{OXA-48}	2015	44	30	100% S	multi-institutional
E. coli	ST13730	$bla_{OXA-244}$	2022	25	25	92% S	multi-institutional; multi-country (9x Türkiye)
E. coli	ST38	bla_{OXA-48}	2015	28	21	95% S	multi-institutional; multi-country
C. freundii complex	ST22	bla_{NDM-5}	2018	57	19	68% R	>80% 1 institute
K. pneumoniae	ST39	bla_{KPC-2}	2022	18	18	100% R	multi-institutional; Ukraine
E. coli	ST38	$bla_{OXA-244}$	2016	32	18	100% S	multi-institutional; multi-country
E. *coli*	ST648	bla_{NDM-5}	2021	17	17	61% R	multi-institutional; multi-country
K. pneumoniae	ST101	bla_{KPC-3}	2022	16	16	100% R	multi-institutional; Ukraine
K. pneumoniae	ST307	bla_{NDM-7}	2017	19	15	93% R	multi-institutional; Morocco
E. cloacae complex	ST1344	bla_{NDM-5}	2025	15	15	93% R	multi-institutional; multi-country (EU)[14]
E. coli	ST167	bla_{NDM-5}	2024	15	15	87% R	>80% 2 institutes
K. pneumoniae	ST23	bla_{NDM-1} a/o bla_{OXA-48}	2022	14	14	93% R	multi-institutional; Ukraine
P. stuartii	N.A.	bla_{NDM-1}	2022	12	12	62% S	multi-institutional; Ukraine

Multi-institutional: at least 5 different submitting laboratories, no lab/hospital > 50%.
Countries mentioned: mix of recent hospitalisation (< 2 months ago), visit or country of birth.
N.A.: not assigned

Clinical/epidemiological characteristics of persons with carbapenemase-producing Enterobacterales based on mandatory notifications in OSIRIS

Between 1 January 2025 and 31 December 2025, 666 CPE positive persons were sampled and notified in OSIRIS (Table 5.2.2.4). This is much higher than the previous years (n=201 in 2021, n=377 in 2022, n=486 in 2023, and n=580 in 2024). The median age of the 666 persons was 60 (range 0 – 100, interquartile range 40 – 74) years and 371 (56%) were male.

In 2025, 30% (202/666) were sampled as part of routine diagnostic procedures rather than risk-based screening, which is similar to the pre-COVID years, but higher than in preceding years (25% (50/201) in 2021, 23% (86/377) in 2022, 24% (118/486) in 2023, and 24% (139/580) in 2024). The most common reported infection among patients with a diagnostic isolate was urinary tract infection (61%, 125/202), which was much higher than previous years (44% in 2021 increasing to 51% in 2024). Most patients with a diagnostic isolate had

no known risk factor reported or it was unknown whether the person had a risk factor (63%) (Figure 5.2.2.3). Hospitalization abroad for at least 24 hours during two months prior to sampling occurred in 7% of patients with a diagnostic isolate, which was comparable to 2024 (9%), 2023 (10%), and 2021 (8%), but lower than in 2022 (21%) (Table 5.2.2.4 and Figure 5.2.2.3). Türkiye (n=5) and Morocco (n=3) were most often reported as countries of hospitalization (Table 5.2.2.5). Of the 127 persons with a diagnostic isolate and no known risk factor, or for whom the presence of risk factors was unknown, 41 (32%) had undergone an invasive medical procedure or had had an invasive medical device within twelve months prior to sampling, 60 (47%) had not had an invasive medical procedure/device while for 26 (20%) persons this information was unknown. Persons with a diagnostic isolate and no known risk factor, or for whom the presence of risk factors was unknown, were older than persons with a risk factor (median age 66 versus 61 years, respectively, p=0.04) and had less often had an invasive medical procedure or device within twelve months prior to sampling (32% versus 51%, respectively, p=0.03). No other differences were observed between the groups.

In 2025, 68% (455/666) of samples were obtained for routine or targeted CPE screening (e.g. on admission, during prolonged hospitalization or as part of selective decontamination regimens), a lower proportion than in previous years (73 – 75% in 2021–2024). Hospitalization abroad for at least 24 hours within two months before sampling was the most common reported risk factor for CPE among persons with a screening isolate in 2025 (54%) which was lower than 2022 (62%) and 2023 (61%), but higher than 2021 (49%) and 2024 (49%) (Table 5.2.2.4 and Figure 5.2.2.3). Ukraine and Türkiye (both n=32), Egypt (n=27) and Morocco (n=20) were most often reported as countries where hospitalization had occurred (Table 5.2.2.5). No risk factor (and thus detected by routine screening and not by targeted screening), or it was unknown whether the person had a risk factor, was reported in 22%, which was lower than 2021 (27%) and 2024 (26%), but higher than in 2022 (18%) and 2023 (19%). Of these 99 persons with no known risk factor, or for whom the presence of risk factors was unknown, 36 (36%) had undergone an invasive medical procedure or had had an invasive medical device within twelve months prior to sampling, 32 (32%) had not had an invasive medical procedure/device while for 31 (31%) persons this information was unknown.

Table 5.2.2.4 *Epidemiological data of notifications of persons carrying CPE, stratified by reason for sampling, OSIRIS, 2025*

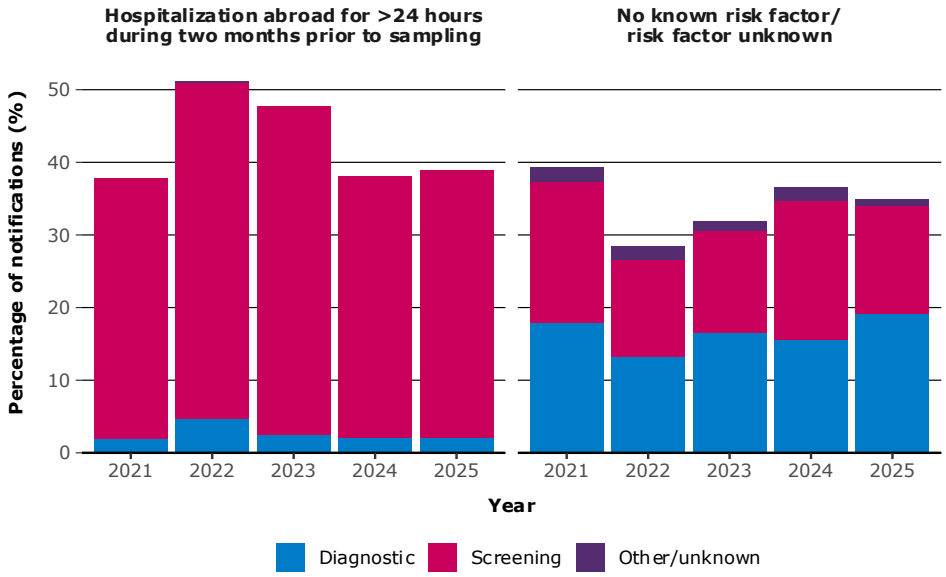
Characteristic	Total[a] N (%)	Diagnostic N (%)	Screening N (%)
N	666	202	455
Location of sampling			
Outpatient/emergency departments or by a general practitioner	322 (48.3)	133 (65.8)	187 (41.1)
Inpatient departments (excl. Intensive care units)	288 (43.2)	61 (30.2)	220 (48.4)
Intensive care units	49 (7.4)	8 (4.0)	41 (9.0)
Other/unknown	7 (1.1)	0 (0.0)	7 (1.5)
Residence			
Living independently	508 (76.3)	171 (84.7)	330 (72.5)
Rehabilitation centre	16 (2.4)	5 (2.5)	11 (2.4)
Nursing or elderly home/facilities for small-scale housing for elderly	28 (4.2)	9 (4.5)	19 (4.2)
Asylum seekers centre	34 (5.1)	3 (1.5)	31 (6.8)
Other/unknown	80 (12.0)	14 (6.9)	64 (14.1)
Invasive medical procedure/device within twelve months prior to sampling[b]			
No	196 (29.4)	88 (43.6)	107 (23.5)
Surgery	205 (30.8)	49 (24.3)	153 (33.6)
Other (incl. endoscopy, cystoscopy, urinary catheter, renal dialysis)	97 (14.6)	27 (13.4)	70 (15.4)
Yes but unknown which invasive procedure(s)	17 (2.6)	3 (1.5)	14 (3.1)
Unknown	151 (22.7)	35 (17.3)	111 (24.4)
Identified risk factors[b]			
Hospitalization abroad for >24 hours during two months prior to sampling	259 (38.9)	14 (6.9)	245 (53.8)
Already known carrier of CPE	24 (3.6)	8 (4.0)	16 (3.5)
Direct contact with a CPE-positive person in the immediate surroundings	4 (0.6)	0 (0.0)	4 (0.9)
Contact with a hospital abroad twelve months prior to sampling in a different way than >24 hours within two months prior to sampling	62 (9.3)	20 (9.9)	41 (9.0)
Travelling abroad twelve months prior to sampling without hospitalization or visiting a hospital	66 (9.9)	29 (14.4)	36 (7.9)
(Prior) stay in a healthcare facility where a (possible) CPE outbreak is/was occurring	18 (2.7)	4 (2.0)	14 (3.1)
No known risk factor/risk factor unknown	233 (35.0)	127 (62.9)	99 (21.8)

[a] Including 9 persons for whom the reason for sampling was unknown
[b] Listed in order of considered importance: in case of multiple answers the person is included in the highest listed answer

Table 5.2.2.5 *Top 5 parts of the world where persons with hospitalization abroad for at least 24 hours during two months prior to sampling were admitted, OSIRIS, 2025*

Characteristic	Total N (%)	Diagnostic N (%)	Screening N (%)
N	259	14	245
Hospitalized in a country in			
Western Asia	63 (24.3)	7 (50.0)	56 (22.9)
Northern Africa	52 (20.1)	4 (28.6)	48 (19.6)
Eastern Europe	46 (17.8)	1 (7.1)	45 (18.4)
Southern Europe	32 (12.4)	1 (7.1)	31 (12.7)
Southern Asia	25 (9.7)	0 (0.0)	25 (10.2)
Other region of the world/>1 region/unknown	41 (15.8)	1 (7.1)	40 (16.3)

Figure 5.2.2.3 *Hospitalization abroad for at least 24 hours during two months prior to sampling and no known risk factor/risk factor unknown among CPE positive persons, stratified by reason for sampling, OSIRIS, 2021-2025*



Outbreaks based on SO-ZI/AMR

In 2025, four new outbreaks with CPE were reported to SO-ZI/AMR (Table 5.2.2.6). See chapter 5.2.7 for more details about SO-ZI/AMR.

Table 5.2.2.6 *Outbreaks of carbapenemase-producing Enterobacterales reported in 2025 to the Early warning and response meeting for Healthcare-associated Infections and Antimicrobial Resistance (SO-ZI/AMR)*

Region	Facility	Micro-organism	Gene(s)	No. of patients
West	Hospital	*E. cloacae* complex	$bla_{\text{OXA-48}}$	11
East	Nursing home	*K. aerogenes*	$bla_{\text{NDM-1}}$	4
West	Rehabilitation clinic	*E. coli*	$bla_{\text{NDM-5}}$	4
East	Hospital	*K. pneumoniae*	$bla_{\text{PKC-2}}$	3

Discussion
In ISIS-AR, the prevalence of carbapenem resistance has increased in 2025 for all Enterobacterales. For *E. coli,* it has increased from 0% in 2021 to 0.04% in 2025. Carbapenem resistance in *K. pneumoniae* is higher, and has increased from 0.09% in 2021 to 0.3% in 2025. Carbapenem resistance in *E. cloacae* complex species is also higher and increased from 0.05% in 2021 to 0.2% in 2025. The carbapenem resistance for the other Enterobacterales species has slightly increased from 0.02% in 2021 to 0.04% in 2025.

The percentage of CPE confirmatory tests performed differed between the various species categories within Enterobacterales even among the isolates with MIC > the clinical R breakpoint, but overall stayed between 52-81%. This was partly a result of lab-specific algorithms for additional testing after automated antimicrobial susceptibility testing, which were not always in accordance with the national guideline. In addition, due to variation in laboratory-specific algorithms, the selection of included laboratories can substantially affect the calculated resistance percentages in nationally aggregated data.

In 2025, the number of persons with carbapenemase-producing Enterobacterales (based both on mandatory notifications and on the number of isolates submitted to the RIVM) was considerably higher than in previous years and exceeded pre-COVID levels. The absolute number of persons with samples taken for diagnostic purposes as well as for routine or targeted screening increased in 2025 compared to previous years, and the proportion of diagnostic isolates/notifications was higher than before. This increase in the absolute numbers of targeted and routine screening samples, together with the relative increase in the share of diagnostic samples, is likely related to the resumption of international travel following the COVID-19 pandemic and the transfer of patients from Ukraine.

Still, in 14% of the persons with CPE, the origin or acquisition remains inexplicable as there were no reported risk factors, or risk factors were unknown, and no invasive medical procedure or invasive medical device within twelve months prior to sampling was reported. This proportion, however, remained stable over the last 5 years.
A considerable part (45%) of the isolates from 2021-2025 fell in one of the detected 320 genetic clusters, including clusters partially containing older isolates (<2021). The fifteen largest clusters had a diversity in species, carbapenem alleles and starting year. Some clusters were a single institute cluster, suggesting nosocomial spread or a point source, some had a link to foreign hospitals or other connections abroad and some showed a mix.

The introduction of Nanopore long-read sequencing on all carbapenemase-producing isolates allows the identification of genetic clusters. Genetic clustering does not prove direct transmission or an outbreak. Isolates that cluster together based on wgMLST may still be different in plasmid content and/or resistome and may lack an epidemiological link in time and place. To identify transmission, information on epidemiological links would be needed.

Conclusions

- The overall percentage of Enterobacterales isolates with elevated MIC value for meropenem or imipenem (i.e., > the screening breakpoint of >0.25 mg/L and >1 mg/L, respectively) was 1.5% in 2025. The overall percentage of Enterobacterales isolates with a resistant MIC for meropenem and/or imipenem was 0.1% in 2025.
- The prevalence of CPE confirmed isolates among *E. coli* was 0.1%, among *K. pneumoniae* 0.4%, *E. cloacae* complex 0.3% and other Enterobacterales 0.1%.
- The prevalence of CRE (confirmed by E-test) among *E. coli* was 0.04%, among *K. pneumoniae* 0.3%, *E. cloacae* complex 0.23% and other Enterobacterales 0.04%.
- In 2025, the number of CPE isolates submitted to the RIVM was considerably higher than in previous years and was succeeding pre- and post-COVID totals. The increase is partially attributable to the transfer of Ukrainian patients to the Netherlands and increased travelling after the COVID-years
- The predominant CPE species in 2025 were *E. coli*, *K. pneumoniae*, *E. cloacae* complex, and *C. freundii* complex, respectively.
- The most frequently identified carbapenemase encoding genes in Enterobacterales were *bla*$_{\text{OXA-48}}$-like (28%), *bla*$_{\text{NDM-5}}$ (20%), *bla*$_{\text{OXA-48}}$ (15%), and *bla*$_{\text{NDM-1}}$ (10%), respectively.
- *bla*$_{\text{OXA-48}}$-like (i.e., *bla*$_{\text{OXA-162}}$, *bla*$_{\text{OXA-181}}$, *bla*$_{\text{OXA-232}}$, *bla*$_{\text{OXA-244}}$, *bla*$_{\text{OXA-245}}$, *bla*$_{\text{OXA-484}}$, *bla*$_{\text{OXA-1205}}$ and *bla*$_{\text{OXA-1207}}$) carrying CPE continues to increase in the Netherlands.
- Notably, 17% of CPE isolates exhibited meropenem MICs ≤0.25 mg/L, as determined by Etest. This finding raises concerns about the ability of semi-automated susceptibility testing systems, such as Vitek, with lower detection limits of 0.25 mg/L, respectively, to reliably identify all CPE, particularly given the EUCAST-recommended screening threshold of >0.125 mg/L. The MIC for meropenem was generally higher for carbapenemase-producing *K. pneumoniae* than for *E. coli* isolates.
- Thirty percent of CPE cases were identified in diagnostic - mainly urine – samples, which is higher than in previous years.
- In 39% of patients, there is a relation with hospitalization abroad for more than 24 hours during the two months prior to sampling (7% and 54% among persons with a diagnostic and screening isolate, respectively), which was higher than in 2022 and 2023 (48 – 51%), but equal to 2021 and 2024. Türkiye, Ukraine, Egypt, and Morocco are the countries that are most often reported.
- In 35% of the CPE positive persons, no known CPE risk factor was identified or it was unknown whether the person had a risk factor (63% and 22% among persons with a diagnostic and screening isolate, respectively), which is within ranges observed in previous years (28 – 39% between 2021 and 2024). Persons with a diagnostic isolate and no known risk factor, or for whom the presence of risk factors was unknown, were older than persons with a risk factor (median age 66 versus 61 years, respectively) and had less often had an invasive medical procedure or device within twelve months prior to sampling (32% versus 51%, respectively).
- In 14% of the CPE positive persons, no known risk factor and no invasive medical procedure or invasive medical device within twelve months prior to sampling was reported, leaving the origin or acquisition of the CPE unexplained. This proportion was stable over time, ranging from 13% to 14% between 2021 and 2024.

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5.2.3 *Carbapenem-resistant and carbapenemase-producing Pseudomonas aeruginosa*

Introduction
Pseudomonas aeruginosa is a common nosocomial pathogen, intrinsically resistant to various broad-spectrum antibiotics. The emergence of multidrug-resistant (MDR) *P. aeruginosa* by acquired resistance mechanisms is a problem of global concern, and in 2024 the World Health Organization classified carbapenem-resistant *P. aeruginosa* as 'high-priority' pathogen.[1]

Methods
Data on carbapenem-resistant and carbapenemase-producing *P. aeruginosa* (CPPA) were obtained from ISIS-AR and the national enhanced CPPA surveillance via Type-Ned.

Prevalence of carbapenem-resistant and MDR P. aeruginosa based on ISIS-AR
From the ISIS-AR database, the first *P. aeruginosa* isolate per patient per year was extracted for the period 2021-2025. To avoid overestimation of the percentage carbapenem-resistant *P. aeruginosa* caused by active screening for highly resistant isolates, only data on diagnostic cultures (as categorized by the reporting laboratory) from blood, cerebrospinal fluid, urine, lower respiratory tract, and wound or pus were included in the analysis. Carbapenem resistance was defined as (1) a positive test for carbapenemase gene detection and/or carbapenemase production and/or (2) phenotypic resistance to meropenem and/or imipenem. The phenotypical tests were reinterpreted according to the 2025 EUCAST breakpoints v15.0 for meropenem (applying the cut-off of >8 mg/L or <14 mm) and/or imipenem (cut-off >4 mg/L or <20 mm). Of note, according to the Dutch HRMO guideline[4], a test for carbapenemase production is only required if phenotypic resistance to carbapenems is present in combination with resistance to tobramycin.

In addition, the percentage of *P. aeruginosa* that was MDR was calculated. Multidrug-resistance was defined as resistance to ≥3 antimicrobials or antimicrobial groups among fluoroquinolones (resistance to ciprofloxacin and/or levofloxacin), aminoglycosides (resistance to tobramycine), carbapenems (resistance to meropenem and/or imipenem), ceftazidime, and piperacillin-tazobactam, based on re-interpretation of test-values according to the EUCAST 2025 breakpoints. Only isolates which were tested for all five groups of antimicrobials were included in the latter analysis. The numbers were based on a selection of 36 medical microbiological laboratories (MMLs) (out of a total of 46 MMLs in the Netherlands), which provided complete data on the last five years (2021 to 2025).

Molecular characteristics of carbapenemase-producing P. aeruginosa *and patient related characteristics based on Type-Ned*
In 2020, the enhanced CPPA surveillance via Type-Ned was implemented. All Dutch MMLs participate and are requested to submit *P. aeruginosa* isolates to the RIVM with an MIC for meropenem of >2 mg/L and/or an MIC for imipenem >4 mg/L and/or carbapenemase production

and/or a detected carbapenemase-encoding gene. Again, it should be noted that according to the Dutch HRMO guideline[4], a test for carbapenemase production is only required if phenotypic resistance to carbapenems is present in combination with resistance to tobramycin. Consequently, isolates that are phenotypically carpapenem resistant but tobramycine susceptible will not be further tested for carbapenemase and will presumably not be submitted to Type-Ned.

A restriction is that the laboratory can only send the first isolate per person per year. The RIVM allows consecutive isolates from the same person if these are *P. aeruginosa* isolates with different carbapenemase-encoding gene combinations when compared to the first isolate. The RIVM confirms the species by MALDI-ToF, determines the MIC for meropenem by Etest, and detects carbapenemase production by the carbapenem inactivation method (CIM).[2] The presence of carbapenemase-encoding genes is assessed by PCR (carba-PCR on *bla*$_{NDM}$, *bla*$_{KPC}$, *bla*$_{IMP}$, *bla*$_{VIM}$, and *bla*$_{OXA}$), next-generation sequencing (NGS) and Nanopore long-read sequencing for all isolates that are CIM positive. The data described in this chapter are based on the first unique CIM-positive *P. aeruginosa* isolate/carbapenemase-encoding allele combination per person with a person ID for the period 2021-2025, and all of these isolates collected in 2025 were included. Samples without a person ID were included for further analysis if it was confirmed that it represented a unique person, based on sex, age and postal code.

Based on the results of whole-genome multi-locus sequence typing (wgMLST), closely related CPPA isolates were grouped in genetic clusters and assigned consecutive cluster numbers. A genetic cluster was defined as ≥2 CPPA isolates that differ ≤15 wgMLST alleles.[3] Assigning genetic cluster numbers in the surveillance started in 2020, but the genetic cluster numbers in the results of this report also include all sequenced *P. aeruginosa* isolates available from (pilot) surveillance studies from previous years available at the RIVM. When multiple isolates within the same cluster were submitted for the same patient, only the first isolate was included in the analysis, also if the different isolates were submitted in different years and/or by different laboratories. In addition to submitting an isolate, Dutch laboratories are also requested to fill in a clinical/epidemiological questionnaire on characteristics of the patient from whom the CPPA isolate was obtained.

Results

Prevalence of carbapenem-resistant and MDR P. aeruginosa based on ISIS-AR

In the ISIS-AR database, 4% (1,108/25,207) of the diagnostic *P. aeruginosa* isolates were carbapenem-resistant in 2025 (Table 5.2.3.1). The percentage of carbapenem-resistant *P. aeruginosa* isolates was slightly higher among *P. aeruginosa* isolates from hospital compared to GP patients. In contrast to previous years, the resistance percentage among patients in intensive care units (ICUs) was similar to the percentages in outpatient and inpatient departments excluding ICUs. The observed proportion of resistance appears to be relatively stable over the 2021-2025 time period, except for a drop in the proportion of carbapenem resistance in *P. aeruginosa* isolates from ICUs in 2025 compared to the previous years 2022-2024 during which the resistance

percentages were higher than in the COVID-years 2020 and 2021 (Figure 5.2.3.1). Of the total number of 1,108 carbapenem-resistant *P. aeruginosa* isolates, for 157 (14%) isolates, data on tests for carbapenemase production was available. Of these, 22 (14%) showed a positive result. Of the 951 carbapenem-resistant *P. aeruginosa* isolates without test results on carbapenemase production, 91% (867/951) were susceptible to tobramycin.

Table 5.2.3.1 *Carbapenem-resistant P. aeruginosa among diagnostic P. aeruginosa isolates in the Netherlands in 2025, based on ISIS-AR data*

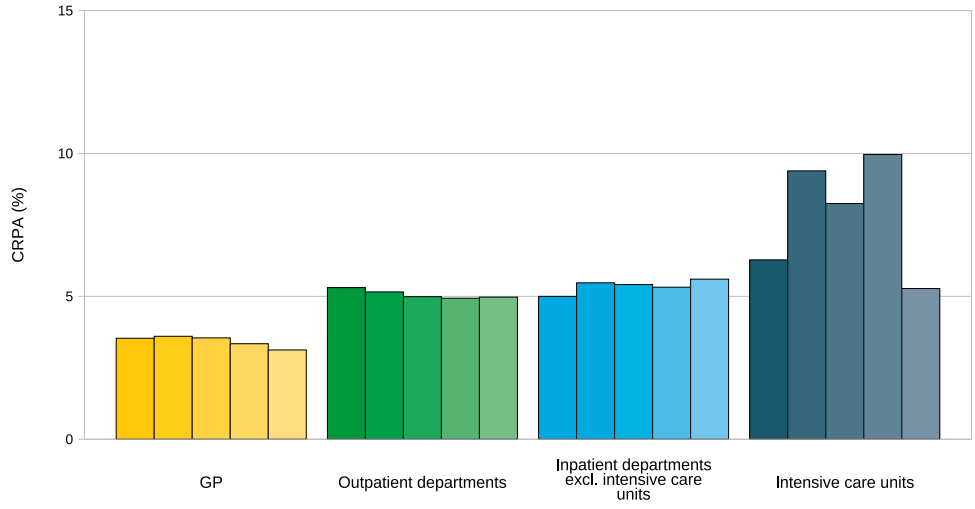
Type of department	Tested isolates, N	Carbapenem-resistant *P. aeruginosa*, N (%)
General practitioners	10,277	321 (3)
Outpatient departments	7,561	376 (5)
Inpatient departments excl. intensive care units	6,838	383 (6)
Intensive care units	531	28 (5)
Total	**25,207**	**1,108 (4)**

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

Numbers are based on a selection of 36 laboratories that continuously reported to the ISIS-AR database in the past five years. The first diagnostic *P. aeruginosa* isolate per patient was selected.

Carbapenem resistance was defined as (1) a positive test for carbapenemase (production) and/or (2) phenotypic resistance to meropenem and/or imipenem. The phenotypical tests were reinterpreted according to the 2025 EUCAST breakpoints for meropenem (applying the cut-off of >8 mg/L or <14 mm) and/or imipenem (cut-off >4 mg/L or <20 mm).

Figure 5.2.3.1 *Percentages of carbapenem-resistant P. aeruginosa among diagnostic P. aeruginosa isolates in the Netherlands (from left to right 2021 to 2025), based on ISIS-AR data*



Numbers are based on a selection of 36 laboratories that continuously reported to the ISIS-AR database in the past five years. The first diagnostic *P. aeruginosa* isolate per patient per year was selected.

Carbapenem resistance was defined as (1) a positive test for carbapenemase (production) and/or (2) phenotypic resistance to meropenem and/or imipenem. The phenotypical tests were reinterpreted according to the 2025 EUCAST breakpoints for meropenem (applying the cut-off of >8 mg/L or <14 mm) and/or imipenem (cut-off >4 mg/L or <20 mm).

GP: General practitioners.

Additional analyses in the 2025 ISIS-AR database showed that 1.2% (n=285) of 24,247 diagnostic *P. aeruginosa* isolates tested for all five groups of antimicrobials included in the MDR definition, were MDR (Table 5.2.3.2) and 64% (181/285) of the MDR isolates were carbapenem-resistant.

Table 5.2.3.2 *Multidrug-resistant (MDR) P. aeruginosa among diagnostic P. aeruginosa isolates in the Netherlands in 2025, based on ISIS-AR data*

Type of department	Tested isolates, N	MDR *P. aeruginosa*, N (%)	Carbapenem-resistant MDR *P. aeruginosa*, N (%)
General practitioners	10,036	38 (0.4)	21 (55)
Outpatient departments	7,253	110 (1.5)	63 (57)
Inpatient departments excl. intensive care units	6,446	125 (1.9)	90 (72)
Intensive care units	512	12 (2)	7 (58)
Total	**24,247**	**285 (1.2)**	**181 (64)**

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

Numbers are based on a selection of 36 laboratories that continuously reported to the ISIS-AR database in the past five years. The first diagnostic *P. aeruginosa* isolate per patient was selected.

Multidrug resistance was defined as resistant to ≥3 antimicrobials or antimicrobial groups among fluoroquinolones, aminoglycosides, carbapenems, ceftazidime, and piperacillin-tazobactam, based on re-interpretation of test-values according to EUCAST 2025; Carbapenem resistance was defined as (1) a positive test for carbapenemase (production) and/or (2) phenotypic resistance to meropenem and/or imipenem. The phenotypical tests were reinterpreted according to the 2025 EUCAST breakpoints for meropenem (applying the cut-off of >8 mg/L or <14 mm) and/or imipenem (cut-off >4 mg/L or <20 mm).

Molecular characteristics of carbapenemase-producing P. aeruginosa and patient related characteristics based on Type-Ned

In the enhanced surveillance, the RIVM received 55 *P. aeruginosa* isolates from samples collected in 2025 through Type-Ned, all of which produced carbapenemase according to the CIM. The CPPA were from 54 patients and these isolates were submitted by 26 MMLs. The following sample materials were reported: seventeen CPPA were from screening swabs, ten were from wound samples, eight from urine samples, seven from sputum, and the remainder from other isolation sites. The majority (51/55) of the CPPA isolates were obtained from materials sampled in hospitals. Of the 55 CPPA isolates submitted in 2025, 96% (53/55) had meropenem MICs above the EUCAST clinical breakpoint of 8 mg/L. One CPPA isolate had an MIC of 1.5 mg/L and no detectable carbapenemase, and one isolate had an MIC of 6 mg/L and carried a *bla*$_{\text{VIM-2}}$ allele. The MICs for imipenem were also assessed and 96% (53/55) were above the clinical EUCAST breakpoint of 4 mg/L.

From 54 of the 55 isolates whole-genome sequencing data was available upon analysis, and revealed that 20 of the 54 (37%) sequenced CPPA isolates carried a *bla*$_{\text{NDM-1}}$ allele, 16 harboured *bla*$_{\text{IMP-1}}$ (30%), and 13 *bla*$_{\text{VIM-}}$

$_2$ (24%) (Figure 5.2.3.2). Two isolates carried *bla*$_{IMP-13}$, one a double *bla*$_{NDM-1}$ and *bla*$_{GES-5}$ allele combination and the remainder was unknown.
Twenty one of the 55 submitted CPPA isolates (38%) were obtained from 20 Ukrainian patients. One Ukrainian patient carried two unrelated CPPA strains harbouring either *bla*$_{NDM-1}$ or *bla*$_{IMP-1}$. Of the isolates from Ukrainian patients, nine harboured a *bla*$_{NDM-1}$ allele and twelve *bla*$_{IMP-1}$.
The overall trend in the past 5 years is an increase in the presence of *bla*$_{NDM-1}$ among CPPA from 7% in 2021 to 36% in 2025 (Figure 5.2.3.2). This could partly be attributed to the fact that 41% (36/88) of all NDM-1-producing CPPA since 2020 is associated with Ukrainian patients, and 59% (52/88) with patients from the Netherlands. Likewise, thirty-one of the 37 (84%) CPPA with *bla*$_{IMP-1}$ were found in Ukrainian patients between 2022 and 2025.

The genetic relations of the 54 sequenced CPPA were assessed by performing MLST and wgMLST (Figure 5.2.3.3). This revealed that most of the isolates belonged to four distinct groups, according to the carbapenemase allele they harbored, and MLST sequence type ST111, ST773, ST1047 and ST2592. In 2025, two and five CPPA ST1047 isolates, four ST2592 isolates, and two CPPA ST235 isolates differed by ≤15 wgMLST alleles and could therefore be considered genetic clusters.[3] The 5 isolates of the large CPPA ST1047 cluster were found among Ukrainian patients (n=5) while the other ST1047 cluster consisted of two Dutch patients. In total, patients belonging to these two clusters had been admitted to four different hospitals. The ST2592 cluster contained isolates of two patients from Ukraine and two patients from the Netherlands, suggesting nosocomial spread in The Netherlands. Between 2021 and 2025, the CPPA isolates that could be typed by MLST revealed a waxing and waning of distinct MLST sequence types through the years (Table 5.2.3.3). However, since 2022, there has been ongoing persistence of globally epidemic ST773 and ST1047 lineages in the top 3 of most commonly detected MLST sequence types in the Netherlands. MLST ST111 remains the most commonly found CPPA sequence type in the Netherlands.

Table 5.2.3.3 *Results of multilocus sequence typing (MLST) of 269 CPPA isolates from 2021-2025**

Species	MLST sequence type	2021	2022	2023	2024	2025	Total
P. aeruginosa	111	18	5	17	28	9	77
	773	2	14	18	17	14	65
	1047		7	4	5	13	29
	235		5	1	5	3	14
	654		4	5	3	1	13
	621	3	4	2	1	2	12
	2592		1	1	2	5	9
	357		3	2	3		8
	Various	7	8	7	12	8	42
	Total	**30**	**51**	**57**	**76**	**55**	**269**

* Red indicates high number of isolates with specific MLST sequence type, while blue indicates low number of isolates with MLST sequence type.

Figure 5.2.3.2 *Numbers of carbapenemase-producing P. aeruginosa (CPPA) per carbapenemase allele (A), and trend in detected carbapenemase genes (B) based on Type-Ned, 2021-2025*

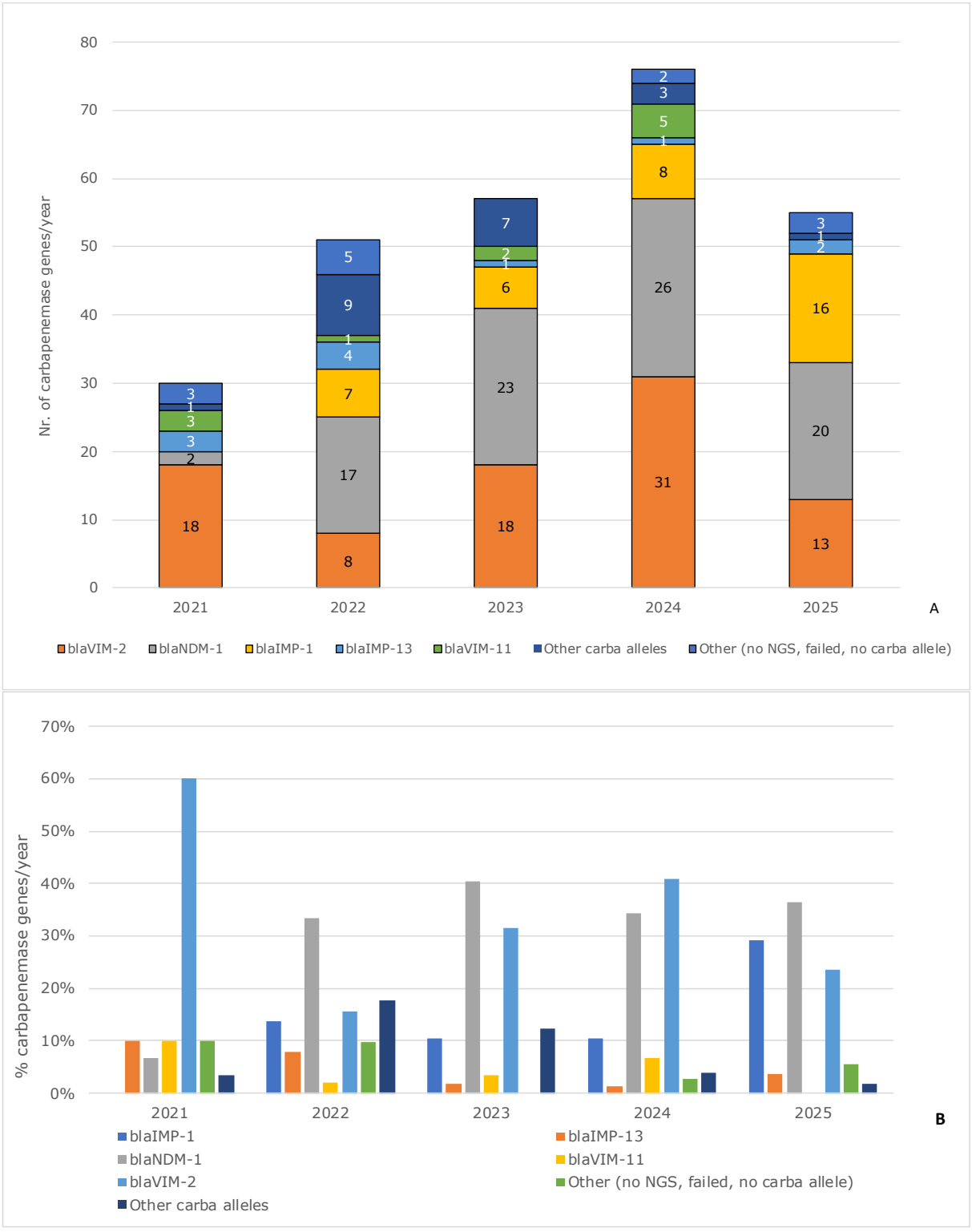
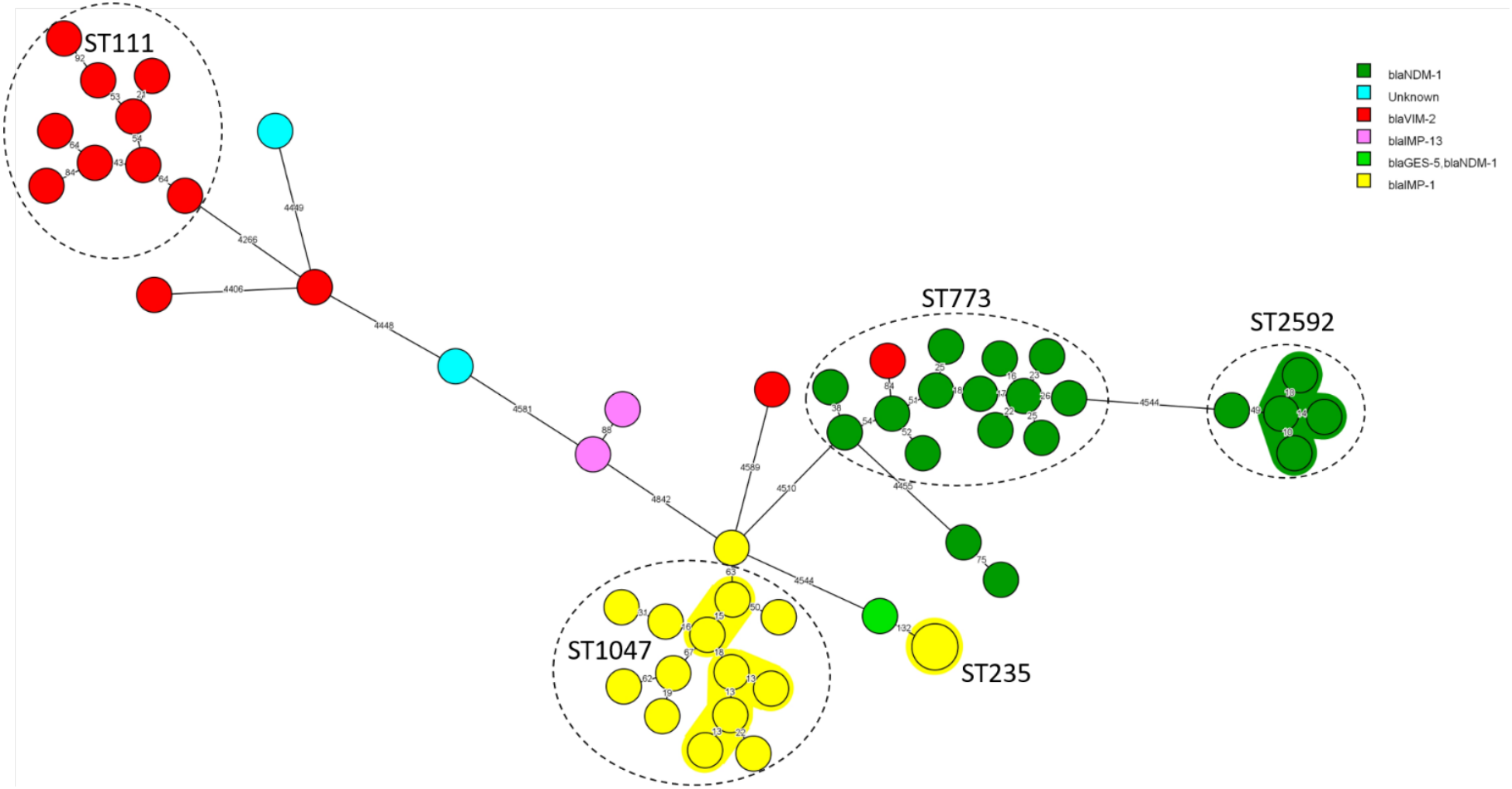


Figure 5.2.3.3 *wgMLST-based minimum spanning tree of 54 CPPA isolates from patients sampled in 2025, based on Type-Ned CPPA surveillance data*



Each node represents an isolate, the numbers on the connecting lines indicate allelic distances between isolates. A colored halo indicates ≥2 isolates differing ≤15 wgMLST alleles.

Clinical/epidemiological characteristics of patients with carbapenemase-producing P. aeruginosa
Clinical/epidemiological questionnaire data in Type-Ned were available for 33 of the 54 CPPA-carrying persons, and 27 were reported to be in-hospital patients. Twenty-six patients (79%) were male and the median age was 46 years (range 24-87 years). Eleven patients (11/33, 33%) were admitted to the ICU at the moment of sampling, 16 (48%) were admitted to a non-ICU hospital department, and six (18%) samples were taken at the outpatient department or in a non-hospital setting. Sixteen questionnaires concerned Ukrainian patients and seventeen concerned non-Ukrainian patients. In the Non-Ukrainian patients, 10/17 samples (59%) were taken for diagnostic purposes. Three patients (3/17, 18%) had been admitted >24 hours in a hospital abroad in the previous two months, namely one in South America, one in Northern Africa, and one in South Asia. Two patients (2/17) were screened because of a current CPPA outbreak in the healthcare institute where they were admitted. Six patients were admitted to the ICU at the moment of sampling, and eight patients (including three of the ICU patients) had (severe) comorbidities.

For 3/16 (19%) of the Ukrainian patients, clinical signs of an infection was mentioned as the reason for taking the sample. Nine patients (9/16, 56%) had been admitted >24 hours in a hospital abroad in the previous two months, and four (4/16, 25%) had been admitted in a hospital abroad in the previous 2-12 months (all in Ukraine).

Discussion
In 2025, in ISIS-AR, 4% of *P. aeruginosa* in diagnostic isolates were resistant to carbapenems. Due to strict diagnostic national guidelines[4], only 14% of these isolates were tested for carbapenemase production or carbapenemase genes, of which 14% were positive. Most isolates without test results were susceptible to tobramycin, which likely explains the missing data, as such isolates are not tested for carbapenemase according to the Dutch national guideline for detecting highly resistant microorganisms[4].

The proportion of carbapenem-resistant *P. aeruginosa* in ICUs (5%) dropped in 2025 compared to the years 2022-2024 during which the percentages were around 8-10%, and was more comparable to the COVID-19 years 2020-2021, when resistance percentages around 6% were calculated. However, no significant and microbiologically relevant decreasing trend since 2021 was observed and as the number of isolates in ICUs are relatively low, these results should be interpreted with caution.

Because of the war between Ukraine and Russia, Ukrainian patients migrated or were transferred to multiple European countries, sometimes carrying highly resistant microorganisms.[6,7] Consequently, the 2022-2025 results of the enhanced CPPA surveillance submitted via Type-Ned were very different to those of 2020 and 2021. Thirty-seven percent of the patients with CPPA isolates submitted in the enhanced surveillance via Type-Ned in 2025 were Ukrainian patients, thereby introducing $bla_{\text{IMP-1}}$ and $bla_{\text{NDM-1}}$ carrying CPPA in the Netherlands, continuing to change the molecular epidemiology. Up until 2021 the most

predominant (61%) carbapenemase-encoding allele in CPPA was *bla*$_{VIM-2}$, in 2022 this was reduced to 16% and dominated the *bla*$_{NDM-1}$ allele in 37% of the isolates until 2025.

Based on the additional epidemiological data we can conclude that more than 40% of the patients with a CPPA infection in the Netherlands had been hospitalized abroad and approximately half had comorbidities reported. Since these results are based on a relatively low number of patients, conclusions regarding the epidemiological characteristics should be drawn with caution.

Of note, the available data most likely underestimate the true burden of carbapenemase-producing *P. aeruginosa* in the Netherlands. According to the NVMM guideline, carbapenemase testing for *P. aeruginosa* is performed only when an isolate is resistant to both imipenem / meropenem and tobramycin. This may introduce selection bias in the submission of putative CPPA isolates for surveillance and is acknowledged as a potential limitation.

Conclusions

- In 2025, in ISIS-AR, 4% of *P. aeruginosa* in diagnostic isolates were resistant to carbapenems. For only 14% of these isolates, information was reported on tests for carbapenemase production; of these, 14% produced carbapenemase. The proportion of carbapenem-resistant *P. aeruginosa* in ICUs was lower compared to the years 2022-2024, but comparable to the COVID-19 years 2020-2021.
- In 2025, 1.2% of the total number of *P. aeruginosa* isolates in ISIS-AR was MDR and 64% of these MDR isolates were carbapenem-resistant.
- In 2025, 55 isolates from 54 patients were submitted to Type-Ned. Thirty seven percent of the patients with CPPA reported in Type-Ned were Ukrainian patients.
- The predominant (37%) carbapenemase-encoding allele in carbapenemase-producing *P. aeruginosa* was *bla*$_{NDM-1}$. In contrast, before the Ukraine/Russia war the dominant carbapenemase encoding allele in CPPA was *bla*$_{VIM-2}$.
- Ukrainian patients mostly carried CPPA with *bla*$_{IMP-1}$ or *bla*$_{NDM-1}$, thereby contributing to the changing molecular epidemiology of CPPA in the Netherlands since 2022.
- Of the isolates submitted to Type-Ned 96% had MICs for meropenem and imipenem above the EUCAST defined clinical breakpoints of 8 mg/L and 4mg/L, respectively.
- The majority (81%) of the Ukrainian patients with CPPA had been hospitalized in a hospital abroad in the previous year, while this proportion was 18% among non-Ukrainian patients. Among the non-Ukrainian patients more than half had severe comorbidities.
- As not all laboratories perform carbapenemase testing, and only a subset of relevant isolates and associated data were submitted to one of both of the surveillance systems ISIS-AR and Type-Ned, the presented data most likely underestimate the true burden of carbapenem-resistant and carbapenemase-producing *P. aeruginosa* in the Netherlands.

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5.2.4 *Carbapenem-resistant Acinetobacter baumannii-calcoaceticus complex*

Introduction
Acinetobacter baumannii is a common nosocomial pathogen. The *A. baumannii-calcoaceticus* complex entails the closely-related species *A. baumannii*, *A. calcoaceticus*, *A. nosocomialis*, *A. pittii*, *A. seifertii* and *A. lactucae* (also known as *A. dijkshoorniae*). While the incidence of multidrug-resistant (MDR) *A. baumannii* in the Netherlands is low, the emergence of MDR *A. baumannii-calcoaceticus* complex with intrinsic and acquired resistance mechanisms is a problem of global concern.[1,2] Therefore, in 2024 the World Health Organization ranked carbapenem-resistant *A. baumannii* as third organism in the 'priority: critical' group.[3]

Methods
Data on carbapenem-resistant *A. baumannii-calcoaceticus* complex (CRAB) were obtained from ISIS-AR and the national enhanced CRAB surveillance via Type-Ned.

Prevalence of carbapenem-resistant A. baumannii-calcoaceticus complex based on ISIS-AR
From the ISIS-AR database the first *A. baumannii-calcoaceticus* complex isolate per patient per year was extracted for the period 2021-2025. To avoid overestimation of the percentage carbapenem-resistant *A. baumannii-calcoaceticus* complex caused by active screening for highly resistant isolates, only data on diagnostic cultures (as categorized by the reporting laboratory) from blood, cerebrospinal fluid, urine, lower respiratory tract, and wound or pus were included in the analysis. Carbapenem resistance was defined as (1) a positive test for carbapenemase production and/or (2) phenotypic resistance to meropenem and/or imipenem. The phenotypical tests were reinterpreted according to the 2025 EUCAST v15.0 breakpoints for meropenem and/or imipenem. The numbers were based on a selection of 36 laboratories (out of a total of 46 laboratories in the Netherlands), which provided complete data on the past five years (2021 to 2025).

Molecular characteristics of carbapenem-resistant and/or carbapenemase-producing Acinetobacter baumannii-calcoaceticus complex and patient related characteristics based on Type-Ned
In 2022, a pilot CRAB surveillance via Type-Ned was performed, and was implemented from 2024 onwards in the national surveillance for highly resistant microorganisms.[2] Participation is voluntary, and not all laboratories will submit all eligible isolates. MMLs are requested to submit *A. baumannii-calcoaceticus* complex isolates to the RIVM with an MIC for meropenem of >8 mg/L and/or an MIC for imipenem >4 mg/L and/or with carbapenemase production and/or with a detected carbapenemase-encoding gene. A restriction is that the laboratory can only send the first isolate per person per year. The RIVM allows consecutive isolates from the same person if these isolates carry other carbapenemase-encoding gene combinations when compared to the first isolate. The RIVM confirms the species by MALDI-ToF, determines the MIC for meropenem by Etest (bioMérieux), and detects carbapenemase production by the carbapenem inactivation method (CIM).[4] The presence of carbapenemase-encoding genes are assessed by PCR (carba-PCR on *bla*$_{\text{NDM}}$, *bla*$_{\text{KPC}}$, *bla*$_{\text{IMP}}$, *bla*$_{\text{VIM}}$, and *bla*$_{\text{OXA-48-like}}$ + *mcr-1*). Next-generation

sequencing (NGS) and Nanopore long-read sequencing is performed for all isolates that are CIM positive and/or have an MIC for meropenem of >8 mg/L as assessed by Etest. The data described in this chapter are based on the first unique CIM-positive *A. baumannii-calcoaceticus* complex species/carbapenemase-encoding allele combination per person with a person ID for 2025, and all of these isolates collected in 2025 were included.
Samples without a person ID were included for further analysis if it was confirmed that it represented a unique person, based on sex, age and postal code.

Based on whole-genome multi-locus sequence typing (wgMLST), genetically closely related CRAB isolates are grouped in genetic clusters and assigned consecutive cluster numbers. A genetic cluster is defined per bacterial species and includes ≥2 CRAB isolates that differ ≤15 wgMLST alleles.[5] Assigning genetic cluster numbers in the CPE/CPPA surveillance started in 2020, but the genetic cluster numbers in the results of this report include all sequenced *A. baumannii-calcoaceticus* complex isolates available from (pilot) surveillance studies at the RIVM.[2] Except the first isolate, clusters of multiple isolates from the same patient, including over multiple years and/or submitted by different laboratories, were not counted. In addition to submitting an isolate, Dutch laboratories are also requested to fill in a clinical/epidemiological questionnaire on characteristics of the patient from whom the CRAB isolate was obtained.

Results

Prevalence of carbapenem-resistant A. baumannii-calcoaceticus complex

Based on the ISIS-AR database, 2% (32/1,423) of the diagnostic *A. baumannii-calcoaceticus* complex isolates were carbapenem-resistant in 2025 (Table 5.2.4.1). Over the past five years, the percentage of carbapenem-resistant *A. baumannii-calcoaceticus* complex isolates has remained at a low level and was consistently higher among diagnostic samples from inpatient departments and intensive care units (ICUs) compared to other types of healthcare settings. Within this low range the annual proportion of resistance varied somewhat between 2021-2025, which may be influenced by the low absolute numbers of tested and resistant isolates (Figure 5.2.4.1).

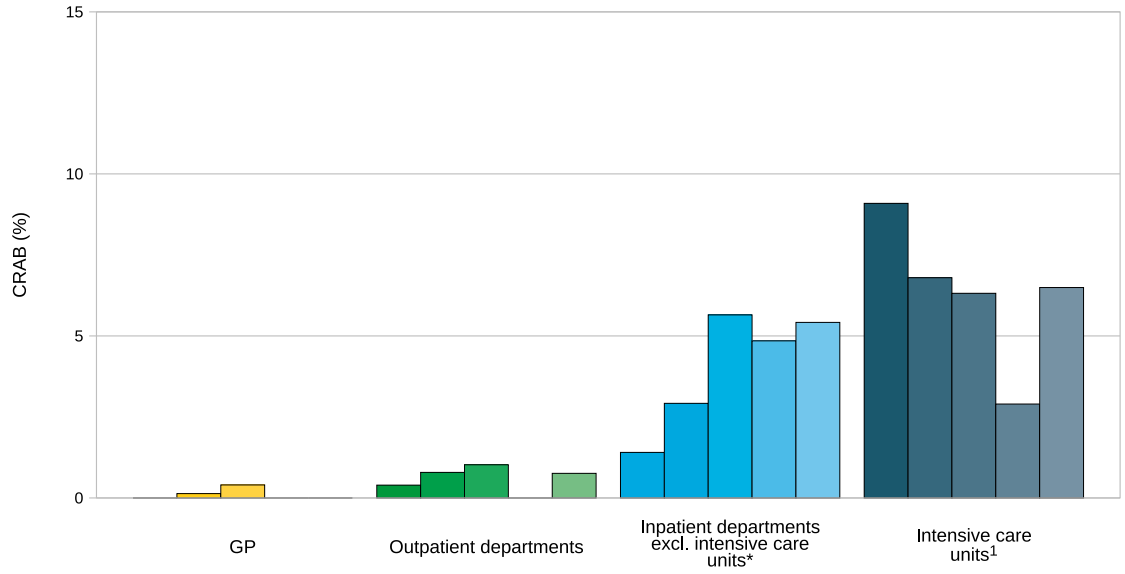
Table 5.2.4.1 *Carbapenem-resistant A. baumannii-calcoaceticus complex in the Netherlands in 2025, based on ISIS-AR data*

Sampling location	Tested isolates, N	Carbapenem-resistant *A. baumannii-calcoaceticus* complex, N (%)
General practitioners	508	0 (0.0)
Outpatient departments	395	3 (0.8)
Inpatient departments excl. intensive care units	443	24 (5) ↑
Intensive care units	77	5 (6)
Total	**1,423**	**32 (2)**

10 ↑	Significant and microbiologically relevant increasing trend since 2020.
10 ↓	Significant and microbiologically relevant decreasing trend since 2020.
10°	Trend not calculated because data from the years before 2024 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

Carbapenem resistance was defined as (1) a positive test for carbapenemase production and/or (2) phenotypic resistance to meropenem and/or imipenem. The phenotypical tests were reinterpreted according to the 2025 EUCAST breakpoints for meropenem (R>8 mg/L or <15 mm) and/or imipenem (R>4 mg/L or <21 mm).

Figure 5.2.4.1 *Percentages of carbapenem-resistant A. baumannii-calcoaceticus complex in the Netherlands (from left to right 2021 to 2025), based on ISIS-AR data*



Numbers are based on a selection of 36 laboratories that continuously reported to the ISIS-AR database in the past five years.

*Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

The first diagnostic *A. baumannii-calcoaceticus* complex isolate per patient per year was selected.

Carbapenem resistance was defined as (1) a positive test for carbapenemase production and/or (2) phenotypic resistance to meropenem and/or imipenem. The phenotypical tests were reinterpreted according to the 2025 EUCAST breakpoints for meropenem (R >8 mg/L or <15 mm) and/or imipenem (R>4 mg/L or <21 mm).

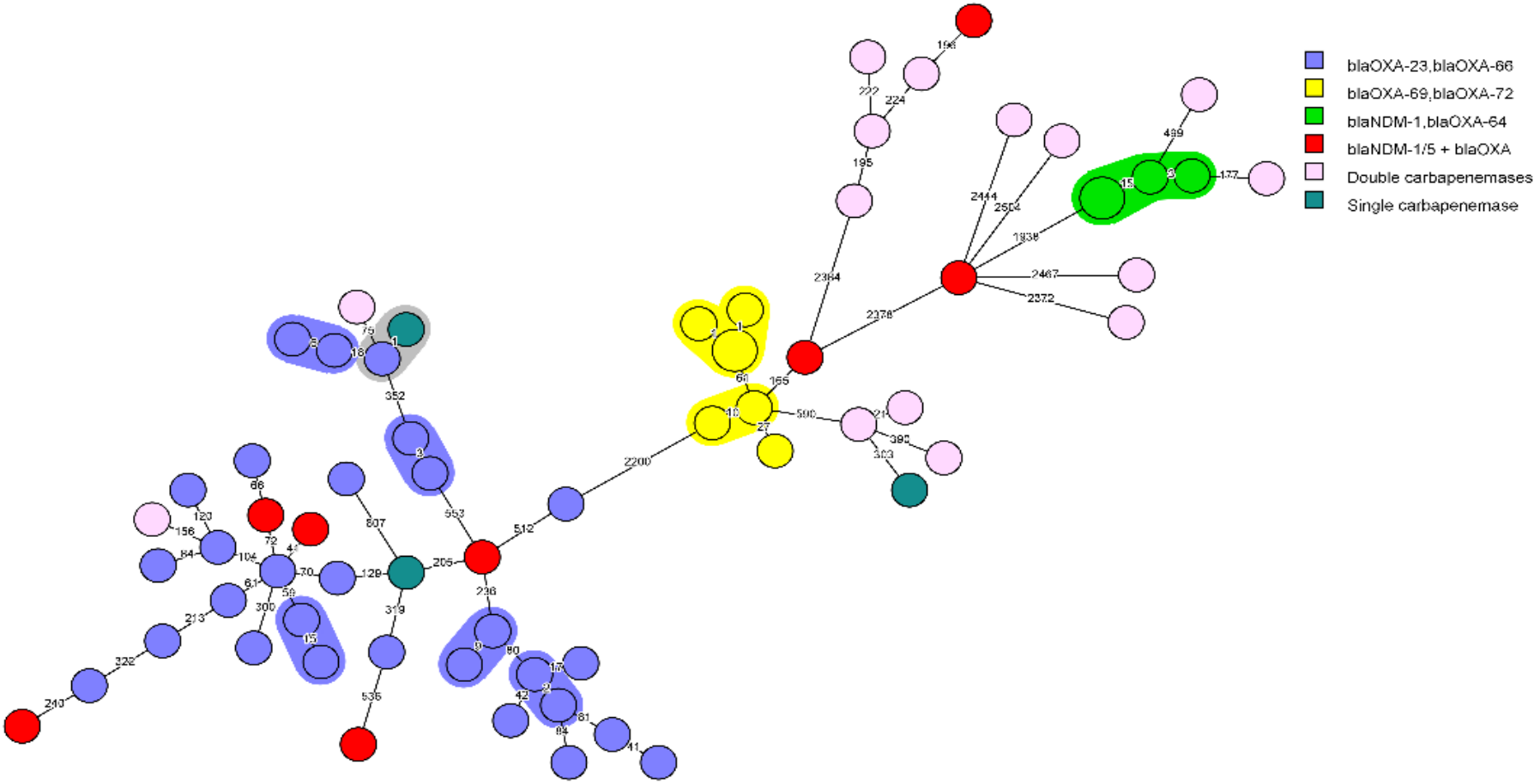
Molecular characteristics of carbapenem-resistant and/or carbapenemase-producing Acinetobacter baumannii-calcoaceticus *complex (CRAB)*

The RIVM received 71 suspected carbapenem-resistant *A. baumannii-calcoaceticus* complex isolates from both diagnostic and screening samples collected in 2025 through Type-Ned, and all produced carbapenemase according to the CIM. The following sample materials were reported: twenty-nine *A. baumannii-calcoaceticus* complex were from screening swabs, seventeen were from wound samples, four from urine samples, two from blood, one from pus, and the remainder from other isolation sites. The majority (65/71) of the *A. baumannii-calcoaceticus* complex were obtained from materials sent in by hospitals.

Of the *A. baumannii-calcoaceticus* complex isolates, 97% (69/71) had an MIC for meropenem above the clinical EUCAST resistance breakpoint of 8 mg/L and are designated CRAB. The 71 *A. baumannii-calcoaceticus* complex isolates were from 66 patients and these isolates were submitted by 32 MMLs. Twenty-four isolates were obtained from 20 Ukrainian patients and 47 isolates were from 46 non-Ukrainian patients. From 67/71 isolates whole-genome sequencing data was available and analysis revealed that 33 of the 67 *A. baumannii-calcoaceticus* complex isolates (49%) carried the *bla*$_{\text{OXA-23}}$ and *bla*$_{\text{OXA-66}}$ carbapenemase gene combination, of which three harboured either an additional *bla*$_{\text{NDM-1}}$, *bla*$_{\text{NDM-5}}$ or *bla*$_{\text{OXA-72}}$ gene. Eight isolates carried *bla*$_{\text{OXA-23}}$ alone or in combination with an OXA-51-like carbapenemase allele (*bla*$_{\text{OXA-64}}$, *bla*$_{\text{OXA-69}}$, *bla*$_{\text{OXA-90}}$, or *bla*$_{\text{OXA-91}}$) and seven carried the *bla*$_{\text{OXA-69}}$/*bla*$_{\text{OXA-72}}$ combination. Nine isolates harboured *bla*$_{\text{NDM-1}}$ in combination with one (n=4, *bla*$_{\text{OXA-64}}$; or n=1 for either *bla*$_{\text{OXA-23,}}$ *bla*$_{\text{OXA-66}}$ or *bla*$_{\text{OXA-120}}$) or two other carbapenemase genes (n=2, *bla*$_{\text{OXA-23}}$/*bla*$_{\text{OXA-66}}$). Three isolates carried *bla*$_{\text{NDM-5}}$ in combination with either *bla*$_{\text{OXA-23}}$, *bla*$_{\text{OXA-23}}$ and *bla*$_{\text{OXA-66}}$, or *bla*$_{\text{OXA-66}}$ and *bla*$_{\text{OXA-72}}$. Seven *A. baumannii-calcoaceticus* complex isolates carried *bla*$_{\text{OXA-72}}$ alone (n=2) or in combination with another carbapenemase gene (n=5, either *bla*$_{\text{OXA-64}}$, *bla*$_{\text{OXA-66}}$, *bla*$_{\text{OXA-69}}$, or *bla*$_{\text{OXA-90}}$) or two carbapenemase genes (*bla*$_{\text{OXA-23}}$/*bla*$_{\text{OXA-66}}$). Eleven *A. baumannii-calcoaceticus* complex isolates carried other more rare carbapenemase genes alone (n=5) or in combination. Of the twenty-four *A. baumannii-calcoaceticus* complex isolates from Ukrainian patients, eight harboured the *bla*$_{\text{OXA-23}}$ and *bla*$_{\text{OXA-66}}$ carbapenemases, and seven the *bla*$_{\text{OXA-69}}$/*bla*$_{\text{OXA-72}}$ combination. One CRAB from a Ukrainian patient carried *bla*$_{\text{NDM-1}}$/*bla*$_{\text{OXA-64}}$ (4%; 1/24) and the remainder had different carbapenemases and combinations. Twenty-six percent (11/43) of isolates from non-Ukrainian patients carried a *bla*$_{\text{NDM}}$-like allele. Of these 11 patients, 7 had risk factor data available and 2 of them had been recently hospitalized abroad.

The genetic relations of the 67/71 sequenced *A. baumannii-calcoaceticus* complex isolates were assessed by performing wgMLST (Figure 5.2.4.2). The isolates were diverse; 67 isolates were assigned to 35 distinct MLST types of which two MLST types, ST231 (n=7) and ST195 (n=5), occurred most often. However, seven groups of two, and two groups of four isolates differed in ≤15 wgMLST alleles and could therefore be regarded as genetic clusters.[5] Six of the nine clusters were from Ukrainian patients, while two clusters were from patients from the Netherlands and one cluster comprised Ukrainian and Dutch patients.

Figure 5.2.4.2 *wgMLST-based minimum spanning tree of 67/71 A. baumannii-calcoaceticus complex isolates from patients sampled in 2025, based on Type-Ned CRAB surveillance data. Each node represents an isolate, the numbers on the connecting lines indicate allelic distances between isolates. A colored halo indicates ≥2 isolates differing ≤15 wgMLST alleles*



Clinical/epidemiological characteristics of patients with carbapenem-resistant and/or carbapenemase-producing A. baumannii-calcoaceticus complex
Clinical/epidemiological questionnaire data in Type-Ned were available for 38 of the 66 persons with an *A. baumannii-calcoaceticus* complex isolate in 2025. Thirty-six of the patients were sampled within a hospital setting. Thirteen (13/38, 34%) were admitted to the ICU at the moment of sampling and 23 (23/38, 61%) were admitted to a non-ICU hospital department. Two patients were sampled while staying in a long-term care facility. Thirty-three patients (50%) were male and the median age was 54 years (range 24-91 years).

Eleven questionnaires concerned Ukrainian patients. For 10/11 of the Ukrainian patients, screening was mentioned as the reason for taking the sample. Ten of the Ukrainian patients had been admitted in a Ukrainian hospital in the previous two months. The Ukrainian patient who was not recently hospitalized abroad had no known risk factors for carrying CRAB.

Twenty-seven questionnaires concerned non-Ukrainian patients. In these patients, 2/27 samples (7%) were taken for diagnostic purposes. Another 2/27 samples were taken for unknown reasons but the sample materials of these patients were blood and urine, and thus expected to be taken for diagnostic purposes as well. For 23 patients, it was mentioned that the reason for sampling was screening. For one patient though, for whom screening was mentioned as the sampling reason, the isolate was cultured in a blood sample, suggesting a diagnostic sampling reason rather than screening. 10/27 patients were admitted to the ICU at the moment of sampling, and eleven patients (including four of the ICU patients) had comorbidities.

Eighteen patients (18/27, 63%) had been admitted >24 hours in a hospital abroad: 17 in the previous two months, and one 2-12 months ago. Of these, six patients had been admitted in a hospital in Western Asia, three in Northern Africa, two in South America, and six patients had been admitted each in a different global region. For one patient the country of recent hospital admission was unknown.
Of the 9 patients without recent hospitalisation abroad, one patient was a known CRAB carrier and for two patients a recent admission to another healthcare institute was mentioned as a risk factor. For six patients, no risk factor for carrying CRAB was reported,

Discussion
In 2025, in ISIS-AR, 2% of *A. baumannii-calcoaceticus* complex in diagnostic isolates were resistant to carbapenems. Since the absolute numbers in diagnostic samples in the Netherlands are low, the resistance percentages cannot be estimated with high precision, making it difficult to reliably assess trends in resistance levels over the past few years. Still, it is clear that the proportion of carbapenem-resistant *A. baumannii-calcoaceticus* complex in inpatient departments and ICUs are higher compared to resistance levels in isolates from general practitioners or outpatient departments. Although *A. baumannii-calcoaceticus* complex is regarded as a predominantly nosocomial pathogen, a large proportion of the diagnostic isolates in the ISIS-AR

database were cultured in samples taken in a general practitioner's setting, which also include samples from long-term care facilities. Still, all carbapenem-resistant isolates in ISIS-AR were sampled in hospital settings.

The 2025 results of the enhanced CRAB surveillance submitted via Type-Ned revealed a genetically highly diverse population of CRAB isolates in the Netherlands. Thirty-four percent of the *A. baumannii-calcoaceticus* complex isolates in the Type-Ned surveillance in 2025 were from samples of Ukrainian patients, and only one of these (4%) carried a *bla*$_{NDM}$-like carbapenemase. Although based on small numbers, NDM-producing CRAB were relatively more often found among isolates retrieved from non-Ukrainian patients (26%). This is in contrast to multiple reports of EU/EEA countries describing occurrence of NDM-producing CPE and CPPA linked to patients originating from Ukraine.[6-8] The absolute numbers of carbapenem-resistant *A. baumannii-calcoaceticus* complex isolates which were analyzed from the ISIS-AR database are not directly comparable to the absolute numbers included in the enhanced CRAB surveillance via Type-Ned, for a number of reasons. For the analysis of resistance percentages in ISIS-AR, only diagnostic samples are included, because the inclusion of screening samples would introduce bias towards higher resistance percentages as a result of selective testing methods for screening samples in laboratories. Furthermore, the selection of included laboratories differs between both surveillance systems and not all eligible isolates are submitted to Type-Ned. Therefore, the data as shown here might be an underestimation of the total CRAB proportion present in the Netherlands.

Nevertheless, from both systems we can conclude that the proportion of carbapenem-resistant *A. baumannii-calcoaceticus* complex is low in the Netherlands and that the most important risk factor for patients to be infected or colonized with carbapenem-resistant *A. baumannii-calcoaceticus* complex is recent admission in a hospital abroad.[9]

Conclusions

- In 2025, in ISIS-AR, 2% of *A. baumannii-calcoaceticus* complex in diagnostic isolates were resistant to carbapenems, with the highest resistance proportions in samples from in-hospital patient departments and ICUs.
- The *A. baumannii-calcoaceticus* complex isolates in the Netherlands are diverse with a high variety of intrinsic and acquired carbapenemase encoding genes, and *A. baumannii-calcoaceticus* complex were from 35 distinct MLST types of which ST231 (n=7) and ST195 (n=5) occurred most often.
- The predominant (49%, 33/67) carbapenemase-encoding gene combination in *A. baumannii-calcoaceticus* complex was *bla*$_{OXA-23}$ and *bla*$_{OXA-66}$, and 18% (12/67) carried a *bla*$_{NDM}$-like carbapenemase.
- All but one Ukrainian patients with carbapenem-resistant *A. baumannii-calcoaceticus* complex had been recently hospitalized in a Ukrainian hospital. Additionally, the majority (63%) of the non-Ukrainian patients had been hospitalized in a hospital abroad.

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5.2.5 *Methicillin-resistant Staphylococcus aureus (MRSA)*

Introduction
The Netherlands remains a country with a low MRSA prevalence. This is probably explained by the strict infection prevention rules (also known as "search and destroy" MRSA policy) imposed in healthcare institutes and the constricted use of antibiotics. To gain insight in the prevalence of MRSA in the Netherlands, several surveillance systems are in place. The ISIS-AR database contains, among others, information regarding *S. aureus* culture and susceptibility testing results from routine practices in medical microbiology laboratories (MML). In addition, since 1989, a more enhanced molecular MRSA surveillance at a national level is performed by the RIVM which includes molecular typing of submitted MRSA isolates. For this enhanced surveillance, the Type-Ned system is used to collect data on the molecular characteristics of circulating MRSA types and clinical/epidemiological characteristics of persons with MRSA.[1]

Methods
Prevalence of MRSA and antibiotic resistance among MRSA isolates, based on ISIS-AR
Data were selected from 36 laboratories that continuously reported complete data to the ISIS-AR database during 2021 to 2025. The first diagnostic isolate per patient per year was included. For general practitioners (GPs), only isolates from wound or pus samples were included. For outpatient departments, inpatient departments (excluding ICUs but including emergency departments), and intensive care units (ICUs), isolates from blood, cerebrospinal fluid, urine, lower respiratory tract, and wound or pus samples were included. Prevalence of MRSA was calculated as the percentage of *S. aureus* isolates for which the MRSA confirmation test (presence of *mecA* or *mecC* gene or *pbp2*) was positive, or, if these test results were lacking, the laboratory interpretation for cefoxitin was R, or, if no data on a cefoxitin test was available the laboratory interpretation for flucloxacillin/oxacillin was R. Additionally, the proportion of MRSA was calculated separately for *S. aureus* blood isolates. For MRSA-defined isolates, resistance levels and time trends were calculated for a set of relevant antibiotics per setting of care. For more details on isolate selection, calculation of resistance levels and the definition of significant and microbiologically relevant trends within ISIS-AR, see section 5.1.1.1.

Molecular characteristics of MRSA and patient related characteristics based on Type-Ned
For the isolate-based MRSA surveillance, Dutch laboratories are requested to submit MRSA complex isolates via the Type-Ned system which are obtained from patients during routine practices. A clinical/epidemiological questionnaire on person characteristics is requested to be completed for each submitted MRSA isolate, except for persons who are part of a contact tracing investigation. Questionnaires related to isolates from employees in a healthcare facility that were screened as part of a local screening programme were excluded.

Molecular typing is performed by multiple-locus variable number of tandem repeat analysis (MLVA), in which detection of the *mecA, mecC* and *lukF-PV* gene (encoding *pbp2* and Panton-Valentine leucocidin,

respectively) are additionally incorporated. MLVA types that differ on one locus in MLVA profile were combined into MLVA-complexes. With the increase in the number of different MLVA-types, MLVA-complex has become less reliable. Therefore, in 2025, new MLVA-types were not assigned to MLVA-complexes anymore, because new MLVA-types often belong to multiple MLVA-complexes. Due to this, the number of isolates without an MLVA-complex is higher compared to previous years.

Since 2020, one isolate per person within a three-year period is eligible to be submitted. Isolates in the database were categorised as either diagnostic (isolated from samples of infection-related materials, i.e., blood, cerebrospinal fluid, sputum, pus, urine or wound) or screening (isolated from human MRSA-screening materials, i.e. swabs from throat, nose, skin, ear, perineum and/or rectum). MRSA of MLVA-complex MC0398 were previously predominantly found in people with livestock contact and therefore labelled as livestock-associated MRSA (LA-MRSA). The first MRSA isolate per person sampled in the period 2021 to 2025 was included in the analyses, with the exception that only the first diagnostic isolate is included when both a screening and a diagnostic sample are submitted from the same person. Samples without a person ID were only included for further analysis if it was confirmed to represent a person not included yet, based on MLVA type, sex, age and postal code, or based on MLVA type, sex, and age if the postal code was unknown. Samples from non-human origin, isolates from Caribbean laboratories and isolates lacking a *mecA* or *mecC* gene were also excluded from molecular analysis.

A semi-random selection of MRSA isolates is analysed through whole-genome sequencing (WGS). It concerns a random selection of 40 isolates per month that meet the following criteria: one isolate per person (per three years), per MLVA type, per laboratory. Isolates were not sequenced in case no person ID was available (e.g. asylum seekers and neonates) or when the surveillance questionnaire was not filled out. All liquor and blood-derived isolates that are not part of the initial selection are additionally included. Sequencing data were used for multi-locus sequence typing (MLST) using SeqSphere software and antimicrobial resistance genes were identified using the ResFinder database.

Clinical/epidemiological data from the persons with included isolates are described for 2025 and compared with the previous four years, for all isolates combined and after stratification into diagnostic and screening isolates.

Results

Prevalence of MRSA and antibiotic resistance among MRSA isolates, based on ISIS-AR

In ISIS-AR, the proportion of diagnostic *S. aureus* isolates in 2025 that was identified as MRSA was 3% (n=1,916/62,929). A higher proportion of 4% was seen for cultures requested by intensive care units (Table 5.2.5.1). In blood isolates, the prevalence of MRSA in 2025 was 2% (n=84/4,068). Figure 5.2.5.1 shows the trends in MRSA prevalence from 2021 to 2025 in all diagnostic isolates, per setting of care. Between 2021 and 2025, overall, the prevalence of MRSA seemed to increase

among cultures requested by GPs, outpatient departments and inpatient departments (excl. ICU) (all from 2% to 3%) and among cultures of ICU patients (3% to 4%). However, changes are small and although the trends were statistically significant, they were not microbiologically relevant according to the applied definitions in NethMap One Health (see methods section 5.1.1.1). Five-year trends in resistance among MRSA isolates from blood cultures did not show an increase either, and remained stable over the past five years.

Antibiotic resistance among MRSA isolates based on ISIS-AR
Five-year trends in resistance among MRSA isolates for a set of relevant antibiotics are shown in figure 5.2.5.2. Between 2021 and 2025, there was a statistically significant and microbiologically relevant decrease of resistance levels for clindamycin (excl. inducible resistance) in cultures from outpatient departments from 20% to 10% and in cultures from inpatient departments (excl. ICU) from 16% to 11%, respectively. Resistance levels for ciprofloxacin in GP cultures decreased from 24% to 17% in the same period. However, as reported in NethMap One Health 2025, the fusidic acid resistance levels increased in the past five years for GPs (27% to 41%), outpatient departments (21 to 35%) and inpatient departments (excl. ICU) (20% to 32%).

Table 5.2.5.1 *Methicillin-resistant S. aureus (MRSA) in the Netherlands in 2025 in diagnostic isolates, based on ISIS-AR data*

Healthcare setting	Tested isolates, N	MRSA, N(%)
GP[1]	20,524	716 (3)
Outpatient departments	23,184	648 (3)
Inpatient departments excl. intensive care units	17,485	489 (3)
Intensive care units	1,736	63 (4)
Total	**62,929**	**1,916 (3)**

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10	No significant and microbiologically relevant time trend.
	For the definition of a microbiologically relevant trend see section 5.1.1.1.

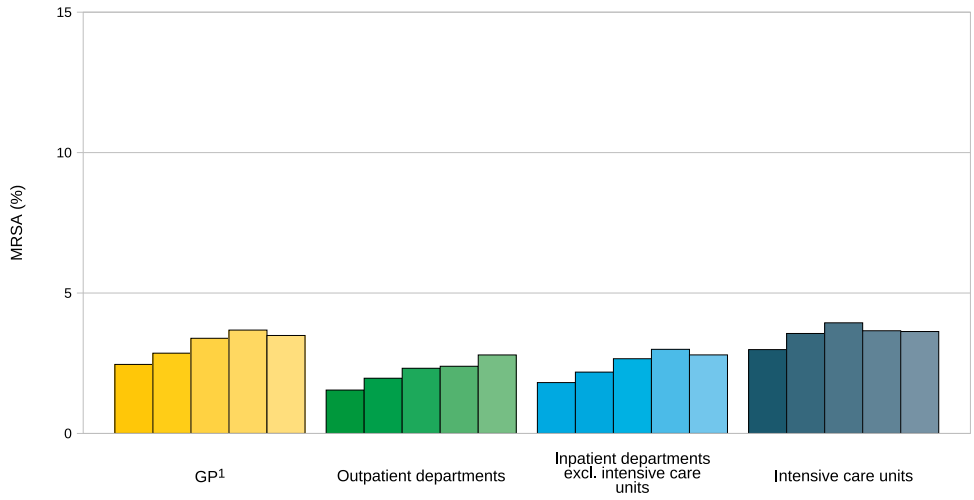
Numbers are based on a selection of 36 laboratories that continuously reported to the ISIS-AR database in the past five years.

The first diagnostic *S. aureus* isolate per patient was selected.

The prevalence of MRSA isolates was based on positivity of MRSA confirmation tests (presence of mecA or mecC gene or pbp2). If these tests were lacking, prevalence was based on re-interpretation of test-values for cefoxitin according to EUCAST 2025 or, if no data on a cefoxitin test was available, for flucloxacillin/oxacillin.

[1] From general practitioner (GP) patients only wound or pus isolates were selected.

Figure 5.2.5.1 *Trends in methicillin-resistant S. aureus (MRSA) in the Netherlands in diagnostic isolates (from left to right 2021 to 2025), based on ISIS-AR data*



Numbers are based on a selection of 36 laboratories that continuously reported to the ISIS-AR database in the past five years.

* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

The first diagnostic *S. aureus* isolate per patient per year was selected.

The prevalence of MRSA isolates was based on positivity of MRSA confirmation tests (presence of mecA or mecC gene or pbp2). If these tests were lacking, prevalence was based on re-interpretation of test-values for cefoxitin according to EUCAST 2025 or, if no data on a cefoxitin test was available, for flucloxacillin/oxacillin.

[1] From general practitioner (GP) patients only wound or pus isolates were selected.

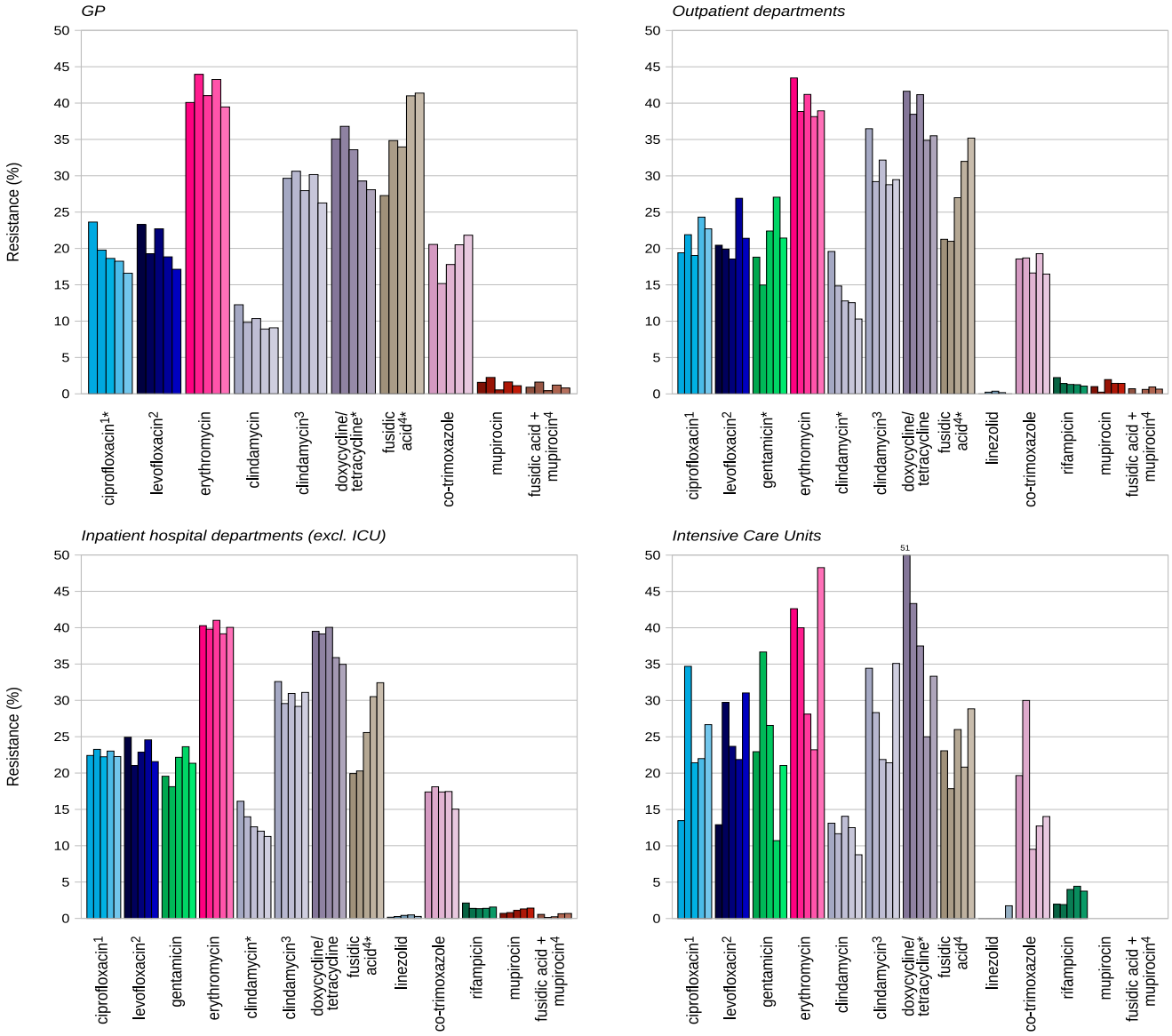
Molecular characteristics of MRSA based on Type-Ned

In 2025, the RIVM received 6,572 *S. aureus* isolates that were *mecA* or *mecC* gene positive and 5,461 isolates fulfilled the selection criteria specified in the methods section. The absolute number of MRSA isolates included in the analysis in 2025 is higher compared to previous four years (minimum: 2,802 isolates in 2021, maximum: 4,847 isolates in 2024) and also higher compared to the annual numbers in the pre-COVID years, both for diagnostic and screening isolates. It is important to mention that during the COVID pandemic in 2020 en 2021 there were significantly lower numbers of submitted MRSA isolates compared to previous years, for both diagnostic and screening isolates.

The majority of isolates in 2025 were cultured from samples submitted to the MML by hospitals (n= 3,469; 64%), followed by GPs (n= 1,521; 28%), municipal health services (n= 189; 3%), treatment centers (n=137; 3%) and long-term care facilities (LTCFs) (n= 95; 2%). Based on the sample material, 63% (n= 3,429) of the isolates were isolated from screening samples. A total of 2,018 isolates (37%) were from materials suggesting a diagnostic (infection-related) reason for sampling, of which the majority were cultured from wound material or pus/punctate/biopsy (1,549/2,018; 77%) and 70 isolates were cultured from blood (3%). For 14 isolates, the material was unknown. The above-mentioned percentages are largely comparable to previous years.

In 2025, 19 methicillin-resistant *Staphylococcus argenteus* (MRSArg) isolates were submitted, of which 12 (63%) were screening isolates. The proportion of screening isolates is lower compared to 2024 (94%).

Figure 5.2.5.2 *Trends in antibiotic resistance (from left to right 2021 to 2025) among diagnostic MRSA isolates in the Netherlands, based on ISIS-AR data*



* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

[1] Resistance to ciprofloxacin is intended to be a class indicator for resistance to fluoroquinolones.

[2] Often, susceptibility to levofloxacin is only tested when resistant to ciprofloxacin. Resistance percentages may, therefore, be biased toward a higher level. For details see section 5.1.1.1.

[3] Including inducible resistance. For the method used to estimate clindamycin resistance including inducible resistance, see section 5.1.1.1.

[4] According to breakpoint for topical use. For more details see section 5.1.1.1.

Note: the number of isolates from the ICU tested for each antibiotic is <100 for each year. From general practitioner (GP) patients only wound or pus isolates were selected.

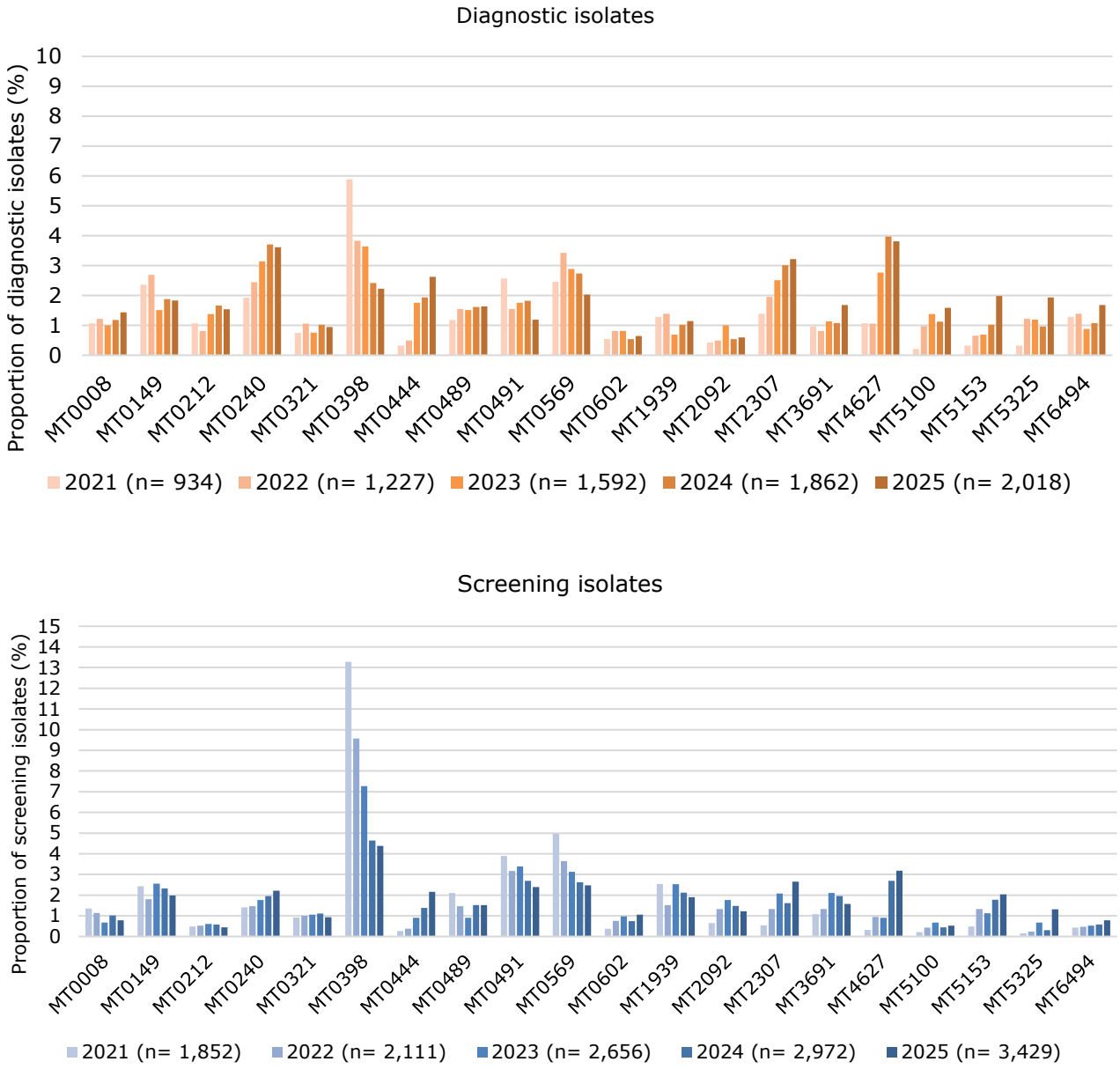
For 2025, the submitted MRSA isolates were classified into 1,255 different MLVA-types. The majority (883 MLVA types; 4,778 isolates) could be grouped into 25 MLVA-complexes (MCs). For 41 MLVA-types (276 isolates) no MC could be assigned and the remaining 331 MLVA-types (407 isolates) were new MLVA-types for which MLVA-complexes are no longer assigned. The most frequently identified MLVA-complexes in 2025 were MC0008 (n=435; 22%), MC0005 (n=333; 17%) and MC0030 (n=202; 10%) among diagnostic isolates and MC0005 (n=556; 16%), MC0008 (n=544; 16%) and MC0398 (n=341; 10%) among screening isolates. Like in the previous years, the proportion MC0398 was higher in screening isolates (10%) than in diagnostic isolates (7%). During the 2021-2025 surveillance period, there has been a decreasing trend in the proportion of MC0398 in both diagnostic (from 12% to 7%) and screening isolates (from 26% to 10%).

Figure 5.2.5.3 shows trends in the top 20 MLVA-types from 2025. The most frequently identified MLVA-types in 2025 were MT4627 (n=77; 4%), MT0240 (n=73; 4%) and MT2307 (n=65; 3%) among diagnostic isolates and MT0398 (n=150; 4%), MT4627 (n=109; 3%) and MT2307 (n=91; 3%) among screening isolates. During the 2021-2025 surveillance period, there has been a decreasing trend in the proportion of MT0398 and MT0569 (both belonging to MC0398) in both diagnostic and screening isolates (Figure 5.2.5.3). Furthermore, MT4627, MT0240, MT0444, MT2307 and MT5153 show an increasing trend among diagnostic and screening isolates and MT0491 is decreasing among screening isolates.

Overall, 27% of the isolates (1,483/5,461) were Panton-Valentine Leukocidin (PVL) positive. Except for 2021 (21%), the proportion of PVL-positive isolates was comparable to previous years. Like in previous years, the proportion of PVL-positive isolates was higher in diagnostic isolates (798/2,018 isolates; 40%) than in screening isolates (679/3,429 isolates; 20%).

In 2025, for 489 (9%) of the MRSA isolates whole-genome sequencing was performed. The isolates belonged to 70 different multi-locus sequence types (STs), of which ST5 was most frequently identified (n= 76; 16%), followed by ST398 (n= 56; 11%), ST8 (n= 45; 9%) and ST6 (n=44; 9%) and ST22 (n= 31; 6%). In the period 2021-2025, the most frequently identified ST among sequenced PVL+ MC0398 was ST1232 (93%; 28/30). Among *S. argenteus*, the majority (14/19; 74%) belonged to ST2250.

Figure 5.2.5.3 *Trends in the twenty most frequently identified MLVA-types of MRSA from 2025 in the Netherlands (2021 to 2025) among diagnostic and screening isolates, based on Type-Ned MRSA surveillance data*



The graph displays the proportions of the 20 most common MLVA-types from 2025 per sampling year.

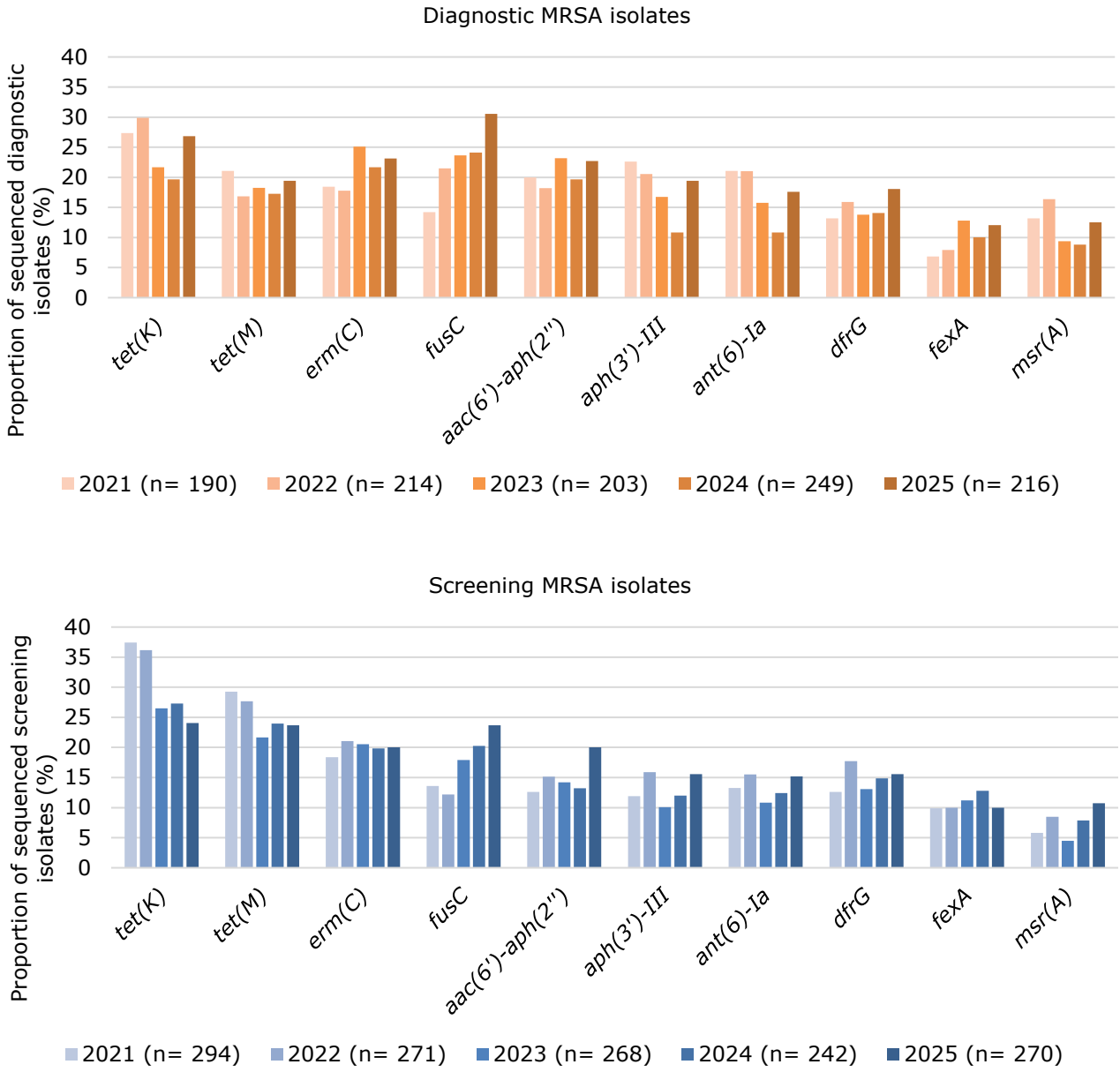
The first MRSA isolate per person sampled in the period 2021 to 2025 was selected, with the exception that the first diagnostic isolate is included when both a screening and a diagnostic sample are submitted from the same person.

Of the 5,461 isolates submitted in 2025, all contained the *mecA* gene except for 18 (0.3%) isolates that contained the *mecC* gene and no *mecA* gene, of which 9 were diagnostic isolates. Besides *mecA*, the antimicrobial resistance (AMR) genes *blaZ* (encoding beta-lactamase; 94%) and *tet(K)* (encoding tetracycline resistance ribosomal protection protein; 28%) were most frequently identified in the genomes of 2,427 sequenced MRSA isolates obtained between 2021 and 2025. The other nine most frequently identified AMR genes in MRSA isolates putatively encode for resistance against tetracyclin (*tet(M)*), erythromycin (*erm(C)*), fusidic acid (*fusC*), aminoglycosides (*aac(6')-aph(2'')*, *aph(3')-III*, *ant(6)-Ia*), trimethoprim (*dfrG*), chloramphenicol (*fexA)* and macrolide, Streptogramin B resistance (*msr(A)*). There is a trend of an increasing proportion of isolates containing the *fusC* gene in both diagnostic and screening isolates (Figure 5.2.5.4). In addition, the proportion of diagnostic isolates containing the *fexA* gene is increasing.[2] A decrease is observed in the proportion of screening isolates containing the *tet(M)* gene and screening isolates with the *tet(K)* gene (Figure 5.2.5.4).

MRSA clusters of special interest
In 2025, MRSA was the second most frequent micro-organism in hospital outbreaks (12/43) reported to the Early warning and response meeting for Healthcare associated Infections and AntiMicrobial Resistance (SO-ZI/AMR). For HRMO outbreaks in LTCFs it was by far the most reported micro-organism (20/24), see Chapter 5.2.7). Besides outbreaks in healthcare settings, there were some outbreaks in the community that required extra attention:

- In 2025, spread of PVL-positive MRSA with MLVA-type MT0240 was observed among students. Students from different cities in the West of the Netherlands were involved, mainly from three different student societies. An outbreak with MT0240 among students was also seen in 2023 and 2024. As MT0240 is a rather common MLVA type of MRSA, a genetic cluster of two or more MT240 isolates can only be noticed after WGS.
- In October 2025 a strong increase of fusidic acid resistant MRSA with MLVA-type MT4627 was reported, that was previously associated with impetigo-outbreaks. The first outbreak with MT4627 was reported in a region in the east of the country in 2019 and this type has slowly spread to other parts of the country in the following years. In the past few years, each year an increase of this MLVA-type was observed during the impetigo-season, approximately in July until October. This MRSA type was also part of a European outbreak.[3]

Figure 5.2.5.4 *Trends in the ten most frequently identified antimicrobial resistance genes in MRSA in the Netherlands (2021 to 2025), based on Type-Ned MRSA surveillance data*



The graph displays the proportion of isolates in which the depicted antimicrobial resistance genes were identified per sampling year.

The *mecA* and *mecC* genes are not included since their presence was part of the isolate inclusion criteria. Furthermore, the *blaZ* gene was not included, since this was present in almost all isolates.

MRSA isolates that were sequenced and fulfilled the inclusion criteria for molecular analysis are included.

Clinical/epidemiological characteristics of patients with MRSA based on Type-Ned
In 2025, the persons from whom MRSA was cultured and submitted to Type-Ned had a median age of 35 years (range 0 - 99) and 2,980 (55%) were male. Based on information provided at sample submission, diagnostic purposes were the reason for sampling in 46% of the persons (2,510/5,461), which is slightly less than the 48-50% of the two last years but much higher than before. Screening was the reason for sampling in 51% (2,784/5,461): in 41% (2,233/5,461) screening was performed because of presumed increased risk for MRSA carriage including active surveillance, and in 10% (551/5,461) because the person was part of a contact tracing investigation. For 3% (n=167) the reason of sampling was unknown.

For 73 of the 5,461 (1%) persons, it was recorded in the questionnaire that they were employees in a healthcare facility that were tested as part of a local screening programme, and for 2,229, including contacts in a contact tracing investigation, no additional data were available. Therefore, additional epidemiological questionnaire data for 2025 were available for 57% (n=3,091) of the persons. This proportion is lower than the last two years (69% and 64% in 2023 and 2024).

In Table 5.2.5.2 an overview of the clinical/epidemiological characteristics of included persons is summarized. Seventy-eight percent (2418/3092) were sampled in the hospital, of which 43% in outpatient departments, 30% in inpatient departments and 4% during their stay in the Intensive care unit. In the group of persons that were sampled for screening/active surveillance, the large majority (94%) met the SRI risk category 1, 2, or 3[4], whereas in diagnostic isolates this proportion was - as expected - much lower (51%), though higher than in the preceding years (2021-2024 (44-46%)). Work-related exposure to livestock animals was reported for 2% of persons with diagnostic samples and 12% of persons with samples that were taken for screening/active surveillance. The latter is comparable with 2024 (13%) but varied between 17 and 25% in the years before. The main group of livestock animals to which this group was exposed were pigs (74%), and from 93% of persons with a livestock-related profession MRSA belonging to MC0398 was sampled. Out of all persons with diagnostic samples with MC0398, the proportion with work related exposure to livestock animals decreased from 38% in 2021 and 22% in 2022-2023 to 14% in 2024 but was 20% (n=17/85) again in 2025. This percentage of persons that were sampled for screening/active surveillance was 76% (n=118/155) in 2025.

The proportion of MRSA positive persons living in an asylum centre was 26%, comparable to the two preceding years. The proportion of persons for whom hospitalization abroad for at least 24 hours during the previous two months was recorded was 144/1757 (8%), comparable to 2022-2024 (7-8%). The main geographic regions of previous hospitalizations in 2025 were Eastern Europe (16%), Western Europe (15%) and Western Asia, including Turkey (15%). The proportion in Eastern Europe increased, from 1-4% in 2021-2022 to 10-12% in 2023-2024 to the present 16%. The proportion in Southern Europe varies over the years: it was 16% in 2024 but now added up to 8%. Ukraine

and Turkey were the most frequently reported countries (13% (18/144) and 11% respectively), followed by Egypt and Belgium (6 and 5%). In 548/1789 (31%) persons an underlying illness was reported (underlying illness unknown in 1,302 persons), with skin disorders (189/548, 34%) and diabetes (29%) being the most mentioned underlying conditions.

Discussion

Calculated from ISIS-AR data, the proportion MRSA among diagnostic *S. aureus* isolates is 3% in 2025. There seems to be a slight increase in resistance over the last five years across different care facilities. Although statistically significant, the trend was not considered microbiologically relevant. Still, from a public health perspective, the small increase each year can have substantial consequences over a longer period, and it matches with the observed annual increase in submitted MRSA isolates for molecular surveillance at RIVM. It should be noted that in 2021-2022 the COVID pandemic had a major influence on Dutch society and healthcare. Therefore, a comparison with these years may be less appropriate. Compared to 2023 and 2024, resistance percentages seem to be relatively stable, except for outpatient departments. Upcoming years should provide more information about MRSA-trends in the Netherlands.

Resistance levels in blood isolates remained consistently low over the years at 2%. ICUs had a 4% resistance, in line with resistance in ICU isolates from all materials.
As described last year, MRSA isolates submitted via GPs, outpatient and inpatient departments (excl. ICUs) show an increase in phenotypic fusidic acid resistance. Among sequenced diagnostic MRSA isolates in 2025, the fusidic acid resistance gene *fusC* is indeed the most common antimicrobial resistance gene (27%). The proportion of isolates with the *fusC* gene is increasing in both diagnostic and screening isolates. Fusidic acid is frequently used in case of skin infections, such as impetigo. In case of impetigo due to fusidic acid-resistant MRSA, both the first and second advised treatment for general practitioners are not effective.[5]

The distribution of risk factors for MRSA was comparable to previous years. However, the percentage for whom work-related exposure to livestock animals is reported decreases. Moreover patients with MRSA infections who were previously admitted to a hospital abroad were increasingly hospitalized in Eastern Europe (Ukraine). Although skin disorders are the most reported underlying condition since 2023, this could be a result of wrongly recording impetigo as an underlying illness instead of a presentation of the MRSA infection.

When interpreting the surveillance results, several factors should be taken into account. Within the ISIS-AR and Type-Ned surveillance, routine culture results and isolates from MMLs are collected. This may overestimate resistance percentages as GPs generally request cultures only in case of clinical treatment failure, leading to selective sampling. This occurs to a lesser extent in hospital departments. Blood samples for culturing are taken routinely in case of suspected bloodstream infection or meningitis, and are, therefore, considered to be the least biased to calculate resistance percentages. On the other hand, MRSA screening isolates originate from selective cultures for MRSA that do not detect

methicillin sensitive isolates and thus cannot be used to calculate the percentage of MRSA among all *S. aureus*. Besides (changes in) selective sampling and culturing, and (changes in) screening practices could also affect outcomes. Therefore, only diagnostic isolates were included to assess MRSA prevalence and diagnostic and screening isolates are shown separately for Type-Ned data. In addition, misclassification of screening and diagnostic isolates might have occurred in the molecular results since distinction between screening and diagnostic isolates is solely based on the material of origin. Furthermore, only 10% of the MRSA isolates are included in the analysis of STs and resistance genes based on a semi-random selection of isolates for sequencing. In this selection, persons with no person ID available are excluded (e.g. asylum seekers and neonates). Laboratories with large numbers of MRSA and common MLVA-types are relatively underrepresented and blood and liquor isolates are relatively overrepresented (see selection criteria for WGS).

From July 2026 onwards, Nanopore long-read sequencing will be implemented in the MRSA surveillance. When whole-genome multilocus sequence typing is automated, all isolates will be assigned to wgMLST clusternumbers and genogroups, which is more reliable than MLVA and MLVA-complexes.

Table 5.2.5.2. *Epidemiological data of 3,091 MRSA positive persons (excluding employees of healthcare facilities) with an isolate in the Type-Ned MRSA surveillance system, with a sampling date in 2025*

	Diagnostic and screening combined[a]		Diagnostic		Screening / active surveillance	
Characteristic	**Data available (N)**	**n (%)**	**Data available (N)**	**n (%)**	**Data available (N)**	**n (%)**
Sampling location (hospital only)						
Outpatient departments	2418	1047 (43)	1194	540 (45)	1205	501 (42)
Inpatient departments (excluding Intensive Care Units)	2418	723 (30)	1194	341 (29)	1205	379 (31)
Intensive Care Units	2418	106 (4)	1194	48 (4)	1205	57 (5)
Other/unknown	2418	542 (22)	1194	265 (22)	1205	268 (22)
Risk factors						
Meeting SRI risk category 1,2, or 3[b,c]	2611	1918 (73)	1237	630 (51)	1326	1246 (94)
Work-related exposure to livestock animals	2164	149 (7)	1094	21 (2)	1043	128 (12)
Pigs	149	111 (74)	21	10 (48)	128	101 (79)
Cattle	149	36 (24)	21	10 (48)	128	26 (20)
Other/unknown	149	2 (1)	21	1 (5)	128	1 (1)
Hospitalization abroad >24 hours during the previous two months	1757	142 (8)	900	32 (4)	840	110 (13)
Western Europe	142	22 (15)	32	5 (16)	110	17 (15)
Western Asia (including Turkey)	142	22 (15)	32	6 (19)	110	16 (15)
Eastern Europe	142	23 (16)	32	5 (16)	110	18 (16)
Other/unknown country	142	75 (53)	32	16 (50)	110	59 (54)
Living in asylum centre	2868	740 (26)	1449	101 (7)	1364	639 (47)

a Including persons for whom the reason for sampling was unknown.

b This question did not appear in all questionnaires and is therefore not completed for all MRSA positive persons.

c SRI risk category 1: the person is known to be MRSA positive; risk category 2: person at high-risk for MRSA carriage; risk category 3: person at low-risk for MRSA carriage; risk category 4: person not suspected of MRSA carriage.

Conclusions

- Compared to 2021, there seems to be a slow increase in MRSA positive cultures in all departments to 3%, and 4% in the ICU. Although the trend is statistically significant, it is not considered microbiologically relevant, and the effect of the COVID-pandemic on MRSA% is unclear - meaning years may not be comparable.
- The absolute number of MRSA isolates submitted for the Type-Ned MRSA surveillance is increasing each year and is higher compared to pre-COVID pandemic levels, both among diagnostic and screening isolates.
- A strong increase was observed in phenotypic fusidic acid resistance among diagnostic MRSA isolates. This corresponds to a clear increase in the fusidic acid resistance gene *fusC* in both screening and diagnostic MRSA isolates.
- The most frequently identified MLVA-types in 2025 were MT4627 (4%), MT0240 (4%) and MT2307 (3%) among diagnostic isolates and MT0398 (4%), MT4627 (3%) and MT2307 (3%) among screening isolates. MLVA-types MT4627, MT0240 and MT2307 showed an increasing trend in the past five years, whereas MT0398 showed a decreasing trend.
- In 2025, 40% of the diagnostic MRSA-isolates carried the PVL-encoding genes, whereas 20% of the screening isolates were PVL-positive.
- The top 10 most occurring antimicrobial resistance genes among MRSA isolates putatively encode for tetracycline, erythromycin, fusidic acid, aminoglycosides, trimethoprim, chloramphenicol and macrolide resistance.
- The majority of persons with samples that were taken for screening/active surveillance, met SRI-category 1,2 or 3[2] (94%). The percentage for whom work-related exposure to livestock animals was the risk factor decreased from 26-27% in 2021-2022 to 13% in 2024 and 2025.
- Hospitalization abroad for at least 24 hours during the previous two months was recorded in 8% of the MRSA positive persons. This percentage remains stable over the years. The main geographic regions of recent hospitalizations abroad of MRSA positive persons were Eastern Europe (16%), Western Europe (15%) and Western Asia, including Turkey (15%).

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5.2.6 *Vancomycin-resistant Enterococci*

Introduction
In the last few years, a considerable number of Dutch hospitals have been confronted with outbreaks of vancomycin-resistant *Enterococcus faecium* (VRE_{fm}). Here we give an overview of available data that describe the epidemiology of VRE in The Netherlands.

Methods
There is no national surveillance program with centrally organised characterisation of VRE-strains in The Netherlands, however, there are two surveillance systems that collect and provide data on VRE_{fm}. VRE_{fm} outbreaks are reported through the Early warning and response meeting for Healthcare associated Infections and Antimicrobial Resistance (SO-ZI/AMR, see section 5.2.7). In addition, based on the national surveillance system of antimicrobial resistance, ISIS-AR, the proportion of vancomycin resistance in *E. faecium* isolates among patients in various healthcare settings in the Netherlands was determined. The prevalence of VRE_{fm} isolates was based on positivity of confirmation tests (molecular detection of *vanA*/*B*), or, if these tests were lacking, on re-interpretation of test-values for amoxicillin/ampicillin and vancomycin according to EUCAST 2025, with VRE_{fm} being defined as resistant to amoxicillin/ampicillin and vancomycin. Both diagnostic isolates (isolates cultured from clinical material) and screening isolates (predominantly rectal swabs) were included. Numbers are based on data from 36 laboratories in the Netherlands that continuously reported to the ISIS-AR database in the past five years. The first diagnostic or screening *E. faecium* isolate per patient was selected.

Results
In 2025, 18 outbreaks with VRE_{fm} in the Netherlands were reported to the SO-ZI/AMR (see section 5.2.7), which were all in hospitals.
This was higher than the number of outbreaks that were reported yearly since 2020 (range 5-9 outbreaks yearly in 2020-2023 and n=14 in 2024), but comparable to the number of 19 VRE outbreaks which were reported in 2019. In total, since the start of SO-ZI/AMR in April 2012, 169 outbreaks with VRE_{fm} have been reported. Outbreaks caused by VRE_{fm} accounted for 20 to 32% of all reported outbreaks in SO-ZI/AMR yearly.
The percentage of diagnostic VRE_{fm} isolates among the total number of *E. faecium* isolates from general practitioners and (outpatient and inpatient) hospital departments in 2025 in the Netherlands based on ISIS-AR is shown in table 5.2.6.1. Figure 5.2.6.1 shows the trend in vancomycin resistance in diagnostic *E. faecium* isolates over the years. The proportion of diagnostic isolates with VRE_{fm} was persistently low, although slight increases can be seen in all hospital departments, with significant and microbiologically relevant trends in outpatient departments and intensive care units.
Based on data from 36 laboratories that continuously report to ISIS-AR, the absolute numbers of VRE_{fm} isolates from screening samples of both GP and hospital departments (out- and inpatient, including intensive care units), were the highest since 2021. The total number of positive screening samples ranged between 132 and 206 in the years 2021-2024, but was 350 in 2025 (Table 5.2.6.2).

Table 5.2.6.1 *Vancomycin-resistant E. faecium (VRE_{fm}) in diagnostic isolates in the Netherlands in 2025, based on ISIS-AR data*

Type of department	Tested isolates, N	VRE, N (%)
General practitioner	475	2 (0.4)
Outpatient departments	499	5 (1.0) ↑
Inpatient departments excl. intensive care units	2,905	19 (0.7)
Intensive care units	598	5 (0.8) ↑
Total	**4,477**	**31 (0.7) ↑**

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10	No significant and microbiologically relevant time trend.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

Numbers are based on a selection of 36 laboratories that continuously reported to the ISIS-AR database in the past five years. The first diagnostic *E. faecium* isolate per patient was selected.

The prevalence of vancomycin-resistant *Enterococcus faecium* (VRE_{fm}) isolates was based on positivity of VRE confirmatory tests, or, if these tests were lacking, on re-interpretation of test-values for amoxicillin/ampicillin and vancomycin according to EUCAST 2025, with VRE_{fm} being defined as resistant to amoxicillin/ampicillin and vancomycin.

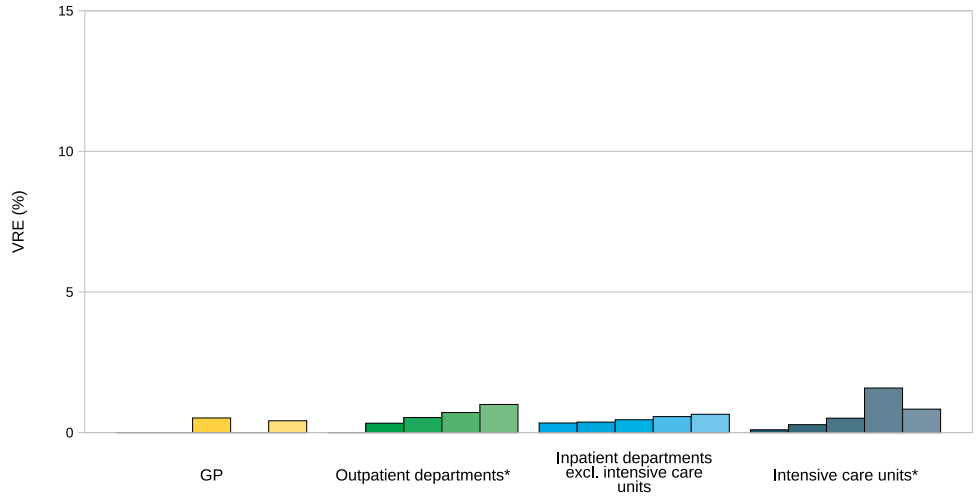
Table 5.2.6.2 *Absolute numbers of vancomycin-resistant E. faecium (VRE_{fm}) isolates in the Netherlands, 2021-2025, based on ISIS-AR data*

	GP and outpatient departments			Inpatient departments including intensive care units			Total		
Year	D	S	Total	D	S	Total	D	S	Total
2021	0	49	49	11	72	83	11	121	132
2022	2	49	51	13	118	131	15	167	182
2023	5	30	35	16	86	102	21	116	137
2024	4	56	60	26	120	146	30	176	206
2025	7	149	156	24	170	194	31	319	350

GP: general practitioners, D: diagnostic, S: screening

Numbers are based on a selection of 36 laboratories that continuously reported to the ISIS-AR database in the past five years. The first diagnostic *E. faecium* isolate per patient was selected, with a preference for the first diagnostic isolate if both diagnostic and screening samples were taken. The prevalence of vancomycin-resistant *Enterococcus faecium* (VRE_{fm}) isolates was based on positivity of VRE confirmatory tests, or, if these tests were lacking, on re-interpretation of test-values for amoxicillin/ampicillin and vancomycin according to EUCAST 2025, with VRE_{fm} being defined as resistant to amoxicillin/ampicillin and vancomycin.

Figure 5.2.6.1 *Trends in percentage of diagnostic vancomycin-resistant E. faecium (VRE$_{fm}$) isolates among the total number of diagnostic E. faecium isolates in the Netherlands (from left to right 2021 to 2025), based on ISIS-AR data*



Numbers are based on a selection of 36 laboratories that continuously reported to the ISIS-AR database in the past five years. The first diagnostic *E. faecium* isolate per patient per year was selected.

* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

The prevalence of vancomycin-resistant *Enterococcus faecium* (VRE$_{fm}$) isolates was based on positivity of VRE confirmatory tests, or, if these tests were lacking, on re-interpretation of test-values for amoxicillin/ampicillin and vancomycin according to EUCAST 2025, with VRE$_{fm}$ being defined as resistant to amoxicillin/ampicillin and vancomycin.

Discussion

The number of reported VRE$_{fm}$ outbreaks in 2025 was higher than the annual number in 2020-2024, but comparable to 2019 and before. The temporary decrease since 2020 could have been related to the COVID-19 pandemic, and a change in infection prevention measures.
Although the total number of screening samples that were tested is unknown, the absolute number of positive screening isolates shows a remarkable increase in 2025 compared to the previous four years. Probably, these higher numbers result from several extensive source and contact tracing investigations related to hospital VRE outbreaks. Such long-lasting outbreaks often comprise VRE testing of large numbers of patients including discharged patients, who had been admitted previously on one of the involved hospital departments. Three of the notified hospital VRE-outbreaks in 2025 lasted more than 6 months, with high total numbers of, mainly only colonized, VRE-positive patients (n=19, n=65 and n=146, see section 5.2.7).
Currently, there are no centrally collected data on molecular typing of VRE$_{fm}$ isolates in the Netherlands, even though the WHO listed VRE$_{fm}$ in the high-risk category.[1] Thus, there are no reliable data available on the molecular epidemiology of VRE$_{fm}$ in Dutch hospitals.

Conclusions

- The number of reported hospital outbreaks with VRE$_{fm}$ in 2025 was higher than in the past four years, but comparable to the number in the pre-COVID years.
- The proportion of VRE$_{fm}$ in infection-related isolates with *E. faecium* in various healthcare settings is still low (below 1%), but slight increases in the previous five years are seen in outpatient hospital departments and intensive care units.
- The absolute number of positive screening VRE$_{fm}$ isolates increased in 2025 compared to the previous four years. This was probably the result of several large, long-lasting hospital VRE outbreaks with extensive contact tracing investigations. The absolute number of diagnostic VRE$_{fm}$ isolates is still low.

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5.2.7 Early warning and response meeting for Healthcare-associated Infections and AntiMicrobial Resistance (SO-ZI/AMR)

Introduction

In 2012, the Early warning and response meeting for Healthcare-associated Infections and AntiMicrobial Resistance (SO-ZI/AMR) was founded.[1,2] Healthcare institutes can report outbreaks of highly resistant microorganisms (HRMO)[3] to the SO-ZI/AMR. Although the primary scope of SO-ZI/AMR is gaining insight in HRMO outbreaks, incidentally non-HRMO outbreaks are reported as well. The SO-ZI/AMR consists of experts in the field of clinical microbiology, infection prevention, elderly care and public health and meets once a month. The SO-ZI/AMR assesses the risk of the outbreak to public health, monitors the course of the outbreak and facilitates – on request of the hospital or long term care facilities (LTCFs) – the acquisition of external expertise. An overview of active outbreaks is reported to professionals involved in infection prevention and control (IPC) on a monthly basis. Outbreaks of special concern are reported with more detailed information in the weekly report of the general Early warning and response meeting.[4] Notification is voluntary, but all hospitals and LTCFs have committed to participate in SO-ZI/AMR via their umbrella organizations (NVZ, NFU, Actiz).[5-7] Moreover since 2017, LTCFs can make use of a financial compensation rule from the NZa (Dutch Healthcare Authority) to cover the costs of detecting and controlling HRMO outbreaks, provided that these outbreaks are reported to SO-ZI/AMR.[8]

Methods

Notifications and monthly updates of outbreaks are submitted through the web-based application system Osiris. Outbreaks can be reported by infection control practitioners, medical microbiologists, or elderly care physicians. The following notification criteria are applied: (a) 2 or more patients infected or colonized with the same HRMO (or non-resistant microorganism) with an epidemiological link, resulting in more than usual outbreak response measures in the healthcare institute, or (b) in case of a highly prevalent HRMO (or non-resistant microorganism) 3 or more patients infected or colonized with the same microorganism with an epidemiological link, resulting in more than usual outbreak response measures in the healthcare institute.

During monthly meetings of the SO-ZI/AMR, each outbreak is categorized in one of three phases with I as lowest, III as highest risk for public health due to uncontrolled spread. In the monthly meetings, the SO-ZI/AMR (re-)assesses the phase of each notified outbreak which was based on the latest information, updated by the notifiers in Osiris. Once an outbreak is contained, it is classified as phase 0. Otherwise, the categories are: Phase I: transmission is under control, all necessary information on the situation is available, active monitoring is in place; phase II: active transmission cannot be ruled out, complete overview on the outbreak has not yet been achieved (active contact screening and/or source tracing and control is still ongoing); phase III: transmission is ongoing in spite of IPC measures, which are thus incomplete or not sufficiently effective.

All outbreaks with a notification date in 2025 were included in the analysis. Only positive patients or clients were included in the calculation of the (median) number of persons per outbreak, and positive healthcare workers were excluded. The duration of an outbreak was defined according to the length of the outbreak as it was registered by the notifier, or, if these data were missing, it was calculated as the duration between the date of reporting by the healthcare institute to the date of the SO-ZI/AMR meeting in which the outbreak was assigned phase 0 (i.e. the end of the outbreak). The reference date of data analysis was July 1, 2026.

Results

Table 5.2.7.1 provides an overview of the outbreaks (n=67) reported in 2025. These were reported by 46 different healthcare institutions: 43 outbreaks in 24 different hospitals and 24 outbreaks in 22 different LTCFs (including 20 LTCF for the elderly, 2 rehabilitation centres, 1 palliative care facility, and 1 healthcare institute with combined hospital and long-term care). Most outbreaks (n=65) ended before July 1 2026 and 2 continued after July 1 2026. The median number of patients (4) involved in outbreaks in hospitals was similar to the previous four years, when median numbers varied between 4 and 6, but was lower compared to 2021 when this number was higher (12). In LTCFs the median number of clients involved was also stable in the previous five years, with a median number of 3.5 in 2025. The maximum number of involved patients was much higher in hospitals compared to LTCF (146 vs 8). The number of reported outbreaks in hospitals with vancomycin-resistant *Enterococcus faecium* (VRE) (n=18) was higher than the annual number of VRE outbreaks reported since 2020 (range 5-9 outbreaks yearly in 2020-2023 and n=14 in 2024). In five of these VRE outbreaks in 2025, more than 10 patients were involved. Three of those lasted more than 6 months, with high numbers of VRE-positive patients (n=19, n=65 and n=146).

Five hospital outbreaks were with carbapenemase-producing (CP) Gram-negatives (2 outbreaks with CP Enterobacterales and 1 with CP *Pseudomonas aeruginosa*, CP *Acinetobacter baumannii* and CP *Acinetobacter variabilis* each). The number of MRSA outbreaks in hospitals (n=12) was similar to 2024 (n=11), but lower than in 2023, when an extraordinarily high number of 20 MRSA hospital outbreaks were reported. In the years 2020-2022, yearly 2-7 MRSA outbreaks were reported. Half (6/12) of the MRSA outbreaks in 2025 were related to paediatric or neonatal wards, which is a similar pattern compared to previous years. Six non-HRMO outbreaks were reported by hospitals. Four of these were outbreaks of *Serratia marcescens* on neonatal wards, one was an outbreak of methicillin-susceptible *S. aureus*, also on a neonatal ward, and one of *Streptococcus pyogenes* on a maternal ward. In LTCFs the vast majority of notified outbreaks in 2025 concerned MRSA, which was also the most reported HRMO in previous years. The total number of 20 MRSA outbreaks in LTCFs was substantially higher than in the years 2020-2023 (with a minimum of n=3 in 2021 and a maximum of n=11 in 2020), but comparable to the pre-COVID-19 period and 2024, with 17 MRSA outbreaks in LTCF reported in both 2019 and 2024.

Overall in 2025, two outbreaks were classified as phase III. One of these concerned an extensive, long-lasting VRE outbreak in a hospital. This was reported to SO-ZI/AMR in March 2025 and involved in total 146 *vanB* VRE-positive patients. Multiple hospital departments were involved, such as surgical and medical departments and an intensive care unit, a very small number of patients had an infection with the outbreak strain, while the majority was only colonized. The outbreak was declared over in November 2025 and the total duration was approximately eight months. The second outbreak in phase III was an outbreak of MRSA in a LTCF for the elderly. The outbreak was notified to SO-ZI/AMR in June 2025 and ended in January 2026. The course of the outbreak was complicated due to the involvement of several MRSA-positive healthcare workers who had worked at different departments of the organization, which facilitated the spread to different locations. Three distinct *mecA*-positive MRSA outbreak strains (MLVA complex (MC) - MLVA type (MT)) were detected: MC0088-MT0088, MC0008-MT0237 and MC0001-MT0151. In total, six MRSA-positive clients and seven healthcare workers tested positive in this outbreak.

Discussion

The total number of reported outbreaks (67) in 2025 was higher than in the previous five years. The lowest number of 27 outbreaks were reported in 2020, which increased again after the COVID pandemic up to 50 in 2024. The number of 67 outbreaks this year was more comparable to 2017-2019, when around 60 outbreaks were reported each year. This trend was similar for both hospitals and LTCF, which may reflect that the attention to HRMO outbreaks has risen again after the potentially waned vigilance during the COVID-19-pandemic and the years onwards. An increase in the number of VRE-outbreaks in hospitals was observed. Six of the reported outbreaks were caused by non-HRMO, which are strictly not the primary scope of SO-ZI/AMR, but which are still incidentally reported by healthcare institutes.

Strikingly, the 43 hospital outbreaks were reported by only 24 hospitals of the total number of 69 hospitals (113 locations) in the Netherlands in 2025.[9] This shows that the majority of hospitals did either not experience notifiable HRMO outbreaks in 2025, or, since notification to SO-ZI/AMR is voluntary, that the medical professionals decided not to notify an outbreak for any reason. The same accounts for LTCFs, of which only 22 notified an HRMO-outbreak.
In LTCFs, increased attention for IPC may have increased the number of notifications and outbreak investigations.
The outbreaks assigned phase III by SO-ZI/AMR in 2025 emphasise the need for continued attention for IPC and well organized IPC infrastructures.

Table 5.2.7.1 *Characteristics of outbreaks reported to the SO-ZI/AMR in 2025*

	Hospitals n=43	**LTCFs[5] n=24**	**Total 2025 n=67**
	n	**n**	**n**
Microorganism (resistance mechanism)[1]			
Staphylococcus aureus (MRSA)	12	20	32
Enterococcus faecium (VRE)	18		18
Enterobacterales (CPE) (various species)	2	2	4
Enterobacterales (ESBL) (various species)	1	2	3
Pseudomonas aeruginosa (CPPA)	1		1
Acinetobacter baumannii (CPAB)	1		1
Acinetobacter variabilis (CP *Acinetobacter*)	1		1
Escherichia coli (FQ and AG-R)	1		1
Non-HRMO outbreaks[2]	6		6
Highest level phase[3]			
phase I	3	3	6
phase II	39	20	59
phase III	1	1	2
Median number of patients/clients[4] (range)	4 (1-146)	3.5 (1-8)	4 (1-146)
Duration outbreak			
<1 month	6	5	11
1-6 months	27	17	44
>6 months	10	2	12

n: number of outbreaks, LTCF: long-term care facilities

[1] MRSA = methicillin-resistant *Staphylococcus aureus*; VRE = vancomycin-resistant *Enterococcus faecium*; CPE = carbapenemase-producing Enterobacterales; ESBL = extended-spectrum β-lactamase producing; CPPA = carbapenemase-producing *Pseudomonas aeruginosa*; CPAB = carbapenemase-producing *Acinetobacter baumannii* complex; CP = carbapenemase-producing; FQ and AG-R = fluoroquinolone- and aminoglycoside-resistant; HRMO = highly resistant microorganism

[2] Six non-HRMO outbreaks in hospitals were reported: four outbreaks with *Serratia marcescens* on neonatal care departments, one *Streptococcus pyogenes* outbreak on a maternal ward and one methicillin-susceptible *S. aureus* outbreak on a neonatal ward

[3] Phase I: transmission is under control, all necessary information on the situation is available, active monitoring is in place; phase II: active transmission cannot be ruled out, a complete overview on the outbreak has not yet been achieved (active contact screening and/or source tracing and control is still ongoing); phase III: transmission is ongoing in spite of infection control measures, which are thus incomplete or not sufficiently effective.

[4] In four outbreaks, one patient and one or more healthcare workers were involved

[5] Including 20 outbreaks in an LTCF for the elderly, 2 rehabilitation centres, 1 palliative care facility, 1 healthcare institute with combined hospital and long-term care

Conclusions

- In total, 67 outbreaks were reported to the SO-ZI/AMR in 2025, which is higher compared to the previous five years, but more or less comparable to the pre-COVID-19 years.
- Only a minority of both hospitals and LTCFs in the Netherlands have notified an HRMO-outbreak to SO-ZI/AMR in 2025.
- The number of VRE outbreaks in hospitals was again notably higher compared to previous years at n=18.
- In LTCFs, the majority of reported outbreaks were with MRSA.
- Most outbreaks had phase II as the highest phase and two outbreaks were classified as phase III, which concerned a long lasting VRE hospital outbreak with a high number of patients involved and an MRSA outbreak in an LTCF.

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5.2.8 Neisseria meningitidis

Introduction
Neisseria meningitidis can cause rare but life-threatening invasive meningococcal disease (IMD). Globally, there is concern about a rise in penicillin non-susceptible meningococcal isolates. Ongoing surveillance is required to assess the development of antibiotic resistance among IMD isolates.

Methods
Isolates cultured from IMD patients are submitted for serogrouping and antibiotic susceptibility testing to the Netherlands Reference Laboratory for Bacterial Meningitis (NRLBM, Amsterdam UMC) by all Dutch microbiological laboratories. The coverage is estimated to be 95% of all IMD cases in the Netherlands.
The MIC for penicillin was determined by Etest using Mueller-Hinton Fastidious Agar (MHF) plates and incubation at 36°C under 5% CO_2 for 18-24 h (susceptible ≤ 0.25 mg/L; resistant > 0.25 mg/L, EUCAST). In case of phenotypic resistance to penicillin, susceptibility to ceftriaxone was also assessed by Etest using MHF plates and incubation at 36°C under 5% CO_2 for 18-24 h. Isolates were classified as susceptible when MIC <0.125 mg/L, in line with EUCAST guidelines.

Results
From 2016-2025, 1,300 IMD cases were defined as patients with culture-positive blood or cerebrospinal fluid (CSF) sample, or patients with culture-negative but PCR-positive blood or CSF sample. For 29 culture-negative PCR-positive cases, a co-submitted blood isolate was available to assess penicillin resistance. In total, 1,066 isolates of 1,300 IMD cases were available for the study period; 312 isolates from meningitis patients (i.e. patients with either CSF-positive culture or with a PCR-positive CSF-sample accompanied by a blood isolate) and 754 isolates from patients with only a positive blood culture (further defined as non-meningitis IMD patients). The number of meningococcal isolates per year in this period ranged between 25 isolates (2021) and 186 isolates (2018). In 2025, in total, 98 meningococcal isolates were submitted.

Thirty-nine (98%) of the 40 received meningococcal isolates from meningitis patients were susceptible to penicillin, and one isolate was resistant (Table 5.2.8.1). For IMD blood isolates, 55 (95%) out of 58 isolates were penicillin susceptible and 3 (5%) were resistant (Table 5.2.8.2). Overall, in the past 10 years, only 14 (1.3%) out of 1,066 isolates displayed phenotypic penicillin resistance (Tables 5.2.8.1 and 5.2.8.2), but all these isolates were susceptible to ceftriaxone.

Discussion
Penicillin-resistant meningococcal isolates have been increasingly detected across the globe. In The Netherlands, penicillin resistance is still rare among isolates from IMD patients, however, in the past three years we do see some incidental cases. The change in the breakpoint for phenotypic penicillin susceptibility by EUCAST in 2021 has not affected this interpretation.

Conclusions

- Penicillin resistance in *N. meningitidis* isolates is rare in the Netherlands. Nevertheless, a small but increasing number of sporadic cases have been detected in the past three years.
- All penicillin-resistant meningococcal isolates were tested susceptible to ceftriaxone.

Table 5.2.8.1 *Penicillin susceptibility of N. meningitidis strains isolated from CSF or blood (in combination with PCR-positive CSF), 2016-2025*

	Penicillin				
	MIC* ≤ 0.25		MIC* > 0.25		Total
	n	%	n	%	
2016	37	**100**	0	**0**	37
2017	46	**100**	0	**0**	46
2018	54	**98**	1	**2**	55
2019	33	**100**	0	**0**	33
2020	14	**93**	1	**7**	15
2021	7	**100**	0	**0**	7
2022	18	**100**	0	**0**	18
2023	27	**100**	0	**0**	27
2024	33	**97**	1	**3**	34
2025	39	**98**	1	**2**	40

* MIC values in mg/L

Table 5.2.8.2 *Penicillin susceptibility of N. meningitidis blood isolates from non-meningitis IMD patients, 2016-2025*

	Penicillin				
	MIC* ≤ 0.25		MIC* > 0.25		Total
	n	%	n	%	
2016	100	**100**	0	**0**	100
2017	128	**99**	1	**1**	129
2018	129	**99**	2	**1**	131
2019	102	**100**	0	**0**	102
2020	39	**100**	0	**0**	39
2021	18	**100**	0	**0**	18
2022	38	**100**	0	**0**	38
2023	60	**97**	2	**3**	62
2024	75	**97**	2	**3**	77
2025	55	**95**	3	**5**	58

* MIC values in mg/L

5.2.9 *Neisseria gonorrhoeae*

Introduction
Neisseria gonorrhoeae is a species of Gram-negative bacteria which can cause gonorrhoea after sexual transmission. Gonorrhoea was the most commonly diagnosed bacterial sexually transmitted infection (STI) at Sexual Health Centres (SHC) in the Netherlands in 2025.[1] Third generation cephalosporins, such as ceftriaxone and cefixime, are the current first-line treatment for gonorrhoea in most countries. In the Netherlands, cefotaxime was the first-line therapy for gonorrhoea from 2003-2006, and ceftriaxone from 2006 onwards. In the past, *N. gonorrhoeae* has developed antimicrobial resistance to all drugs used for treatment of gonorrhoea. While resistance to ceftriaxone has been reported in Europe only incidentally, resistance levels globally surpass 5% in several countries.[2]

Methods
The national Gonococcal Resistance to Antimicrobials Surveillance (GRAS) programme started in 2006, collecting epidemiological data on gonorrhoea and resistance patterns of isolated strains obtained via SHC across the Netherlands. In 2025, 15 out of the 24 SHC participated in GRAS, which together accounted for 82% of SHC gonorrhoea diagnoses. Diagnosis of gonorrhoea is made by PCR on patients' materials. For GRAS, additional culture and susceptibility testing using Etest, are performed. The aim is to perform culture and susceptibility testing for all gonorrhoea patients in these SHC, but due to logistical and financial restrictions in practice there is a culture performed for around 75% of PCR-positive patients. Isolates are tested for susceptibility to ciprofloxacin, cefotaxime, ceftriaxone, and azithromycin. In 2025, additional testing for tetracycline was added in response to the emerging use of doxycycline post-exposure prophylaxis (Doxy-PEP) for STI prevention. Resistance levels are calculated using the EUCAST breakpoints for resistance.[3]

Results
The yearly national number of gonorrhoea diagnoses reported by SHC was around 6,000 from 2016 to 2020, and increased since then to 14,297 diagnoses in 2025. Between 2016 and 2025, the number of SHC participating in GRAS ranged from 14 in 2020 to 17 in 2018, but was 15 in most years. The percentage of diagnoses including a susceptibility test result was stable around 33% in the past 10 years (33.3% (4768/14,297) in 2025, Figure 5.2.9.1). In 2025, 77% of isolates were from men who have sex with men (MSM), 10% from women and 10% from men who have sex with women. Gonococcal resistance to ciprofloxacin was around 30% between 2016 and 2018 but increased since then and was 59.7% in 2025. Resistance to cefotaxime has been slowly decreasing since 2018 and was 0.2% in 2025. For azithromycin, resistance increased from 4.7% in 2016 to 30.6% in 2023, but decreased to 21.9% in 2025 (Figure 5.2.9.2). Tetracycline resistance was measured in 2025 only, and was 57.1%.

2025 marks the first year that ceftriaxone resistance was reported in the Netherlands. This person contracted gonorrhoea in South-East Asia and was diagnosed upon return to the Netherlands. The strain was resistant

to ceftriaxone (MIC 0.19 mg/L, MIC of >0.125 mg/L is considered resistant), cefotaxime (MIC 0.38 mg/L), azithromycin (MIC >256 mg/L), tetracycline (MIC 6 mg/L) and ciprofloxacin (MIC 2 mg/L). Despite measured phenotypic resistance, treatment with 1000 mg of ceftriaxone was successful, and there was no further sexual contact reported in the Netherlands.

Figure 5.2.9.1 *Number of reported gonorrhoea diagnoses at all 24 Sexual Health Centres and number and percentage of diagnoses including an antimicrobial susceptibility test result at Sexual Health Centres participating in GRAS, 2016-2025*

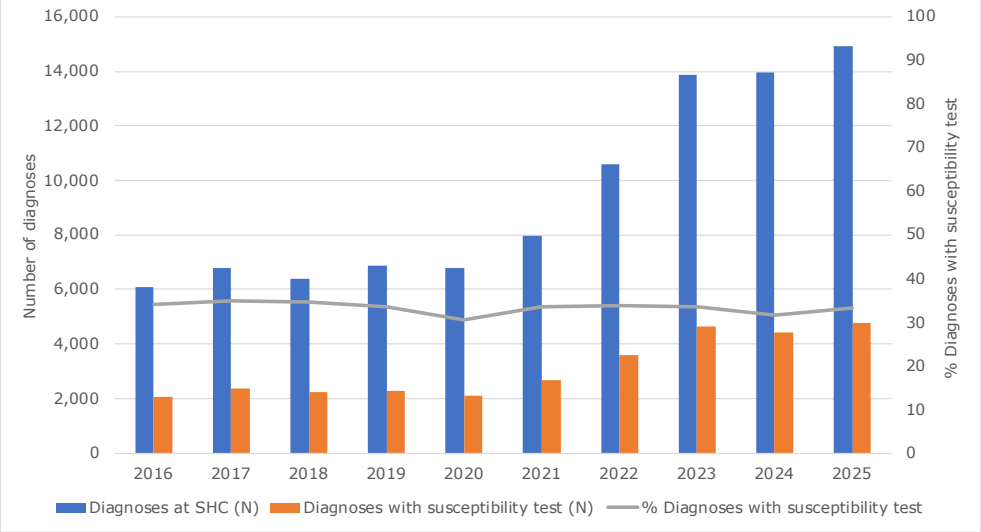
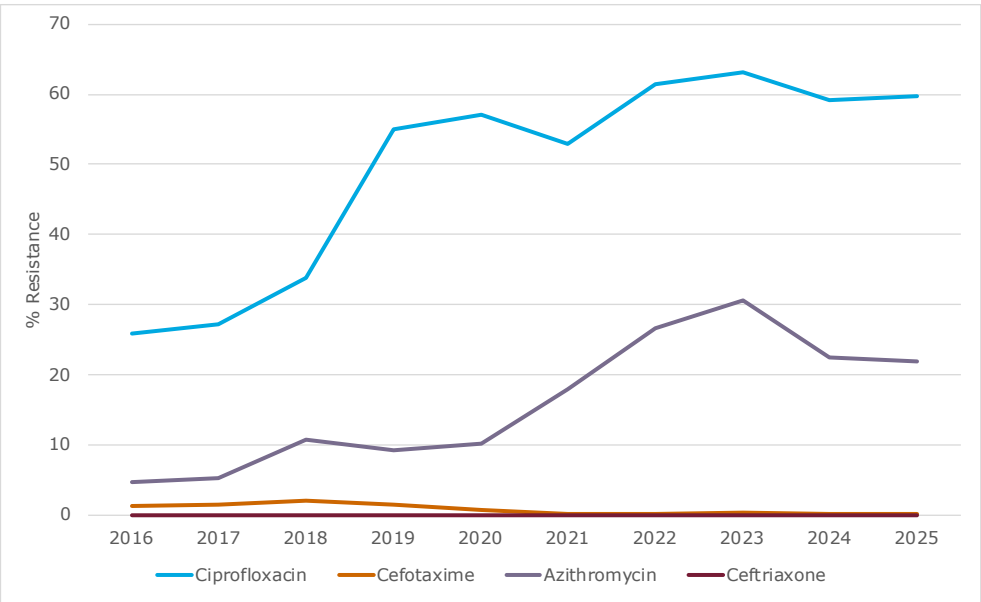


Figure 5.2.9.2 *Trends in antimicrobial resistance among Neisseria gonorrhoeae (following EUCAST breakpoints) in the Netherlands, 2016-2025. In 2025, 1 case of ceftriaxone resistance was reported*



In the MIC distribution of ceftriaxone a shift is observed since 2021 where the proportion of isolates with an MIC < 0.008 mg/L decreased and the proportion of isolates with slightly higher MIC values (MIC 0.016

mg/L) increased (Figure 5.2.9.3a). For azithromycin a shift towards higher MICs is also observed over time. (Figure 5.2.9.3b).

Discussion

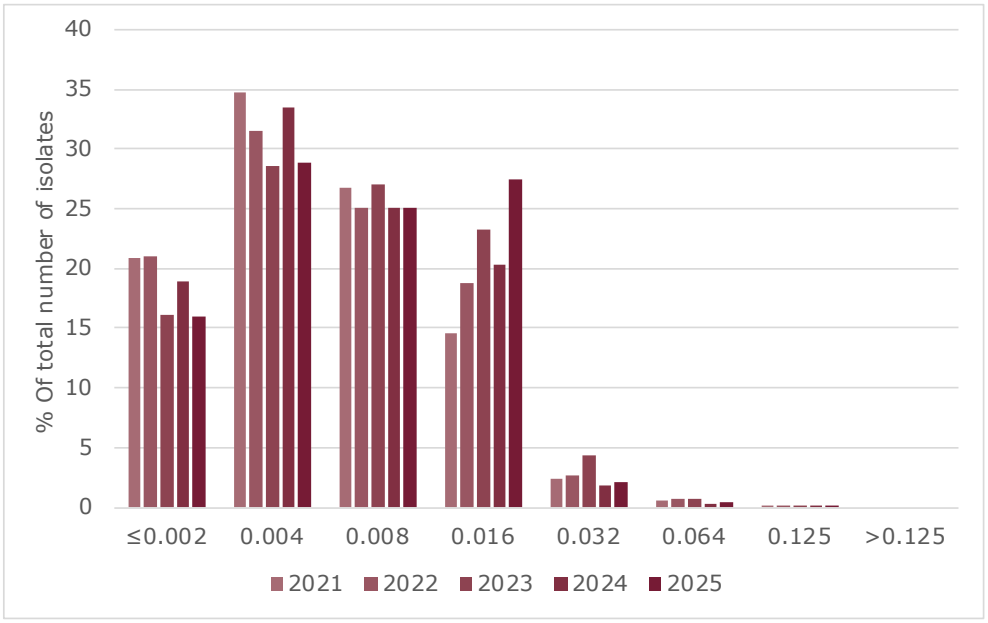
As in previous years, in 2025 for one-third (33.3%) of all gonorrhoea diagnoses at the SHC susceptibility test results were available. Susceptibility test results are not available for all gonorrhoea cases because some SHC do not participate in GRAS, and within participating SHC only ~75% of PCR confirmed cases are cultured, of which ~50% are culture negative, making susceptibility testing impossible. In the Netherlands, the recommended treatment for gonorrhoea is a single injection with ceftriaxone (500 or 1000 mg).

This year, tetracycline was added to the GRAS panel in response to the emerging use of Doxycycline post-exposure prophylaxis (Doxy-PEP) for STI prevention. Clinical trials have demonstrated Doxy-PEP to be potentially effective in reducing the incidence of chlamydia and syphilis, but its effect on gonorrhoea is dependent on existing tetracycline resistance levels. Although Doxy-PEP is not recommended in the Netherlands, 4% of MSM attending SHC in 2025 reported recent use.[1] Given the high prevalence of tetracycline resistance (57%) among *N. gonorrhoeae* in the Netherlands, Doxy-PEP is unlikely to impact gonorrhoea incidence and might increase the incidence of tetracycline-resistant gonorrhoea.

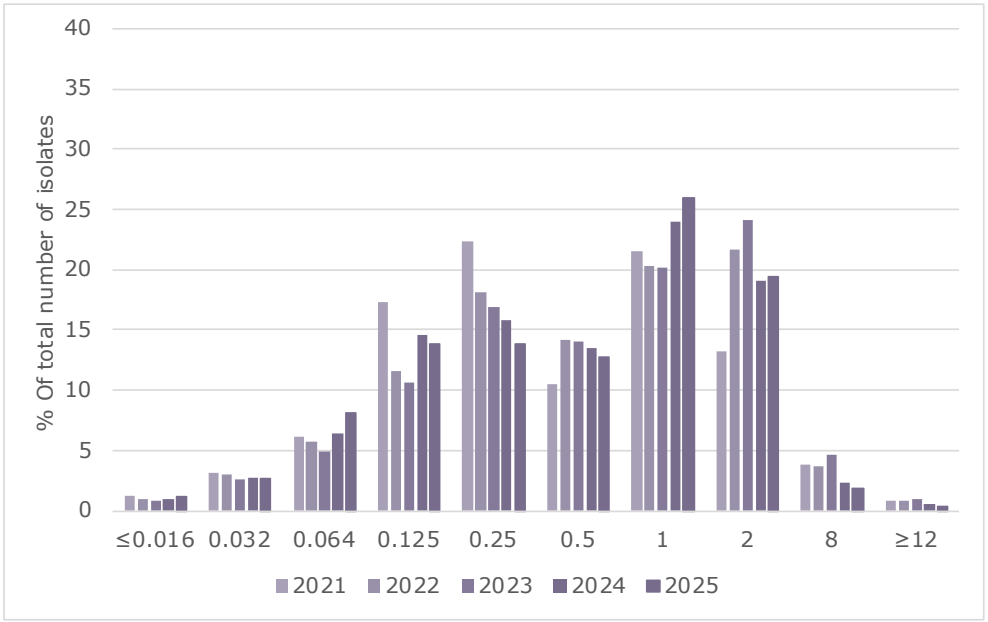
In 2025 also the first case of ceftriaxone resistance was reported in the Netherlands. This case concerned an imported infection, and since the patient did not report any further sexual contacts within the Netherlands and was successfully treated, onward transmission was prevented. This finding is in line with the higher prevalence of ceftriaxone resistance observed abroad, especially in South-East Asia[2], suggesting that the first detected cases in the Netherlands are more likely to be imported rather than originating locally. However, since overall susceptibility tests are available for only one third of gonorrhoea patients at the SHC, it is likely that not all imported resistant cases will be detected especially in asymptomatic persons - and the possibility of future local transmission of a resistant strain cannot be excluded. These developments underscore the importance of a continued effort to monitor the prevalence and emergence of antimicrobial resistance in gonococci in a systematic way, especially since also the number of gonorrhoea infections is rising.

Figure 5.2.9.3 *MIC distributions of ceftriaxone and azithromycin for Neisseria gonorrhoeae, 2021-2025*

A: MIC distribution for ceftriaxone. Following EUCAST breakpoints, an MIC of >0.125 mg/L is considered resistant



B: MIC distribution for azithromycin. Following EUCAST breakpoints, an MIC of 1 mg/L is considered the epidemiological cut-off value for resistance



Conclusions

- Thanks to the GRAS programme, around 33% of gonorrhoea diagnoses from SHC include susceptibility testing results each year.
- In 2025, ceftriaxone resistance was reported for the first time in an imported infection. There was no further transmission following this case in the Netherlands.
- Resistance to ciprofloxacin, tetracycline, and azithromycin remains high.

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5.2.10 Mycobacteria

5.2.10.1 *Mycobacterium tuberculosis* complex

Introduction

Tuberculosis (TB) remains one of the deadliest infectious diseases worldwide. Although the incidence is slowly declining globally, it has been estimated that a significant proportion of the global population is still latently infected by its main causative agent; *Mycobacterium tuberculosis*. In the Netherlands we have reached the elimination phase in the native population; more than 80% of TB cases which are diagnosed are acquired outside the Netherlands and/or in persons born abroad.

Worldwide, the development and spread of resistant *M. tuberculosis*, which hampers the adequate treatment of tuberculosis, is a concern. In the Netherlands, all cultured isolates of *M. tuberculosis* complex are sent to the RIVM for confirmation of species identification, susceptibility prediction/testing and whole genome sequencing (WGS) typing. The results are used to guide the anti-tuberculosis therapy of individual patients, to support cluster investigations, and for national TB surveillance.

Methods

In the Netherlands, tuberculosis is a notifiable disease. This means that every confirmed TB case must be reported by the physician and/or MML to the Municipal Public Health Service (GGD) within one day.
Around 30 MMLs in the Netherlands are involved in performing diagnostic tests for TB and all of these cultured *M. tuberculosis* complex isolate are sent to the RIVM. These isolates are immediately subjected to WGS for susceptibility prediction and fingerprinting. Fingerprinting data is used to identify potential genetic clusters and to support TB source contact tracing performed by Municipal Health Services. Since 2020, all *M. tuberculosis* complex isolates are initially screened by WGS for the presence of resistance mutations confidently associated with a raised MIC to any of the first line drugs.[1]

In the absence of such mutations, isolates are determined to be susceptible to standard first line therapy and no further testing is performed. If resistance mutations are detected, phenotypic resistance testing is performed to confirm the genotypic findings and to screen for additional undetected resistance.[1,2,3,4] As parenteral drugs are no longer part of the TB treatment regimen we no longer routinely predict resistance against streptomycin. From 2020 onwards, we also monitor resistance to pyrazinamide (PZA), for which the combination of the results of WGS and phenotypic testing (a composite reference standard) yield more reliable predictions, than phenotypic testing alone. Comparisons of molecular and phenotypic resistance testing have been described by Jajou et al[2] and Walker et al[3]. These studies form the basis of the current testing algorithm[4].

From 2024 we started monitoring the prevalence of fluoroquinolone resistance mutations in isolates sensitive to the first line drugs as these agents may be added to first line therapy. From 2024 a prediction of the fluoroquinolone susceptibility has been included in the standard report.

Results
After a decrease in the number of notified TB cases between 2019 and 2022, in 2023 and 2024 the annual number increased again. In 2025 the number of notified TB cases increased further by 13%; from 768 patients in 2024 to 871 patients in 2025.

In 2025, 566 (65%) of the 871 notified TB cases, were confirmed with a positive culture. Isolates from all 566 confirmed cases were received by the RIVM and subjected to WGS.

Approximately 90% of these isolates were susceptible to first line antimycobacterial drugs as no relevant resistance mutations were detected. In 10% (57/566) of the isolates resistance to one or more antimycobacterial drugs was detected. This mainly concerned isoniazid (INH) resistance (Figure 5.2.10.1.1). In total 11 multi-drug resistant (MDR) TB cases (defined as resistant to at least both isoniazid and rifampicin) were detected, and additionally 2 non-MDR TB cases with resistance to at least rifampicin (RR) (Figure 5.2.10.1.2).

Figure 5.2.10.1.1 *Yearly percentage of antibiotic resistance among M. tuberculosis complex isolates 2011-2025*

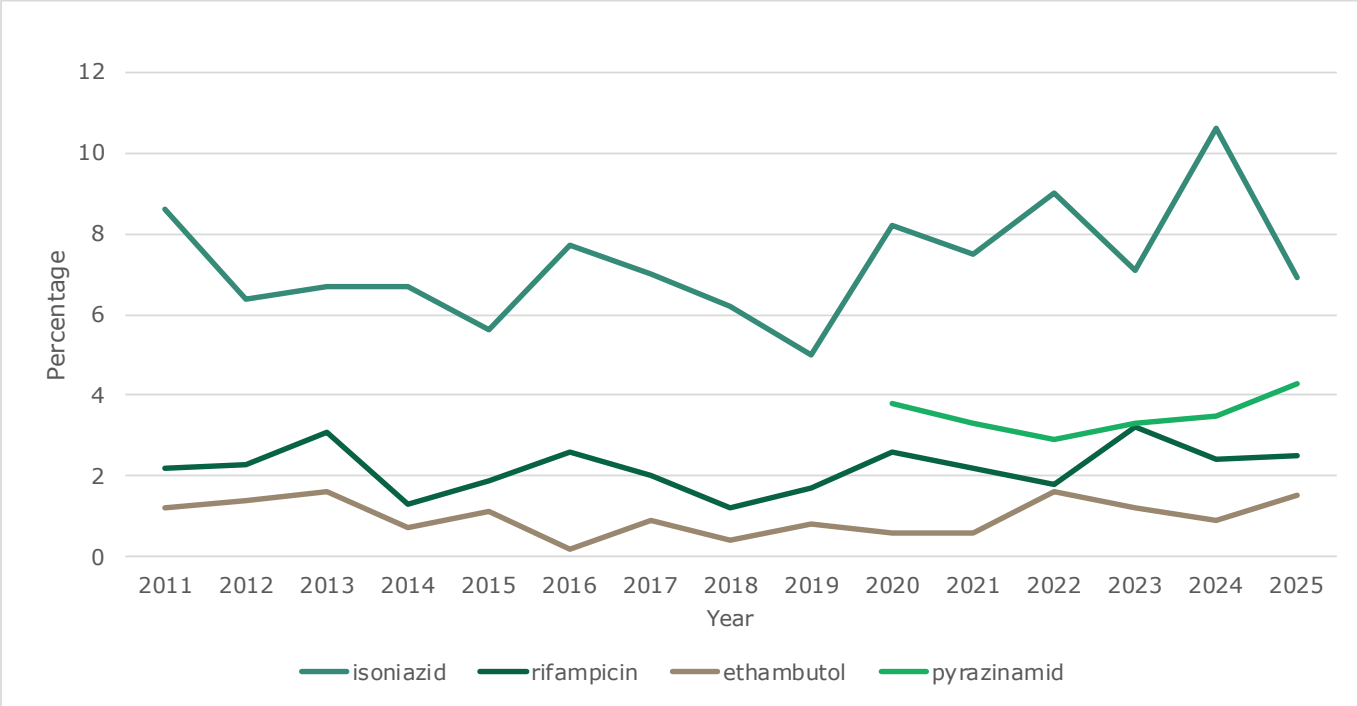
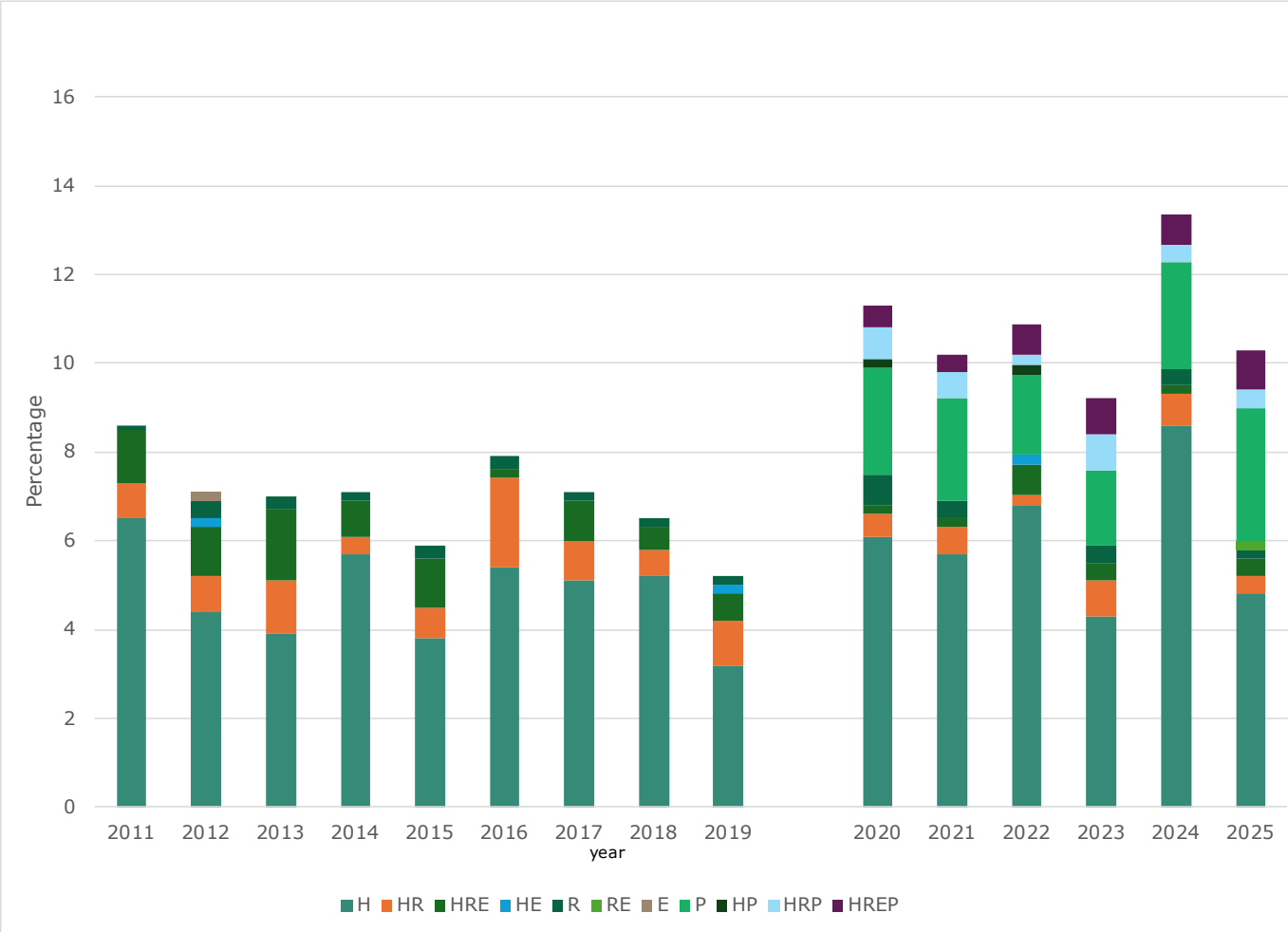


Figure 5.2.10.1.2 *Percentage combined antibiotic resistance for M. tuberculosis complex isolates 2011-2025*



In 2024 thirteen isolated tested resistant to fluoroquinolones and in 2025 nine isolates tested resistant. These observations were initially based on the detection of resistance mutations in WGS data from isolates for which resistance to at least one agent was predicted (and subsequently confirmed by phenotypic testing).

MDR and RR TB cases represented 2.3% (13/566) of the culture positive cases diagnosed in 2025, which is comparable to the combined MDR and RR resistance in 2024 (2.4%).
No transmission of MDR-TB was seen in the Netherlands in 2025.

Discussion
In 2025, 10% (57/566) of the isolates tested in the Netherlands revealed any form of resistance, compared to 13.4 % (72/536) in 2024. The number of MDR isolates in the Netherlands, was stable in 2024 and 2025, representing slightly more than 2% of all isolates, a total of 13 MDR/RR-TB cases in 2025. The increase of INH resistance reported in 2024 was primarily due to a single cluster which was brought under control in 2025.

The extended hospitalization, complicated MDR-TB treatment, and contagious nature of this disease continues to justify special attention for infections caused by resistant TB Worldwide, resistance is an important aspect in TB control. As the majority of TB cases in The Netherlands are diagnosed in patients originating from high prevalence areas, it remains important to continue the structural surveillance to support the efforts to prevent and ultimately eliminate local transmission in particular of resistant strains.

Conclusions

- In 2025, resistance to first line antimycobacterial drugs has remained stable compared to previous years.
- The alarming increase in INH resistance in 2024, was brought under control in 2025.
- The number of MDR-TB cases was also stable in recent years (average of 10/12 cases per year). This trend is carefully monitored.
- A gradual increase of the number of TB cases in the Netherlands is ongoing, in 2024 an increase of 8.3% and in 2025 an increase of 13.0 % compared to the previous year.

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5.2.10.2 Nontuberculous mycobacteria

Introduction
Nontuberculous mycobacteria (NTM) are emerging as important causative agents of opportunistic infections in humans. The NTM are a highly diverse group of >200 species with important variation in virulence and antimicrobial susceptibility patterns. Antibiotic treatment regimens differ by species, but combination regimens of 2 to 4 drugs are the norm, with macrolide antibiotics as the core for most species. NTM are typically acquired from the environment and onward human transmission is exceedingly rare. Hence, the current diagnostics in the Radboudumc-RIVM expertise laboratory focus on species identification and antimicrobial susceptibility testing.

Methods
The Radboudumc–RIVM expertise laboratory receives clinical samples or cultured isolates sent voluntarily from all MMLs in the Netherlands. From clinical samples, NTM are detected by real-time PCR followed by amplicon sequencing. For cultured isolates, identification to (sub)species level is achieved by whole genome sequencing.

Antimicrobial susceptibility testing is performed using broth microdilution, according to Clinical and Laboratory Standards Institute guidelines (CLSI, M24-A3). Clarithromycin is tested as class representative of the macrolide antibiotics.

Results
We received 783 NTM isolates of 653 persons for identification and/or antimicrobial susceptibility testing in 2025; we received 877 isolates in 2024 and 871 in 2023. Fifty percent of all submitted isolates are members of the *Mycobacterium avium* complex, with *M. avium* representing 24% of the total number of submitted isolates (Figure 5.2.10.2.1).

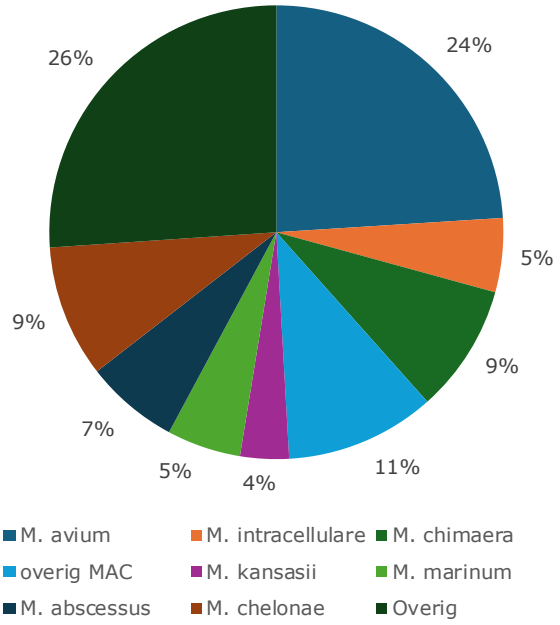
Of 173 *Mycobacterium avium* isolates, 6 (3%) proved macrolide-resistant. Three of 55 (5%) submitted *M. abscessus* isolates showed acquired amikacin resistance.

The Radboudumc and affiliated hospitals which it serves as an MML submitted 5281 clinical samples which yielded another 381 NTM isolates of 238 persons, with similar species distribution.

Discussion
The slight reduction in number of submitted isolates compared to previous years likely reflects the increased uptake of NTM identification tools (MALDI-TOF, line probe assays) by MMLs; the reduction was mostly seen in requests for ‘identification only’; identification of NTM is the crucial step in determining their clinical significance and avirulent or low-virulent species do not require submission for susceptibility testing. In part, it also results from the extension of the number of hospitals for which Radboudumc performs full mycobacteriology diagnostics. *Mycobacterium avium* complex isolates still predominate, in line with previous reports from the Netherlands and neighboring countries.[1] Macrolide-resistance in *M. avium* complex bacteria and amikacin-resistance in *M. abscessus* are rare and always an acquired resistance.

Prior studies in the Netherlands identified macrolide monotherapy for immunomodulation as a key cause of macrolide-resistance in *M. avium* complex bacteria.[2] Amikacin-resistance in *M. abscessus* resulted from prior exposure to inhaled or topical aminoglycoside therapies in all identified cases.

Figure 5.2.10.2.1 *Species distribution among NTM isolates submitted to RadboudUMC-RIVM in 2025*



Note: The *Mycobacterium avium* complex consists of 14 established species, of which *M. avium*, *M. intracellulare* and *M. chimaera* are most frequently isolated.

Conclusions

- Compared to the previous two years, in 2025 a lower number of NTM isolates was submitted to the expertise laboratory, likely due to increased uptake of efficient routine identification tools (e.g. MALDI-TOF) in MMLs.
- Half of the submitted isolates belong to the *M. avium* complex, which are important opportunistic pathogens.
- Acquired macrolide-resistance among *M. avium* complex isolates remains rare at 3%, but does signify the complexities of treatment.

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5.2.11 Helicobacter pylori

Introduction
Helicobacter pylori is a Gram-negative curved bacterium that resides only on the gastric epithelium. Primary colonization often occurs during childhood and can last a lifetime. The global prevalence of *H. pylori* carriage is estimated to range between 20%-30% in Northern and Central European countries, to over 70% in parts of Asia, Africa and Southern Europe.[1] *H. pylori* is an important factor in the etiology of a wide range of gastric disorders including peptic ulcer disease, chronic gastritis, Mucosa-Associated Lymphoid Tissue (MALT) lymphoma, and gastric cancer.[2] In the past decades, this highly prevalent infection has been treated with various antimicrobial regimens, and concerns about antimicrobial resistance in this pathogen are rising, also in the Netherlands.[3,4] In this section we describe for a selection of frequently used agents the prevalence and trends in antimicrobial resistance in *H. pylori* in the Netherlands during the period 2021-2025.

Methods
Data were selected from the ISIS-AR database. Isolates sampled from gastro-intestinal mucosa, pus, and normally sterile tissue or liquid were all included because we could not distinguish gastric specimens specifically. Further data selection as well as the calculation of resistance levels and time trends were executed using the same methods as those described in section 5.1.1.1.

Results
In total, 2830 *H. pylori* isolates were included over the period 2021-2025, of which 538 isolates were sampled in 2025. In table 5.2.11.1 resistance levels for 2025 are presented. Five-year trends in resistance are shown in figure 5.2.11.1.

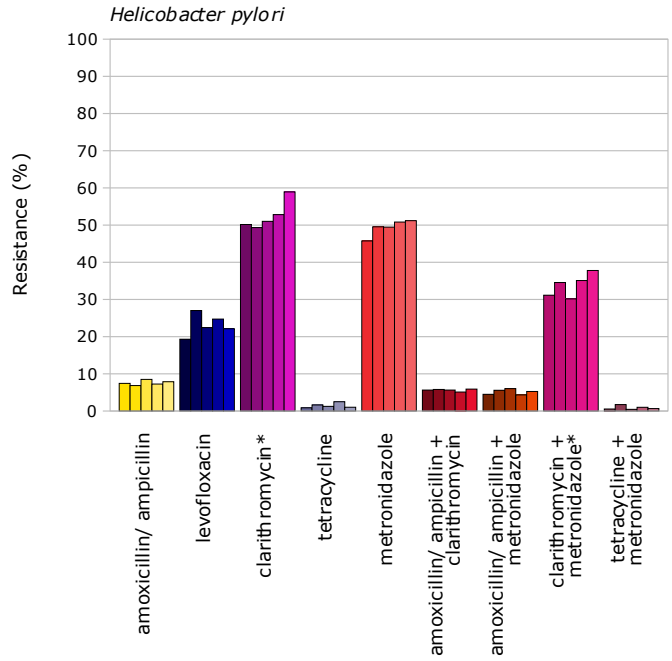
Discussion
For the culture of *H. pylori* and subsequent phenotypical antimicrobial susceptibility testing, a biopsy from the gastric epithelium is required. However, an *H. pylori* infection is primarily diagnosed using non-invasive methods such as a stool antigen test or a urea breath test. Only when empirical treatment was unsuccessful, a biopsy is likely to be performed. Therefore, the results may be biased towards higher antibiotic resistance levels compared to resistance levels in the total population with an *H. pylori* infection. Nevertheless, because the degree of bias is assumed to be constant over the years, we expect the calculated time trends to be a valid estimate of the changes in antibiotic resistance through the years.

Table 5.2.11.1 *Resistance levels (%) among 538 H. pylori isolates sampled from gastro-intestinal mucosa, pus and normally sterile tissue or liquid, ISIS-AR 2025*

	H. pylori
Antibiotic	
amoxicillin/ampicillin	8
levofloxacin	22
clarithromycin	59 ↑
tetracycline	1.0
metronidazole	51
Empiric therapy combinations	
amoxicillin/ampicillin + clarithromycin	6
amoxicillin/ampicillin + metronidazole	5
clarithromycin + metronidazole	38 ↑
tetracycline + metronidazole	0.7

10 ↑	Significant and microbiologically relevant increasing trend since 2021.
10 ↓	Significant and microbiologically relevant decreasing trend since 2021.
10°	Trend not calculated because data from the years before 2025 did not meet the criteria for trend analysis.
10	No significant and microbiologically relevant time trend.
-	Resistance not calculated.
	For the criteria for trend analysis and the definition of a microbiologically relevant trend see section 5.1.1.1.

Figure 5.2.11.1 *Trends in antibiotic resistance (from left to right 2021 to 2025) among gastro-intestinal mucosa, pus and normally sterile tissue or liquid isolates of H. pylori in ISIS-AR*



Warning: The Y-axis of this figure differs from the standard format. The Y-axis is scaled up to 100%.

* Trend is significant and microbiologically relevant (for details see section 5.1.1.1).

Key findings

- Resistance to **amoxicillin/ampicillin** remained low at 8% (2024: 7%), continuing the consistently low resistance levels observed for this agent over the past 5 years and supporting its continued role in standard combination regimens.
- Resistance to **doxycycline/tetracycline** remained very low at 1.0% (2024: 2%), the lowest of all agents tested, confirming this as a reliable component of rescue therapy regimens.
- **Clarithromycin** resistance rose further to 59% (2024: 53%) and now shows a significant and microbiologically relevant increasing trend — the first such trend identified for this agent since reporting began in 2020. This is a clinically important development, as **clarithromycin** forms part of the first-choice combination therapy for *H. pylori* eradication, and resistance at this level substantially undermines the expected efficacy of standard triple therapy.
- **Metronidazole** resistance remained high and essentially unchanged at 51% without a significant trend. **Levofloxacin** resistance was stable at 22%.
- For first-choice combination treatment — **amoxicillin/ampicillin + clarithromycin** — combined resistance was 6% remaining low despite the sharp rise in **clarithromycin** resistance alone. This apparent discrepancy suggests that **clarithromycin** resistance does not yet frequently co-occur with **amoxicillin** resistance in the same isolate, though the rising **clarithromycin** trend warrants close monitoring of this combination going forward.
- If first-choice treatment fails, recommended rescue regimens are **tetracycline + metronidazole** and **amoxicillin/ampicillin + metronidazole**, with combined resistance of 0.7% and 5% respectively (2024: 1% and 4%) — both remaining low and providing reliable fallback options.
- **Clarithromycin + metronidazole** combined resistance rose to 38% (2021: ~30%) and now shows a significant and microbiologically relevant increasing trend. As this combination is sometimes used as an alternative regimen in case of beta-lactam allergy, the rising resistance further narrows the range of effective non-rescue treatment options and reinforces the importance of avoiding **clarithromycin**-based regimens without prior susceptibility testing where feasible.

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5.2.12 *Clostridioides difficile*

Introduction
After recognition of *C. difficile* ribotype (RT) 027 outbreaks in 2005, surveillance programs were initiated worldwide. The Dutch sentinel surveillance started in 2009 to monitor the *C. difficile* infection (CDI) incidence and characteristics. From 2022 onward, the CDI sentinel surveillance is conducted in 5 centers (3 academic, 2 general hospitals) geographically spread over the Netherlands. Decreased susceptibility and resistance of *C. difficile* to anti-CDI antibiotics has been reported, most notably in North America.[1,2] We here describe (1) epidemiologic and (2) molecular trends in *C. difficile* based on 2025 surveillance data, and (3) resistance to anti-CDI antibiotics in patients with recurrent CDI (rCDI) based on 2023-2024 surveillance data.

Methods
(1) Inclusion criteria for surveillance are: hospitalized patients with a clinical picture compatible with CDI and a positive CDI diagnostic test (toxin enzyme-immunoassay, or toxigenic *C. difficile* PCR), or presence of pseudomembranous colitis. The web-based system OSIRIS was used to capture epidemiological data such as location of onset, disease severity, disease course (ICU admission, and/or surgery), and CDI-attributable mortality. Severe CDI is defined as meeting ≥1 of the following criteria: (i) bloody diarrhoea, (ii) pseudomembranous colitis, (iii) diarrhoea with dehydration, (iv) diarrhoea with hypoalbuminemia, (v) temperature >38.0°C with leukocytosis. To calculate CDI incidence rate, the number of included CDI cases was divided by the number of clinical patient days of all admitted patients in the participating medical centers.

(2) Of the included cases from (1), *C. difficile* isolates or fecal samples are submitted to the CDI Expertise Center for culture and typing. Sentinel surveillance cohort isolates were whole genome sequenced (WGS, Illumina 150bp paired-end) and PCR ribotyped.[3,4] The latter is still included for comparison with historic data. Besides, an *ad hoc* typing service is offered for all microbiology laboratories in the Netherlands for samples/isolates of patients with severe disease or samples/isolates from a suspected outbreak.

(3) The 2023-2024 surveillance included 539 CDI cases of which 64 patients had recurrent CDI (rCDI). Of rCDI cases, 60 isolates were available for testing with agar dilution for antibiotic susceptibility to metronidazole, vancomycin and fidaxomicin using EUCAST breakpoints, and 62 for short read WGS. After *de novo* assembly (Velvet), CARD/resfinder/MEGARES/AMRfinder+ databases were used to identify resistance determinants, while *rpoB* and *rpoC* loci (mutations which can be associated with fidaxomicin resistance) were manually assessed (by alignment to the reference sequence from strain CD630).

Results
(1) In 2025, 280 cases from the 5 surveillance centers (median age 69 years, IQR 58-77) met surveillance inclusion criteria, of which 198 *C. difficile* isolates could be cultured and subsequently typed. Epidemiological characteristics over time are shown in Table 5.2.12.1.

CDI incidence was 3.4 cases/10,000 patient days, which is stable compared to previous (non-COVID19 pandemic) years. The percentage of patients with severe disease was 21% (95%CI 15.9-25.5), similar to pre-COVID19 in 2019-2021. Of the included cases, 244 had data on CDI treatment available. Overall, antibiotics used for treatment were similar compared to 2024: 44% of patients were treated with vancomycin for 10-14 days, 28% received fidaxomicin for 10-14 days, 4.5% metronidazole, 2.9% extended fidaxomicin scheme, 1.2% vancomycin taper and pulse. Eighteen percent did not receive CDI treatment.

(2) The distribution of circulating types was stable compared to previous years, see Figure 5.2.12.1 for distribution of STs and RTs. Sequence Type (ST) 2 (n=25, 12.6%, includes RT014/020), ST8 (n=27, 13.6%, includes RT002), and ST11 (n=15, 7.6%, includes RT078/126) were the dominant STs. RT014/020 continued to be the most prevalent accounting for 20.7% of isolates, comparable to previous years. One isolate belonged to the hypervirulent ST1, RT181 (not depicted in figure 1); this RT has not previously been detected in the Netherlands, and was possibly contracted abroad. We received 25 samples for *ad hoc* typing of severe cases or suspected outbreaks. Among these, one transmission event was confirmed. No ST1 was detected in those 25 samples.

(3) MIC90 for the 60 isolates tested from the 2023-2024 rCDI cohort was 0.25 mg/L (range 0.0625-0.25) for metronidazole, 2 mg/L (1-2) for vancomycin and 0.25 mg/L (0.0625-0.5) for fidaxomicin. No resistant isolates were identified. WGS identified a P*nimB*G mutation, associated with medium-dependent metronidazole resistance[5] in one isolate. Seven distinct *rpoB*/*rpoC* non-synonymous mutations were identified in 29 isolates; none of these showed reduced fidaxomicin susceptibility.

Discussion

Epidemiological characteristics of CDI cases and distribution of circulating types were comparable to previous years. The one hypervirulent and multidrug resistant RT181 isolate encountered in 2025 belongs to the hypervirulent ST1, clade 2 lineage, which includes RT 016/027/036/176/244/955. Reports from Eastern European countries including Romania, Bulgaria, Hungary and from Greece indicate that RT181 is an emerging, multidrug-resistant lineage promoting resistance selection and spread.[6,7] Sporadic cases have been reported in Denmark, France, Belgium, Ireland and Italy.

No resistance to metronidazole, vancomycin and fidaxomicin was identified in isolates of patients with rCDI. MIC90 for vancomycin was 2 mg/L, one step below the EUCAST breakpoint based on epidemiological cut-off values (ECOFFs), though there are no conclusive data regarding the relation between vancomycin MIC and clinical outcome, and luminal concentrations of vancomycin can far exceed this cut-off.[8] While *rpoB* or *rpoC* variants were observed in nearly half of the surveillance isolates, these particular variants do not appear to be associated with reduced fidaxomicin susceptibility in our test results.

Conclusions

- Epidemiological characteristics of CDI in 2025 were comparable to previous years.
- One hypervirulent (ST1, RT181) and multidrug resistant *C. difficile* isolate was detected, possibly imported from abroad. The presence of hypervirulent and drug-resistant strains (promoting selection and spread) should be considered in cases of CDI diagnosed in patients transferred from hospitals abroad, particularly from Eastern and Southern European countries.
- MIC90 for vancomycin in the 60 isolates tested from the 2023-2024 rCDI was one step below the EUCAST breakpoint based on epidemiological cut-off values (ECOFFs).
- No resistance to metronidazole, vancomycin and fidaxomicin was identified in isolates of Dutch patients with recurrent CDI in 2023-2024.

Table 5.2.12.1 *Key epidemiological characteristics of C. difficile surveillance over the years 2009-2024*

Surveillance period	2015-2016	2016-2017	2017-2018	2018-2019	2019-2021[3,4]	2022[5]	2023	2024	2025
Incidence									
Per 10,000 patient-days	3.1	3.0	2.9	3.1	3.2	3.2	2.8	3.4	3.4
Location of onset									
Within healthcare facility	58%	59%	55%	54%	55%	53%	44%	56%	52%
At home	42%	41%	45%	46%	45%	47%	56%	44%	48%
Course and outcome[1]									
Severe CDI[1]	21%	17%	20%	16%	21%	30%	40%	27%	21%
Uncomplicated course[2]	89%	87%	87%	90%	89%	83%	87%	89%	87%
Deaths contributable to CDI	2%	2%	3%	1%	2%	1%	4%	2%	3%
PCR ribotype 027									
Prevalence	1.2%	0.6%	1.2%	0.6%	0.2%	0.9%	0.0%	0.0%	0.0%
N reported 027 outbreaks-sentinel surveillance	0	0	0	0	0	0	0	0	0
N reported 027 outbreaks-ad hoc typing	0	1	0	0	0	0	0	0	0

1 Severe CDI is defined as bloody diarrhoea and/or diarrhoea with hypovolaemia or hypoalbuminaemia (<20 g/L) and/or with fever (T >38.0°C) and leucocytosis (WBC count >15x10⁹/l), and/or with pseudomembranous colitis.

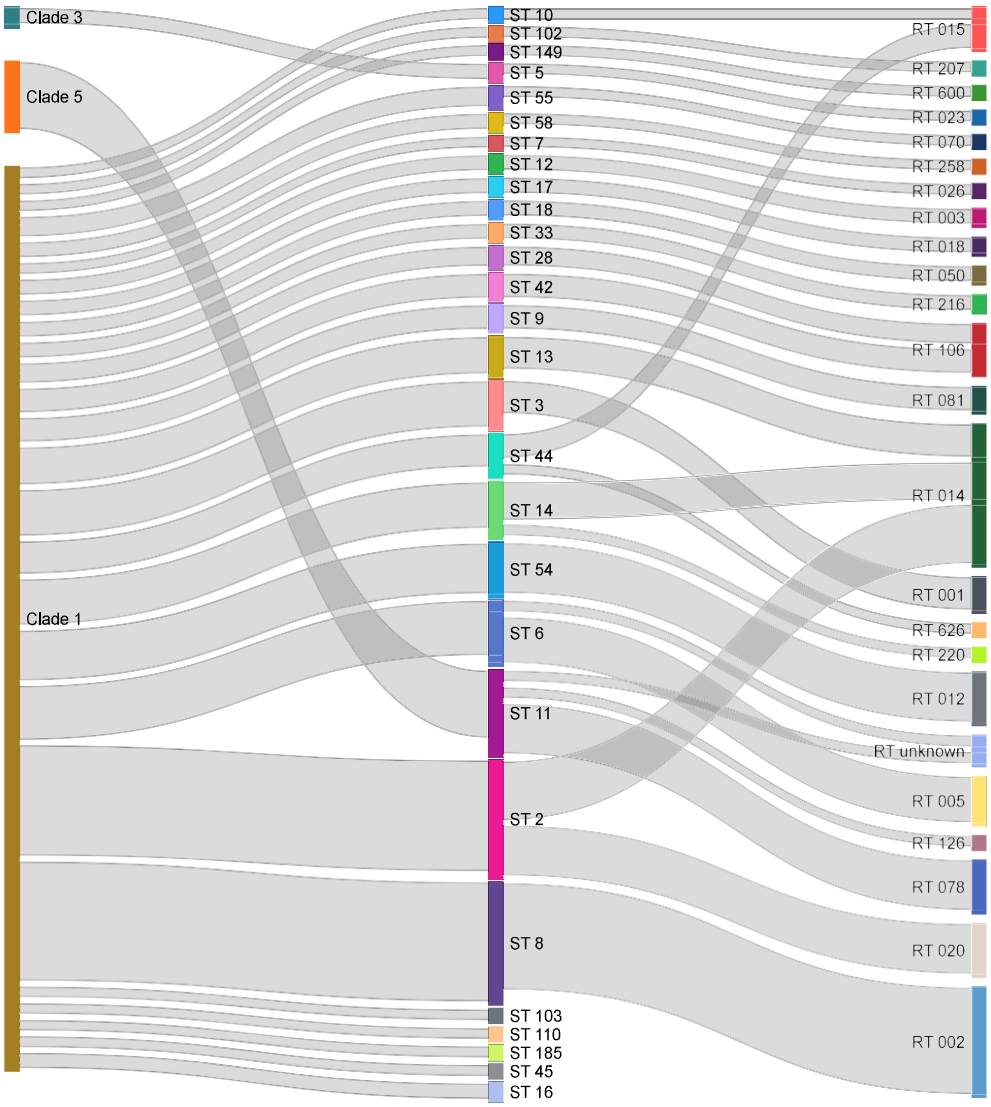
2 Uncomplicated course is defined as not admitted to the intensive care unit as a consequence of the C. difficile infection, no need for surgery as a consequence of the C. difficile infection and no death within 30 days after sample date.

3 Sentinel surveillance period May 2019 - January 2021.

4 Data on complicated course and mortality from between the 2nd of November 2020 until the 10th of January 2021 were excluded due to technical issues with absence of some answer possibilities, indicating missingness at random.

5 In 2022, as part of a restructuring effort, the number of participating hospitals was reduced from 22 to five.

Figure 5.2.12.1 *Sankey diagram of the distribution of C. difficile clade and Sequence Type (ST) with corresponding Ribotype (RT). Isolates of the 2025 sentinel surveillance with available WGS data and connection count >1 are shown (n=180).*



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5.2.13 *Antibiotic susceptibility profile of clinically relevant anaerobic bacteria isolated from human clinical specimens*

Introduction
Antibiotic resistance among anaerobic bacteria is gradually rising in the Netherlands and in other countries, multi-drug resistant anaerobic bacteria are reported (1). Therefore, treatment of infections caused by these pathogens could be complicated, emphasizing the importance of regular surveillance and gaining insight in the mechanisms behind antibiotic resistance. Each year we report the susceptibility profile of anaerobic bacteria isolated from human clinical specimens at the University Medical Center Groningen. EUCAST introduced several modifications among the breakpoints of antibiotics for anaerobic bacteria, hereby differentiating between the different genera/species and improving antibiotic treatment of infections in which they play a role.

Methods
Anaerobic bacterial isolates were derived from a variety of clinical samples, e.g. orthopedic, abdominal, head and neck, and blood samples, and were identified using MALDI-TOF MS (Bruker Daltonics, Bremen, Germany). Clinically relevant isolates (e.g. sterile specimens from sterile sites, with no risk of contamination by commensal bacteria from nearby intact mucous membranes) were subjected to antibiotic susceptibility testing using Etest (BioMerieux).

The MIC for amoxicillin was assessed for almost all isolates. The exceptions were the genera *Bacteroides*, *Parabacteroides*, *Phoceiacola* and *Prevotella*, since they are assumed to be intrinsically resistant. The MIC for amoxicillin was only assessed for isolates which produced no beta-lactamase. For isolates belonging to either of the genera mentioned above, the MIC for meropenem was determined and beta-lactamase production was assessed using a cefinase disk. Amoxicillin-clavulanic acid was tested for all Gram-negative bacteria. The presence of the *cfiA* gene in *B. fragilis* was assessed using MALDI-TOF MS, which plays an important role in meropenem resistance. The MIC for clindamycin was assessed for all isolates. The MIC for metronidazole was assessed for all species, except *Actinomyces* species, bifidobacteria and cutibacteria due to intrinsic resistance. Results are interpreted using the Clinical breakpoints v15.0 and the "When there are no breakpoints" guidance document from EUCAST. The MIC50, MIC90 and resistance percentage was calculated for each antibiotic - genus/species combination if at least 10 isolates were tested.

Results
An overview of the obtained MIC50, MIC90 and resistance percentage is shown in Table 5.2.13.1.
Resistance rates for amoxicillin, amoxicillin-clavulanic acid and clindamycin among most gram-negative anaerobic bacteria remained relatively stable. For example, the percentage clindamycin resistant *Bacteroides* isolates varied between 31.6% and 41.2% in the last four years. The susceptibility profile of amoxicillin for *Bacteroides*, *Parabacteroides*, *Phoceiacola* and *Prevotella* was omitted, as it does not provide a realistic picture of the resistance present among these genera

due to selective testing. Remarkably, the only (former) *Bacteroides* species susceptible for amoxicillin and not producing beta-lactamase were *Bacteroides pyogenes* (4/5) and *Ezakiella coagulans* (2/2), all with MICs <0.19 mg/L. There seems to be a trend of increasing resistance for clindamycin among *Porphyromonas* species from none in 2022 to 25% in 2025, and *Prevotella* species, from 19% in 2022 to 30% in 2025. Most of the clindamycin resistant *Prevotella* isolates were observed among *P. baroniae*, *P. bivia*, *P. denticola*, *P. jejuni* and *P. timonensis*. All resistant *Porphyromonas* (4/16) and *Prevotella* isolates (21/71) had an MIC >256 mg/L and all susceptible isolates had very low MICs. The only clindamycin-resistant *Veillonella* isolate had an MIC of 1 mg/L, just above the breakpoint.

Resistance rates for both metronidazole and meropenem remained stable across all included bacterial species over the last four years, including *Bacteroides* (0-1% for metronidazole and 6-12% for meropenem) and *Prevotella* (1-4% for metronidazole and 1-2% for meropenem). In 2025, six of 103 *Bacteroides* isolates were resistant for meropenem, four were identified as *Bacteroides fragilis*, one as *Bacteroides ovatus* and one as *Bacteroides thetaiotaomicron*. According to the MALDI-TOF MS results, all four *B. fragilis* isolates harbored the *cfiA* gene in their genome. The resistant isolates had MICs ranging from 4 mg/L to >32 mg/L, above the clinical breakpoint for meropenem of 1 mg/L according to the EUCAST guidelines. One *P. bivia* isolate was resistant for meropenem with an MIC of 4 mg/L. One *B. fragilis* isolate and one *P. bivia* isolate were resistant to metronidazole. The latter was not resistant to other antibiotics tested. None of the *Bacteroides* (and related genera) isolates were resistant to both meropenem and metronidazole.

Among the gram-positive anaerobes, resistance for amoxicillin was observed mainly among the clostridia. Clindamycin resistance was observed among all gram-positive anaerobic genera and varied, from 4% (8/200) among *C. acnes* to 90% (9/10) among *Clostridium perfringens* isolates. For most gram-positive anaerobes the rate of clindamycin resistance remained stable. Resistance for clindamycin among clostridia (excluding *C. difficile* and *C. perfringens*) increased from roughly 55% in the last two years to 75% this year. Resistance to metronidazole was detected in one *Clostridium ramosum* isolate (MIC 6 mg/L).

Table 5.2.13.1 *MIC50, MIC90 and resistance percentage of clinically anaerobic isolates in 2025*

	Amoxicillin			Co-amoxiclav			Clindamycin		
	MIC50	**MIC90**	**%R**	**MIC50**	**MIC90**	**%R**	**MIC50**	**MIC90**	**%R**
Gram-negative anaerobes									
Bacteroides spp. (103)[a]	nd[b]	nd	nd	0.094	16	15.5	3	>256	39.8
Fusobacterium spp. (38)	0.047	1.5	13.2	<0.016	0.016	5.3	0.032	0.094	0.0
Porphyromonas spp. (14-16)[c]	0.016	0.047	12.5	<0.016	0.064	0.0	<0.016	>256	25.0
Prevotella spp. (71)	nd	nd	nd	<0.016	0.125	nd[d]	0.023	>256	29.6
Veillonella spp. (36)	0.5	1.5	36.1	0.125	0.75	19.4	0.125	0.25	2.8
Gram-positive anaerobes									
Actinomyces spp. (112)[e]	0.064	0.25	3.6	nd	nd	nd	0.125	>256	17.0
Anaerococcus spp. (38)	0.032	0.125	0.0	nd	nd	nd	0.047	>256	26.3
Atopobium spp. (12)	0.094	0.25	8.3	nd	nd	nd	0.75	1.5	66.7
Bifidobacterium spp. (12)	0.19	0.5	8.3	nd	nd	nd	0.032	0.5	8.3
Clostridium spp. (37)[f]	0.25	1	24.3	nd	nd	nd	3	32	75.7
Clostridium perfringens (10)	0.023	0.047	0.0	nd	nd	nd	3	6	90.0
Cutibacterium spp. (42)[g]	0.125	0.25	0.0	nd	nd	nd	0.047	0.5	9.5
Cutibacterium acnes (200)	0.064	0.19	2.0	nd	nd	nd	0.047	0.125	4.0
Finegoldia magna (77)	0.125	0.25	0.0	nd	nd	nd	1	>256	57.1
Parvimonas micra (28)	0.032	0.064	0.0	nd	nd	nd	0.38	1.5	25.0
Peptoniphilus spp. (56)	0.016	0.064	0.0	nd	nd	nd	0.5	>256	46.4
Peptostreptococcus spp. (15)	0.125	0.5	6.7	nd	nd	nd	0.19	0.5	6.7

a Bacteroides spp.: including genera which were previously named Bacteroides: *Ezakiella spp*., and *Phocaeicola* spp.

b Not determined.

c Not all isolates were tested for all antibiotics.

d No breakpoint available

e *Actinomyces* spp.: including genera which were previously named *Actinomyces*: *Gleimia* spp., *Schaalia* spp., and *Winkia* spp.

f *Clostridium* spp. : excluding *C. perfringens* and *C. difficile*, but including genera which were previously named *Clostridium*: *Enterocloster* spp., *Lacrimispora* spp., *Hathewaya* spp., *Hungatella* spp., *Terrisporobacter* spp.

g *Cutibacterium* spp.: excluding *C. acnes*.

Table 5.2.13.1 (continued) *MIC50, MIC90 and resistance percentage of clinically anaerobic isolates in 2025*

	Metronidazole			Meropenem		
	MIC50	**MIC90**	**%R**	**MIC50**	**MIC90**	**%R**
Gram-negative anaerobes						
Bacteroides spp. (103)[a]	0.38	0.75	1.0	0.125	0.75	5.8
Fusobacterium spp. (38)	<0.016	0.125	0.0	nd	nd	nd
Porphyromonas spp. (14-16)[c]	0.032	0.094	0.0	nd	nd	nd
Prevotella spp. (71)	0.19	1	1.4	0.032	0.094	1.4
Veillonella spp. (36)	1	3	8.3	nd	nd	nd
Gram-positive anaerobes						
Actinomyces spp. (112)[e]	nd	nd	nd	nd	nd	nd
Anaerococcus spp. (38)	0.19	0.5	0.0	nd	nd	nd
Atopobium spp. (12)	0.125	1	0.0	nd	nd	nd
Bifidobacterium spp. (12)	nd	nd	nd	nd	nd	nd
Clostridium spp. (37)[f]	0.38	1.5	2.7	nd	nd	nd
Clostridium perfringens (10)	0.38	1.5	0.0	nd	nd	nd
Cutibacterium spp. (42)[g]	nd	nd	nd	nd	nd	nd
Cutibacterium acnes (200)	nd	nd	nd	nd	nd	nd
Finegoldia magna (77)	0.125	0.38	0.0	nd	nd	nd
Parvimonas micra (28)	0.064	0.19	0.0	nd	nd	nd
Peptoniphilus spp. (56)	0.25	1.0	0.0	nd	nd	nd
Peptostreptococcus spp. (15)	0.064	0.38	0.0	nd	nd	nd

a Bacteroides spp.: including genera which were previously named Bacteroides: *Ezakiella spp*., and *Phocaeicola* spp.

b Not determined.

c Not all isolates were tested for all antibiotics.

d No breakpoint available

e *Actinomyces* spp.: including genera which were previously named *Actinomyces*: *Gleimia* spp., *Schaalia* spp., and *Winkia* spp.

f *Clostridium* spp.: excluding *C. perfringens* and *C. difficile*, but including genera which were previously named *Clostridium*: *Enterocloster* spp., *Lacrimispora* spp., *Hathewaya* spp., *Hungatella* spp., *Terrisporobacter* spp.

g *Cutibacterium* spp.: excluding *C. acnes*.

Discussion

The already existing meropenem resistance among *Bacteroides* species continues to be present and is stable. In all the resistant *B. fragilis* isolates the *cfiA* gene encoding a metallo-beta-lactamase was present, which correlated with their resistance to a carbapenem antibiotic. The presence of this gene was not observed in the susceptible *B. fragilis* isolates. In the resistant non-*fragilis* isolates the presence of a gene encoding this enzyme was not assessed. One of these isolates was identified as *B. thetaiotaomicron* with an MIC for meropenem of >32 mg/L. The molecular mechanism behind this resistance is unknown.

There seems to be a trend of increasing resistance for clindamycin among *Porphyromonas* species and *Prevotella* species. Most of the resistant *Prevotella* isolates were observed among *P. baroniae*, *P. bivia*, *P. denticola*, *P. jejuni* and *P. timonensis*.

Conclusions

- Clinicians should be aware of the fact that *Bacteroides* isolates can be resistant to carbapenem antibiotics
- Metronidazole resistance among *Bacteroides* and *Prevotella* remains at the same low rate as in previous years
- Tendency of increased clindamycin resistance among *Prevotella* and *Porphyromonas* species.

References

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5.2.14 *Aspergillus fumigatus and Candida (Candidozyma) auris*

Introduction
Antifungal resistance is increasingly reported in both yeasts and molds. Since 2013 resistance pathogen surveillance is performed in *Aspergillus fumigatus*, which can cause both chronic pulmonary aspergillosis and acute invasive disease. In *A. fumigatus,* triazole resistance is primarily selected for in the environment through exposure to azole fungicides. Signature resistance mutations, e.g. TR_{34}/L98H or TR_{46}/Y121F/T289A, are associated with environmental resistance selection. Surveillance is performed to determine resistance levels in hospitalized patients and trends in the distribution of resistance mutations.

Another concern is *Candidozyma* (*Candida*) *auris,* a fluconazole-resistant yeast, that is spreading globally and across Europe. A recent report of the European Center for Disease Prevention and Control (ECDC) shows the highest *C. auris* case numbers in Spain, Greece, Italy, Romania and Germany.[1] The Netherlands is among nine countries reporting imported cases only (stage 1).[1] In the Netherlands there is no formal surveillance program for *C. auris*, but medical microbiology laboratories are asked to send *C. auris* isolates to the national mycology reference laboratory for identification, resistance testing and whole genome sequencing.

Methods
A. fumigatus
In five University Medical Centers (UMCs) and five teaching hospitals all clinical *A. fumigatus* isolates from patient samples were screened for triazole resistance using a four-well agar plate (VIPcheck™, MediaProducts, Groningen, the Netherlands). Three wells contain agars supplemented with itraconazole, voriconazole and posaconazole at breakpoints concentrations, and one well acts as growth control. When clinical isolates grow on one of the triazole containing wells they are sent to the mycology reference laboratory for MIC-testing (according to the EUCAST microbroth dilution method) and sequence-analysis of the Cyp51A gene. The resistance frequency is calculated by dividing the number of patients with an azole-resistant culture by the total number of patients with an *A. fumigatus* isolate that was screened for triazole resistance in the participating hospitals.

C. auris
For *C. auris*, isolation of the organism is notified voluntarily to the mycology reference laboratory. Upon notification, patient information regarding travel history, presence of invasive candidiasis, infection control measures and possible secondary cases was collected by a standardized questionnaire. Species identification was confirmed using MALDI-TOF MS, and the EUCAST microdilution reference method was used for antifungal susceptibility testing. Illumina whole-genome sequencing (WGS) was performed to determine clades, assess phylogenetic clustering, and identify antifungal resistance markers.

Results
In 2025 *A. fumigatus* isolates from 1,661 culture-positive patients were screened for triazole resistance, including 866 (range 67 to 358 per center) patients from UMCs and 795 (range 55 to 232 per center) patients

from teaching hospitals. Overall, 141 (8.5%) patients harbored an azole-resistant *A. fumigatus,* with 12.5% (108 of 866 patients) in UMCs, and 4.2% (33 of 795 patients) in teaching hospitals (Table 5.2.14.1). Of those 141 patients, a total of 143 azole-resistant isolates (some patients harbored mixed genotypes) were analyzed for the presence of resistance mutations in the Cyp51A-gene. A tandem repeat (TR_{34} or TR_{46}) resistance mutation was detected in 107/143 isolates (74.8%), of which 79 (55.2%) TR_{34} and 28 (19.6%) TR_{46}.

In 2025 eleven cases of *C. auris* were reported (Figure 5.2.14.1) who were admitted to nine different hospitals in the Netherlands. All cases were linked to travel and/or admission to a hospital abroad, of which five in Europe, two in the Middle East, two in Asia and one in Africa. For one case the travel history was unknown. All patients were colonized with *C. auris* and there was no nosocomial transmission noted. WGS showed nine Clade I isolates and two belonging to Clade III. Nine isolates showed non-wildtype MICs for fluconazole and one isolate was non-wildtype for both fluconazole and the echinocandins.

Discussion

Azole resistance frequency in *A. fumigatus* in 2025 remained stable in teaching hospitals compared with previous years, with 4.2% of the patients harboring an azole-resistant isolate compared to 4.6% in 2024. In contrast the overall frequency of azole-resistant *A. fumigatus* in UMCs was with 12.5% higher compared to previous years but comparable to 2019. A threshold of 10% is recommended to consider initial antifungal therapy that covers azole resistance in patients with invasive aspergillosis, i.e. an azole combined with echinocandin or with liposomal amphotericin B. However, it must be noted that our surveillance is pathogen-based and the underlying *Aspergillus* disease is not systematically documented. Moreover, resistance percentages per institution fluctuate over the years, due to the relatively low numbers of isolates and therefore these should be interpreted with caution.

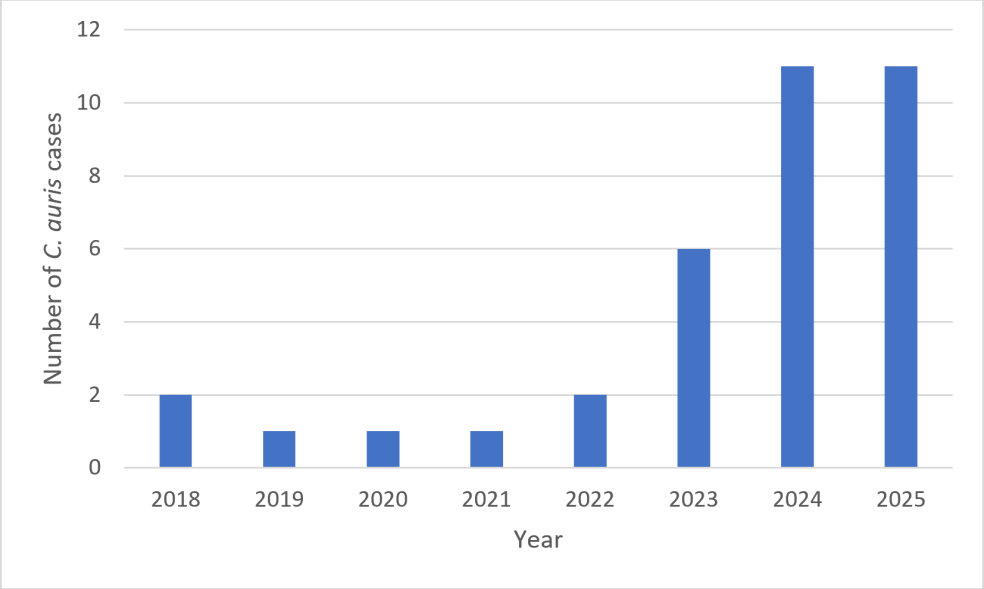
The number of reported *C. auris* cases in The Netherlands remains low, despite increasing numbers being reported across Europe.[1] Stringent infection control measures in patients at increased risk of *C. auris* carriage remain the cornerstone for keeping the prevalence low as all patients could be linked to travel or hospital admission in countries with a high *C. auris* prevalence. One patient harboured a multidrug-resistant isolate, showing a non-wildtype phenotype for azoles and echinocandins. An infection caused by this strain will likely not respond to treatment with first choice antifungals (echinocandins) and leaves very limited alternative treatment options.

Table 5.2.14.1 *Triazole resistance proportion in unselected clinical A. fumigatus isolates in 5 University Medical Centers and 5 teaching hospitals, 2018-2024*

	2019		2020		2021		2022		2023		2024		2025	
	Screened	Azole R (%)	Screened	Azole R (%)	Screened	Azole R (%)	Screened	Azole R (%)	Screened	Azole R (%)	Screened	Azole R (%)	Screened	Azole R (%)
UMCs														
ErasmusMC	102	18 (17.6)	108	12 (11.1)	142	17 (12)	119	7 (7.6)	114	10 (8.8)	141	9 (6.4)	171	20 (11.7)
LUMC	90	14 (15.6)	83	8 (9.6)	103	7 (6.8)	81	12 (14.8)	65	9 (13.8)	73	3 (4.7)	67	7 (10.4)
Radboudumc	230	23 (10)	193	20 (10.4)	205	25 (12.2)	175	18 (10.3)	172	13 (7.6)	328	25 (7.6)	358	44 (12.3)
UMCG	230	27 (11.7)	181	31 (17.1)	209	28 (13.4)	206	27 (13.1)	188	25 (13.8)	109	12 (11.0)	153	20 (13.1)
AmsterdamUMC	51	6 (11.8)	172[a]	16 (9.3)	173	20 (11.6)	175	16 (9.1)	110	18 (16)	115	23 (20.0)	117	17 (14.5)
Total UMCs	**703**	**88 (12.5)**	**737**	**87 (11.8)**	**832**	**97 (11.7)**	**756**	**80 (10.6)**	**649**	**75 (11.6)**	**766**	**72 (9.4)**	**866**	**108 (12.5)**
Teaching hospitals														
Medisch Spectrum Twente	90	2 (2.2)	95	2 (2.1)	182	8 (4.4)	98	2 (2.0)	140	5 (3.6)	167	4 (2.4)	232	10 (4.3)
St Antonius Hospital	177	10 (5.7)	193	15 (7.8)	151	12 (7.9)	211	15 (7.1)	155	11 (7.1)	170	10 (5.9)	188	9 (4.8)
PAMM*	147	8 (5.4)	150	3 (2)	129	6 (4.7)	141	4 (2.8)	114	1 (0.9)	37	1 (2.7)	55	4 (7.4)
CWZ	90	6 (6.7)	163	7 (4.3)	120	8 (6.7)	99	6 (6.1)	92	4 (4.4)	140	8 (5.7)	167	2 (1.2)
Isala	222	18 (8.1)	183	10 (5.5)	222	20 (9)	237	11 (4.6)	204	6 (3.0)	153	8 (5.2)	153	8 (5.2)
Total teaching hospitals	**726**	**42 (6.1)**	**784**	**37 (4.7)**	**804**	**54 (6.7)**	**786**	**38 (4.8)**	**705**	**27 (3.8)**	**667**	**31 (4.6)**	**795**	**33 (4.2)**

[a] Includes both VUmc and AMC, since 2020 AmsterdamUMC.
* PAMM did not service Catherina Hospital and Maxima Medisch Center in 2024 and 2025.

Figure 5.2.14.1 *Number of C. auris cases per year in the Netherlands*



Conclusions

A. fumigatus

- In 2025 the triazole resistance frequency in *A. fumigatus* was 12.5% in UMCs and 4.2% in teaching hospitals
- In all UMCs, the triazole resistance frequency in *A. fumigatus* was above 10%, which was not the case for the teaching hospitals.
- Overall, 74.8% of azole-resistant isolates harbored a TR-mediated resistance mechanism, of which 55.2% harbored TR34 and 19.6% TR46.

C. auris

- The number of *C. auris* cases remains low, and all are associated with travel and/or hospital admission in endemic countries.
- There has been no evidence for local transmission or outbreaks of *C. auris* within healthcare settings, which is likely due to stringent infection control measures.

References

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5.2.15 General antiviral resistance

The current antimicrobial resistance (AMR) awareness and monitoring activities along with the preventive/mitigation measures still focus largely on antibacterial resistance, notorious for the death of thousands worldwide, each year. Importantly, resistance to drugs and therapies occurs in a vast array of other pathogens as well, from viruses and parasites to fungi and others.

Like other resistance phenomena, antiviral drug pressure confers survival advantage to subpopulations of viral isolates relatively less susceptible to the drug effect, driving the emergence of resistant viral isolates. Spontaneous mutations due to drug exposure can also occur and alter the virus genetic stability, pathogenicity and transmissibility. High viral replicative loads, elevated viral mutation rates and prolonged drug exposure (specifically inadequate antiviral therapy or inappropriate dosages) also favour the selection of resistant virus isolates, rendering antiviral drugs ineffective.

On the clinical aspect, the concern around antiviral resistance is to limit its significance and manifestations, along with reducing the possibility of mutants' development and transmission, particularly to immunocompromised and vulnerable populations.
Noteworthy, efforts to analyse antiviral treatment failure should rely on systematic antiviral resistance monitoring activities for all relevant treatable viral infections, along with enhanced characterisation of both antiviral susceptibility and underlying drivers for the emergence of resistance events.

In the Netherlands, antiviral resistance monitoring is carried out by several clinical virology laboratories and working groups.
Since 2009, NethMap entailed data on the systematic monitoring of antiviral resistance for Influenza viruses' treatments. Herein, the update on Influenza antiviral resistance data is provided. Data on antiretroviral resistance in HIV is provided in the annual report of Stichting HIV monitoring (SHM)[1]. Below we have listed an overview of the main findings from the 2025 SHM report:

Baseline antiretroviral drug resistance

- Between 2015 and 2024, 39% of individuals newly diagnosed with HIV in the Netherlands underwent baseline screening for HIV drug resistance. Clinically significant drug resistance was identified in 11.4%.
- The rate of baseline drug resistance increased from 5% in 2015 to 20% in 2024. This increase was largely driven by HIV-1 subtype A6 IN L74I resistance associated polymorphism, impacting cabotegravir susceptibility only.
- To date, baseline drug resistance has had no observed impact on antiretroviral treatment response. We found no differences in rates of virological suppression between participants with and without baseline drug resistance.

Acquired antiretroviral drug resistance

- Of 24,028 participants in HIV care through 2024, 3,022 (12.6%) were tested for acquired HIV drug resistance. Clinically significant resistance was identified in 1,633 (6.8%) participants.
- Between 2000 and 2024, the proportion of sequences with clinically significant resistance associated mutations decreased from 78.1% to 31.1%.
- Resistance to newer treatment strategies, including second-generation integrase inhibitors and long-acting cabotegravir/rilpivirine, has been documented and requires future monitoring.
- Participants with a history of acquired drug resistance were less likely to be virologically suppressed at last observation than participants without a history of acquired drug resistance (92% vs 83%, respectively), attesting to the ongoing importance of adherence support.

Besides these, there are ongoing studies on antiviral susceptibility monitoring accounting other viral infections, such as Hepatitis B virus (HBV), Hepatitis C virus (HCV), Herpes virus, Varicella Zoster virus (VZV), Cytomegalovirus (CMV), Mpox, Respiratory Syncytial virus (RSV) and SARS-CoV-2. Systematic resistance monitoring is not implemented for any of the above viruses.

There have been few documented instances of antiviral resistance observed among the aforementioned viral pathogens. Consequently, these pathogens are currently not the focus of attention within this report. Still, some interesting results are worth mentioning.
For HBV and HCV genomic resistance monitoring using whole genome sequencing is implemented as part of the enhanced molecular surveillance conducted by RIVM and AUMC respectively for those samples from cases that are mandatory reported to RIVM. This enhanced molecular surveillance includes analyses of HBV positive acute cases, chronic HBV positive cases with sexual risk behaviour, and acute and chronic HCV positive cases with MSM as risk behaviour. In HBV, no clinically relevant resistance was observed, in line with the current understanding that the development of resistance in HBV is not expected. In most obtained whole genome HCV sequences (83%) no resistance mutations were identified that would influence the recommended initial treatment regime according to the "HCV richtsnoer".[2] In nearly 20% of obtained sequences clinically relevant resistance mutations were identified that could have influenced the initial preferred treatment regime. Such mutations were identified in multiple genotypes, including 1a, 1b and 3a with also known intrinsic resistance mutations in genotype 3b infections. Of note, in all cases with identified resistance mutations at least one of the alternative recommended regimes from the HCV richtsnoer remained fully susceptible.

Finally, in the 4th quarter of 2025 the use of nirsevimab (Beyfortus) for RSV-immunisation of neonates until 1 year of age, as part of the National Immunisation Program was implemented. Results of the first year of use will become available later in 2026, including molecular analysis of breakthrough infections and associated antiviral susceptibility.

References

1. Stichting HIV Monitoring. Monitoring reports. Amsterdam. Available from: HIV Monitoring Report | Stichting hiv monitoring
2. HCV Richtsnoer - Home - Hepatitis C

5.2.15.1 Influenza virus

Introduction
When vaccination against influenza is unavailable or proves ineffective due to antigenic mismatch with circulating influenza viruses, influenza antiviral drugs may be used for (post-exposure) prophylaxis as well as treatment of influenza cases with (expected) severe course of disease. In the Netherlands, the following antiviral drugs are approved for use: 1) the M2 ion channel blockers (M2B) amantadine and rimantadine, 2) the neuraminidase inhibitors (NAI) oseltamivir and zanamivir, and 3) the acidic endonuclease inhibitor baloxavir marboxil (BXM). M2B are active against type A viruses only, whereas NAI and BXM are effective against both influenza type A and B viruses. M2B and BXM inhibit viral replication by preventing uncoating of the virus or viral genome replication in the host cell, respectively. In contrast, NAI inhibit the release of progeny virions from the cell, thereby limiting the infection of surrounding cells. Since 2010, seasonal influenza type A viruses have become fully resistant to M2B. Surveillance of antiviral susceptibility in seasonal human influenza viruses has been conducted in the Netherlands for NAIs since the 2005/2006 season and for BXM susceptibility since the 2019/2020 season.[1,2]

Methods
Monitoring of influenza virus antiviral susceptibility is incorporated into the integrated clinical and virological primary care surveillance of acute respiratory infections (ARI), which utilizes data and specimens obtained by the Nivel Netherlands Institute for Health Services Research Primary Care Database sentinel general practitioner (GP) network. The specimens are analysed at the National Institute for Public Health and the Environment (RIVM) location of the Dutch National Influenza Centre (NIC). In addition, a subset of influenza virus-positive specimens identified in clinical diagnostic laboratories is submitted for further characterization to the Erasmus Medical Centre location of the Dutch NIC. This includes assessment of antiviral susceptibility. For viruses obtained from both sources, patient information regarding antiviral treatment, travel history, and immune competence status in the 14 days preceding specimen collection is collected. Furthermore, influenza viruses obtained through the community-based participatory surveillance of ARI (Infectieradar) are also included in the antiviral susceptibility assessments at RIVM. However, for these viruses, no patient data concerning antiviral treatment, travel history, or immune competence status in the 14 days preceding specimen collection is collected.

Antiviral susceptibility is monitored using whole genome Nanopore sequencing to detect known amino acid changes associated with reduced susceptibility to both NAIs and BXM. For a subset of influenza viruses, susceptibility to NAIs is assessed using an enzyme inhibition assay, which determines the drug's 50% inhibitory concentration (IC_{50}). This assay is used to confirm the impact of known amino acid changes associated with reduced antiviral susceptibility and to identify novel markers or combinations of markers. Susceptibility to NAIs is defined by the fold increase in IC_{50} over the wild-type median. For type A viruses: normal inhibition (NI) <10-fold, reduced inhibition (RI) 10–100-fold,

highly reduced inhibition (HRI) >100-fold. For type B viruses: NI <5-fold, RI 5–50-fold, HRI >50-fold.

Community use of antiviral drugs is monitored using data from the Foundation for Pharmaceutical Statistics (SFK), which collects dispensing information from more than 98% of community pharmacies in the Netherlands. These pharmacies serve 16.5 million people, representing 90.9% of the Dutch population (preliminary count May 2026).

Results

Table 5.2.15.1.1 displays an overview of the antiviral susceptibility of influenza viruses since the 2020/2021 respiratory season. From the 2020/2021 season through the 2022/2023 season and in the 2024/2025 season, no or only a limited number of viruses with reduced susceptibility (<1%) to NAIs and BXM were detected. In the 2023/2024 season, double mutant A(H1N1)pdm09 viruses carrying amino acid substitutions NA-I223V and NA-S247N (30/890, 3.4%) emerged. These showed phenotypically RI by oseltamivir and NI by zanamivir. In the 2025/2026 season, such double mutants (40/665, 6.0%) re-emerged. In addition, in 2025/2026 one other double mutant virus carrying NA-I223T and NA-S247N and one virus carrying only NA-I223M were detected. These mutants showed also phenotypically RI by oseltamivir and NI by zanamivir. Furthermore, two A(H1N1)pdm09 viruses with the NA-H275Y substitution were detected. These mutants showed phenotypically HRI by oseltamivir and NI by zanamivir. Among A(H3N2) and B/Victoria lineage viruses from the 2025/2026 season only one antiviral susceptibility relevant mutant was detected, namely an A(H3N2) virus carrying the NA-K249E substitution. This substitution has previously been associated with RI by oseltamivir. However, phenotypic testing showed NI by oseltamivir and zanamivir.
No amino acid changes previously associated with reduced BXM susceptibility were detected in any of the viruses analysed from the 2025/2026 season.

Figure 5.2.15.1.1 shows the dispensing of oseltamivir since 2020 in the Netherlands, as reported by the SFK. Community pharmacy dispensations of oseltamivir peak in parallel with periods of increased influenza virus circulation, except for the peak in December 2020 which was not related to true prescriptions but seemed to be attributable to stockpiling (>100 DDD/prescription) in the absence of influenza virus circulation due to COVID-19 preventive measures. According to SFK for the Netherlands, zanamivir has not been dispensed since 2020, and BXM has not been dispensed at all since its EU authorization in early 2021.

Table 5.2.15.1.1 *(Highly) reduced inhibition/susceptibility of influenza viruses by neuraminidase inhibitors (NAIs) and baloxavir marboxil (BXM) in the Netherlands, 2020/2021 - 2025/2026 respiratory seasons*[1]

Season	A(H1N1)pdm09		A(H3N2)		B	
	NAI	BXM	NAI	BXM	NAI	BXM
2020/2021[2]	ND	ND	0/20	ND	0/1	ND
2021/2022	1/432 (<1%)[3]	0/285	3/1772 (<1%)[4]	2/1158 (<1%)[5]	0/62	0/41
2022/2023	3/647 (<1%)[6]	0/505	0/367	0/321	0/436[7]	0/424
2023/2024	33/890 (3.7%)[8]	0/678	0/509	0/483	0/49	0/34
2024/2025	4/703 (<1%)[9]	0/465	0/690	0/647	1/334 (<1%)[10]	0/296
2025/2026[11]	44/665 (6.6%)[12]	0/529	0/789	0/748	0/17	0/15

[1] Combined results obtained with phenotypic (virus isolates) and genotypic (clinical specimens) assays. Season defined as week 40 of the first year through week 39 of the following year. Abbreviations: NAI = neuraminidase inhibitor; BXM = baloxavir marboxil; ND = not done.

[2] During the winter period 2020/2021 no influenza viruses were detected. Only very late in the season after COVID-19 measures were partly lifted in summer 2021 few influenza viruses were detected and analysed for antiviral susceptibility.

[3] One virus with NA-H275Y associated with highly reduced inhibition by oseltamivir and normal inhibition by zanamivir was detected; additional data on treatment status of the patient unknown.

[4] Three viruses with NA-N329R associated with reduced inhibition by zanamivir and normal inhibition by oseltamivir were detected; by phenotypic testing two were indeed reduced inhibited by zanamivir with fold-change just over the threshold for reduced inhibition and one was normal inhibited by both oseltamivir and zanamivir. All three viruses came from the same submitter. Influenza antiviral treatment history of all three patients was unknown.

[5] Two viruses showed the amino acid substitution PA-E23G, previously associated with mild reduced susceptibility to baloxavir marboxil. By phenotypic testing at the WHO CCs for influenza in Tokyo and Atlanta of one virus, the virus was clearly reduced susceptible for baloxavir marboxil. One patient was hospitalized. The status of the other patient was unknown. For both patients no antiviral exposure data were available.

[6] One virus with NA-I223V and NA-S247N (double mutant) was detected. All but one double mutant viruses detected in the 2023/2024 season and phenotypically tested showed reduced inhibition by oseltamivir (median fold-change 12.3; range 10.4-16.1) and normal inhibition by zanamivir. The sequences of one clinical specimen contained NA-D199G/D(91%G) and NA-H275Y/H(8%Y), previously associated with 17-fold reduced and 221 to 1637-fold highly reduced inhibition by oseltamivir, respectively. However, the virus isolate used for phenotypic testing contained NA-D199G/D(24%G) and NA-H275Y/H(75%Y) and therefore the phenotypic outcome is mainly driven by NA-H275Y. The patient did not receive influenza antiviral treatment prior to specimen collection. One virus with NA-H275Y was detected, previously associated with highly reduced inhibition by oseltamivir and normal inhibition by zanamivir. Additional data on treatment status of the patient was unknown.

[7] A cluster of B/Victoria viruses emerged almost exclusively in The Netherlands with NA-K360E previously associated with highly reduced inhibition by peramivir. However, by phenotypic testing of 9 of the 89 viruses detected they appeared normal inhibited by peramivir, likely due to additional compensating amino acid substitutions A395V and L396F/S in the close vicinity of the 360 position in the 3D structure of the neuraminidase.

[8] Thirty viruses with NA-I223V and NA-S247N (double mutant) were detected that caused mild reduced inhibition by oseltamivir (median fold-change 12.3; range 10.3-16.1) and normal inhibition by zanamivir by phenotypic test of 14 of these viruses. One virus with NA-I233T previously associated with reduced inhibition by oseltamivir (9-15 fold) and normal inhibition by zanamivir was detected. Additional data on treatment status of the patient unknown. The virus could not be isolated for phenotypic testing. Two viruses with NA-H257Y previously associated with highly reduced inhibition by oseltamivir but normal inhibition by zanamivir were detected. Of one patient the treatment status was known; the virus with NA-H275Y was retrieved during oseltamivir therapy and confirmed highly reduced inhibited by oseltamivir and normal inhibited by zanamivir in phenotypic test. The other virus could not be isolated for phenotypic testing.

[9] Four viruses with NA-H257Y previously associated with highly reduced inhibition by oseltamivir but normal inhibition by zanamivir were detected. Of one patient the treatment status was known; the virus with NA-H275Y was retrieved during oseltamivir therapy and confirmed highly reduced inhibited by oseltamivir and normal inhibited by zanamivir in phenotypic test. For the other three viruses no isolate was available for phenotypic testing.

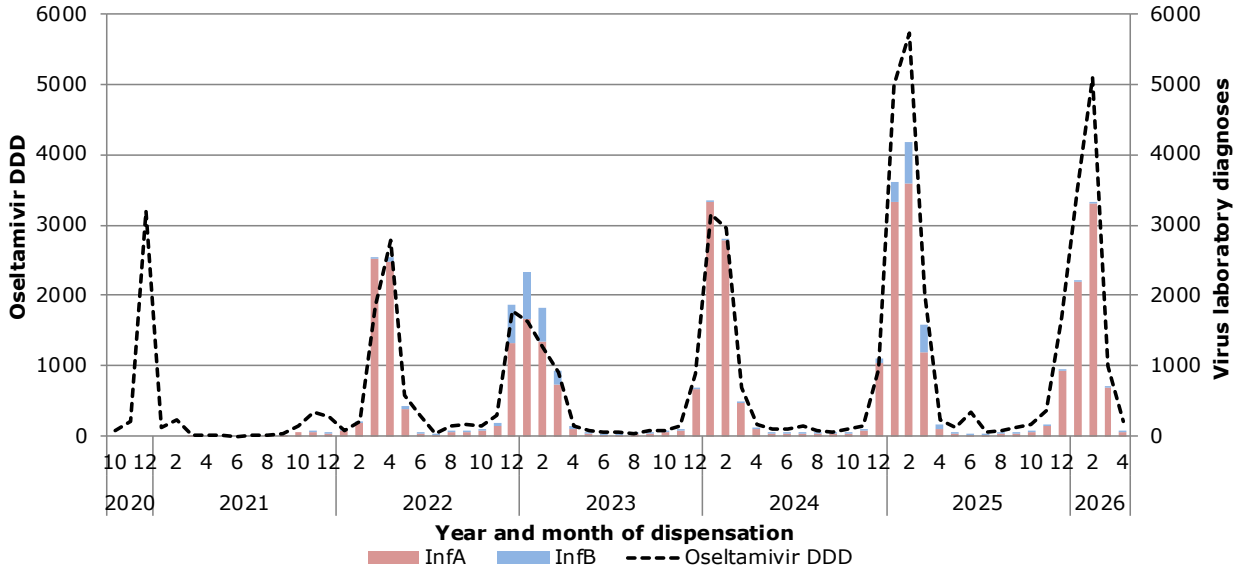
[10] One virus with NA-M464T previously associated with reduced inhibition by peramivir was detected and appeared also reduced inhibited by zanamivir (5.1-fold) but normal inhibited by oseltamivir by phenotypic test. The patient was not treated with antiviral drugs.

[11] Preliminary data up to week 20/2026.

[12] Forty viruses with NA-I223V and NA-S247N (double mutant) causing mild reduced inhibition by oseltamivir (median fold-change 13.3; range 7.4-15.6) and normal inhibition by zanamivir by phenotypic test of 12 of these viruses. Seven patients reported no use of antivirals and for 33 patients the antiviral treatment status was unknown. One virus with NA-I223T and NA-S247N (double mutant) causing mild reduced inhibition by oseltamivir (fold-change 15.4) and normal inhibition by zanamivir by phenotypic test. The antiviral treatment status of the patient was unknown. One virus with NA-I223M causing mild reduced inhibition by oseltamivir (fold-change 11.7) and normal inhibition by zanamivir by phenotypic test. The antiviral treatment status of the patient was unknown. Two viruses with NA-H257Y previously associated with highly

reduced inhibition by oseltamivir but normal inhibition by zanamivir were detected. The antiviral treatment status of the patient was unknown. Phenotypic testing of one virus confirmed highly reduced inhibited by oseltamivir and normal inhibited by zanamivir. The other virus was not available for phenotypic testing.

Figure 5.2.15.1.1 *Community pharmacy dispensations of oseltamivir in the Netherlands, 2020/2021 - 2025/2026 respiratory seasons*



Shown are the Defined Daily Doses (DDD) cumulated by month. Data kindly provided by Foundation for Pharmaceutical Statistics (SFK), the Netherlands.

For context, influenza virus type (InfA) and type B (InfB) laboratory diagnoses by 13 laboratories consistently reporting to the virology weekly records (virologische weekstaten) over 2020-2026 are shown. Data kindly provided by the Dutch Working Group for Clinical Virology.

Discussion

From the 2020/2021 season until the 2022/2023 season and in the 2024/2025 season, a very low proportion of tested influenza viruses in the Netherlands showed NAI reduced susceptibility, similar to global levels.[3] During the 2023/2024 season, double mutant A(H1N1)pdm09 virus carrying NA-I223V and NA-S247N emerged, which exhibit RI by oseltamivir. In the 2024/2025 this double mutant was not detected in the Netherlands. However, such double mutants re-emerged in the 2025/2026 season. This might be due to a high proportion of A(H1N1)pdm09 viruses that contained the single NA-S247N amino acid substitution (overall 437/665; 66%) from the start of the season, increasing the odds for emergence of double mutant viruses. NA-S247N reduces the susceptibility for oseltamivir to a level just below the RI threshold. The acquisition of the NA-I223V or the NA-I223T amino acid substitution in NA-S247N containing viruses further reduced the susceptibility for oseltamivir above the RI threshold. We are actively monitoring whether A(H1N1)pdm09 viruses carrying NA-S247N continue to circulate over summer 2026 and into the upcoming 2026/2027 season in the Netherlands. No naturally occurring BXM-reduced susceptible viruses were detected in the Netherlands, consistent with previous years and their very low global prevalence.[3] As the 2025/2026 season illustrated, ongoing genomic surveillance and phenotypic testing remain essential to promptly detect the emergence of reduced antiviral susceptibility and safeguard effective treatment options.

Conclusions

- In the 2025/2026 season, double mutant A(H1N1)pdm09 influenza viruses containing NA-I223V and NA-S247N showing reduced inhibition by oseltamivir and normal inhibition by zanamivir re-emerged in the Netherlands.
- Reduced inhibition by oseltamivir was found in 6.2% of A(H1N1)pdm09 viruses sequenced.
- All A(H3N2) and B viruses tested from the 2025/2026 season showed normal inhibition by oseltamivir and zanamivir.
- No reduced susceptibility to baloxavir marboxil (BXM) was detected in the 2025/2026 season, consistent with previous years.
- Community pharmacy dispensing of oseltamivir remains low with sharp increases during every influenza epidemic.
- Community pharmacies have not dispensed zanamivir since late 2020 and baloxavir marboxil (BXM) since its 2021 registration.

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5.2.16 Shigella

Introduction
Shigellosis is an infection caused by *Shigella* bacteria. Humans are the only reservoir for the four *Shigella* species: *S. sonnei, S. flexneri, S. boydii* and *S. dysenteriae*. All species can cause diarrheal illness, that can be bloody and prolonged. Severe illness (dysentery) is more commonly caused by *S. dysenteriae* serotype 1, and can be fatal. Rare post-infectious complications include reactive arthritis and hemolytic uremic syndrome (HUS). The primary route of transmission is the fecal-oral-one and occurs either directly through person-to-person contact or indirectly via contaminated food or water. In the Netherlands, shigellosis is a notifiable disease and is often associated with international travel and with sexual activity among men who have sex with men (MSM).

Antibiotic treatment is recommended for severe infections, as well as for infections of any level of severity in individuals at increased risk of severe disease.[1] Antimicrobial resistance of *Shigella* spp. against commonly used antibiotics such as ciprofloxacin, third-generation cephalosporins, and to a lesser extent, azithromycin, is a problem that is increasing worldwide, and one that was preceded by resistance against ampicillin, chloramphenicol and co-trimoxazole. Multi-drug resistance is also being more frequently reported, particularly among MSM.[2] In the Netherlands, azithromycin and ceftriaxone are currently recommended as respective oral and intravenous empirical treatment options for severe infections. The use of ciprofloxacin is only recommended for infections with proven sensitivity to this drug.

Methods
Phenotypic antimicrobial sensitivity data from 2021 to 2025 were extracted from the ISIS-AR-surveillance database. ISIS-AR's selection criteria are described in Chapter 5.1.1. Additionally, travel history and transmission route data obtained from the Dutch registration system for notifiable infectious diseases (OSIRIS) were linked to the extracted ISIS-AR data based on 4-digit postal code, gender, age and date of notification, where possible. Antimicrobial resistance outcomes were available for a broad selection of antibiotic agents, while confirmatory tests were available for the presence of Carbapenemase-producing Enterobacterales (CPE). Due to the limited amount of data on macrolide resistance, a reliable analysis of the level of resistance of *Shigella* spp. against this class of antibiotics was not feasible. Multi-drug resistance (MDR) was defined as resistance to ceftazidime, cefotaxime/ceftriaxone, ciprofloxacin and cotrimoxazole.

Results
In 2025, as in previous years, *S. sonnei* (n=210; 50.5%) and *S. flexneri* (n=166; 39.9%) were the most frequently identified species in ISIS-AR, followed by *S. boydii* (n=9; 2.2%) and *S. dysenteriae* (n=5; 1.25%) (Table 5.2.16.1). In 6.3% of the isolates, the *Shigella* species was not specified.

Table 5.2.16.1 *Number of tested human Shigella isolates per species per year, based on ISIS-AR data, 2021-2025*

	2021	2022	2023	2024	2025
	n=182	n=349	n=495	n=397	n=416
S. sonnei	79	217	334	205	210
S. flexneri	84	105	126	154	166
S. boydii	6	9	9	15	9
S. dysenteriae	2	11	5	6	5
Shigella species not specified	11	7	21	17	26

As expected, resistance percentages for amoxicillin/ampicillin (70.4%) and cotrimoxazole (54.7%) were very high across species, although inter-species differences exist (Table 5.2.16.2). The percentage of isolates resistant to ciprofloxacin and third-generation cephalosporins was also high, with percentages of 37.2% and 38.0% for ciprofloxacin and of 39.2% and 22.6% for cefotaxime/ceftriaxone resistance, in *S. sonnei* and *S. flexneri* respectively, in 2025. Over the past five years, resistance to third-generation cephalosporins and ciprofloxacin in *S. sonnei* isolates showed a modest increase. The percentage of MDR *S. sonnei* isolates was higher compared to *S. flexneri* and has since 2021 been fluctuating between 2.6% and 8.3%. Among MSM, the percentage of MDR *S. sonnei* isolates has typically remained above 10%, except in 2024, when it was 9%. A peak in resistance among *S. flexneri* samples was observed in 2024 for both third-generation cephalosporins and ciprofloxacin, with lower percentages in 2025 (Figure 5.2.16.1 and 5.2.16.2). There were no positive CPE-confirmatory test results, and no meropenem/imipenem resistant isolates among *S. flexneri* and *S. sonnei* isolates.

For patients with available OSIRIS data (80% of 416 patients in 2025), 52.6% (173/329) acquired the infection abroad and 23.7% (79/334) had MSM contact in the week before onset of symptoms, resistance percentages for these groups are shown in Table 5.2.16.2. Fluctuations in resistance percentages are largely driven by longstanding clusters identified by whole genome sequencing (WGS), each associated with characteristic resistance profiles, becoming more dominant in certain years or acquiring additional resistance. At the same time, new clusters continue to be identified, contributing to the observed variability in resistance patterns over time.

The European Centre for Disease Prevention and Control (ECDC) has issued a warning about the increasing spread of MDR *Shigella* strains in Europe, especially among MSM.[3] This was first noted between 2020 and 2022. Since 2023, several WGS-defined clusters, some longstanding on others more recently identified, have been responsible for the majority of MDR observed among MSM. In England, more than half of *S. sonnei* isolates in MSM were resistant to all three clinically relevant antimicrobial agents ciprofloxacin, azithromycin and/or ceftriaxone in 2025, compared to a MDR of 16% among *S. sonnei* isolates in MSM in 2025 in the Netherlands.[4] These higher reported resistance levels in England can be (partially) explained by several factors: 1) the MDR

definitions used in England differ from ours; 2) resistance-level-analyses are based on genotypic data rather than phenotypic data; and 3) azithromycin is not included in our MDR definition, because there is no established clinical breakpoint for azithromycin resistance in *Shigella* spp.

Table 5.2.16.2 *Resistance (%) of human Shigella isolates, total and stratified, in the Netherlands in 2025*

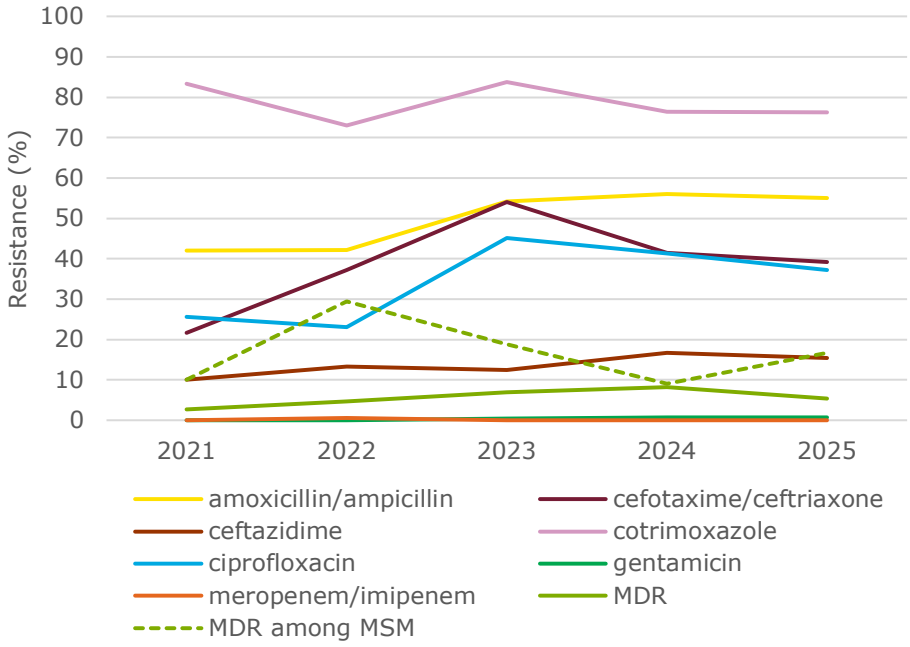
		Species		Persons at increased risk of infection	
	Total	***S. sonnei***	***S. flexneri***	**Acquired abroad**	**MSM**
	n=416	**n=210**	**n=166**	**n=173**	**n=79**
amoxicillin/ ampicillin	70.4	55.1	91	52.7	96.6
cefotaxime/ ceftriaxone	30.1	39.2	22.6	23.6	47.9
ceftazidime	12.2	15.4	9.15	8.2	25.4
cotrimoxazole	54.7	76.3	27.7	63.2	44.3
ciprofloxacin	37.3	37.2	38	22.8	58.6
gentamicin	1	0.7	1.6	0.8	0
meropenem/ imipenem	0	0	0	0	0
CPE	0	0	0	0	0
MDR	3.4	5.3	1.6	3.1	8.2

MSM, men who have sex with men in the week before onset of symptoms

CPE, Carbapenemase-producing Enterobacterales

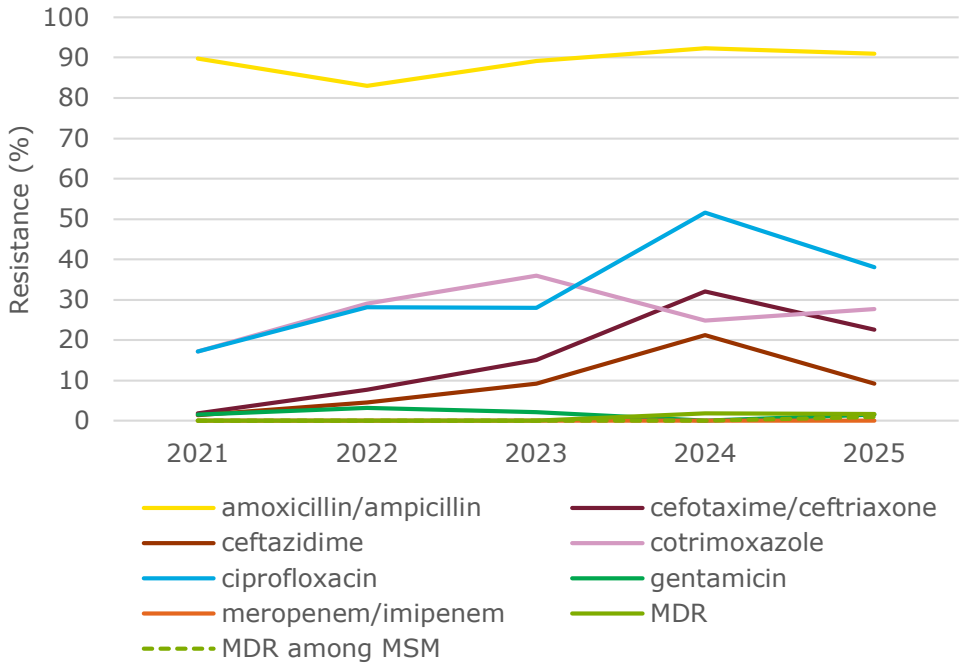
MDR, Multi-drug resistant: defined as resistance to all of the following antibiotic agents (classes): ceftazidime, cefotaxime/ceftriaxone (3GCS), ciprofloxacin (fluoroquinolones) and cotrimoxazole (sulfonamides)

Figure 5.2.16.1 *Resistance trends (%) of human S. sonnei isolates, from 2021-2025*



MDR, Multi-drug resistant: defined as resistance to all of the following antibiotic agents (classes): ceftazidime, cefotaxime/ceftriaxone (3GCS), ciprofloxacin (fluoroquinolones) and cotrimoxazole (sulfonamides)
MSM, men who have sex with men in the week before onset of symptoms

Figure 5.2.16.2 *Resistance trends (%) of human S. flexneri isolates, from 2021-2025*



MDR, Multi-drug resistant: defined as resistance to all of the following antibiotic agents (classes): ceftazidime, cefotaxime/ceftriaxone (3GCS), ciprofloxacin (fluoroquinolones) and cotrimoxazole (sulfonamides)

MSM, men who have sex with men in the week before onset of symptoms

Conclusions

- In 2025, as in the previous 5 years, *S. sonnei* and *S. flexneri* were the most frequently identified species, comprising 50% and 40% of the 416 isolates extracted from the ISIS-AR-surveillance database, respectively.
- For most antibiotics, resistance percentages were higher among the MSM population compared to the overall population.
- Following an increase of resistance to third-generation cephalosporins and ciprofloxacin among *S. sonnei* isolates up to 2023, resistance has since remained high and relatively stable at around 40%. The overall percentage of MDR *S. sonnei* isolates has been fluctuating since 2021 between 2.6% and 8.3%, although this percentage has typically remained above 10% among MSM-isolates.
- Resistance percentage of S*. flexneri* isolates for ciprofloxacin and third-generation cephalosporins was lower than in 2024, when the highest resistance percentages were observed since 2021. MDR was a way less common phenomenon for *S. flexneri* than for *S. sonnei*, also among MSM.

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6 Antimicrobial resistance in zoonotic bacteria

This chapter describes susceptibility test results as determined in 2025 for the zoonotic pathogens *Salmonella enterica*, *Campylobacter* spp., Shiga-toxin producing and enteropathogenic *E. coli*, and *Yersinia* spp. For data extracted from the ISIS-AR database, the laboratory methods used and the selection of isolates are described in chapter 5.1.1. For the phenotypic data in this chapter, epidemiological cut-off values (www.eucast.org) were used for the interpretation of minimum inhibitory concentrations (MIC). Epidemiological cut-off (ECOFF) values are in most cases lower than clinical breakpoints; therefore, depending on the antibiotic, non-wild-type susceptible isolates (i.e. isolates displaying MICs above the ECOFFs) cannot be classified as clinically resistant. For the purpose of this report, we designated all non-wild-type susceptible isolates as "resistant", and specified this per antibiotic if necessary. The results of Shiga-toxin producing and enteropathogenic *E. coli* are based solely on genotypic data.

6.1 Salmonella

Introduction

In this chapter, we report data on antimicrobial resistance among zoonotic non-typhoidal *Salmonella* (ntS), including *S*. Paratyphi B, variant Java, isolates obtained from human clinical patients, animals, and food-samples. Human infections with ntS may lead to a form of gastrointestinal illness that is usually self-limiting, and that typically involves nausea, fever, diarrhea, and abdominal discomfort. Unlike S. Paratyphi B *sensu stricto,* human paratyphoid infections with *S*. Paratyphi B var. Java, stand out in the sense that they commonly infect poultry, while *not* typically causing typhoidal disease.

Carriage of ntS serotypes is widely distributed among domestic and wild animals. These animals are often asymptomatic carriers that shed ntS in their feces. Fecal-oral transmission to humans may occur through direct or indirect contact with infected animals or their feces. However, most infections arise from the consumption of contaminated animal products, such as meat or eggs.

Antibiotic treatment for human ntS infections is only recommended for individuals at increased risk of complications and in case of severe infection. For infections with fluoroquinolone-sensitive *Salmonella* strains in adults, ciprofloxacin is generally recommended as the treatment of choice. For infections with unknown sensitivity, either azithromycin (oral route) or a third-generation cephalosporin is recommended.[1]

Methods

Phenotypic antimicrobial sensitivity data (MICs and diameters) from human salmonellosis patients between 2016 and 2025 were extracted from the ISIS-AR-surveillance database, which includes data from all connected laboratories. Additionally, detailed serotype information obtained from *Salmonella* isolates sent to the RIVM by clinical

laboratories on a voluntary basis was linked to the extracted ISIS-AR data based on 4-digit postal code, gender, age, and date of notification, where possible. Only the first isolate per patient, per serotype per year was included in this report to avoid repeated sampling causing bias in the calculation of resistance levels and time trends. Antimicrobial resistance proportions of *Salmonella enterica* from ISIS-AR were determined according to EUCAST antimicrobial susceptibility testing guidelines for amoxicillin/ampicillin, third-generation cephalosporins (ceftazidime and cefotaxime/ceftriaxone), cotrimoxazole, gentamicin, ciprofloxacin, and meropenem/imipenem. Confirmatory tests were available for the presence of Carbapenemase-producing Enterobacterales (CPE). We do not present macrolide-resistance data as the limited number of available data did not allow for reliable analysis.

Non-human isolates from 2025 were obtained from healthy food-producing animals, food products of animal origin, and other food products. All non-human isolates were subjected to phenotypic antimicrobial susceptibility testing based on MICs and interpreted using ECOFF values. These non-human resistance data originated from a diversity of programs, including: (a) *Salmonella* isolates originating from the national control program in poultry (mainly broilers and laying hens); (b) *Salmonella* isolates obtained from caecal samples of pigs and veal calves collected at slaughter, and; (3) *Salmonella* isolates from food products (e.g. meat and products thereof). All samples from animals and food were collected by the Dutch Food Safety Authority (NVWA) in the framework of the national AMR monitoring program (Decision 2020/179/EU). *Salmonella* isolates originating from animals were analysed for antibiotic susceptibility by Wageningen Bioveterinary Research (WBVR) and isolated from food products were analyzed by Wageningen Food Safety Research (WFSR).

Results

Of 1683 patients in ISIS-AR in 2025, 1341 (79.7%) could be linked to ntS serovar information of isolates sent to the RIVM. Of these, similar to what was found in previous years, *S.* Enteritidis was the most frequently identified serovar in human ntS-infections in the Netherlands (n=543; 40.5%), followed by *S.* Typhimurium (n=149; 11.1%) and *S.* Typhimurium Monophasic variant (n=75; 5.6%) (Table 6.1.1).

Table 6.1.1 *Number of human patients per year by most prevalent (n≥20) non-typhoidal Salmonella serovars in humans in the Netherlands in 2025 based on ISIS-AR. This only includes isolates from patients which could be linked to serovar information from isolates received by the RIVM from clinical laboratories*

	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
Total	**925**	**742**	**813**	**865**	**531**	**598**	**756**	**1098**	**1271**	**1341**
Enteritidis	230	167	204	317	145	136	263	454	514	543
Typhimurium	171	129	163	99	78	107	65	97	157	149
Monophasic	182	153	128	118	110	112	79	110	122	75
Chester	6	7	13	15	4	6	26	45	37	47
Paratyphi B var. Java	19	12	13	19	7	2	15	21	37	45
Newport	9	12	16	14	8	14	17	16	19	35
Saintpaul	10	6	12	10	2	6	10	10	19	33
Stanley	7	10	12	12	3	1	7	20	19	21
Other serotypes	291	246	252	261	174	214	274	325	347	393

A total of 545 isolates from non-human sources were tested in 2025. These sources included broilers (n=290), laying hens (n=168), pigs (n=59), cattle (n=13), and a diversity of other sources, including herbs and other animals (such as sheep, turkey, duck, and shrimps) (n=15). The most frequently identified serotypes among these isolates were *S.* Enteritidis (n=165; 30.3%), *S.* Infantis (n=86; 15.8%), and *S.* Paratyphi B var. Java (n=82; 15.0%) (Table 6.1.3).

Overall resistance

In 2025, high resistance proportions were those concerning (fluoro)quinolones, with ciprofloxacin resistance of 32.2% and 26.1% in human and non-humans isolates, respectively (Table 6.1.2 and 6.1.3). Among non-human isolates, high proportions of resistance to sulfamethoxazole (28.1%), trimethoprim (24.6%) and tetracyclines (19.1%) were observed. Testing of human isolates was limited to the cotrimoxazole (sulfamethoxazole/trimethoprim) combination, for which average resistance across serovars was rare (4.0%), compared with non-human isolates, of which 18.3% (10/545) were resistant to both sulfamethoxazole and trimethoprim.

Among serovars with at least 20 isolates in 2025, high rates of ciprofloxacin resistance were observed for *S.* Chester and *S.* Enteritidis in human isolates and for *S.* Infantis and *S.* Paratyphi B var. Java in non-human isolates. No meropenem resistance was detected in human or non-human isolates in 2025.

Table 6.1.2 *Resistance percentages (%) of the most prevalent (n≥20) non-typhoidal Salmonella serovars in human isolates, in the Netherlands in 2025 (N tested), according to EUCAST guidelines*

	All serovars (1341)	Enteritidis (543)	Typhimurium (149)	Typhimurium monophasic (75)	Chester (47)	Paratyphi B var. Java (45)	Newport (35)	Saintpaul (33)	Stanley (21)
amoxicillin/ ampicillin	18.4	12.8	28.8	65.8	40.4	4.5	11.4	6.1	14.3
cefotaxime/ ceftriaxone	1.4	0.6	0.7	2.7	2.1	2.3	2.9	0.0	0.0
ceftazidime	1.2	0.7	0.7	0.0	2.1	0.0	2.9	0.0	0.0
gentamicin	2.9	0.0	6.1	4.2	0.0	2.6	7.1	0.0	0.0
cotrimoxazole	4.0	0.2	9.0	11.0	8.5	2.3	11.4	6.1	0.0
ciprofloxacin	32.2	48.5	12.0	11.3	97.6	2.5	9.1	32.3	0.0
meropenem/ imipenem	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
CPE	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

CPE, Carbapenemase-producing Enterobacterales

Table 6.1.3 *Resistance percentages of the most prevalent (n≥20) non-typhoidal Salmonella serovars in non-human isolates, in the Netherlands in 2025 (number of isolates tested), according to ECOFF values*

	All serovars (545)	Enteritidis (165)	Infantis (86)	Paratyphi B var. Java (82)	Virchow (34)	Typhimurium monophasic (27)	Mbandaka (23)	Derby (20)	Typhimurium (20)
ampicillin	12.5	0.0	20.9	20.7	0.0	74.1	0.0	5.0	35.0
cefotaxime	0.7	0.0	1.2	1.2	0.0	0.0	0.0	0.0	0.0
ceftazidime	0.4	0.0	1.2	0.0	0.0	0.0	0.0	0.0	0.0
gentamicin	0.7	0.0	1.2	0.0	2.9	3.7	0.0	0.0	5.0
tetracycline	19.1	0.0	83.7	1.2	0.0	70.4	0.0	10.0	20.0
sulfamethoxazole	28.1	0.0	84.9	58.5	2.9	70.4	0.0	10.0	25.0
trimethoprim	24.6	0.0	48.8	100.0	0.0	22.2	0.0	5.0	0.0
ciprofloxacin	26.1	11.5	87.2	46.3	2.9	11.1	0.0	0.0	0.0
nalidixic acid	25.9	11.5	87.2	47.6	2.9	11.1	0.0	0.0	0.0
chloramphenicol	2.9	0.0	2.3	2.4	0.0	22.2	0.0	5.0	10.0
azithromycin	0.4	0.0	1.2	0.0	0.0	3.7	0.0	0.0	0.0
meropenem	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
tigecycline	1.1	0.0	7.0	0.0	0.0	0.0	0.0	0.0	0.0
amikacin	0.4	0.0	1.2	0.0	0.0	0.0	0.0	0.0	0.0

Resistance of (monophasic) S. Typhimurium and S. Enteritidis in humans and animals

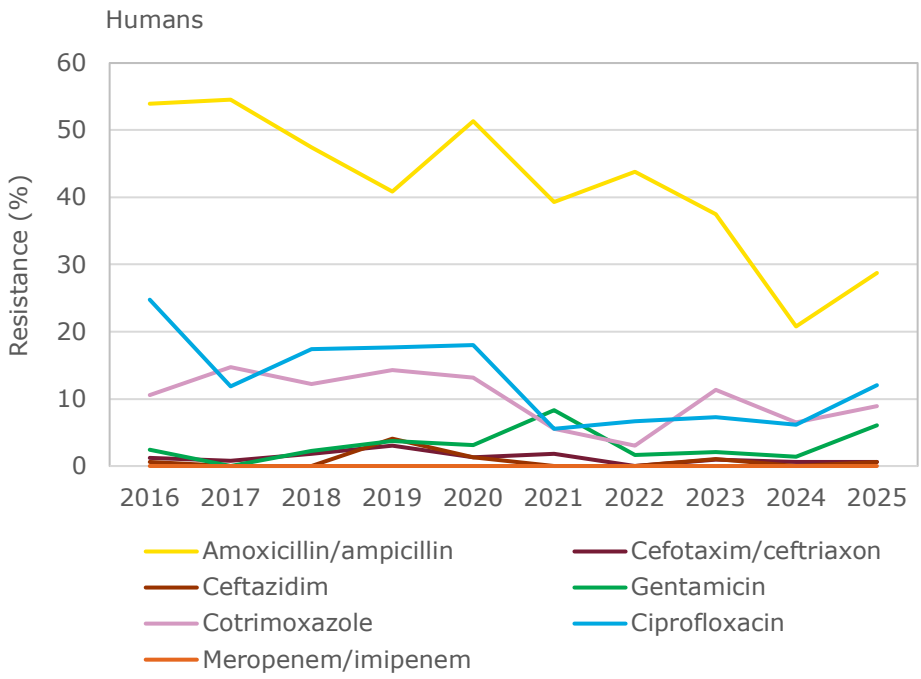
S. Typhimurium
Pigs and cattle serve as important animal reservoirs for *S.* Typhimurium and its monophasic variant.[2] For human *S.* Typhimurium and monophasic *S.* Typhimurium isolates (Table 6.1.2), resistance percentages were high for amoxicillin/ampicillin (28.8% and 65.8%), and moderately high for cotrimoxazole (9.0% and 11.0%) and ciprofloxacin (12.0% and 11.3%). Resistance to the third-generation cephalosporins was rare. Long-term resistance trends of human *S.* Typhimurium isolates are shown in Figure 6.1.1. The percentage of amoxicillin/ampicillin resistant isolates has long been extremely high, although it appears to have decreased slightly in recent years. A similar pattern is observed for ciprofloxacin, albeit to a somewhat lesser extent. For human samples, resistance to other antibiotics, including cotrimoxazole, gentamicin and third-generation cephalosporins, has remained relatively stable over the same period.
Resistance proportions among non-human isolates of *S.* Typhimurium and its monophasic variant were also high for ampicillin, tetracycline and sulfamethoxazole, especially among pigs (Table 6.1.4). Chloramphenicol and trimethoprim resistance was particularly prevalent among *S.* Typhimurium isolates obtained from pigs. However, results should be interpreted with care due to low number of isolates.

Table 6.1.4 *Resistance percentages of S. Typhimurium and S. Typhimurium monophasic (N tested) isolated from non-human sources in 2025*

	***S.* Typhimurium (20)[a]**		***S.* Typhimurium monophasic (27)[b]**
	Broilers (8)	**Pigs (7)**	**Pigs (20)**
ampicillin	25.0	71.4	85.0
cefotaxime	0.0	0.0	0.0
ceftazidime	0.0	0.0	0.0
gentamicin	12.5	0.0	5.0
tetracycline	25.0	28.6	80.0
sulfamethoxazole	25.0	42.9	80.0
trimethoprim	0.0	0.0	25.0
ciprofloxacin	0.0	0.0	15.0
nalidixic acid	0.0	0.0	15.0
chloramphenicol	12.5	14.3	30.0
azithromycin	0.0	0.0	5.0
meropenem	0.0	0.0	0.0
tigecycline	0.0	0.0	0.0
amikacin	0.0	0.0	0.0

[a] Including 5 isolates from other non-human sources: veal calves (3), beef (1), and laying hens (1).
[b] Including 7 isolates from other non-human sources: broilers (6), and veal calves (1).

Figure 6.1.1 *Resistance (%) trends for human S. Typhimurium 2016-2025*



S. Enteritidis

In the Netherlands, laying hens and their eggs are the main reservoir of *S.* Enteritidis.[2] For human *S.* Enteritidis isolates in 2025, resistance against fluoroquinolones was high (ciprofloxacin: 48.5%; Table 6.1.2). This percentage occurs within the context of an upward trend over the last 10 years, and is even higher than the previous peak percentage in 2022 (Figure 6.1.2). Although these high percentages cannot be fully explained, it may be partly attributable to a substantially higher rate of ciprofloxacin resistance among strains isolated from travellers, something which may also explain why fluoroquinolone resistance was lower during the 2020/2021 COVID-19 pandemic period with travel restrictions. Third-generation cephalosporins resistance among human *S*. Enteritidis isolates was rare, and no meropenem resistant isolates were found.

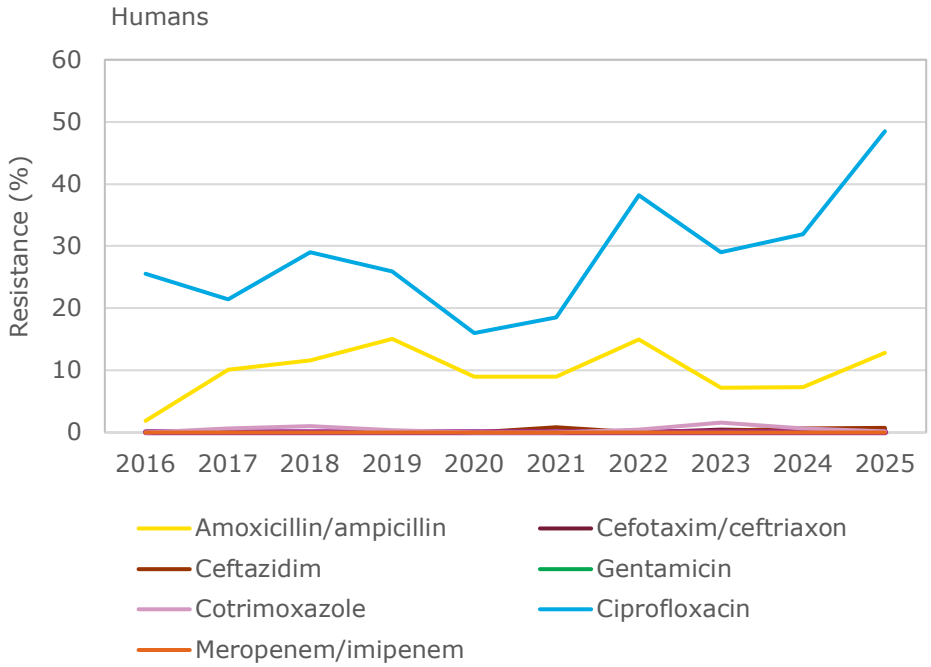
Similar to previous years, fluoroquinolone-resistance percentages among isolates from laying hens and broilers were lower (8.6% and 26.1%, respectively) than among isolates from humans (Table 6.1.5).

Table 6.1.5 *Resistance percentages of S. Enteritidis (N tested) isolated from non-human sources in 2025*

	***S*. Enteritidis (165)[a]**	
	Laying hens (139)	**Broilers (23)**
ampicillin	0.0	0.0
cefotaxime	0.0	0.0
ceftazidime	0.0	0.0
gentamicin	0.0	0.0
tetracycline	0.0	0.0
sulfamethoxazole	0.0	0.0
trimethoprim	0.0	0.0
ciprofloxacin	8.6	26.1
nalidixic acid	8.6	26.1
chloramphenicol	0.0	0.0
azithromycin	0.0	0.0
meropenem	0.0	0.0
tigecycline	0.0	0.0
amikacin	0.0	0.0

[a] Including 3 isolates from other non-human sources: dough (1), duck (1), and veal calves (1).

Figure 6.1.2 *Resistance (%) trends for human S. Enteritidis, 2016-2025*



ESBL/pAmpC-producing and multidrug resistant Salmonella enterica in humans and animals
The global emergence of human infections with multidrug-resistant *Salmonella* strains including both fluoroquinolone resistance and resistance against beta-lactams, including cephalosporins, through the production of extended-spectrum beta-lactamases (ESBL) and plasmid-mediated AmpC (pAmpC), results in severe limitations of antimicrobial treatment of human infections. In 2025, the percentage of human genotypically confirmed ESBL/pAmpC-producing *Salmonella* isolates was 1.3% (18/1341). The most frequently identified resistance gene was *bla*CTX-M-55. Among these isolates, 66.7% (12/18) were also resistant to ciprofloxacin. In non-human isolates, genotypically confirmed ESBL/pAmpC-producing *Salmonella* was detected twice in 2025 (0.4%; 2/545).

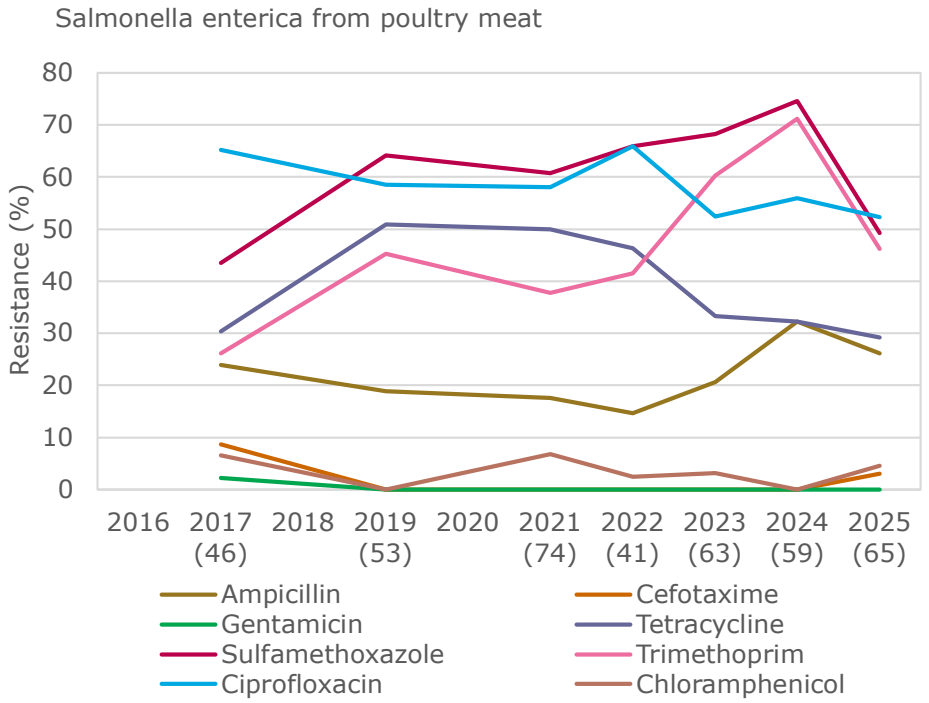
Resistance among Salmonella enterica isolates from broiler meat, pork, and other meat sources
The occurrence of ciprofloxacin, sulfamethoxazole and trimethoprim resistance was very high among Dutch/EU broiler meat (Table 6.1.6 and Figure 6.1.3). Overall, resistance proportions in Dutch/EU broiler meat appear to be relatively stable. Only resistance to trimethoprim shows an increasing trend up to 2024. However, trends should be interpreted with caution, as the observed resistance proportions are influenced by the underlying distribution of serotypes.

Table 6.1.6 *Resistance (%) of Salmonella enterica isolated from different types of raw meat in the Netherlands in 2025*

	Dutch/EU broiler meat (65)[a]	Pork (11)	Other meat (19)[b]
ampicillin	26.2	45.5	10.5
cefotaxime	3.1	0.0	0.0
ceftazidime	1.5	0.0	0.0
gentamicin	0.0	0.0	0.0
tetracycline	29.2	54.5	5.3
sulfamethoxazole	49.2	36.4	10.5
trimethoprim	46.2	9.1	10.5
ciprofloxacin	52.3	9.1	10.5
nalidixic acid	53.8	9.1	5.3
chloramphenicol	4.6	9.1	5.3
azithromycin	1.5	0.0	0.0
meropenem	0.0	0.0	0.0
tigecycline	7.7	0.0	0.0
amikacin	1.5	0.0	0.0

[a] Fresh chicken meat sampled at retail and chicken neck skin from verification projects, excluding imported broiler meat.
[b] Other meat includes sheep (7), veal calves (6), beef (3), duck (1), and imported broiler meat (1) and shrimp (1).

Figure 6.1.3 *Trends in resistance (%) of Salmonella enterica isolated from Dutch/EU broiler meat, in the Netherlands from 2017-2025*



Conclusions

- In 2025, the proportion of ntS samples with resistance to (fluoro)quinolones (ciprofloxacin, nalidixic acid) remained high in both human and non-human ntS isolates, whereas resistance to third-generation cephalosporins remained rare.
- None of the tested human and non-human ntS isolates were found to produce carbapenemases.
- Over the past 10 years, the percentage of amoxicillin/ampicillin resistant human *S*. Typhimurium isolates has been extremely high, although it appears to have decreased slightly in recent years (29% in 2025). A similar pattern is observed for ciprofloxacin, albeit to a somewhat lower level (12% in 2025). Resistance to other classes of antibiotics has remained relatively stable over the same period.
- Among non-human *S*. Typhimurium isolates, resistance to sulfamethoxazole and tetracycline was high, especially in pigs, although trends over time are difficult to interpret due to the limited sample size.
- Among human *S*. Enteritidis isolates the percentage of isolates resistant to ciprofloxacin is high (49% in 2025), and has been increasing since 2016.
- Compared to humans, fluoroquinolone resistance in *S*. Enteritidis isolates from laying hens and broilers was much lower in 2025 (9% and 26%), although significant fluctuations over time have been observed.
- The occurrence of resistance to ciprofloxacin and sulfamethoxazole in *S.* enterica isolates from Dutch/EU broiler meat has been consistently high over the past 10 years. Trimethoprim resistance, however, has been increasing up to 2024.

References

1. SWAB richtlijn antimicrobiële therapie voor acute infectieuze diarree, 2023. https://swab.nl/nl/exec/file/download/259
2. Teunis G, Dallman TJ, Zając M, et al. Attributable sources of the five most prevalent non-typhoidal Salmonella serovars across ten European countries. Bacteria and Bacterial Diseases. J Infect. 2025;91(5):106632.

6.2 Campylobacter

Introduction

According to the European legislation[1], antibiotic resistance monitoring of zoonotic bacteria includes *Campylobacter jejuni* (*C. jejuni*) and *Campylobacter coli* (*C. coli*) as important food-borne pathogens. In this chapter, the occurrence and trends in antimicrobial resistance in *C. jejuni* and *C. coli* are described. Isolates were obtained from samples collected from food animals, meat and humans.

Methods

Isolation of campylobacters from faecal samples was performed according to the guidelines of the EURL Campylobacter by direct inoculation of faecal material on two different selective media: mCCDA and Butzler. After 48 hours incubation at 37 ^{0}C under microaerobic conditions presumptive campylobacter colonies are pure cultured and identified by MALDI-TOF mass spectrometry (MALDI Biotyper®, Bruker). In case of confirmed identification, one *C. coli* and one *C. jejuni* is analysed. Susceptibility testing was performed by broth microdilution according to ISO 20776-1:2019 under ISO 17025 accreditation RvA TESTING L 389 and L 014 in a standard antimicrobial panel designed for testing campylobacter, which contains six antibiotics representing antibiotic classes relevant for treatment of human infections caused by Campylobacter (erythromycin, gentamicin and ciprofloxacin) or included for monitoring purposes (chloramphenicol, ertapenem and tetracycline)[2]. Within this monitoring program non-wild type susceptible isolates (exhibiting MIC-values above the ECOFF), obtained from farm animals and food are classified as resistant. These isolates most probably contain an acquired resistance mechanism, but may not be clinically resistant.

Data on antimicrobial resistance in human campylobacteriosis cases were extracted from the Infectious Diseases Surveillance Information System for Antimicrobial resistance (ISIS-AR) at the RIVM. In case of patients with multiple isolates of the same species within 60 days, only the first isolate was selected, to avoid repeated sampling causing bias in the calculation of resistance levels and time trends.

Results

6.2.1 Campylobacter in animals and food

Bacterial isolates

In 2025, 66 *C. jejuni* and 38 *C. coli* isolates obtained from caecal samples of broilers, 68 *C. jejuni* and 28 *C. coli* isolates from faecal samples of turkeys, 242 *C. jejuni* and 94 *C. coli* from caeca of veal calves as well as 287 *C. coli* from caecal samples of slaughter pigs were tested for antimicrobial susceptibility. In addition, 192 *C. jejuni* and 100 *C. coli* isolates obtained from chicken meat and neck skin were included in the monitoring.

Antimicrobial resistance levels
Table 6.2.1.1 summarizes the aggregated MIC distributions and antimicrobial resistance rates for all *C. jejuni* and *C. coli* strains isolated in 2025 from caecal or faecal samples of broilers, turkeys, veal calves, and pigs. Table 6.2.1.2a and 6.2.1.2b show the species specific resistance rates for *C. jejuni* and *C. coli* from broilers (isolated either from caeca, meat or neck skin), turkeys, veal calves, and pigs (limited to *C. coli*). Trends in resistance of *C. jejuni* in broilers and poultry meat are shown in figures 6.2.1.1a and 6.2.1.1b and trends in resistance of *C. coli* in broilers and poultry meat are shown in figures 6.2.1.2a and 6.2.1.2b. National surveillance data for *Campylobacter* spp. isolated from humans are summarized in figure 6.2.1.3 and table 6.2.1.3, with data available from2002 and 2009 onward, respectively).

Broiler chickens, neck skin and, chicken meat and turkeys
For Campylobacter strains derived from poultry sources in 2025, resistance percentages were determined for isolates obtained from caecal samples, samples of neck skin and chicken meat from broiler chickens, and faecal samples from turkeys. Table 6.2.1.2a shows high resistance levels for tetracycline in *C. jejuni* isolates obtained from broiler caecal samples (60.6%) as well as in isolates from chicken meat and neck skin, ranging from 54.3% to 75.9%. Resistance to tetracycline was substantially lower in *C. jejuni* from turkeys (25.4%). In 2025, high levels of resistance to ciprofloxacin were observed in all poultry sources: broilers (68.2%), chicken meat (68.1%), chicken neck skin (83.3%) and turkeys (60.3%). Resistance to chloramphenicol, erythromycin and gentamicin was not detected in *C. jejuni* from poultry sources in 2025.

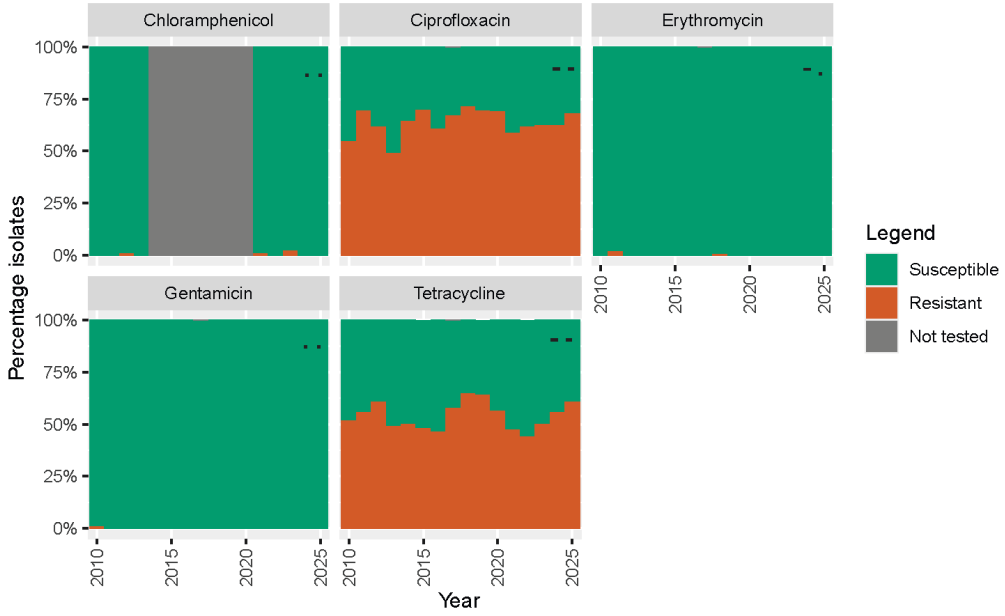
Looking at the trends in antimicrobial resistance in *C. jejuni*, as shown in Figure 6.2.1.1a and 6.2.1.1b, levels of resistance for ciprofloxacin in *C. jejuni* from broilers and chicken meat remain persistently high in the period from 2010 to 2025. In the same period, a yearly but non-significant increase of tetracycline resistance is observed in *C. jejuni* from broiler caeca, but not in chicken meat.
Higher resistance proportions were observed for all antimicrobials in *C. coli* isolates from broilers and chicken meat, compared to *C. jejuni* isolates from the same sources. Figures 6.2.1.2a and 6.2.1.2b display fluctuating high levels of resistance in *C. coli* isolates to tetracycline, both from broilers and chicken meat, with a steep increase of tetracycline resistance in 2025 compared to 2024, which is not observed in *C. coli* isolates from chicken meat. However, this increase should be interpreted with care due to the low number of isolates included (n=38). During the period 2021 -2025, ciprofloxacin resistance in *C. coli* from broilers increased to extremely high levels of resistance above 85% from 2023 onwards. Very high levels of resistance to ciprofloxacin were also observed in *C. coli* isolates from chicken meat (89.1%) and chicken neck skin (86.1%) in 2025 (table 6.2.1.2b). As in former years, gentamicin resistance in *C. coli* from broilers and poultry meat was not detected. Unlike *C. jejuni*, macrolide resistance is observed annually in *C. coli*, with resistance rates less than 10% since 2019.

Table 6.2.1.1 *MIC distributions (in %) for Campylobacter jejuni (N = 308) isolated from caecal samples of broilers and veal calves as well as C. coli (N = 419) isolated from caecal samples of broilers, veal calves and pigs in 2025*

***C. jejuni,* broilers and veal calves**	**MIC (%) distribution mg/L**															**R%**	**95% CI**
(N = 308)	**0.06**	**0.125**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**1024**		
Chloramphenicol						30.8	58.1	8.4	2.6							0.0	0.0 - 1.2
Ciprofloxacin		39.6	8.8	1.0	0.3		1.6	20.8	22.1	4.9	1.0					50.6	44.9 - 56.4
Erythromycin					52.9	41.2	5.8									0.0	0.0 - 1.2
Ertapenem		68.5	20.1	6.8	3.2	0.6	0.6									-	-
Gentamicin			91.6	8.4												0.0	0.0 - 1.2
Tetracycline				15.6	1.9			0.6	1.9	1.9	22.4	55.5				82.5	77.8 - 86.6

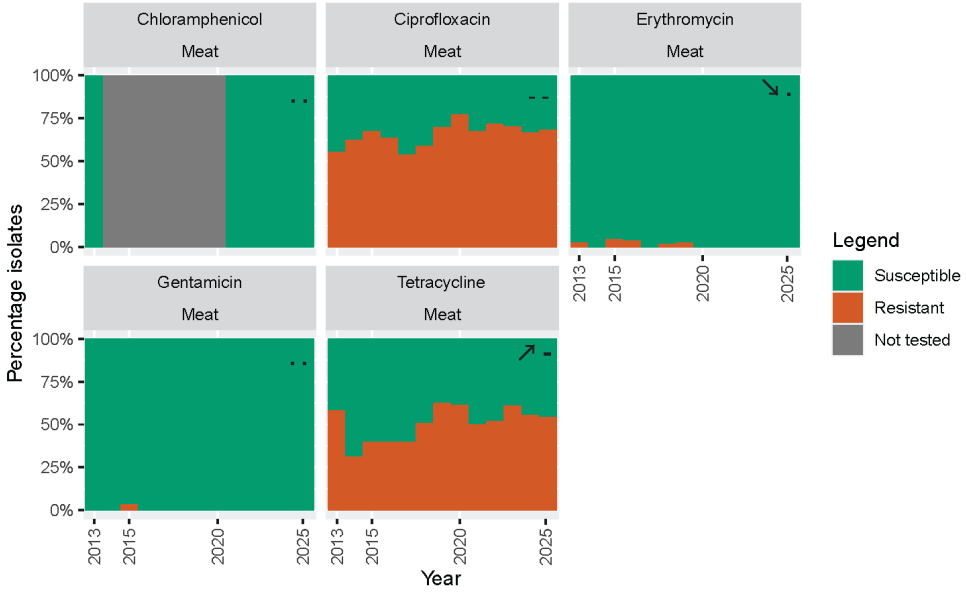
***C. coli,* broilers, veal calves and pigs**	**MIC (%) distribution mg/L**															**R%**	**95% CI**
(N = 419)	**0.06**	**0.125**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**1024**		
Chloramphenicol						3.6	43.7	43.4	9.3							0.0	0.0 - 0.1
Ciprofloxacin		48.4	13.1	1.2	0.2	0.2	3.6	11.0	14.8	7.2	0.2					37.2	32.6 - 42.1
Erythromycin					27.9	38.2	17.2	5.0	0.7	0.2	0.2	0.2	0.5	0.5	9.3	11.7	8.8 - 15.2
Ertapenem		33.2	27.9	16.5	13.6	6.4	1.4	1.0								-	-
Gentamicin			37.5	59.7	1.2					1.7						1.7	0.7 - 3.4
Tetracycline				17.4	1.9	0.7	0.7	0.5	1.2	1.7	8.8	67.1				80.0	75.8 - 83.7

Figure 6.2.1.1a *Trends in resistance of Campylobacter jejuni from broilers, 2010-2025*



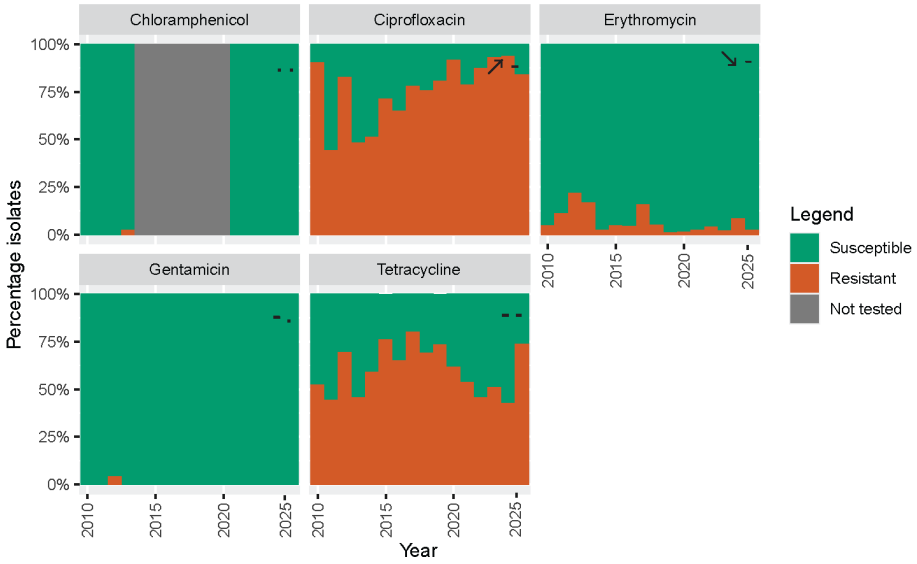
Percentage (%) of resistant *C. jejuni* isolates against different antibiotics, isolated from caecal samples from broilers in the period 2010-2025 in the Netherlands. The symbols indicate the trend in percentage of resistant isolates per antibiotic, the first symbol indicates the trend during the period 2010-2025, the second symbol indicates the trend during the last 5 years (2021-2025), with ↗ indicating an increasing trend in resistant isolates, ↘ indicating a decreasing trend in resistant isolates, - no trend. • means statistical trend analysis could not be performed, due to a lack of (resistant) isolates.

Figure 6.2.1.1b *Trends in resistance of Campylobacter jejuni from chicken meat, 2013-2025*



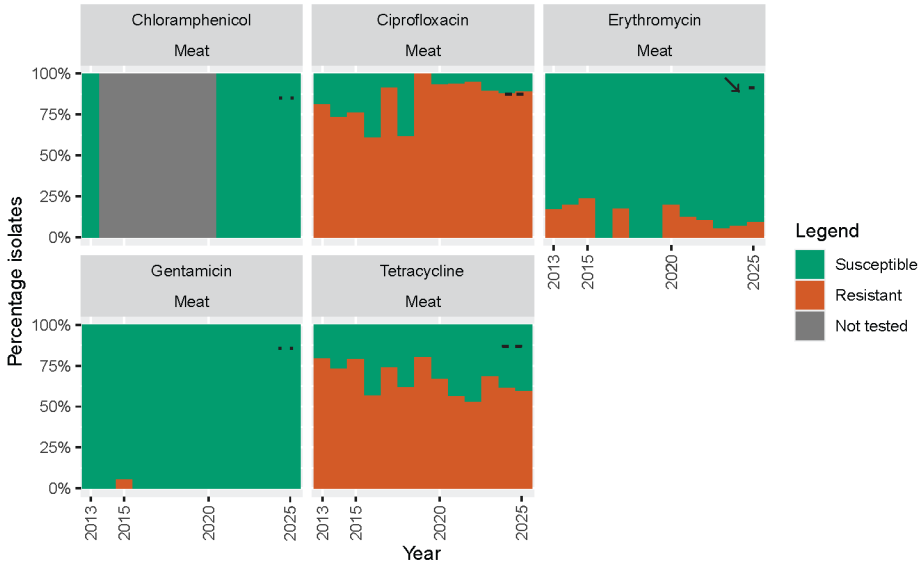
Percentage (%) of resistant *C. jejuni* isolates against different antibiotics, isolated from chicken meat samples in the period 2013-2025 in the Netherlands. The symbols indicate the trend in percentage of resistant isolates per antibiotic, the first symbol indicates the trend during the period 2013-2025, the second symbol indicates the trend during the last 5 years (2021-2025), with ↗ indicating an increasing trend in resistant isolates, ↘ indicating a decreasing trend in resistant isolates, - no trend. • means statistical trend analysis could not be performed, due to a lack of (resistant) isolates.

Figure 6.2.1.2a *Trends in resistance of Campylobacter coli from broilers, 2010-2025*



Percentage (%) of resistant *C. coli* isolates against different antibiotics, isolated from caecal samples from broilers in the period 2010-2025 in the Netherlands. The symbols indicate the trend in percentage of resistant isolates per antibiotic, the first symbol indicates the trend during the period 2010-2025, the second symbol indicates the trend during the last 5 years (2021-2025), with ↗ indicating an increasing trend in resistant isolates, ↘ indicating a decreasing trend in resistant isolates, - no trend. • means statistical trend analysis could not be performed, due to a lack of (resistant) isolates.

Figure 6.2.1.2b *Trends in resistance of Campylobacter coli from chicken meat, 2013-2025*



Percentage (%) of resistant *C. coli* isolates against different antibiotics, isolated from chicken meat samples in the period 2013-2025 in the Netherlands. The symbols indicate the trend in percentage of resistant isolates per antibiotic, the first symbol indicates the trend during the period 2013-2025, the second symbol indicates the trend during the last 5 years (2021-2025), with ↗ indicating an increasing trend in resistant isolates, ↘ indicating a decreasing trend in resistant isolates, - no trend. • means statistical trend analysis could not be performed, due to a lack of (resistant) isolates.

Table 6.2.1.2a *Resistance percentages of C. jejuni isolated from caecal and faecal samples, nek skin and meat in 2025*

	***C. jejuni* (R%)**				
	Broilers caeca	**Chicken meat**	**Chicken neck skin**	**Turkeys caeca**	**Veal calves caeca**
	N=66	**N=138**	**N=54**	**N=67**	**N=242**
Chloramphenicol	0.0	0.0	0.0	0.0	0.0
Ciprofloxacin	68.2	68.1	83.3	61.2	45.9
Erythromycin	0.0	0.0	0.0	0.0	0.0
Gentamicin	0.0	0.0	0.0	0.0	0.0
Tetracycline	60.6	54.3	75.9	25.4	88.4

Table 6.2.1.2b *Resistance percentages of C. coli isolated from caecal and faecal samples, nek skin and meat in 2025*

	***C. coli* (R%)**					
	Broilers caeca	**Chicken meat**	**Chicken neck skin**	**Turkeys caeca**	**Veal calves caeca**	**Pigs caeca**
	N=38	**N=64**	**N=36**	**N=28**	**N=94**	**N=287**
Chloramphenicol	0.0	0.0	0.0	0.0	0.0	0.0
Ciprofloxacin	84.2	89.1	86.1	100.0	75.5	18.5
Erythromycin	2.6	9.4	16.7	17.9	37.2	4.5
Gentamicin	0.0	0.0	2.8	0.0	7.4	0.0
Tetracycline	73.7	59.4	75.0	100.0	98.9	74.6

Veal calves and fattening pigs
Starting in 2021, mandatory monitoring of antimicrobial resistance in *Campylobacter* has been extended to include *C. jejuni* and *C. coli* from veal calves (< 1 year) as well as *C. coli* obtained from slaughter pigs. Resistance proportions are depicted in table 6.2.1.2.
As in previous years, very high percentages of tetracycline resistance were measured for *C. jejuni* and *C. coli* from calves (88.4–98.9%), as well as for *C. coli* from pigs (74.6%). In veal calves resistance to ciprofloxacin was also high in both *C. jejuni* and *C. coli* (45.9 – 75.5%). Substantially lower levels of ciprofloxacin resistance were found in *C. coli* from pigs (18.4%), which reflects the limited use of quinolones in this animal sector. In *C. jejuni* from calves, resistance to chloramphenicol, erythromycin, and gentamicin was not observed. As in previous years, erythromycin resistance was common in *C. coli* from calves (37.5%), but this percentage was lower than in 2024 (44.8%). In *C. coli* from calves resistance to gentamicin was observed in 7.4% of the strains, while no resistance to chloramphenicol was found. In *C. coli* from pigs resistance to erythromycin was rare (<5%) and resistance against chloramphenicol and gentamicin was not detected.

6.2.2 *Campylobacter in humans*

In 2025, 4856 campylobacteriosis cases were registered in ISIS-AR, which is lower than 2024 (n=5472) and 2023 (n = 5199) and pre-COVID years (average 2017-2019, n = 5028). During the COVID-19 pandemic the number of isolates was lower (average 2020-2021, n = 4071). Resistance levels in isolates from human patients were

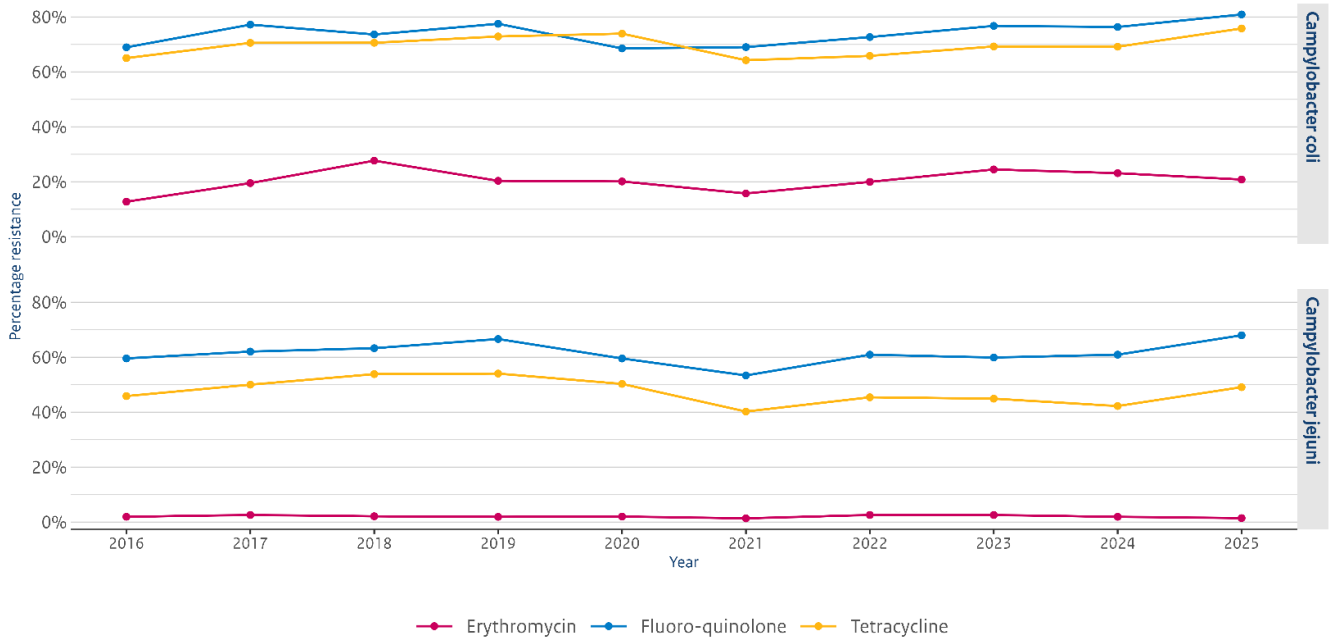
determined for ciprofloxacin, tetracycline and erythromycin, and are shown in table 6.2.1.3 and figure 6.2.1.3. Figure 6.2.1.3 shows a gradual increase of ciprofloxacin and tetracycline resistance from 2016 to 2019. In 2020 and 2021, however, resistance levels for all measured antibiotics dropped, most likely due to a substantial reduction in travel-related campylobacteriosis as a result of the COVID-19 lockdown, which is associated with higher resistance levels than domestically acquired campylobacteriosis. Because data on travel history it not available, this cannot be confirmed.
In 2025, the resistance level for ciprofloxacin in human *Campylobacter* spp. isolates was 69.4%, which is a public health concern. This percentage was higher than in 2023 (61.3%) and 2024 (62.4%), and also higher compared with pre-pandemic years. Tetracycline resistance had a similar trend, with 52.5% resistance in 2025, compared with 47.0% in 2023 and 44.9% in 2024. In contrast to ciprofloxacin, it was still lower than pre-pandemic years. Erythromycin resistance was still low with 3.6% in 2025.

Table 6.2.1.3 shows the resistance levels for human *C. jejuni* and *C. coli* isolates since 2016, with higher resistance proportions for *C. coli* isolates than *C. jejuni* isolates. In 2022-2025, the resistance levels for *C. jejuni* and *C. coli* isolates were back or even above at pre-pandemic levels, except for tetracycline and erythromycin resistance in *C. jejuni*, which were still lower than before the pandemic.

Table 6.2.1.3 *Resistance in C. jejuni and C. coli isolated from humans from 2021 – 2025*

		2021		2022		2023		2024		2025	
		N	R%	N	R%	N	R%	N	R%	N	R%
Fluoro-quinolone	*C. jejuni*	2957	53.4	3648	60.9	4160	59.9	4536	60.9	4084	68.0
	C. coli	229	69.0	362	72.7	378	76.7	494	76.3	528	80.9
	Totaal	3186	54.5	4010	62.0	4538	61.3	5030	62.4	4612	69.4
Tetra-cycline	*C. jejuni*	2775	40.2	3405	45.4	3922	44.9	4340	42.2	3952	49.1
	C. coli	218	64.2	351	65.8	364	69.2	473	69.1	512	75.8
	Totaal	2993	42.0	3756	47.3	4286	47.0	4813	44.9	4464	52.2
Erythro-mycin	*C. jejuni*	3008	1.3	3695	2.6	4183	2.6	4532	1.9	4098	1.4
	C. coli	229	15.7	356	19.9	372	24.5	476	23.1	524	20.8
	Totaal	3237	2.3	4051	4.1	4555	4.3	5008	3.9	4622	3.6

Figure 6.2.1.3 *Trends in resistance (%) of Campylobacter jejuni and coli. isolated from humans between 2016 and 2025*



Conclusions

- In 2025, resistance levels to quinolones and tetracycline in *C. jejuni* isolates from caecal samples of broilers and meat remained at a high level.
- Resistance to erythromycin was not detected in *C. jejuni* isolates from broilers and poultry meat, but is was observed at low levels in *C. jejuni* from veal calves and in *C. coli* from broilers and poultry meat. As in former years, a notably higher level of erythromycin resistance was observed in *C. coli* from veal calves compared to the other animal sectors.
- The high level of ciprofloxacin resistance in human *Campylobacter* spp. continues to be a public health concern. In 2025, resistance levels increased further compared with previous years to nearly 70% of all isolates.
- Resistance to erythromycin, first choice antibiotic in human medicine for campylobacteriosis, remained low for *C. jejuni, which is responsible for most of human infections*.

References

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6.3 Shiga-toxin producing *E. coli* (STEC) and enteropathogenic *E. coli* (EPEC)

Introduction

Shiga-toxin producing *Escherichia coli* (STEC) is a bacterial zoonotic agent associated with human disease with varying clinical manifestations, including diarrhea, hemorrhagic colitis and hemolytic uremic syndrome (HUS), a leading cause of acute renal failure among children. The natural reservoir of STEC is the gastrointestinal tract of ruminants, especially cattle and small ruminants [1]. Although, therapeutic treatment of STEC infections with antimicrobials is not regularly advised, monitoring AMR in STEC from symptomatic human cases is useful in assessing the risk of transmission of resistant bacteria, and resistance genes, from ruminants to humans.

Methods

Isolates from human clinical cases (N=397) consisting of multiple STEC/aEPEC/tEPEC[1*] O157:H7 and non-O157:H7 serotypes, were analysed by Illumina whole-genome sequencing for the presence of antimicrobial resistance (AMR) markers. The set consisted of 73 STEC/EPEC O157:H7 isolates and 324 STEC/EPEC non-O157:H7 isolates. All isolates were obtained from the RIVM national laboratory surveillance of STEC.

Results

The most frequently occurring non-O157:H7 isolates consisted of: O26 (n=55), O103 (n=30), O146 (n=26), O145 (n=22), O63 (n=18), O128 (n=12), O71 (n=11), and other O-types (n=150).
Unlike previous NethMap STEC reports, only genotypic analyses of AMR-markers were performed this year. Therefore, direct comparisons between genotypic resistance markers detected in 2025 and phenotypic resistance results reported in previous years were not possible.

Table 6.3.1 shows the percentage of pathogenic *E. coli* isolates in which AMR markers were detected by WGS. Overall, AMR markers were more frequently detected among non-O157:H7 STEC/EPEC isolates than among O157:H7 isolates. Significant differences were observed for AMR-markers associated with ampicillin ($\chi 2$, $p=0.0427$), ciprofloxacin ($\chi 2$, $p=0.0327$), sulfamethoxazole ($\chi 2$, $p<0.0001$), and trimethoprim ($\chi 2$, $p=0.0018$) resistance as well as for multiple-class AMR marker carriage[2*]($\chi 2$, $p=0.0032$). In contrast, cefotaxime-associated resistance markers occurred at similar frequencies in both groups, while no meropenem resistance determinants were detected in either group.

Table 6.3.1 *Percentage of pathogenic E. coli isolates from humans in the Netherlands carrying antimicrobial resistance markers in 2025*

E. coli	**O157:H7**	**Other serotypes**
	N=73	**N=324**
Ampicillin	2.7	10.2
Cefotaxime	2.7	3.4
Ciprofloxacin	5.5	14.8
Gentamicin	0.0	2.2
Meropenem	0.0	0.0
Sulfamethoxazole	0.0	19.4
Trimethoprim	0.0	12.0
Multidrug resistence	2.7	15.7

Among the multiple-class AMR marker carriage non-O157:H7 isolates, the most frequently represented serotypes were O103:H2 (n=11) and O26:H11 (n=7).

Table 6.3.2 shows the distribution of individual genotypic resistance marker profiles. Based on these results, non-O157:H7 STEC/EPEC isolates showed a greater diversity of resistance markers than O157:H7 isolates. In O157:H7 isolates, the only detected resistance markers were the extended spectrum beta-lactamase gene *bla*$_{\text{CTX-M-15}}$, associated with resistance to ampicillin (2.7%) and cefotaxime (2.7%), and the fluoroquinolone-associated resistance genes *qnrB19* (2.7%) and *qnrS1* (2.7%).
Among non-O157:H7 isolates, the most frequently detected resistance markers or profiles included the sulfonamide resistance genes *sul2* (12.4%) and *sul1* + *sul2* (6.8%), the beta-lactamase gene *bla*$_{\text{TEM-1B}}$ (5.9%), the trimethoprim resistance gene *dfrA1* (4.9%), and the fluoroquinolone-associated markers *qnrS1* (3.7%) and *gyrA* p.S83L (3.1%).
In total, 2.7% of O157:H7 and 3.4% of non-O157:H7 isolates carried beta-lactamase genes associated with resistance to third-generation cephalosporins such as cefotaxime.
AMR markers were more frequently detected among non-O157:H7 STEC/EPEC isolates than among O157:H7 isolates, with significant differences for several antimicrobial classes. Greater marker diversity was also observed among non-O157:H7 isolates, although this likely partly reflects the greater serotype diversity of this group.

Markers associated with resistance to third-generation cephalosporins occurred at similarly low frequencies in both groups (2.7% in O157 and 3.4% in non-O157), while no meropenem resistance markers were detected. Among non-O157 isolates with genotypic resistance markers across multiple antimicrobial classes, O103 and O26 were most frequently represented.
As only genotypic resistance was assessed this year, direct comparison with phenotypic resistance data from previous NethMap One Health reports was not possible.

Table 6.3.2 *Percentage of antimicrobial resistance profiles of pathogenic E. coli isolates from humans in the Netherlands in 2025*

Antimicrobial: ampicillin	**O157:H7**	**Other serotypes**
Class: beta lactams	**N=73**	**N=324**
bla$_{\text{CTX-M-3}}$	0.0	0.31
bla$_{\text{CTX-M-15}}$	2.74	0.31
bla$_{\text{CTX-M-117}}$, *bla*$_{\text{CTX-M-15}}$	0.0	0.31
bla$_{\text{DHA-1}}$	0.0	0.31
bla$_{\text{DHA-1}}$, *bla*$_{\text{CTX-M-15}}$	0.0	0.31
bla$_{\text{TEM-1A}}$	0.0	0.62
bla$_{\text{TEM-1B}}$	0.0	5.86
bla$_{\text{TEM-1D}}$	0.0	0.31
bla$_{\text{TEM-1A}}$, *bla*$_{\text{CTX-M-15}}$	0.0	0.31
bla$_{\text{TEM-1A}}$, *bla*$_{\text{CTX-M-55}}$	0.0	0.31
bla$_{\text{TEM-1B}}$, *bla*$_{\text{CTX-M-15}}$	0.0	0.62
bla$_{\text{TEM-1C}}$, *bla*$_{\text{CTX-M-3}}$	0.0	0.62
Antimicrobial: cefotaxime	**O157:H7**	**Other serotypes**
Class: beta lactams	**N=73**	**N=324**
bla$_{\text{CTX-M-3}}$	0.0	0.93
bla$_{\text{CTX-M-15}}$	2.74	1.23
bla$_{\text{CTX-M-55}}$	0.0	0.31
bla$_{\text{CTX-M-117}}$, *bla*$_{\text{CTX-M-15}}$	0.0	0.31
bla$_{\text{DHA-1}}$	0.0	0.31
bla$_{\text{DHA-1}}$, *bla*$_{\text{CTX-M-15}}$	0.0	0.31
Antimicrobial: ciprofloxacin	**O157:H7**	**Other serotypes**
Class: fluoroquinolones	**N=73**	**N=324**
gyrA p.D87G	0.0	0.31
gyrA p.S83L	0.0	3.09
parC p.A56T	0.0	0.31
parC p.S57T	0.0	0.62
parE p.I355T	0.0	4.01
qnrB4	0.0	0.31
qnrB19	2.74	0.93
qnrS1	2.74	3.70
qnrS13	0.0	1.23
qnrB4, *qnrS1*	0.0	0.31

Table 6.3.2 (continued) *Percentage of antimicrobial resistance profiles of pathogenic E. coli isolates from humans in the Netherlands in 2025*

Antimicrobial: gentamicin	**O157:H7**	**Other serotypes**
Class: aminoglycoside	**N=73**	**N=324**
aac(3)-Iia	0.0	1.85
ant(2'')-Ia	0.0	0.31
Antimicrobial: meropenem	**O157:H7**	**Other serotypes**
Class: carbapenem	**N=73**	**N=324**
No resistance markers		
Antimicrobial: sulfamethoxazole	**O157:H7**	**Other serotypes**
Class: sulfonamides	**N=73**	**N=324**
sul1	0.0	0.31
sul2	0.0	12.35
sul1, *sul2*	0.0	6.79
Antimicrobial: trimethoprim	**O157:H7**	**Other serotypes**
Class: trimethoprim	**N=73**	**N=324**
dfrA1	0.0	4.94
dfrA5	0.0	0.93
dfrA7	0.0	1.23
dfrA14	0.0	2.47
dfrA17	0.0	0.62
dfrA36	0.0	1.23
dfrA1, *dfrA12*	0.0	0.31
dfrA1, *dfrA36*	0.0	0.31

Conclusions

- Genotypic AMR markers were more frequent and more diverse in non-O157:H7 STEC/EPEC isolates than in O157:H7 isolates.
- Significantly higher prevalences of genotypic AMR markers associated with resistance to ampicillin, ciprofloxacin, sulfamethoxazole, and trimethoprim, as well as markers associated with resistance to multiple antimicrobial classes, were found more frequently in non-O157:H7 isolates compared with O157:H7 isolates.
- Genotypic surveillance identified O103:H2 and O26:H11 as the most frequently represented serotypes among non-O157:H7 isolates carrying resistance-associated markers for multiple antimicrobial classes.
- Genotypic AMR markers associated with third-generation cephalosporins were uncommon and occurred at similar frequencies in both groups.

References

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6.4 Yersinia

Introduction

Human food-borne yersiniosis is primarily caused by the *Yersinia enterocolitica* species. *Y. enterocolitica* is a zoonotic Gram-negative bacterial pathogen that mostly infects humans through contaminated food. The majority of infections cause mild, self-limiting gastrointestinal disease with diarrhea that generally does not require treatment. Abdominal pain related to mesenteric lymphadenitis may occur, and may be mistaken for appendicitis. Bacteremia is rare, and mostly limited to young or immunocompromised children. Post-infectious sequelae such as reactive arthritis or erythema nodosum may occur, especially in older children and adults.

Pigs and rodents represent *Y. enterocolitica's* main natural reservoir, from where it spreads to humans via contaminated meat and/or environmental routes such as contact with soil or water. *Y. pseudotuberculosis* is a distinct *Yersinia* species that can be found in an array of mammals and birds, and is the second most commonly reported *Yersinia* species causing human infection. Clinical disease with acute pseudo-appendiceal pain is more common with *Y. pseudotuberculosis* than with *Y. enterocolitica*. Other zoonotic species such as *Y. frederiksenii*, *Y. intermedia* and *Y. kristensenii* may cause gastrointestinal disease in humans as well, but such infections are rare.

The evidence-base for appropriate antimicrobial treatment of human yersiniosis is limited.[1] However, in cases were antibiotics are considered necessary, ciprofloxacin and third-generation cephalosporins are recommended treatment options for infections with susceptible strains. Worldwide, beta-lactamase production among *Yersinia* species is common, resulting in wide-spread amoxicillin/ampicillin and first-generation cephalosporin resistance.[2]

Methods

Human yersiniosis data were extracted from the ISIS-AR-surveillance database. ISIS-AR's selection criteria are described in chapter 5.1.1.1, and include a selection of laboratories that provided complete data in the last five years. Antimicrobial resistance proportions of *Y. enterocolitica* were determined for amoxicillin/ampicillin, third-generation cephalosporins (ceftazidime and cefotaxime/ceftriaxone), cotrimoxazole, gentamicin, ciprofloxacin, and meropenem/imipenem. We do not present macrolide-resistance data as limited available data did not allow for reliable analysis.

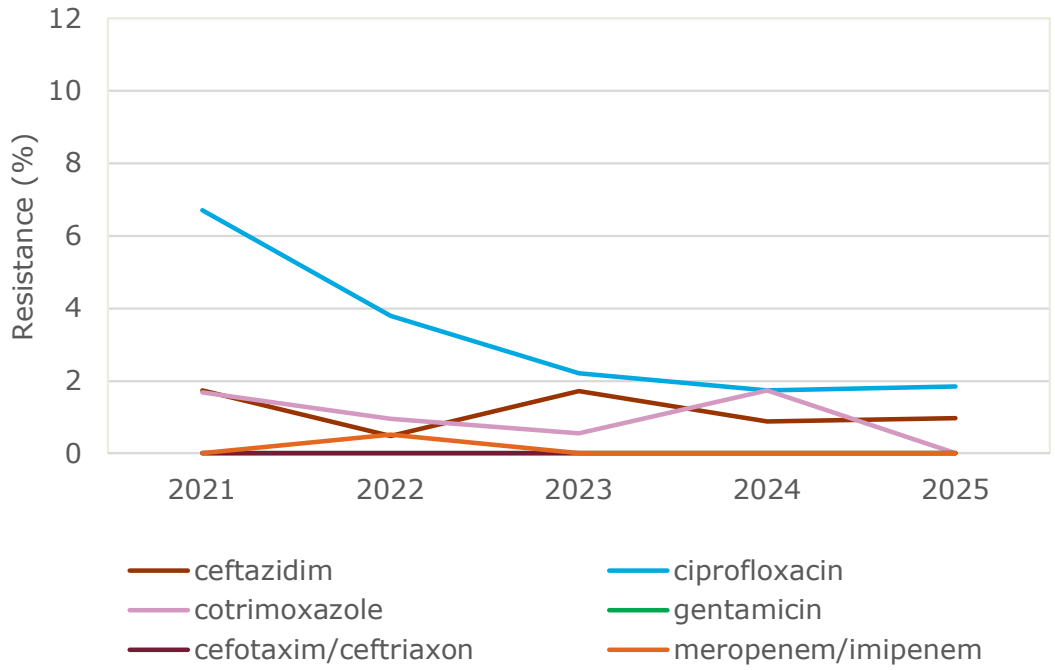
Results

In 2025, the majority of human yersiniosis cases were caused by *Y. enterocolitica* (90%), followed by *Y. pseudotuberculosis* (2%;see Table 6.4.1). Over the past five years, a decreasing trend was observed for ciprofloxacin resistance from 6.7% in 2021 to 1.9% in 2025, the origin of which is unclear. The proportions of resistance to third-generation cephalosporins, cotrimoxazole, and gentamicin for this species have remained stable at levels below 2% in the same period (Figure 6.4.1).

Table 6.4.1 *Number of tested human Yersinia isolates per species, based on ISIS-AR data*

	2021	2022	2023	2024	2025
	n=216	n=245	n=232	n=292	n=249
Yersinia enterocolitica	182	216	197	239	224
Yersinia pseudotuberculosis	11	3	12	7	5
Yersinia frederiksenii	8	11	10	13	3
Other *Yersinia* spp. and *Yersinia* not specified	15	15	13	33	17

Figure 6.4.1 *Trends in resistance (%) of human Y. enterocolitica isolates, 2021-2025*



Amoxicillin/ampicillin resistance levels are not shown, but have remained consistently high at approximately 98%.

Conclusions

- As expected, *Y. enterocolitica* was the most common *Yersinia* species (90%).
- Over the past five years, a decreasing trend was observed for ciprofloxacin resistance from 6.7% to 1.9%, the origins of which is unclear, while resistance to third-generation cephalosporins and cotrimoxazole has remained below 2%.

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7 Antimicrobial resistance in commensal bacteria from farm animals and food

This chapter describes the susceptibility profiles of commensal bacteria from the gastro-intestinal tract from farm animals and derived meat in accordance with EFSA guidelines[1] and European legislation[2]. The level of antimicrobial resistance (AMR) in bacteria inhabiting the intestinal tract directly reflects the selection pressure as a result of the use of antibiotics in animals, especially over time. In addition, the level of antibiotic resistance in commensal bacteria in food is monitored closer to the consumer to track the spread of resistant genes and bacteria through the food chain. *E. coli* is included as indicator organism for the Gram-negative bacterial population. After a discontinuation of seven years, enterococci were included in the AMR monitoring program again as representatives of the Gram-positive bacterial population. Reintroduction of Enterococcus to the program allows for better tracking of the prevalence and spread of AMR among Gram-positive bacteria. This report provides resistance data for enterococci in slaughter pigs. EFSA[1] prescribes the sampling strategy and isolation methodology of bacteria from caeca of randomly selected food-producing animals at slaughter with the aim to detect the occurrence and trends in resistance at the bacterial population level in food-producing animals. In the Netherlands, this monitoring is conducted in slaughter pigs and broilers since 1998. From 2005 onwards, resistance in isolates from both dairy cattle, veal calves and meat samples have been included. In the years 2010 and 2011, samples of individual dairy cattle were collected at slaughter houses; in all other years pooled or individual faecal samples were collected at dairy farms. Until 2012, pooled veal calf samples were collected at farms. Monitoring programs in veal calves at farms stopped in 2012. From then onwards, the monitoring program for veal calves was carried out similar as for pigs and poultry by collecting samples from caeca of individual veal calves at slaughterhouses, and resistance levels were reported separately for white and rosé veal calves.

7.1 General AMR surveillance

7.1.1 Escherichia coli from farm animals and food

Introduction

In this chapter, information is presented on resistance in *E. coli,* as indicator organism for the occurrence and trends in resistance in Gram-negative bacteria in the gastro-intestinal tract of food-producing animals and meat in the Netherlands.

The EU legislation on monitoring and reporting of antimicrobial resistance in zoonotic and commensal bacteria (2020/1729/EU) was implemented in 2021. Indicator commensal *E. coli* isolates obtained from samples of caecal content taken at slaughter, and from samples of fresh meat taken at the border control posts have to be gathered and examined.

Methods

Bacterial isolation of *E. coli* is performed on MacConkey agar plates, either by direct inoculation of the sample using a cotton swab (faecal samples) or after overnight incubation of a 10% suspension in Buffered Peptone Water (meat samples). Per sample one randomly picked colony is pure cultured and identified by MALDI-TOF mass spectrometry (MALDI Biotyper®, Bruker). In case of confirmed identification, one *E. coli* isolate is analysed per sample. This includes susceptibility testing by broth microdilution according to ISO 20776-1:2019 with mandatory panels of antimicrobials performed under ISO 17025 accreditation RvA TESTING L 389 and L 014. Test results are interpreted using epidemiological cut-off values (ECOFFs) published by the European Committee on Antimicrobial Susceptibility Testing (EUCAST).[3] In this chapter, non-wild type susceptible isolates (exhibiting MIC values above the ECOFF) are classified as resistant. These isolates likely harbour acquired resistance mechanism, although they may not be clinically resistant to certain antibiotics.

In 2025, trend-analysis was done for broilers, pigs, dairy, and veal calves (including white and rosé) to estimate the trends in resistance levels in the period since 2010 until now, as well as for the most recent five-year period (2021-2025). Statistical analysis was based on the methods described by Hesp et al. (2019), estimating the incidence rate ratio (IRR) based on the proportion of resistant isolates for every livestock species and antibiotic using a generalized linear model with a Poisson distribution. Analysis was performed in R software.

Results

Bacterial isolates

In 2025, randomly isolated *E. coli* obtained from caecal samples of broilers (n=308) , pigs (n=301), veal calves (n=329), faecal samples of dairy cattle (n=317) were tested for antimicrobial susceptibility. For the first time since 2011, faecal samples from turkeys (n=145) collected at farms were included, along with 588 *E. coli* isolates obtained from fresh meat including beef (retail n=177; import n=130), pork (retail n=159; import n=30), and lamb (retail n=92).

Resistance levels

Table 7.1.1.1 shows resistance levels, presented as MIC-distributions, of 1248 *E. coli* isolates obtained from caecal samples from broilers, pigs, and veal calves collected at slaughter and faecal samples of dairy cows collected at farms in 2025. Table 7.1.1.2 presents resistance percentages per animal species and includes resistance data of *E. coli* obtained from faecal samples of turkeys collected at farms. Trends in resistance levels from 1998 to 2025 are shown in figure 7.1.1.1 and information on trends in multidrug resistance in the different animals sectors is shown in figure 7.1.1.2.

Table 7.1.1.3 presents resistance percentages of 756 *E. coli* isolates collected from fresh beef and pork collected at retail and import as well as fresh lamb collected at retail in the Netherlands in 2025.

Table 7.1.1.1 *MIC distribution (in %) and resistance percentages (R%) for all E. coli (N=1248) isolated as indicator organism from intestines of food producing animals in the Netherlands in 2025*

E. coli	**MIC (%) distribution mg/L**																			
N = 1248	**0.015**	**0.03**	**0.06**	**0.125**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**1024**	**2048**	**R%**	**95% CI**
ampicillin							1.4	20.5	53.7	6.7	0.5		17.2						17.7	15.6 - 19.4
cefotaxime					99.7			0.2		0.1									0.3	0.1 - 0.8
ceftazidime					94.6	5.0		0.2			0.1								0.3	0.1 - 0.8
gentamicin						58.1	38.4	2.0	0.1		0.3	1.1							1.5	0.9 - 2.4
tetracycline								66.3	11.9	0.2	0.2	0.5	20.8						21.5	19.2 - 23.9
sulfamethoxazole										48.1	28.0	5.8	0.2				17.9		17.9	15.9 - 20.2
trimethoprim					33.2	43.8	7.7	0.4	0.0	0.0	0.1	14.8							14.9	13.0 - 17.0
ciprofloxacin	84.3	8.0	0.2	0.6	5.1	1.1	0.2	0.2	0.0	0.2	0.1								7.5	6.1 - 9.1
nalidixic acid									91.3	2.7	0.5	0.4	0.6	4.6					6.0	4.8 - 7.5
chloramphenicol										89.0	3.0	1.3	0.6	6.1					7.9	6.5 - 9.6
azithromycin*								5.4	46.8	44.0	3.0	0.2	0.2		0.5				0.8	0.4 - 1.5
colistin							99.0	1.0											0.0	0.0 - 0.3
meropenem		99.9	0.1																0.0	0.0 - 0.3
tigecycline					94.7	5.3													0.0	0.0 - 0.3
amikacine									96.1	3.9									0.0	0.0 - 0.3

The white areas indicate the dilution range tested for each antimicrobial agent. Values above this range indicate MIC values > the highest concentration in the range. Values at the lowest concentration tested indicate MIC-values ≤ the lowest concentration in the range. Vertical bars indicate the epidemiological cut-off values (ECOFF), used as breakpoints.
* tentative ECOFF set by EUCAST.

For most drugs or drug classes, resistance levels varied between the different animal sectors (Table 7.1.1.2). The highest resistance levels were observed in broilers, turkeys, slaughter pigs and white veal calves, lower levels in rosé veal calves, and the lowest levels of resistance were observed in isolates from dairy cattle. Overall, the highest resistance levels were detected for ampicillin, tetracycline, sulfamethoxazole and trimethoprim. These drug classes are the most frequently used classes in farm animals in the Netherlands. In addition, higher levels of resistance (>10%) were also observed for (fluoro)quinolones in broilers and turkeys, and for chloramphenicol in veal calves and pigs. The use of chloramphenicol has been banned for many years in the animal sector, but cross-resistance exists between chloramphenicol and florfenicol, which is registered for and used in farm animals. Low resistance (<5%) was noticed for azithromycin, cefotaxime, ceftazidime, gentamicin and tigecycline. Resistance to colistin, meropenem and amikacin was not detected.

Table 7.1.1.2 *Resistance percentages (R%) of E. coli isolated from faecal samples of broilers, pigs, veal calves (white and rosé), dairy cows and dairy goats in the Netherlands in 2025*

	Broilers	**Pigs**	**Veal calves**		**Dairy cows**	**Turkeys**
Faecal samples	**N = 308**	**N = 301**	**White, N = 200**	**Rosé, N = 125**	**N = 314**	**N = 145**
ampicillin	26.6	20.3	25.5	14.4	2.8	35.9
cefotaxime	1.0	0.3	0.0	0.0	0.0	0.7
ceftazidime	1.0	0.3	0.0	0.0	0.0	0.7
gentamicin	2.9	0.3	4.0	0.8	0.0	1.4
tetracycline	17.9	25.9	41.5	30.4	4.5	44.8
sulfamethoxazole	23.1	22.9	25.0	17.6	3.8	17.9
trimethoprim	14.0	23.3	24.0	11.2	3.4	13.8
ciprofloxacin	24.0	2.3	3.5	4.0	0.3	13.8
nalidixic acid	22.7	0.3	0.5	1.6	0.3	8.3
chloramphenicol	2.3	11.0	19.5	12.0	1.6	6.9
azithromycin	0.0	1.3	2.5	0.8	0.0	0.7
colistin	0.0	0.0	0.0	0.0	0.0	0.0
meropenem	0.0	0.0	0.0	0.0	0.0	0.0
tigecycline	0.0	0.0	0.0	0.0	0.0	0.7
amikacin	0.0	0.0	0.0	0.0	0.0	0.0

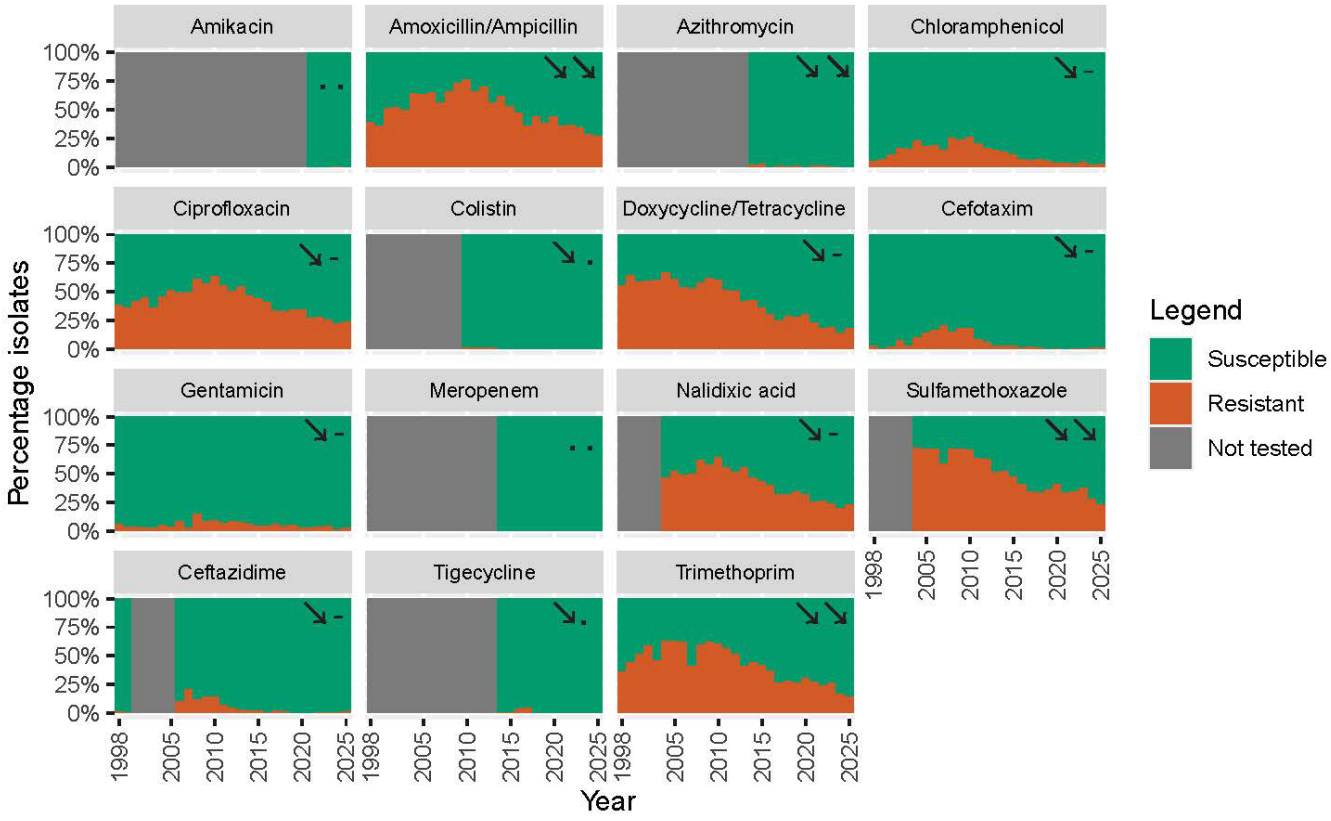
Fluoroquinolone resistance
Fluoroquinolones (FQ) resistance in *E. coli* from broilers remained the highest amongst the animal sectors included, with 24.0% ciprofloxacin resistance in 2025, followed by 13.8% FQ resistance in turkeys (Table 7.1.1.2). In *E. coli* isolated from other animal species FQ resistance was low: 3.5% in white veal calves, 4.0% in rosé veal calves, 2.3% in slaughter pigs, and 0.3% in dairy cattle. Resistance to fluoroquinolones in *E. coli* isolated from meat was tested in 2025 for beef and pork collected at retail and import, as well as for *E. coli* from lamb collected at retail (Table 7.1.1.3). FQ resistance levels were low in retail beef (2.8%) and pork (0.8%) and very low in imported beef (0.8%) and pork (0.1%) The highest FQ resistance (7.6%) was observed in *E. coli* from lamb meat.

Resistance against extended-spectrum cephalosporins (cefotaxime and ceftazidime)
Since 2019, the prevalence of resistance against extended-spectrum cephalosporins (ESC-R) in randomly selected indicator *E. coli* has declined over time and is now rarely observed in caecal and faecal samples from farm animals. In 2025, four ESC-R *E. coli* isolates were identified in caecal samples: three isolates originating from broiler chickens (1%) and one isolate (0.1%) from a slaughter pig showed resistance to cefotaxime. In addition, one ESC-R *E. coli* was identified in a faecal sample from a turkey farm (0.7%) (Table 7.1.1.2). Amongst the indicator *E. coli* obtained from meat samples, ESC-R *E. coli* were incidentally detected in retail meat, including beef (1.1% cefotaxime resistance) and lamb (2.2% cefotaxime resistance), but not in pork. No ESC-E. coli were identified amongst indicator *E. coli* from imported meat (beef and pork (Table 7.1.1.3).

Broiler chickens

Resistance proportions of commensal *E. coli* isolated obtained from caecal samples of broiler chickens stayed below 30% for all antibiotic classes for the second year in a row (Table 7.1.1.2). Resistance levels were similar compared to 2024, with the highest levels of resistance observed for ampicillin, (fluoro)quinolones (ciprofloxacin and nalidixic acid), sulfamethoxazole, trimethoprim and tetracycline (between 17.9 – 26.6%). Resistance to cefotaxime, ceftazidime and gentamicin was low (<5%), while resistance to amikacin, azithromycin, colistin, meropenem and tigecycline was not detected amongst indicator *E. coli*. Trend-analysis (based on linear regression) of resistance in *E. coli* over the period 2021-2025 showed decreasing patterns for amoxicillin/ampicillin, azithromycin, sulfamethoxazole and trimethoprim (Figure 7.1.1.1a).

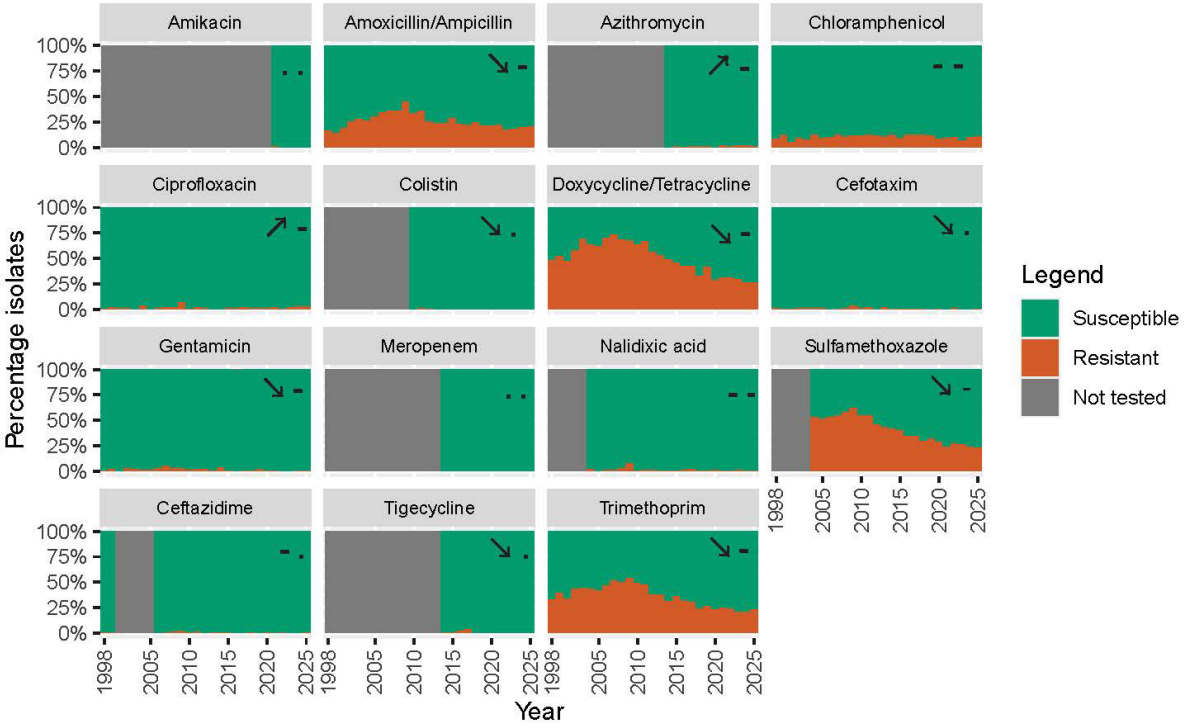
Figure 7.1.1.1a (broilers - caeca) *Percentage (%) of resistant indicator E. coli isolates against different antibiotics, isolated from faecal samples from broilers in the period 1998-2025 in the Netherlands*



The symbols indicate the trend in percentage of resistant isolates per antibiotic, the first symbol indicates the trend during the period 2010-2025, the second symbol indicates the trend during the last 5 years (2021-2025), with ↗ indicating an increasing trend in resistant isolates, ↘ indicating a decreasing trend in resistant isolates, - no trend. • means statistical trend analysis could not be performed, due to a lack of (resistant) isolates.

Slaughter pigs
Resistance levels stayed below 30% in slaughter pigs for all antibiotic classes for the third year in a row (Table 7.1.1.2). The overall resistance proportion stabilised in slaughter pigs with some fluctuation in resistance between the different antibiotic classes (Figure 7.1.1.1b). For ampicillin, sulfamethoxazole, tetracycline and trimethoprim resistance levels stabilised between 20% and 30%. Chloramphenicol resistance tend to increase to 11.0% compared to 9.9% in 2024 and 6.3% in 2023, although differences were not statistically tested. Low levels of resistance (<5%) were observed for azithromycin, cefotaxime and (fluoro)quinolones, whereas resistance to amikacin, colistin, gentamicin, meropenem and tigecycline was not detected. Based on linear regression analysis, the level of resistance of indicator *E. coli* from slaughter pigs stabilised in the last five years.

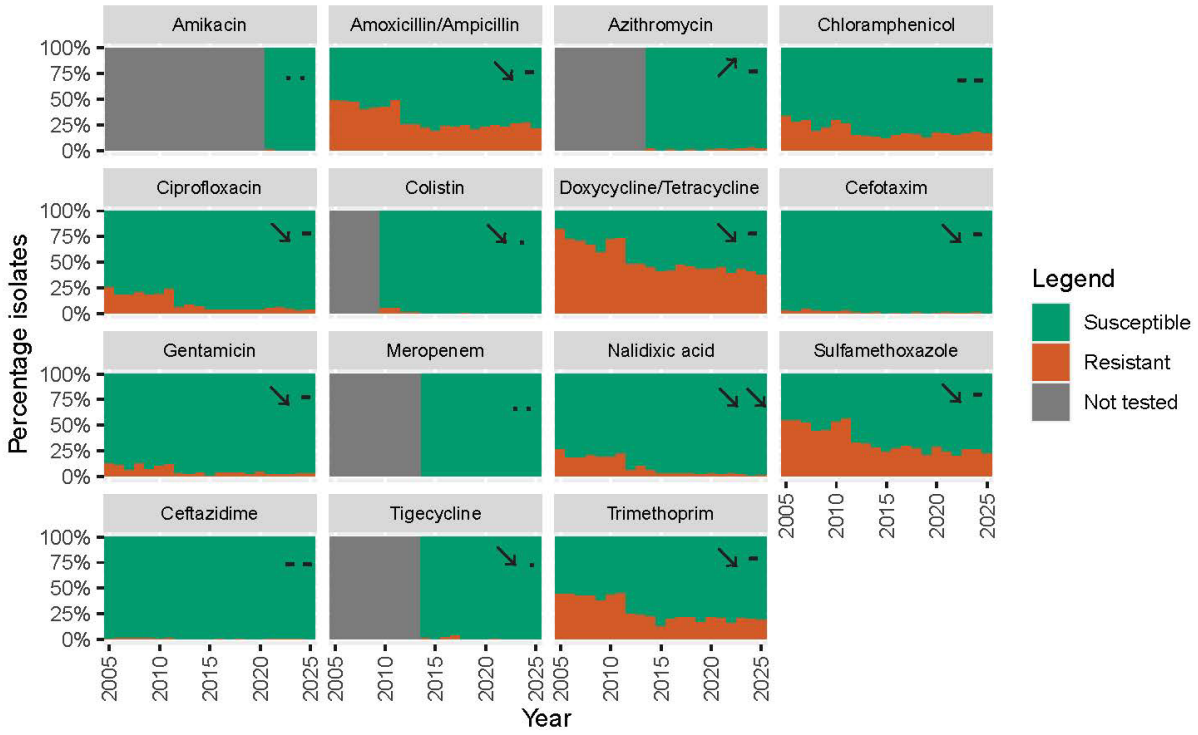
Figure 7.1.1.1b (pigs - caeca) *Percentage (%) of resistant indicator E. coli isolates against different antibiotics, isolated from faecal samples from pigs in the period 1998-2025 in the Netherlands*



The symbols indicate the trend in percentage of resistant isolates per antibiotic, the first symbol indicates the trend during the period 2010-2025, the second symbol indicates the trend during the last 5 years (2021-2025), with ↗ indicating an increasing trend in resistant isolates, ↘ indicating a decreasing trend in resistant isolates, - no trend. • means statistical trend analysis could not be performed, due to a lack of (resistant) isolates.

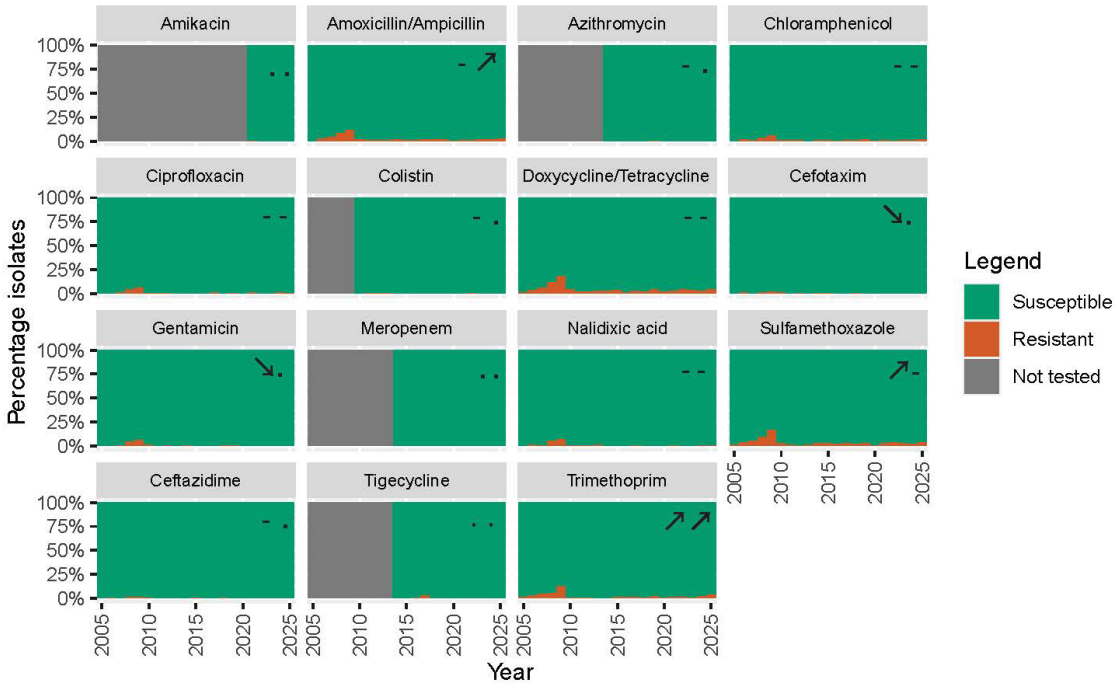
Veal calves
Resistance data for white and rosé veal calves are reported separately, due to the difference in production systems. As in previous years, higher resistance levels were measured in isolates from white, compared to those from rosé veal calves (Table 7.1.1.2). Figure 7.1.1.1c illustrates the trends in resistance in *E. coli* isolated from both types of veal calves combined. Resistance levels were relatively stable over time, with a clear decrease in 2012, which was the year in which the sampling strategy changed from sampling at farm at variable ages to sampling at slaughterhouse. This has influenced the results from 2012 onwards, because most antibiotic usage is in the younger calves and less in the period before slaughter. The ratio of sampled white veal calves versus rosé veal calves changed from 50/50% to 60/40% in 2016, and to 70/30% in 2017 onwards, which better reflects the proportions of slaughtered white and rosé calves in The Netherlands. After 2017, resistance levels in calves stabilized (Figure 7.1.1.1c), with large differences in resistance percentages between the two types of livestock farms. In 2025, although not statistically tested, differences in resistance amongst the two farming types decreased as a result of declining resistance in white calves to tetracycline (from 53.5% to 41.4%), sulfamethoxazole (from 34.1% to 25.0%), and trimethoprim (from 28.1% to 24.0%), while in rosé calves, resistance to tetracycline (from 18.8% to 30.4%) and trimethoprim (from 5.4% to 11.2%) increased remarkably, and to a lesser extent that to sulfamethoxazole (from 14.3% to 17.6%) (Table 7.1.1.2). Moreover, resistance to ampicillin in white calves has decreased compared to 2024 (from 34.1 to 25.5%). Resistance to azithromycin, gentamicin and fluoroquinolones was low (<5%) in the different types of veal calves. In addition, no resistance was observed for amikacin, colistin, meropenem and tigecycline. (Table 7.1.1.2). In the last five years, the resistance of indicator *E. coli* from veal calves stabilised (Figure 7.1.1.1c).

Figure 7.1.1.1c (veal calves - caeca) *Percentage (%) of resistant indicator E. coli isolates against different antibiotics, isolated from faecal samples from veal calves in the period 2005-2025 in the Netherlands*



The symbols indicate the trend in percentage of resistant isolates per antibiotic, the first symbol indicates the trend during the period 2010-2025, the second symbol indicates the trend during the last 5 years (2021-2025), with ↗ indicating an increasing trend in resistant isolates, ↘ indicating a decreasing trend in resistant isolates, - no trend. • means statistical trend analysis could not be performed, due to a lack of (resistant) isolates.

Figure 7.1.1.1d (dairy cows - faeces) *Percentage (%) of resistant indicator E. coli isolates against different antibiotics, isolated from faecal samples from dairy in the period 2005-2025 in the Netherlands*



The symbols indicate the trend in percentage of resistant isolates per antibiotic, the first symbol indicates the trend during the period 2010-2025, the second symbol indicates the trend during the last 5 years (2021-2025), with ↗ indicating an increasing trend in resistant isolates, ↘ indicating a decreasing trend in resistant isolates, - no trend. • means statistical trend analysis could not be performed, due to a lack of (resistant) isolates.

Dairy cattle

Resistance in *E. coli* isolated from dairy cattle was traditionally low compared to pigs, broilers and veal calves (Table 7.1.1.2), reflecting the low use of antibiotics in dairy farming. Notably, resistance to ampicillin, tetracycline, sulfamethoxazole and trimethoprim is still low (<5%) but increased to the highest levels since 2010. As in previous years resistance to the 3rd generation cephalosporins was not detected.

Turkeys

In 2025, indicator *E. coli*, obtained from faecal samples of turkeys, was analysed as part of a policy-supporting project that also analysed other animal sectors not included in the European antimicrobial resistance monitoring program. For this purpose 29 farms were sampled (5 samples per farm) resulting in 145 samples. Due to the dependence between the samples originating from a single farm the results must be interpreted with care. Compared to the other animal sectors included in the monitoring, resistance percentages were the highest for ampicillin (35.9%) and tetracycline (44.8%). In addition, FQ resistance was at the second highest level (13.8%) after broilers (24.0%). Furthermore, resistance percentages for chloramphenicol, sulfamethoxazole, trimethoprim were in the lower ranges with 6.6%, 17.9% and 13.8% respectively. Resistance to azithromycin, cefotaxime, gentamicin and tigecycline was rare (<1%) and no resistance was detected for colistin and meropenem.

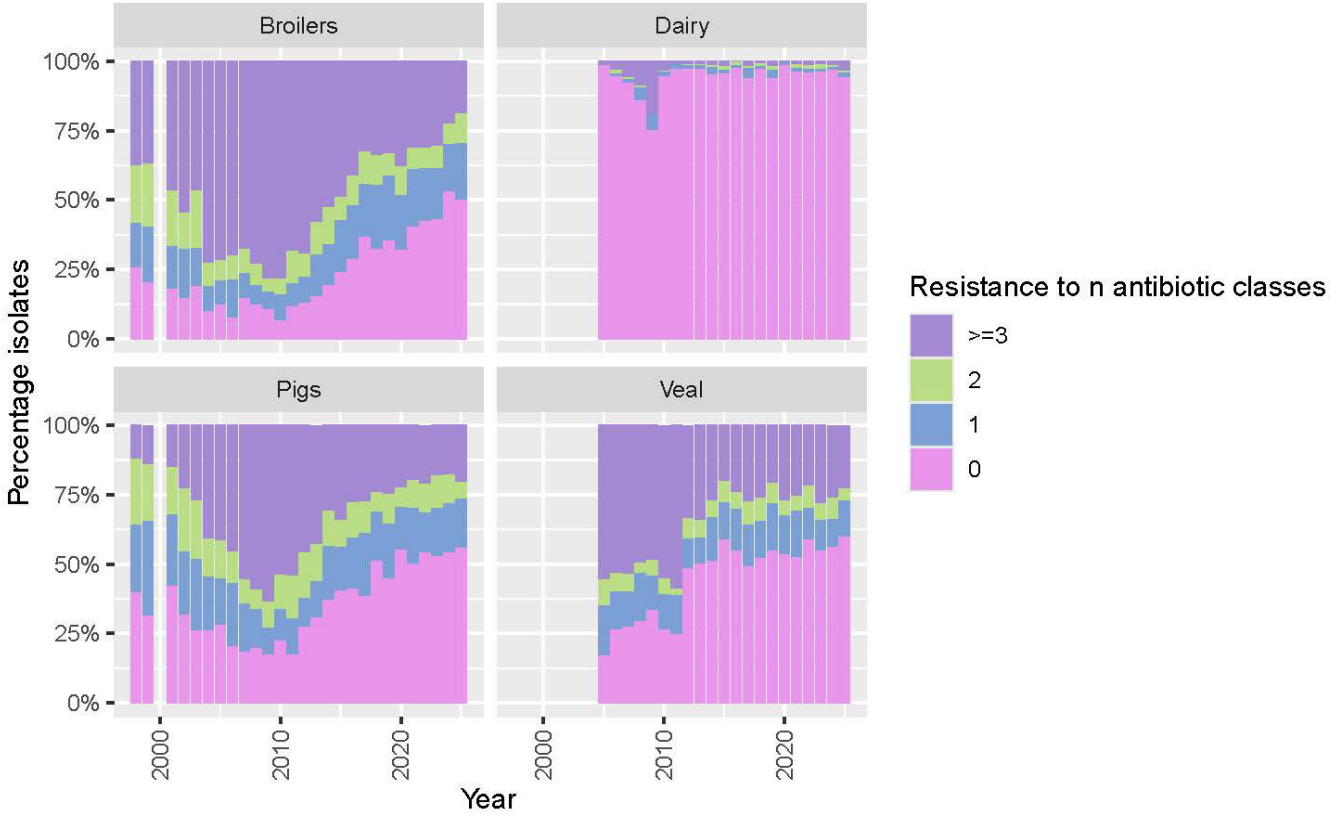
The comparison with the figures from 2011 (based on 100 faecal samples from 20 farms) reveals a significant decrease in resistance in this animal sector. In 2011 we observed 80.0% resistance to ampicillin and tetracycline; 66.3% to sulfamethoxazole; 43.2% to chloramphenicol and 31.6% to ciprofloxacin[4]. The current AMR data reflect the effect of the reduction of selective pressure due to the substantial decrease in antibiotic use in the turkey sector in this period[5].

Multidrug resistance
Multidrug resistance is defined as resistance to three or more of the following antimicrobial classes: aminopenicillins (ampicillin), 3rd gen. cephalosporins (cefotaxime), carbapenems (meropenem), aminoglycosides (gentamicin and amikacin), tetracyclines (tetracycline), tigecycline, sulfonamides (sulfamethoxazole), folate pathway inhibitors (trimethoprim), (fluoro)quinolones (ciprofloxacin), phenicols (chloramphenicol), macrolides (azithromycin), and polymyxins (colistin). The data on multidrug resistance over the years are shown in figure 7.1.1.2.

Following an increase in multidrug resistance observed until 2000–2012, the overall level of multidrug resistance has since decreased in *E. coli* isolates across all food animal sectors. In general, the level of multidrug resistance continuously decreased in *E. coli* from broiler chickens as well as in slaughter pigs. For broilers, a clear decline was observed in the period 2020-2025, from 38.1% in 2020 to approximately 31% in the years 2021-2023, followed by a further, sharp decline in 2024 to 22.6% and 19.8% in 2025. In pigs, an earlier decrease in the level of multidrug resistance was observed in the last decade (2014 – 2024) from 33.9% in 2014 to 17.9% in 2024. The level of multidrug resistance stabilised in slaughter pigs to 17.6% in 2025. In veal calves, the level of multidrug resistance has fluctuated in the last decade, ranging between 20.7% to 28.1%. In 2025, the level of multidrug resistance was recorded at 26.5%, remaining within this range. The percentage of multidrug resistance in *E. coli* from dairy cattle was low at 3.5% but this value doubled compared to 2024 (1.7%) and was the highest level measured since 2010. Future monitoring results will help determine whether this increase is transient or indicative of a longer-term trend.

In contrast to the decreasing trend observed in multidrug resistance in most farm animal species, the percentage of fully susceptible *E. coli* from various animal species was lower in 2025 compared to 2024. The decline in the percentage of pan-susceptible isolates was most evident in dairy cattle (from 96.6% in 2024 to 73.6% in 2025) and in broilers (from 53.2% in 2024 to 40.9% in 2025). The percentage of pan-susceptible isolates in slaughter pigs (52.8%) and veal calves (49.2%) also slightly declined compared to 2024. Future findings will help determine whether these changes reflect annual variation or an emerging trend.

Figure 7.1.1.2 *Percentage (%) of indicator E. coli isolates, isolated from faecal samples from broilers and pigs (1998-2025), dairy and veal calves (2005-2025), in the Netherlands, being resistant to none (0), 1, 2 or 3 or more antibiotic (AB) classes*



Isolates resistant to 0 antibiotic classes are classified as fully susceptible isolates, isolates resistant to 3 or more antibiotic classes are classified as multi-resistant isolates.

E. coli from meat

Table 7.1.1.3 presents resistance percentages of *E. coli* isolated from fresh meat (beef, pork and lamb) sampled at retail as well as from imported meat (beef and pork) sampled at border control posts by the Dutch Food and Consumer Product Safety Authority (NVWA). Fresh retail meat comprises meat produced in the Netherlands, but also in other EU countries. Imported meat originates from outside EU. This includes the UK and countries outside Europe.

Overall, levels of resistance in *E. coli* from retail beef was low ranging, from 0 – 7.9% across the different antimicrobials tested. Notably, resistance in *E. coli* from imported beef was even lower. No resistance to ceftazidime, colistin, meropenem or tigecycline was detected in both retail and imported beef, while resistance to ampicillin, cefotaxime, chloramphenicol, and azithromycin was also absent in imported beef. For retail pork, *E. coli* resistance levels were higher than in retail beef for almost all antibiotic classes. The highest levels of resistance were observed in ampicillin, tetracycline, sulfamethoxazole and trimethoprim ranging from 12.6% to 14.5%. Similar to beef, resistance was lower in *E. coli* from imported pork for most antibiotics, but the small number of isolates (n=30) precludes drawing conclusions regarding the difference between retail pork and imported pork.

For *E. coli* derived from lamb (in retail), resistance levels were slightly higher than in 2024, but resistance remained below 10% for all antibiotic classes, except tetracycline (13%).

Table 7.1.1.3 *Resistance percentages (R%) of E. coli isolated from raw meat in the Netherlands in 2025*

	Beef	Beef	Pork	Pork	Lamb
	Fresh, retail	Fresh, import	Fresh, retail	Fresh, import	Fresh, retail
Products	**N = 177**	**N = 130**	**N = 159**	**N = 30**	**N = 145**
Ampicillin	5.6	0.0	12.6	3.3	7.6
Cefotaxime	0.6	0.0	0.0	3.3	1.1
Ceftazidime	0.0	0.0	0.6	0.0	0.0
Gentamicin	1.1	0.8	2.5	3.3	4.3
Tetracycline	7.9	5.4	14.5	10.0	13.0
Sulfamethoxazole	5.6	2.3	14.5	3.3	9.8
Trimethoprim	4.0	0.8	13.2	3.3	7.6
Ciprofloxacin	2.3	0.8	5.0	10.0	6.5
Nalidixic acid	2.8	0.8	3.8	6.7	5.4
Chloramphenicol	1.7	0.0	4.4	3.3	6.5
Azithromycin	0.0	0.0	0.6	0.0	1.1
Colistin	0.0	0.0	0.0	0.0	0.0
Meropenem	0.0	0.0	0.0	0.0	0.0
Tigecycline	0.0	0.0	0.0	0.0	0.0
Amikacin	1.1	0.8	0.6	6.7	0.0

7.1.2 Enterococci from farm animals

Introduction
According to the European legislation[2] antibiotic resistance monitoring of enterococci includes *Enterococcus faecium* (*E. faecium*) and *Enterococcus faecalis* (*E. faecalis*) as indicator bacteria for resistance in Gram-positive bacteria. Enterococci are a non-mandatory part of the monitoring program. In 2025, enterococci from caecal samples of slaughter pigs were analysed.

Methods
Enterococci are isolated from caecal material by bacterial culturing on Slanetz and Bartley agar plates. Presumptive colonies are pure cultured and identification is performed by MALDI-TOF mass spectrometry (MALDI Biotyper®, Bruker). In case of confirmed identification, one *E. faecium* and one *E. faecalis* is analysed. Susceptibility testing is performed by broth microdilution according to ISO 20776-1:2019 under ISO 17025 accreditation RvA TESTING L 389 in a standard antimicrobial panel designed for testing enterococci. The panel contains twelve different antibiotics representing most antibiotic classes relevant for treatment of human infections caused by Gram-positive bacteria. Test results are interpreted using epidemiological cut-off values (ECOFFs) published by the European Committee on Antimicrobial Susceptibility Testing (EUCAST).[3] In this chapter non-wild type susceptible isolates are classified as resistant. These isolates probably contain acquired resistance mechanism, but may not necessarily be clinically resistant to certain antibiotics.

Results
Bacterial isolates
In 2025, 150 *E. faecium* and 53 *E. faecalis* isolates were isolated from 301 samples of caecal material from slaughter pigs and tested for antimicrobial susceptibility by broth microdilution.

Resistance levels
Table 7.1.2.1 presents resistance percentages of *E. faecium* and *E. faecalis* isolates obtained from slaughter pigs. In *E. faecium*, resistance levels were relatively high for Synercid (quinopristin/dalfopristin; 60.0%) and tetracycline (39.3%), whereas resistance to ampicillin (18.7%), erythromycin (13.3%) and chloramphenicol (2.7%) was less frequently found. In *E. faecalis*, resistance levels were substantially higher for tetracycline (60.4%), erythromycin (32.1%) and chloramphenicol (15.1%), with complete absence of resistance to ampicillin and Synercid. Resistance to linezolid and tigecycline was present at low levels (<4%) in both *E. faecium* and *E. faecalis*. Importantly, resistance to antibiotics of critical or high importance to human health (ciprofloxacin, daptomycin, gentamicin, teicoplanin, and vancomycin) according to the List of Medically Important Antimicrobials of the WHO[6] was very low (<1%) or not detected in both bacterial species.

Table 7.1.2.1 *Resistance percentages (%) of Enterococcus faecalis and E. faecium isolated from slaughter pigs in the Netherlands in 2025*

Slaughter pigs	***E. faecium***	***E. faecalis***
2025	**N=150**	**N=53**
Ampicillin	18.7	0.0
Chloramphenicol	2.7	15.1
Ciprofloxacin	0.7	0.0
Daptomycin	0.0	0.0
Erythromycin	13.3	32.1
Gentamicin	0.0	0.0
Linezolid	2.0	3.8
Synercid	60.0	0.0
Teicoplanin	0.0	0.0
Tetracycline	39.3	60.4
Tigecycline	1.3	1.9
Vancomycin	0.0	0.0

Conclusions

- Over the period 2021-2025, levels of resistance in *E. coli* stabilised in broilers, pigs and veal calves for most antibiotics.
- In 2025, a slight increase in resistance in *E. coli* from dairy resulted in a notable decline in the proportion of pan susceptible isolates from 96.6% in 2024 to 73.6% in 2025.
- As in previous years, in 2025, resistance to ampicillin, chloramphenicol, tetracycline, sulfamethoxazole and trimethoprim was commonly observed (>10%) amongst indicator *E. coli* in broilers (except for chloramphenicol), pigs, and veal calves
- Also in 2025, the highest FQ resistance levels were found in *E. coli* from broiler chickens with 24.0%, followed by 13.8% in turkeys. This in contrast with the low prevalence (<5%) in pigs, veal calves, and dairy cattle.
- Resistance to third generation cephalosporins was low (≤1%) or not detected amongst (randomly isolated) indicator *E. coli* from caecal or faecal samples of farm animals.
- For most antibiotics tested, levels of resistance in *E. coli* from caecal samples of rosé veal calves were lower than those from white veal calves. However, the difference in resistance levels between the two types of farms has decreased.
- In turkeys, resistance levels of indicator *E. coli* from faecal samples substantially decreased compared to 2011, probably reflecting the effect of the considerable reduction in use of antibiotics in this sector.
- *E. coli* isolates from retail beef and pork showed low levels of resistance with even lower levels in *E. coli* from imported beef and pork.
- For *E. coli* obtained from lamb (at retail), resistance levels were slightly higher than in 2024, but remained (< 10%) for all antibiotic classes, except for tetracycline (13%).
- In enterococci (*E. faecium* and *E. faecalis*) derived from caecal samples of slaughtered pigs, resistance to erythromycin and

tetracycline was frequently found in *E. faecium*, but the highest levels were observed in *E. faecalis*. Resistance to ampicillin was only detected in *E. faecium*. Resistance to ciprofloxacin, daptomycin, gentamicin, linezolid, tigecycline, teicoplanin, and vancomycin was absent or present at low levels (<4%).

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7.2 Specific AMR surveillance

7.2.1 Extended-spectrum cephalosporins resistant Enterobacterales in farm animals and food

Third and fourth generation cephalosporins, collectively referred to here as extended-spectrum cephalosporins (ESC), are considered one of the highest priority critically important antimicrobials in human medicine, and resistance can occur through several mechanisms[1]. Two of these mechanisms, Extended-spectrum beta-lactamases (ESBLs) and AmpC production, can occur on encoded on plasmids and be exchanged between various species of the Enterobacterales family, including *Escherichia coli*, *Salmonella enterica* and *Enterobacter cloacae*. These isolates are described in this chapter as ESBL/pAmpC producers. In *E. coli*, a third mechanism for resistance to ESC is the upregulation of the chromosomally located AmpC, a gene present in all *E. coli* that does not confer resistance in its wildtype form. These isolates are described here as AmpC promotor mutants.

This section describes the results of the characterisation of non-selective isolated ESC-resistant indicator *E. coli* and selective isolated ESC-resistant *E. coli* in farm animals and food, as well as of ESC-resistant Salmonella. All ESC-resistant *E. coli* and *Salmonella* from farm animals and food are analysed by whole genome sequencing (WGS) since the EU legislation (2020/1729/EU) was implemented in 2021.

7.2.1.1 Indicator ESC-resistant *E. coli* from farm animals and food products

Introduction

Random (non-selective) isolation of indicator *E. coli* from caecal samples of broilers, slaughter pigs, veal calves and dairy cows and food products is described in chapter 7.1.1. The prevalence of ESC-resistance in these *E. coli* provides data on the prevalence of the total population of *E. coli* that are present in the livestock sector and food in the Netherlands. The phenotype of these bacteria was determined by measuring the minimum inhibitory concentration (MIC) and comparing these to the epidemiological cut-off values described by EUCAST.

Methods

E. coli are considered suspected ESBL/pAmpC producers or AmpC promotor mutants when a reduced susceptibility of the isolate is measured against the ESC cefotaxime and/or ceftazidime. After confirmation of the phenotype, WGS is performed using the Illumina Nextera sequence technology. A standardised analysis pipeline was used to assess quality control and perform assembly of the WGS data[2]. Analysis of the resistance mechanisms was determined using Resfinder 4.5 including Pointfinder[3].

Results

The screening of indicator E. coli for ESC-resistant isolates has been performed since 1998, see figure Table 7.2.1.1.1. Between 2000 and 2009, the prevalence increased considerably, especially in broilers, but since the reduction of antimicrobial usage in farm animals, the prevalence has decreased. While no ESC-resistant isolates were found in

any livestock sector in 2019, approximately 2-5 isolates have been found annually since then. In 2025, four isolates were found to carry an ESBL gene or show no confirmed resistance mechanism: one isolate from broilers contained the CTX-M-1 gene, one isolate from broilers contained the TEM-52 gene, one isolate from broilers with no known genotype (WGS) for ESBL phenotype, and one isolate from turkey contained the CTX-M-15 gene (Table 7.2.1.1.1). As in the previous two years, no chromosomal AmpC promoter mutations were detected among the 2025 isolates.

In food products, no poultry meat was included among the categories tested for indicator ESC-resistant E. coli screening in 2025. Among the categories that were tested, ESC-resistant E. coli were detected in fresh retail lamb meat (3 of 111 batches, 2.7%) and in imported frozen pork (1 of 35 batches, 2.9%); no ESC-resistant isolates were detected in domestic or imported beef, or in domestic fresh pork.

Figure 7.2.1.1.1 *Trends in ESC resistance (%) of indicator E. coli isolated from faecal samples of broilers, slaughter pigs, veal calves and dairy cows*

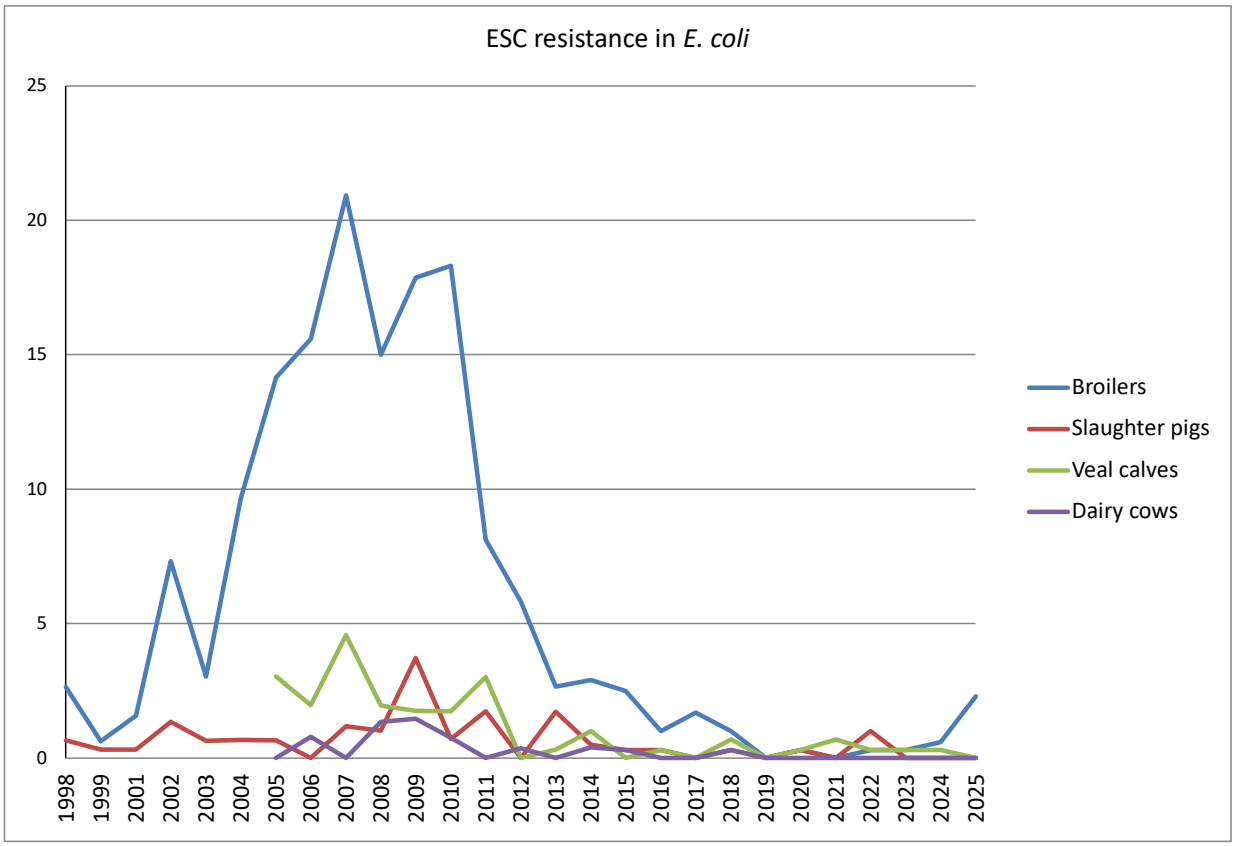


Table 7.2.1.1.1 *ESBL/pAmpC-genes and chromosomal AmpC mutations found in E. coli isolates with reduced susceptibility to ESC derived from broilers, veal calves, slaughter pigs, dairy cows and turkey (only 2011, 2012 and 2025) during 2007-2025*

	ESC-resistant *E. coli* isolated from						Beta-lactamase genes										
Year	**Broilers[c]**	**Veal calves**	**Slaughter pigs**	**Dairy cows[d]**	**Turkeys**	**Total ESBL suspected (n)**	**CTX-M-1-group[a]**	**CTX-M-2**	**CTX-M-9-group**	**TEM-52**	**TEM-20**	**SHV-12[b]**	**SHV-2**	**CMY-2**	**chromosomal *ampC***	**no gene found**	**Total *E. coli* (n)**	**% ESBL of total *E. coli***
2007	9	6	2	0	*n.t.*	**17**	3	1		3				1	2	7	539	**3,2**
2008	66	4	3	2	*n.t.*	**75**	38	5	1	9			2	12	3	5	1026	**7,3**
2009	53	2	11	2	*n.t.*	**68**	34	7		2	1	8	1	12	3		894	**7,6**
2010	52	3	2	2	*n.t.*	**59**	21	6		5	1	9	4	5	3	5	1002	**5,9**
2011	23	5	5	0	6	**39**	9			8		9	2	3	3	5	1096	**3,6**
2012	26	2	0	1	0	**29**	8			4		8		5		4	1328	**2,2**
2013	13	1	4	0	*n.t.*	**18**	7			4		3		3	1		1371	**1,3**
2014	11	3	2	0	*n.t.*	**16**	8			1		4			1	2	1519	**1,1**
2015	10	0	1	1	*n.t.*	**12**	3		2	1		1		2	3		1283	**0,9**
2016	3	1	1	0	*n.t.*	**5**	2			1				1	1		1492	**0,3**

[a] All were *bla*$_{\text{CTX-M-1}}$, only in 2011 one *bla*$_{\text{CTX-M-3}}$ gene was found in an isolate from a veal calf.

[b] One combination of *bla*$_{\text{SHV-12}}$ together with *bla*$_{\text{TEM-52}}$ occurred in 2012 in one broiler isolate.

[c] In broilers, three combinations were found: in 2008: *bla*$_{\text{CTX-M-1}}$ with *bla*$_{\text{CTX-M-2}}$; in 2009: *bla*$_{\text{CTX-M-1}}$ with *bla*$_{\text{SHV-12}}$ and *bla*$_{\text{CTX-M-1}}$ with *bla*$_{\text{SHV-12}}$ and *bla*$_{\text{CMY-2}}$.

[d] In dairy cows, one combination of *bla*$_{\text{CMY-42}}$ with *bla*$_{\text{TEM-190}}$.

n.t. : not tested.

Table 7.2.1.1.1 (continued) *ESBL/pAmpC-genes and chromosomal AmpC mutations found in E. coli isolates with reduced susceptibility to ESC derived from broilers, veal calves, slaughter pigs, dairy cows and turkey (only 2011, 2012 and 2025) during 2007-2025*

	ESC-resistant *E. coli* isolated from						Beta-lactamase genes											
Year	**Broilers[c]**	**Veal calves**	**Slaughter pigs**	**Dairy cows[d]**	**Turkeys**	**Total ESBL suspected (n)**	**CTX-M-1-group[a]**	**CTX-M-2**	**CTX-M-9-group**	**TEM-52**	**TEM-20**	**SHV-12[b]**	**SHV-2**	**CMY-2**	**chromosomal *ampC***	**no gene found**	**Total *E. coli* (n)**	**% ESBL of total *E. coli***
2017	5	0	0	0	*n.t.*	**5**	2			1			2				1194	**0,4**
2018	3	2	0	0	*n.t.*	**5**	2					3			2		1198	**0,4**
2019	0	0	0	0	*n.t.*	**0**											1209	**0,0**
2020	1	1	1	0	*n.t.*	**3**	1						1			1	1103	**0,3**
2021	0	2	0	0	*n.t.*	**2**	1									1	1206	**0,2**
2022	1	1	3	0	*n.t.*	**5**	1			1					2	1	1276	**0,4**
2023	1	1	0	0	*n.t.*	**2**	2										1185	**0,2**
2024	2	1	0	0	*n.t.*	**3**	1					2					1196	**0,3**
2025	3	0	0	0	*1*	**4**	2			1						1	522	**0,8**
Total	282	35	35	8	7	**367**	145	19	3	41	2	47	12	44	24	32	21639	**1,7**

[a] All were *bla*$_{\text{CTX-M-1}}$, only in 2011 one *bla*$_{\text{CTX-M-3}}$ gene was found in an isolate from a veal calf.

[b] One combination of *bla*$_{\text{SHV-12}}$ together with *bla*$_{\text{TEM-52}}$ occurred in 2012 in one broiler isolate.

[c] In broilers, three combinations were found: in 2008: *bla*$_{\text{CTX-M-1}}$ with *bla*$_{\text{CTX-M-2}}$; in 2009: *bla*$_{\text{CTX-M-1}}$ with *bla*$_{\text{SHV-12}}$ and *bla*$_{\text{CTX-M-1}}$ with *bla*$_{\text{SHV-12}}$ and *bla*$_{\text{CMY-2}}$.

[d] In dairy cows, one combination of *bla*$_{\text{CMY-42}}$ with *bla*$_{\text{TEM-190}}$.

n.t. : not tested.

7.2.1.2 Selectively isolated ESC-resistant *E. coli* from farm animals and food products

Introduction
The ESC-resistant indicator *E. coli* described in chapter 7.2.1.1 provide insight into the total prevalence of ESC-resistance in the farm animal population. The selectively isolated *E. coli* described here provide insight of the prevalence at the level of individual animals. Selection is performed according to protocols provided by the European Reference Laboratory for Antimicrobial Resistance. Isolation from faeces and caecal content occurs by incubating 1 gram of material in 9 ml of buffered peptone water overnight at 37 °C. While samples from pigs, veal calves and dairy cows represent individual animals per flock, for broiler chickens the caecal contents of 10 animals from a single flock are pooled since 2022 due to a change in EU legislation (2020/1729/EU). Selective isolation is performed on MacConkey agar plates supplemented with 1 mg/L of cefotaxime according to the EURL AR, Laboratory Protocol; Isolation of ESBL, AmpC and carbapenemase-producing *E. coli* from caecal samples.[4]

Methods
The isolation from food products is performed by adding 25 grams of product to 225 ml of buffered peptone water and incubating overnight at 37 °C. Selective screening is performed on plates of MacConkey agar plates supplemented with 1 mg/L of cefotaxime according to the EURL AR, Laboratory Protocol; Isolation of ESBL, AmpC and carbapenemase-producing *E. coli* from meat samples.[4]

Presumptive resistant *E. coli* colonies are subcultured and species identification is performed using MALDI-TOF (Bruker Biotyper). The MIC of isolates is determined as described in chapter 7.1.1 using a panel of antibiotics specifically aimed at beta-lactamase producing Enterobacteriaceae, EUVSEC-2. The genotype of all ESC-resistant *E. coli* was confirmed using WGS, as described in chapter 7.2.1.1.

Results
The results of the selective isolation in 2025 of ESC-resistant *E. coli* from farm animals are described in table 7.2.1.2.1. Both the number of suspected ESC-resistant isolates is included, as well as the number of isolates for which the genotype could be confirmed via WGS. In figure 7.2.1.2.1 the prevalence of the confirmed ESC-resistant *E. coli* from farm animals are compared between the livestock sectors over time, now extended through 2025. The genes responsible for the ESC-resistant phenotype based on WGS are summarized per livestock sector in table 7.2.1.2.2.

The prevalence of ESC-resistant *E. coli* decreased in **broilers** from 14.6% in 2024 to 10.4% in 2025 (32/308). All resistant isolates carried a transferable ESBL or plasmid AmpC gene; unlike previous years, no chromosomal *ampC* promotor mutants were detected. CTX-M-1 remained the most frequently detected gene (40.6% of resistant isolates), followed by SHV-12 (21.9%), CTX-M-55 (12.5%) and CTX-M-65 (9.4%). The plasmid-encoded AmpC gene CMY-2 was detected in 2 isolates (6.3%).

As in previous years, chromosomal mutations in the promoter region of the AmpC gene remained the most frequently detected resistance mechanism in **pigs**, accounting for 60.0% of resistant isolates (18/30). The overall prevalence of ESC-resistant *E. coli* decreased slightly to 10.0% of samples (30/301) from 13.6% in 2024. CTX-M-1 was the predominant ESBL variant, detected in 30.0% of resistant isolates (9/30, including 1 isolate in which the promotor mutation and $bla_{\text{CTX-M-1}}$ co-occurred).

In **veal calves**, the prevalence of ESC-resistant *E. coli* remained highest among all farm animal sectors and continued to differ markedly between the two sub-populations: 39.9% in white veal calves (81/203) and 24.6% in rosé veal calves (30/125), in line with the 44.6% and 21.9% recorded in 2024. CTX-M-15 and CTX-M-32 were the most prevalent ESBL variants in white veal calves (34.8% and 26.8% of white calves' resistant isolates respectively); the continued high proportion of CTX-M-32 is consistent with the expansion of this lineage in veal calves reported in previous years.

The prevalence of ESC-resistant *E. coli* in **dairy cows** decreased to 18.3% of samples (58/317) in 2025, from 22.9% in 2024. As in recent years, CTX-M-15 was by far the dominant gene, detected in 69.0% of resistant isolates (40/58), consistent with the shift towards CTX-M-15 dominance reported in this sector over the past decade[5].

In 2025, **turkey** farms were sampled for the first time since 2011 as part of a policy supporting project (see paragraph 7.1.1). ESC-resistant *E. coli* were detected in 6.9% of samples (10/145), all of which carried CTX-M-15. The prevalence of ESC-resistant *E. coli* in faecal samples of turkey is similar to 2011 with 6.3% (MARAN 2012).

Figure 7.2.1.2.1 *Trends in prevalence of confirmed ESBL/pAmpC-producing E. coli and chromosomal AmpC-mutant E. coli in faecal samples of broilers, pigs, white and rosé veal calves and dairy cows from 2014-2025 determined by using selective isolation*

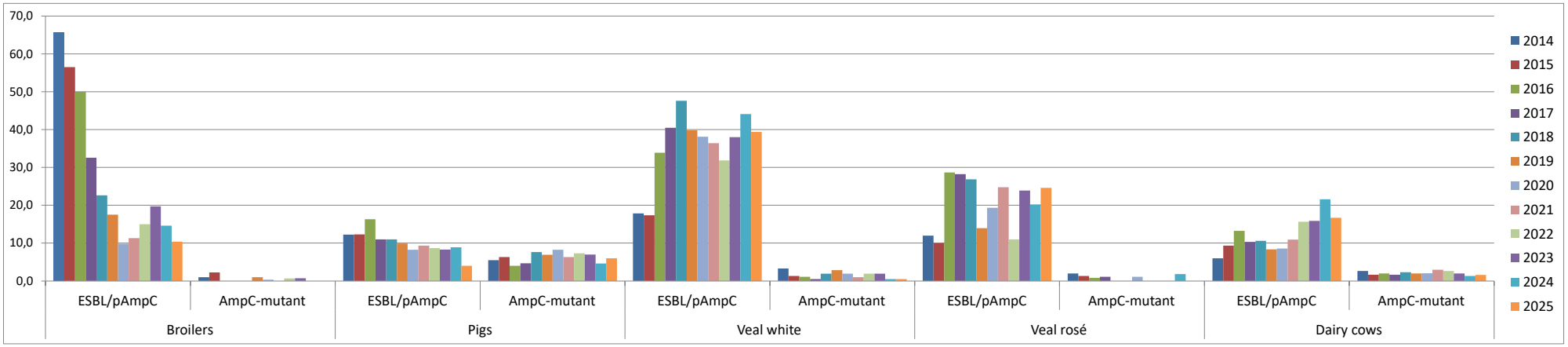


Table 7.2.1.2.1 *Proportion of E. coli isolates showing resistance to ESC derived from selective culturing of faecal samples from broilers, slaughter pigs, veal calves, dairy cows and turkey collected in 2025*

	N samples	N ESC-resistant *E. coli*	% ESC-resistant *E. coli*	N ESBL/ pAmpC carrying *E. coli*	% ESBL/ pAmpC carrying *E. coli*	N AmpC promotor mutants	% AmpC promotor mutants
Broilers	308	32	10,4	32	10,4	0	0
Pigs	301	30	10	12	4	18	6
Veal calves white	203	81	39,9	80	39,4	1	0,5
Veal calves rosé	126	31	24,6	31	24,6	0	0
Dairy cows	317	58	18,3	53	16,7	5	1,6
Turkey	145	10	6,9	10	6,9	0	0
Total	1400	242	17,3	218	15,6	24	1,7

Table 7.2.1.2.2 *Beta-lactamases identified in E. coli derived from selective culturing of faecal samples of broilers, slaughter pigs, veal calves, dairy cows and turkey in 2025*

		Broilers	Slaughter pigs	Veal calves		Dairy cows	Turkey	Total
				White	Rose			
CTX-M-1 group	CTX-M-1	13	9	19	7	4		52
	CTX-M-15	2	1	22	17	40	10	92
	CTX-M-32		1	25	5			31
	CTX-M-55	4		6		3		13
CTX-M-8/25 group	CTX-M-8			1				1
CTX-M-9 group	CTX-M-14		1	1	1	1		4
	CTX-M-65	3		2		1		6
TEM	TEM-52			2	1	1		4
	TEM-52C	1						1
SHV	SHV-12	7		1		2		10
CMY	CMY-2	2						2
DHA	DHA-1			1		1		2
Chromosomal ampC	-42 C>T		18	1		5		24
	n.-1C>T		1*					1*
Total		32	30	81	31	58	10	242

* n.-1C>T has been identified in a sample harbouring -42 C>T also, hence already accounted for there

Results of selective isolation and molecular typing of ESC-resistant E. coli in food products

Selective isolation of ESC-resistant *E. coli* was performed from food for human consumption, including samples from fresh meat, poultry, fish and fresh herbs and imported goods from outside the EU. Similar to the selective isolation of ESC-resistant *E. coli* from farm animals, described above, the selective isolation is more sensitive than the non-selective isolation method described in chapter 7.1.1.

In 2025, 2,640 samples were analysed, of which 2,086 were domestic produced and 496 were samples of food imported from outside the EU (58 samples of fresh herbs are not clearly attributable to either category and are excluded from this split), table 7.2.1.2.3. A total of 107 isolates were suspected ESC-resistant *E. coli* of which 98 were confirmed ESBL or plasmid-encoded AmpC producing isolates, and 1 isolate contained a mutation in the chromosomal AmpC promotor which is associated with ESC-resistance. A further 8 suspected isolates yielded no confirmed ESC-resistance mechanism with WGS.

The prevalence of ESC-resistant *E. coli* are compared to previous years in figure 7.2.1.2.2 for the domestically produced conventional food sources. The genes responsible for the ESC-resistant phenotype based on WGS are summarized per food category in table 7.2.1.2.4.

The prevalence of ESC-resistant *E. coli* on domestically produced **beef** and **pork** remained relatively low, as in previous years. On beef, ESC-resistant *E. coli* were detected in 1.1% of samples (6/532); this is within the range of natural year-to-year variation seen since 2014 (0.3-2.3%). On pork, ESC-resistant *E. coli* were detected in 0.5% of domestic samples (3/560) and 0.8% of imported samples (2/254), consistent with the low prevalence (<2%) reported in these meat samples since 2014.

In **veal**, ESC-resistant *E. coli* were isolated from 4.2% of meat samples (8/189), all ESBL-positive and predominantly carrying CTX-M-15, which appears to fall within the natural variation seen in this category (2.7-7.0% in recent years).

The detection of ESC-resistant *E. coli* from domestically produced **chicken** (poultry meat) was essentially unchanged at 18.3% of fresh meat samples (78/426), compared to 18.8% in 2024, continuing the relatively stable prevalence seen since 2021. SHV-12 and TEM-52 variants were the most frequently detected genes in chicken meat, together with CTX-M-1, CTX-M-15 and CTX-M-55.

Imported **aquaculture** (frozen fish) showed ESC-resistant *E. coli* in 2.1% of batches (4/188), including CTX-M genes and, in one pangasius sample from Vietnam, the AmpC gene DHA-1 which broadly consistent with the low, fluctuating prevalence (0.7-12.5%) reported in this category in previous years.

Fresh herbs (58 batches) yielded no confirmed ESBL/AmpC-producing *E. coli* in 2025.

Table 7.2.1.2.3 *Prevalence of ESC-resistant E. coli isolates from raw meat, poultry, aquaculture and fresh herbs in the Netherlands in 2025*

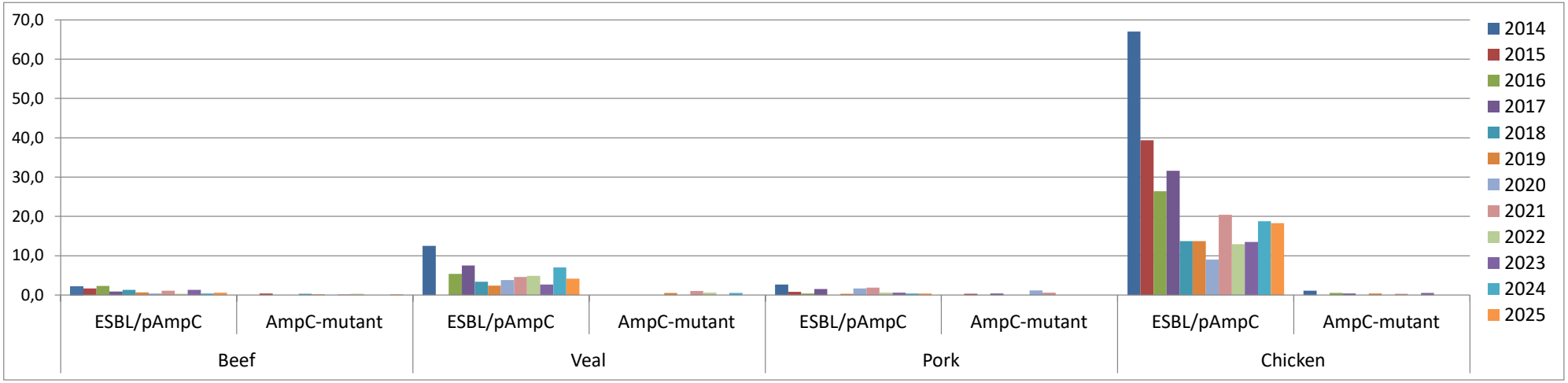
Animal source	N samples	N ESC-resistant *E. coli*	% ESC-resistant *E. coli*	N ESBL/ pAmpC carrying *E. coli*	% ESBL/ pAmpC positive	N AmpC promotor mutants	% AmpC promotor mutants
Beef	532	6	1,1	3	0,6	1	0,2
Veal	189	8	4,2	8	4,2	0	0
Pork	560	3	0,5	2	0,4	0	0
Chicken	651	80	12,3	79	12,1	0	0
Non-conventional meat	154	3	1,9	0	0	0	0
Imported pork	254	2	0,8	1	0,4	0	0
Imported chicken	54	1	1,9	1	1,9	0	0
Imported aquaculture/wild caught fish	188	4	2,1	4	2,1	0	0
Fresh herbs	58	0	0	0	0	0	0
Total	**2640**	**107**	**4,1**	**98**	**3,7**	**1**	**0,04**

Table 7.2.1.2.4 *Beta-lactamases identified in E. coli from raw meat products, poultry and aquaculture in the Netherlands in 2025*

	Beta-lactamase gene	Chicken	Pork	Beef	Veal	Non-conventional meat	Imported chicken	Imported aquaculture/wild caught fish	Total
CTX-M-1 group	CTX-M-1	8			2	2			12
	CTX-M-15	5	1			5			11
	CTX-M-32		1	1					2
	CTX-M-55	13			1				14
	CTX-M-55; LAP-2	1							1
	CTX-M-55; OXA-10							1	1
	CTX-M-14; CTX-M-55							1	1
	CTX-M-64*							1	1
CTX-M-9 group	CTX-M-9	1							1
	CTX-M-14	1							1
	CTX-M-65	1					1		2
TEM	TEM-52	15							15
	TEM-106	1							1
	SHV-12; TEM-207	1							1
SHV	SHV-12	29	1						30
	CMY-2; SHV-12	1							1
CMY	CMY-2	2							2
DHA	DHA-1; LAP-2						1		1
Chromosomal ampC	-42 C>T		1					1	
Total		**79**	**3**	**4**	**8**	**0**	**1**	**4**	**99**

*CTX-M-64 is a CTX-M-1/CTX-M-9 hybrid variant

Figure 7.2.1.2.2 *Trends in prevalence of confirmed ESBL/AmpC-producing E. coli and chromosomal AmpC-mutant E. coli in fresh meat of broilers, pigs, veal calves and dairy cows from 2014-2025 determined by using selective isolation*



ESC-resistant Salmonella

Introduction
Salmonella is a zoonotic pathogen carried by food-producing animals (poultry, pigs, cattle) and transmitted to humans mainly through contaminated animal products such as meat. ESBL- or AmpC-producing *Salmonella* are of particular concern in a food-safety context, as they are considered critically important antimicrobials for treating severe or invasive salmonellosis in humans.[6]

Methods
Isolates from animal and food sources were subjected to phenotypic antimicrobial susceptibility testing. Isolates with reduced susceptibility to cefotaxime and/or ceftazidime were confirmed by whole genome sequencing (WGS) to identify the underlying ESBL/AmpC resistance mechanism.

Results
Of the 111 *Salmonella* isolates analysed from animal and food sources in 2025, 2 were confirmed ESBL/AmpC producing isolates on WGS, both from chicken meat: 1 *S*. Heidelberg from Dutch retail chicken meat preparation carrying the plasmid borne AmpC gene CMY-2, and 1 *S*. Infantis from imported (salted) chicken meat preparation carrying CTX-M-65 (belonging to the CTX-M-9 group).

Table 7.2.1.2.5 *Beta-lactamases identified in Salmonella isolates in 2025 (n=2)*

Serovar	CTX-M-65	CMY-2	Total
Heidelberg		1	1
Infantis	1		1
Total	**1**	**1**	**2**

Table 7.2.1.2.6 *Beta-lactamases identified in Salmonella isolates collected in 2007-2025*

Year	CTX-M-1-group[a]	CTX-M-2[b]	CTX-M-3	CTX-M-8	CTX-M-9-group[c]	TEM-52	TEM-20	SHV-12[d]	CMY-2[e]	ACC-1	DHA-1	DHA-12	Total ESBL	Total *Salmonella* tested	% ESBL of total *Salmonella*
2007	9	13				17	2	4	2				47	1514	3.1
2008	25	12		1	1	13	1		6	2			61	2149	2.8
2009	12	4			2	3		1	9				31	2232	1.4
2010	8	3			1	2		3	4				21	1715	1.2
2011	5	3			1	1		2	13				25	1444	1.7
2012	14	5			2	2			10	1			34	1795	1.9
2013	1	3		5	4	5	1		36				55	1369	4.0
2014	6			2	3	1			21				33	1688	2.0
2015	13	2			6	1			12				34	1761	1.9
2016[f]	7				15	2			10		1		36	2117	1.7
2017[g]	3				23			1	3		1		31	1697	1.8
2018[g]	2		1	1	8				2				14	1718	0.8
2019	4				11			1	3				19	1880	1.0
2020					4				2				6	1310	0.5
2021	2				5			1	2				10	1264	0.8
2022[h]	4	2		1	6			2	32				47	1503	3.1
2023	10			1	4	1		1	2			1	20	2139	0.9
2024	13				5	2		1	2				23	1759	1,3
2025					1				1				2	111	1,8
Total	138	47	1	11	102	50	4	17	172	3	2	1	549	31165	1.8

[a] contains *bla*$_{CTX-M-1}$, *bla*$_{CTX-M-55}$, *bla*$_{CTX-M-15}$, *bla*$_{CTX-M-3}$ and a combination with *bla*$_{CMY-2}$ (n=2, 2014, 2015).
[b] In 2008 one combination of *bla*$_{CTX-M-2}$ with *bla*$_{TEM-52}$ was found in *S*. Paratyphi B var Java.
[c] contains *bla*$_{CTX-M-9}$, *bla*$_{CTX-M-14}$ and *bla*$_{CTX-M-65}$.
[d] In 2007 three *S.* Concord were found containing both *bla*$_{SHV-12}$ and *bla*$_{CTX-M-15}$.
[e] In 2015 a combination of *bla*$_{CMY-2}$ and *bla*$_{TEM-52}$ was found in *S*. Oranienburg and a combination of *bla*$_{CMY-2}$ with *bla*$_{CTX-M-1}$ in *S*. Molade.
[f] In 2016, one *S.* Minnesota isolate obtained from poultry meat at NVWA was not included in the molecular analysis.
[g] In 2017 and 2018 only human isolates were molecularly characterised.
[h] in 2022 a total of 33 *Salmonella* isolates obtained from imported fresh or processed meat were included which results in an increase of the % ESBL-positive isolates compared to former years.

Conclusions

- ESC-resistant E. coli in broilers decreased from 14.6% in 2024 to 10.4% in 2025 and remained exclusively ESBL/pAmpC-mediated, with no chromosomal ampC promotor mutants detected.
- The prevalence of ESC-resistant E. coli in pigs decreased to 10.0% of samples (30/301) from 13.6% in 2024. Chromosomal ampC promotor mutations remained the dominant resistance mechanism in pigs, accounting for 60.0% of resistant isolates (18/30), consistent with previous years.
- Veal calves had the highest prevalence of ESC-resistant E. coli among farm animal sectors (39.9% white, 24.6% rosé), CTX-M-32 remained highly prevalent in white calves, consistent with the previously reported expansion of this lineage.
- The prevalence of ESC-resistant E. coli in dairy cows decreased from 22.9% in 2024 to 18.3% in 2025, CTX-M-15 was the dominant gene (69.0% of resistant isolates).
- In faecal samples of turkey, ESC-resistant E. coli were detected in 6.9% of samples, all carrying CTX-M-15. The prevalence is similar to 2011 when ESC-resistant E. coli isolates were detected in 6.3% of the samples.
- In food, ESC-resistant E. coli prevalence in 2025 was broadly stable relative to 2024 in beef, veal, pork, chicken and aquaculture products, all remaining within the range of fluctuation seen since 2014; chicken remains the food category with the highest prevalence.
- Of the animal- and food-origin Salmonella isolates, 2 out of 111 were confirmed ESBL/AmpC producers, both from chicken meat (CMY-2 and CTX-M-65).

References

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7.2.2 Carbapenemase-producing Enterobacterales (CPE) in farm animals, companion animals and food

7.2.2.1 Farm animals

Introduction
Carbapenem antibiotics are banned for use in animals in Europe under EU legislation[1] to prevent the spread of antibiotic resistance, as carbapenems are last-resort drugs for treatment of certain human infections. Carbapenems are classified by the European Medicine Agency as Category A ("Avoid").[2] To identify potential sources for spread of Carbapenemase-producing Enterobacterales (CPE) via the food chain to humans, it is important to continuously monitor farm animals and meat. Although CPE is still rarely found in farm animals, the European Food Safety Authority (EFSA) has recently reported CPE in farm animals and meat thereof in a growing number of EU countries.[3] In the Netherlands, monitoring of CPE in farm animals was started in 2012. No CPE were found until 2024.

Methods
Passive screening
Based on the outcomes of the antimicrobial susceptibility testing, all randomly isolated indicator *E. coli*, *Salmonella* as well as selectively cultured extended-spectrum cephalosporins (ESC)-resistant *E. coli* isolates are screened for resistance to meropenem as indicator for the presence of carbapenem resistance genes.

Active screening based on selective culturing
As part of the mandatory AMR program[4], faecal samples of farm animals are screened for the presence of CPE according to the EURL-AR protocol 'Isolation of ESBL-, AmpC- and carbapenemase-producing *E. coli* from caecal samples' based on non-selective enrichment, followed by culturing on chromogenic plates.[5] More specifically, an overnight enrichment step in BPW (1 gram sample in 9 ml BPW) is followed by inoculation onto two chromogenic agar plates (ChromID® CARBA agar and ChromID® OXA agar plates, BioMérieux). After incubation, plates are inspected visually for growth of CPE suspected colonies (both *E. coli* and other Enterobacterales) and identified by MALDI-TOF (MALDI Biotyper® Sirius System, Bruker).

Active screening based on PCR
To enhance the sensitivity of the screening, all faecal samples are screened in parallel for specific carbapenem resistance genes with an in-house Real-Time multiplex PCR. This is important in an environment with a very low anticipated prevalence of carbapenem resistance as PCR is expected to have a higher sensitivity than culture methods. Samples are grown overnight in Buffered Peptone Water (BPW) with 0.25 mg/L ertapenem and 50 mg/L vancomycin. After incubation, five individual samples are pooled in lysis buffer, and DNA is isolated with a bead method. A multiplex Real-Time PCR (in-house) is targeting NDM, KPC, VIM, IMP, OXA-48, IMI and FRI carbapenemase genes. In case of a positive PCR result, a step-wise analysis is performed to confirm the results: 1. Singleplex Real-Time PCR test is performed on purified DNA of the 5 individual samples of the pool; 2. If the PCR test is positive, the

original faecal sample and corresponding broth culture of suspected positive samples were inoculated for bacterial isolation on commercial selective plates (ChromID® CARBA agar and ChromID® OXA agar and MacConkey agar plates with 0.125 mg/L ertapenem all selective for Enterobacterales) as well as sheep blood agar plates (HIS) with 0.125 mg/L ertapenem (selective for *Shewanella* spp); 3. DNA is isolated from CPE-suspected bacteria that grown on the selective agar plates, after MALDITOF identification, Real-Time PCR is performed. The phenotype of CPE-suspected isolates is determined with broth microdilution. The presence of CPE genes is confirmed using whole-genome sequencing.

Results
In 2025, 1,255 samples of farm animals were examined for the presence of carbapenemase-producing Enterobacterales. These included caecal samples from broiler chickens (n = 308), fattening pigs (n = 301), and veal calves (n = 329) collected at slaughterhouses, as well as manure samples (floor samples) from dairy farms (n = 317). Additionally, 145 faecal samples (floor samples) from turkeys were examined.
As a result of the selective culturing one CPE isolate was identified in a faecal sample of a dairy cow. The CPE was isolated from the ChromID® OXA plate and identified as an E. coli ST372 harbouring a blaOXA-181 gene on an IncX3 plasmid. The source of this OXA-181-producing CPE in the dairy cattle could not be identified. The Netherlands Food and Consumer Product Safety Authority (NVWA) conducted extensive follow-up investigations, collecting approximately 200 rectal swabs from individual animals present at the farm including calves of different ages, young stock, dry cows and lactating cows. No CPE was detected in the samples from this follow-up investigation. Consequently, the risk of CPE spreading from this farm is considered low.
The PCR screening of the same 1255 samples did not result in the finding of additional CPE.

In conclusion, CPE has been detected in farm animals for the second consecutive year. Although the prevalence of CPE in farm animals is still low, this finding emphasises the importance of a continuous screening program, followed by molecular analysis of potential carbapenemase-producing bacteria for confirmation. Screening for carbapenemase-producing bacteria in livestock will continue in 2026.

7.2.2.2 Companion animals

Introduction
Carbapenemase-producing Enterobacterales (CPE) have been reported sporadically in companion animals in several Europe countries, although the prevalence remains relatively low. CPE have been identified in dogs from Germany[6,7], Spain[8], France[9], UK[10], Portugal[11,12] and Switzerland[13,14,15]. Recent European studies indicate that companion-animal CPE can belong to internationally recognised high-risk clones and carry mobile elements similar to those found in human healthcare settings, highlighting their relevance from a One Health perspective[11,13,16,17].

In the Netherlands, monitoring for CPE in companion animals in the Netherlands was initiated in 2015. The screening for CPE comprised of an initial retrospective study and a prospective study, and no CPE was detected up to 2016 (MARAN 2017). In 2017, the first finding was a *bla*$_{\text{OXA-48}}$ producing *E. coli*, isolated from a dog faecal sample (MARAN 2018). In 2018, *bla*$_{\text{OXA-48}}$ and *bla*$_{\text{OXA-181}}$ producing *E. coli* were detected in two additional dog samples, that originated from different parts of the Netherlands. No CPE were detected during monitoring from 2019 to 2021. A bla$_{\text{OXA-48}}$-producing *E. coli* was subsequently identified in a dog in 2022 while no CPE were detected in dogs and cat in 2023. In 2024, *bla*$_{\text{NDM-1}}$ producing *E. coli* was identified in a dog faecal sample.

Methods
Because the prevalence of CPE in companion animals is expected low and CPE are frequently multi-resistant, dog faecal samples were preferentially selected from animals with recent antimicrobial treatment. This selection criterion was not considered suitable for cats, which are less frequently treated with antimicrobials. Therefore, a randomized, stratified subset of cat faecal samples submitted to the VMDC was examined. In 2025 the CPE screenings protocol was slightly adapted. For each sample, 0.5 gram faeces was suspended in 4.5 mL TSB broth supplemented with 50 mg/L vancomycin and incubated overnight at 37 °C. Following enrichment, the broth was cultured overnight at 37°C on ChromID Carba-Smart agar (BioMerieux). For molecular screening, 200 µl of enrichment broth from up to 5 samples were pooled, followed by total DNA extraction. PCR was performed to detect NDM[18], KPC[19], IMP[20], VIM[20], OXA-group-23, -24, -51, -58[21] and OXA-group-48[22].

Results
In 2025, 102 faecal samples from dogs and 100 faecal samples from cats submitted to the Veterinary Microbiological Diagnostic Center (VMDC) of Utrecht University were examined. One faecal sample from a dog with intermittent diarrhoea was positive for *E. coli* carrying *bla*$_{\text{OXA-48}}$. In a second dog faecal sample, qPCR identified *bla*$_{\text{OXA-23}}$, but no bacteria were recovered by culture. Two additional dog samples were positive for *bla*$_{\text{OXA-10}}$. Because *bla*$_{\text{OXA-10}}$ is a class D β-lactamases without carbapenemase activity, and bacterial culture was negative, these samples were considered negative for CPE. Both dogs had intermittent diarrhoea of which one was treated with metronidazole before sampling. No CPE-suspected isolates were detected in the 100 faecal cat samples.

The detection of *bla*$_{OXA-48}$ producing *E. coli* in a dog demonstrates the value of continued surveillance for CPE in companion animals. Combined selective culture with molecular screening allows the detection of carbapenemase-associated genes and confirmation of clinically relevant carbapenemase-producing bacteria. Continued surveillance is warranted to detect the introduction and possible spread in companion animals, and screening at the VMDC will continue in 2026.

7.2.2.3 Food

Introduction

As part of the mandatory AMR program[4], fresh meat samples from retail and import are screened by WFSR for the presence of CPE according to the EURL-AR protocol 'Isolation of ESBL-, AmpC- and carbapenemase-producing *E. coli* from fresh meat, based on non-selective enrichment, followed by culturing on chromogenic plates.[23]

Analysing the presence of carbapenem resistant bacteria in food products is part in the annual AMR monitoring program in the Netherlands. In recent years, carbapenem resistant bacteria have been incidentally isolated from imported food products other than meat. In total one carbapenemase-producing *E. coli* and 14 carbapenemase-producing *Enterobacter cloacae* isolates have been found in food products between 2017-2023. Shrimps was with 9 isolates the most dominant source, followed by four isolates from Tilapia, one from Salicornia and one from fresh coriander. The identified carbapenem genes were diverse including: *bla*$_{IMI}$, *bla*$_{FLC}$, *bla*$_{NDM}$, *bla*$_{FRI}$, *bla*$_{OXA-9-10}$. This shows that imported food is a potential risk for spread of carbapenem resistance through the environment. Based on the number of analysed consignments, the estimated annual incidence is considered low (<1%).

Methods

Active screening based on selective culturing

Food samples of pork -, beef -, and calf meat, fresh herbs, fish, and shellfish are screened for the presence of CPE according to the EURL-AR protocol 'Isolation of ESBL-, AmpC- and carbapenemase-producing *E. coli* from fresh meat' based on non-selective enrichment, followed by culturing on chromogenic plates.[23] In more detail, an overnight enrichment step in BPW (25 gram sample in 225 ml BPW) is followed by inoculation on two chromogenic agar plates (ChromID® CARBA agar and ChromID® OXA agar plates , BioMérieux). After incubation, plates are inspected visually for growth of CPE suspected colonies (*E. coli, Klebsiella and Enterobacter* and identified by MALDI-TOF (MALDI Biotyper® Sirius System, Bruker). In case a suspected carbapenem resistant colony was isolated the carbapenemase gene was confirmed by WGS analysis.

Active screening based on PCR

In addition to the culture based screening, a selection of imported food samples were screened with an in-house Real-Time multiplex PCR. This DNA-based screening is species independent and possibly more sensitive. Per samples 25 gr of food product was added to BPW and after overnight incubation for 20 h at 37 °C, 150 µl of the enrichment was used for DNA extracting. Three different multiplex Real-Time PCR

methods targeting (IMP and OXA-48), (KPC, NDM and VIM) and (FRI and IMI) carbapenemase genes were used for the screening.

Results

Active screening based on selective culturing

In 2025, 188 samples of frozen fish originating from fish farms in South-East Asia and South-America as well as of shrimps, mainly from farms in South-America and Asia, were screened for the presence of CPE through selective culturing. In addition, 277 samples pork, 266 samples of beef, 17 samples of turkey meat and 426 samples of chicken meat all sampled at retail, 189 samples of calf meat from wholesale, and 35 and 184 batches of imported pig and beef meat respectively, 58 batches of imported herbs, were screened for the presence of CPE. From one sample fresh herb (mint leaves from Spain) a CPE was isolated. Further analysis of this isolate resulted in the identification of a *Enterobacter cloacae* complex isolate with a *bla*$_{\text{IMI-3}}$ gene.

Active screening based on PCR

In the active screening based on PCR a total of 374 samples were analysed including 158 samples from frozen fish, shrimps and shellfish which were not included in the screening based on selective culturing. DNA samples were screened for the presence of carbapenem resistance genes with the three multiplex qPCR. As in previous years a relative high number of samples of (124 out of 374) DNA samples were positive with the OXA-48 primer set. A possible explanation for the high prevalence of OXA-48 is the link of these samples to water environments in which *Shewanella* spp. are commonly present often carrying chromosomal blaOXA-48-like genes.[24] In two imported samples from frozen shrimps a positive PCR signal was detected, for IMI and VIM and for KPC in frozen fish. Selective culturing to confirm the presence of bacteria carrying these genes was not included in the protocol.

Our findings confirm earlier reports on the presence of CPE in imported herbs and seafood in the Netherlands[25,26] reflecting the high consumption of antimicrobials in the countries of origin, specifically in aquaculture as an environment with a high selective pressure advantageous for resistant bacteria. The active monitoring of (imported) food will be continued in 2026.

Conclusions

- In 2025, CPE has been detected in farm animals for the second consecutive year. The source of this *E. coli* carrying a *bla*$_{\text{OXA-181}}$ gene in dairy cattle could not be identified.
- CPE are incidentally found in dogs in the Netherlands. In 2025, *E. coli* carrying *bla*$_{\text{OXA-48}}$ was found in a faecal sample from a dog. As in previous years, CPE was not detected in cats.
- CPE is sometimes also found in food products. In 2025, an *Enterobacter cloacae* complex isolate carrying a *bla*$_{\text{IMI-3}}$ gene was identified in a fresh herb sample from Spain.

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7.2.3 Colistin resistance in farm animals and food

Introduction
The use of colistin in farm animals in Europe is increasingly restricted due to concerns about rising resistance. This restriction is due to the discovery of the plasmid-mediated resistance gene *mcr-1* in 2016[1] and the recognition of colistin as a crucial antibiotic for the treatment of multidrug-resistant infections in humans. In the same year, *mcr-1* was reported in farm animals and meat in the Netherlands.[2] In 2020, a diagnostic test before prescribing colistin was strongly recommended, and overall sales of colistin for animal use in the EU fell significantly. According to the latest report of the Netherlands Veterinary Medicines Authority (SDa) colistin use in farm animals in the Netherlands has decreased for the fifth consecutive year (2021-2025)[3]. The use in pigs (primarily weaned piglets) and laying hens decreased compared to 2024. (Almost) no colistin is used in broilers, turkeys, dairy cattle, veal calves, other cattle, and meat rabbits.

To monitor the prevalence of *mcr*-positive bacteria in farm animals as a potential source linked to the food chain, screening of faecal samples for *mcr*-positive Enterobacterales began in 2016 and was implemented into the national AMR monitoring program in animal and food to date.

Methods
For this purpose, purified DNA of pooled BPW + 2mg/L colistine cultures (five samples per pool) of faecal samples of farm animals are tested for the presence of *mcr-1*, *mcr-2*, *mcr-3*, *mcr-4* and *mcr-5* using an in house designed multiplex Real-Time PCR based on the updated EURL-AR protocol[4]. From 2022 onwards, the PCR screening of the samples was extended with *mcr-6*, *mcr-7*, *mcr-8*, *mcr-9* and *mcr-10* using an extra inhouse designed multiplex RT-PCR. In case of a PCR positive pool, individual samples are tested, followed by direct culturing of the original BPW broth on MacConkey agar with 2 mg/L colistin.

Results
In 2025, 1,255 samples of farm animals were examined. These included caecal samples from broiler chickens (n = 308), fattening pigs (n = 301), and veal calves (n = 329) collected at slaughterhouses, as well as faecal samples (floor samples) from dairy farms (n = 317). Additionally, 145 faecal samples (floor samples) from turkeys were included in the monitoring. As a result of the screening, *mcr*-1 positive *E. coli* were identified in two samples from broilers (0.6%), two from pigs (0.7%) and one veal calf sample (0.3%). Furthermore, colistin resistance was not detected in the randomly isolated indicator *E. coli* from caecal or faecal samples of farm animals (Table 7.1.1.2). These results confirm the long-term low prevalence of *mcr*-positive bacteria in farm animals and probably reflects the low use of this antibiotic. Table 7.1.1.3 shows that colistin resistance was also not observed amongst indicator *E. coli* isolates obtained from retail meat (beef, pork and lamb) and imported meat (beef and pork) indicative of the low prevalence of colistin resistance in bacteria from meat.

Conclusions

- As in previous years, the prevalence of *mcr*-positive *E. coli* in farm animals was low. This probably reflects the low use of this antibiotic.
- In randomly selected indicator *E. coli* from meat products resistance to colistin was not observed indicative of the low prevalence of colistin resistance in bacteria from meat.

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7.2.4 MRSA surveillance in livestock and humans living/working on farms

Introduction
Two decades ago, MLST clonal complex (CC) 398 has emerged in livestock and persons in contact with livestock in multiple countries, including the Netherlands[1,2]. This subtype of MRSA is referred to as livestock-associated MRSA (LA-MRSA). The most important risk factor for carriage of LA-MRSA is professional contact with livestock, especially pigs, poultry and veal calves. During the last decade, the detected number of MRSA infected persons without direct contact with livestock, seems to be increasing[3]. To monitor these trends, in 2018, a national project on surveillance of MRSA in humans, livestock, and meat products was started. The objective of this project was to assess possible changes in the rate or nature of MRSA transmission between animals and humans.

Methods
The project is a collaboration between NVWA, RIVM, WBVR and WFSR. MRSA isolates obtained from various sources result in prevalence data in different animal reservoirs over the years. In addition, the genomes of the MRSA isolates are analysed using various Illumina platforms. Animal related MRSA isolates are collected from three surveillance programs[3] and this year also data from the pig baseline study (see below nr. 4) is included:

1. Surveillance livestock project in livestock and persons living or working on a farm.
   This surveillance is described in van Duijkeren et al., 2025[4] and executed under Zoonoses Directive 2003/99/EC. Within this surveillance program successively one livestock sector is investigated for the presence of MRSA. In 2024 and 2025 pig farms and persons working and/or living on these farms were sampled. Dust was collected using three wipes in one barn per farm that housed pigs older than 16 weeks of age. The farm was considered positive if at least one of the dust samples contained MRSA bacteria. Farmers and persons living and/or working on the farm sent in a nose swab by regular mail. Culture methods were used as described in van Duijkeren *et al.,* 2025[4].
2. National MRSA surveillance in livestock.
   In this surveillance caecal /faecal samples collected at slaughter and/or at a farm are collected and investigated for MRSA as described in van Duijkeren et al., 2025[4].
3. National MRSA surveillance in meat.
   Every year, Dutch retail meat samples and this year also imported meat are collected and investigated for MRSA.
4. Pig baseline study
   For this study nose swabs of pigs are taken at slaughter. Twenty nose swabs per slaughter batch were pooled in four pools containing five nose swabs each. This study was performed following the Commission Implementing Decision EU 2023/1017.

The genomes of the animal-related MRSA isolates are compared with the genomes of MRSA isolates from genogroup (GG) 0398 collected in the Dutch national MRSA surveillance in humans. See for the description of the Dutch national MRSA surveillance in humans, chapter 5.2.5.

A molecular comparison of the isolates obtained in 2024-2025 took place as described in van Duijkeren *et al*., 2026[3].

In 2025, susceptibility testing of MRSA was performed on all isolates originating from caeca of pigs (n=37), one isolate per nose swab (n=172) as well as one isolate per dust sample (n=62) from pig farms. MRSA isolates were tested for antimicrobial susceptibility with broth microdilution according to ISO standards in a harmonised antibiotic panel advised by EFSA using commercially available Sensititre plates (Thermofisher Scientific, panel EUST). The MIC-values were interpreted with ECOFFs as advised by EUCAST (https://mic.eucast.org/)

Results

MRSA prevalence on farms in caecal samples and on meat

MRSA prevalence in animals on farms

In 2024-2025, 213 pig farms were sampled for MRSA. The overall proportion MRSA positive farms was 67.6%. Thirty-three farms were organic farms, with a proportion of MRSA positive farms of 12.1%. This is significantly lower than among the 180 conventional farms sampled (77.8%, Table 7.2.4.1). The proportion of positive conventional farms is not significantly different from the prevalence found in 2020 when 149 farms were sampled and 113 (76%) were MRSA positive. However, the prevalence was significantly higher than for any other type of livestock farms sampled in previous years (Table 7.2.4.1).

MRSA prevalence in persons living and/or working on pig farms

In 2024-2025, 91 persons living and/or working on 59 pig farms participated in the study. From those 91 persons, thirty persons, derived from twenty-four pig farms, carried MRSA (33.0%). This MRSA prevalence was even higher when looking at persons living and/or working on conventional pig farms. 28 persons from a total of 68 participants (41.2%), derived from 23 conventional farms, tested MRSA positive. Compared to MRSA carriage in persons living/working on an organic pig farm (8.7%, two persons, derived from one farm), or any other type of livestock farm (0.9-12.7%) this is significantly higher (Table 7.2.4.1).

Table 7.2.4.1 *MRSA prevalence on farms and in persons living/working on the farm 2018-2025*

Year	Animal	MRSA positive farms (n)	Total no of farms sampled (n)	Preva-lence (%)	95% CI	Mrsa positive humans (n)	Total no of humans sampled(n)	Derived from n farms (n)	Preva-lence (%)	95% CI
2024/2025	Pigs organic	4	33	12.1	4.8-27.3	2	23	1	8.7	2.4-26.8
2024/2025	Pigs conventional	140	180	77.8	71.2-83.2	28	69	23	41.2	30.3-53.0
2023	Sheep	7	156	4.5	2.2-9.0	5	80	3	6.3	2.7-13.8
2022	Veal calves	44	173	25.4	19.5-32.4	7	55	7	12.7	6.3-24.0
2020/2021	Dairy cows	11	181	6.2	3.4-10.6	1	107	1	0.9	0.2-5.1
2020	Pigs	113	149	75.8	68.4-82.0	ns	ns	ns	-	-
2018/2019	Broilers	0	195	0.0	0.0-2.0	4	133	4	3.0	3.4-10.3

ns=not sampled.

Table 7.2.4.2 *MRSA found in caecal samples collected in 2021-2025*

	Year				
Animal species	**2021 % (n/N)**	**2022 % (n/N)**	**2023 % (n/N)**	**2024 % (n/N)**	**2025 % (n/N)**
Pigs	15.1 (15/100)	16.0 (48/300)	13.7 (41/300)	16.6 (50/302)	12.3 (37/301)
White veal calves	44 .3 (31/70)	28.2 (58/207)	-	40.3 (75/186)	-
Rosé veal calves	0.0 (0/32)	2.0 (2/100)	-	6.1 (7/114)	-
Dairy cows	1.0 (1/102)	0.3 (1/300)	-	-	-
Broilers	1.0 (1/102)	-	0.3 (1/290)	-	0.6 (2/308)

MRSA prevalence in caecal samples
In 2025, caecal/faecal samples from the national surveillance taken at slaughter for the monitoring of antimicrobial resistance in zoonotic and commensal bacteria (EU decision (EU) 2020/1729) were investigated. Caecal samples are only collected from animals raised and slaughtered in the Netherlands.
MRSA was found in caecal samples from 37/301 (12.3%) pigs and 2/308 (0.6%) broilers. Caecal samples from veal calves and faecal samples from dairy cattle were not investigated in 2025 (Table 7.2.4.2).
The data should be interpreted with care, as caecal or faecal samples are not the preferred sample for MRSA. The data, however, are available from the routine surveillance and as they are collected in the same way each year, trends in time can be analysed. The prevalence found in pigs and broilers in 2025 was comparable to the prevalence found in previous years (2021 to 2024).

MRSA prevalence on meat
In 2025, a total of 1,644 retail meat samples were investigated. Retail meat is always derived either from the Netherlands or from countries within the EU. Table 7.2.4.3 shows the amount tested and the number of MRSA positive samples per meat product over the years 2018-2025. In 2025, there were no significant differences in MRSA prevalence on meat compared to 2024. Pork is contaminated with MRSA (5.7%), but that is not significantly different from sampled beef (4.2%) and veal (6.3%), sampled at retail. This year, also imported pork and imported beef were sampled. Prevalence for these were 14.2% and 6.9% respectively. Import means always, derived from outside the EU. MRSA prevalence in imported pork was significantly higher ($p=0.0061$, two-tailed Z-test) compared to pork derived from the Netherlands or EU.

Table 7.2.4.3 *MRSA found on meat (products) between 2018-2025*

Year	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**	**2025**
Sample	**%(n/N)**	**%(n/N)**	**%(n/N)**	**%(n/N)**	**%(n/N)**	**%(n/N)**	**%(n/N)**	**%(n/N)**
Sheep/goat meat	no data	no data	2.2	12.4	no data	4.6	4.3	no data
			(1/46)	(37/299)		(7/151)	(7/162)	
95% CI			0.0-11.5	8.9-16.7		1.9-9.3	1.8-8.7	
Pork	5.9	8.4	3.5	no data	7.2	6.9	8.4	5.7
	(8/135)	(25/296)	(3/57)		(13/180)	(20/291)	(25/297)	(16/283)
95% CI	2.6-11.34	5.5-12.2	1.1-14.6		3.9-12.0	4.3-10.4	5.5-12.2	3.5-9.0
Pork import	no data	no data	no data	no data	no data	no data	no data	14.3
								(15/105)
95% CI								8.9-22.2
Beef	2.1	3.8	no data	no data	6.1	3.9	5.5	4.2
	(3/140)	(2/11)			(9/14)	(17/432)	(17/309)	(11/263)
95% CI	0.4-6.1	1.9-6.8			2.8-11.3	2.3-6.2	3.2-8.7	2.4-7.3
Beef import	no data	no data	no data	no data	no data	no data	no data	6.9
								(45/651)
95% CI								5.2-9.1
Poultry-meat	22.0	19.9	16.5	8.6	9.3	10.4	7.9	no data
	(29/132)	(50/251)	(45/248)	(28/324)	(18/194)	(20/192)	(36/455)	
95% CI	15.2-30.0	15.2-25.4	13.6-23.5	5.8-12.3	5.6-14.3	6.5-15.6	5.6-10.8	
Veal	no data	no data	3.8	6.9	9.1	13.6	10.4	6.3
			(2/52)	(18/261)	(15/164)	(25/184)	(21/201)	(12/192)
95% CI			0.5-13.2	4.1-10.7	5.2-14.6	9.0-19.4	6.6-15.5	3.6-10.6
Other meat	no data	no data	0.0	20.0	14.3	4.5	0	no data
			(0/4)	(4/20)	(3/21)	(1/22)	(0/106)	
95% CI			0.0-60.2	5.7-43.7	3.1-36.3	0.1-22.8	0.0-3.4	

* Most "other" samples in 2024 derived from venison from UK and New-Zealand.

MRSA prevalence in nose swabs – Base line study at slaughter
In 2025, 172 slaughter batches were investigated. All batches were MRSA positive. In one batch only two out of four pools were MRSA positive. All other slaughter batches resulted in four pools MRSA positive.

Resistance levels of MRSA in pigs
The proportion of resistance of the MRSA isolates from pigs caeca at slaughter, nose swabs from the baseline study at slaughter and dust samples from pig farms sampled in 2025 to various antimicrobial drugs are depicted for each type of sample in Table 7.2.4.4. In 2025, as expected for MRSA, all isolates tested resistant against (benzyl)penicillin and cefoxitin. High levels of resistance were also observed for tetracycline. This is in line with the known levels (~100%) of tetracycline resistance in LA-MRSA.

Resistance levels differ a little depending on isolation source. Overall, resistance levels for some antimicrobials (e.g. quinupristin/dalfopristin, tiamulin and trimethoprim) were lower in isolates collected from pig caeca compared to isolates from dust and nasal swabs.

Resistance levels in MRSA isolates from pig caeca remained equal compared to 2024 (Nethmap/MARAN 2024).

Finally, no or very low resistance was detected against the following reserved and highly critically important antibiotics for humans: fusidic acid, linezolid, mupirocin, rifampicin, or vancomycin.

Table 7.2.4.4 *Resistance percentages (R%) of MRSA isolated from dust samples from pig farms and from caeca and nose swabs from pigs at slaughter in 2025*

Antibiotic	Pig farms dust (N=90)	Pigs at slaughter caeca (N=50)	Pigs at slaughter Nose swab (N=82)
cefoxitin	100.0	100.0	100.0
chloramphenicol	27.4	17.9	18.6
ciprofloxacin	0.0	2.6	5.2
clindamycin	45.2	43.6	46.5
erythromycin	33.9	41.0	32.6
fusidic acid	1.6	0.0	1.2
gentamicin	19.4	20.5	25.6
kanamycin*	8.1	5.1	13.4
linezolid	0.0	0.0	0.0
mupirocin	0.0	0.0	0.0
penicillin	100.0	100.0	100.0
quinupristin/dalfopristin	22.6	17.9	20.3
rifampicin	0.0	0.0	0.6
streptomycin	1.6	2.6	1.7
sulfamethoxazole	0.0	0.0	2.3
tetracycline	100.0	100.0	94.8
tiamulin	22.6	17.9	21.5
trimethoprim	51.6	41.0	69.8
vancomycin	0.0	0.0	0.0

*Resistance to kanamycin may be underestimated with the current tentative ECOFF.

Genetic analyses of MRSA isolates

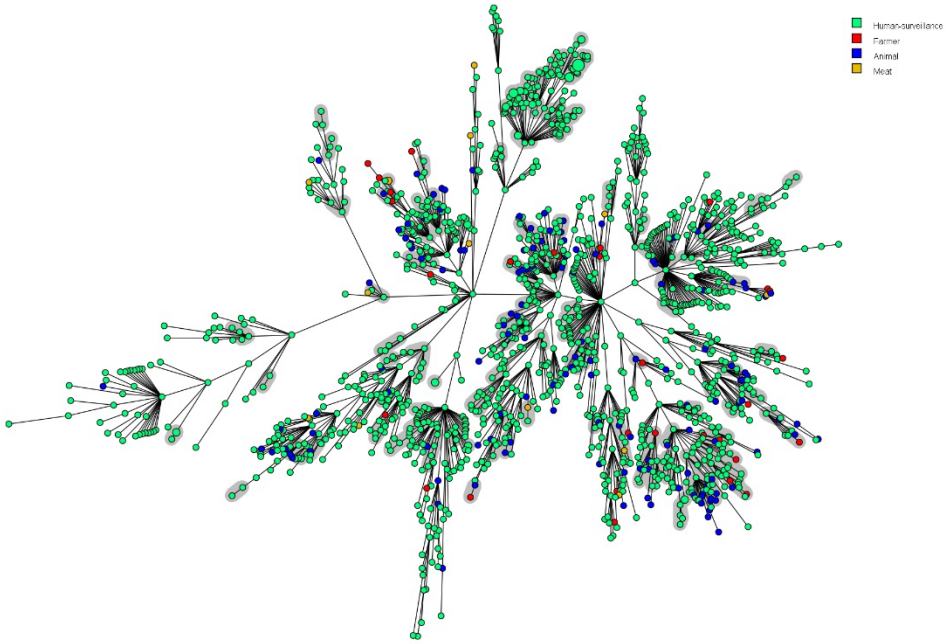
All MRSA isolates, except three isolates belonged to GG0398, and carried the *mecA* gene. The three non-GG0398 isolates carried the *mecC* gene and belonged to GG0130 (n=2) or GG009 (n=1). Two of these isolates were derived from meat and one from a pig caecum (GG0130).

From the 30 human MRSA carriers, 21 (70%) lived or worked on a farm that contained MRSA positive pigs. The isolates from all MRSA-carriers from MRSA positive farms were compared to the isolates derived from the pigs on their farm using whole genome MLST (wgMLST). This resulted in three cases of highly comparable (< 16 loci difference) MRSA isolates in farmer and animals at the farm. In two cases the isolates differed 16 to 30 loci and the isolates from the other 16 persons differed more than 100 loci.

In total, we compared 162 pig-related GG0398 isolates (from pig meat, pigs and farmers) to 1,234 human GG0398 isolates from the national MRSA surveillance using wgMLST analyses. (fig 1). The animal-related isolates are genetically diverse and spread over the wgMLST minimum spanning tree (Figure 7.2.4.1). In total, 36 pig-related isolates and 38 isolates from the national MRSA surveillance formed 23 mixed genetic clusters (< 16 loci difference). In two clusters, isolates derived from a known infection (wound and urinary tract infection) were genetically

related to a pig-related isolate (one from meat and one from a pig). In addition, two pig-pig clusters, both containing two isolates were detected. These two clusters contained four isolates, all derived from a different farm.

Figure 7.2.4.1 *wgMLST minimum spanning tree of GG0398 including 162 pig, meat, farmer isolates from 2024-2025 and 1,234 isolates derived from the human MRSA national surveillance 2019-2025*



Discussion

Farms investigated in 2024-2025 show a difference in MRSA prevalence between conventional and organic pig farms. A lower proportion of MRSA positive farms within organic farming compared to conventional farming has been speculated to be the result of lower antibiotic usage in organic farming[5]. On the other hand, we must interpret the results with care. Organic farming has more spacious housing for the pigs and the animals live partly outside. Therefore, it cannot be ruled out that these differences have an influence on the culturing results of dust samples.

The persisting high prevalence on conventional pig farms and at slaughter poses a potential threat to persons living and/or working on these farms or working at slaughter houses, especially for persons in direct contact with the animals. Living or working on an organic farm poses less risk of MRSA contamination than living/working on a conventional farm.

The presence of similar MRSA isolates present in both pigs and persons living or working on the same farm confirms MRSA transmission at the farm. In addition, 3% of the GG0398 MRSA isolates from humans collected in the national MRSA surveillance show genetic relatedness to MRSA isolates from pigs. In two cases such an isolate was recovered from a human infection.

On meat, the highest prevalence is found on imported pork. Generally, it is believed that contaminated meat is not an important transmission

route for MRSA for the population at large, especially because the meat is usually sufficiently heated before consumption. In some studies performed abroad, however, food handling has been implicated as a transmission route[6,7] and our study shows a human infection MRSA isolate that is genetically related to a MRSA isolate derived from pig meat.

Conclusions

- Still a high percentage, 67.6% of pig farms and 100% of sampled slaughter batches are MRSA positive. This prevalence is significantly higher than for any other type of livestock. As a result, there is also no decrease in MRSA prevalence visible in caecal samples from pigs at slaughter and all slaughter batches sampled in the baseline study are MRSA positive.
- MRSA is present on 12% of organic pig farms, compared to 78% of conventional pig farms.
- MRSA prevalence among persons living or working on organic farms (8.7%) is lower than among persons working or living on conventional pig farms (41.2%).
- In two cases, MRSA isolates from a human infection were genetically related to pig isolates from 2024-2025, including one isolate from pig meat.
- MRSA is found on pork, veal and beef. Imported pork is more contaminated than pork obtained from retail.
- MRSA isolates from pigs show very low to no resistance to antimicrobials that are important for human medicine: fusidic acid, linezolid, mupirocin, rifampicin, and vancomycin.

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8 Supplements

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8.2 Overview of antimicrobial resistance in human surveillance programs included in NethMap One Health 2026

Table S1 *Overview of antimicrobial resistance surveillance programs included in NethMap One Health 2026*

Surveillance program	Origin of isolates	Availability	Sources 2026	Central or decentral susceptibility testing	Method of susceptibility testing
Surveillance programs aimed at resistance surveillance in specific pathogens					
CPE	GP, hospital, LTCF	2011-	Nationwide	Central testing	Gradient testing, Carba-PCR, next generation sequencing, Nanopore long-read sequencing
CPPA	GP, hospital, LTCF	2020-	Nationwide	Central testing	Gradient testing, Carba-PCR, next generation sequencing, Nanopore long-read sequencing
CRAB	GP, hospital, LTCF	2022-	Nationwide	Central testing	Gradient testing, Carba-PCR, next generation sequencing, Nanopore long-read sequencing
MRSA	GP, hospital, LTCF	2008-	Nationwide	Central testing	MLVA typing, whole genome sequencing
Neisseria meningitidis	Hospital	1994-	Nationwide	Central testing	Gradient testing
Neisseria gonorrhoeae	SHC	2006-	15 out of 24 SHC	Decentral testing	Gradient testing

ISIS-AR = Infectious disease surveillance information system on antibiotic resistance; CPE = carbapenemase-producing Enterobacterales; CPPA = carbapenemase-producing *Pseudomonas aeruginosa*; CRAB = carbapenem-resistant *Acinetobacter baumannii-calcoaceticus* complex; MRSA = methicillin-resistant *Staphylococcus aureus*; GP = general practice; LTCF = long-term care facility; SHC = sexual health centres; UMCG = University Medical Centre Groningen; NIC-ErasmusMC = National Influenza Centre Erasmus Medical Centre location; WHO-CC = World Health Organization collaborating centre; MLVA = multiple-locus variable number of tandem repeat analysis

Table S1 (continued) *Overview of antimicrobial resistance surveillance programs included in NethMap One Health 2026*

Surveillance program	Origin of isolates	Availability	Sources 2026	Central or decentral susceptibility testing	Method of susceptibility testing
Surveillance programs aimed at resistance surveillance in specific pathogens					
Mycobacterium tuberculosis	General population	1993-	Nationwide	Primarily central testing	Whole genome sequencing, additional phenotypic testing
Influenza antiviral drugs	Community, GP, hospital	2005-	NIVEL GP sentinels, hospital/regional laboratories, Infectieradar	central testing (RIVM, NIC-ErasmusMC, WHO-CC London)	Whole genome Nanopore sequencing, Neuraminidase enzyme inhibition assay
Resistance among anaerobic pathogens	Hospital	2010-	UMCG	Central testing	Gradient testing
Clostridioides difficile	Hospital, LTCF	2005-	5 hospitals	(de)central testing	Agar dilution
Azole resistance in *Aspergillus fumigatus*	Hospital	2011-	5 university hospitals + 5 teaching hospitals	Central testing	EUCAST microbroth dilution methodology

ISIS-AR = Infectious disease surveillance information system on antibiotic resistance; CPE = carbapenemase-producing Enterobacterales; CPPA = carbapenemase-producing *Pseudomonas aeruginosa*; CRAB = carbapenem-resistant *Acinetobacter baumannii-calcoaceticus* complex; MRSA = methicillin-resistant *Staphylococcus aureus*; GP = general practice; LTCF = long-term care facility; SHC = sexual health centres; UMCG = University Medical Centre Groningen; NIC-ErasmusMC = National Influenza Centre Erasmus Medical Centre location; WHO-CC = World Health Organization collaborating centre; MLVA = multiple-locus variable number of tandem repeat analysis