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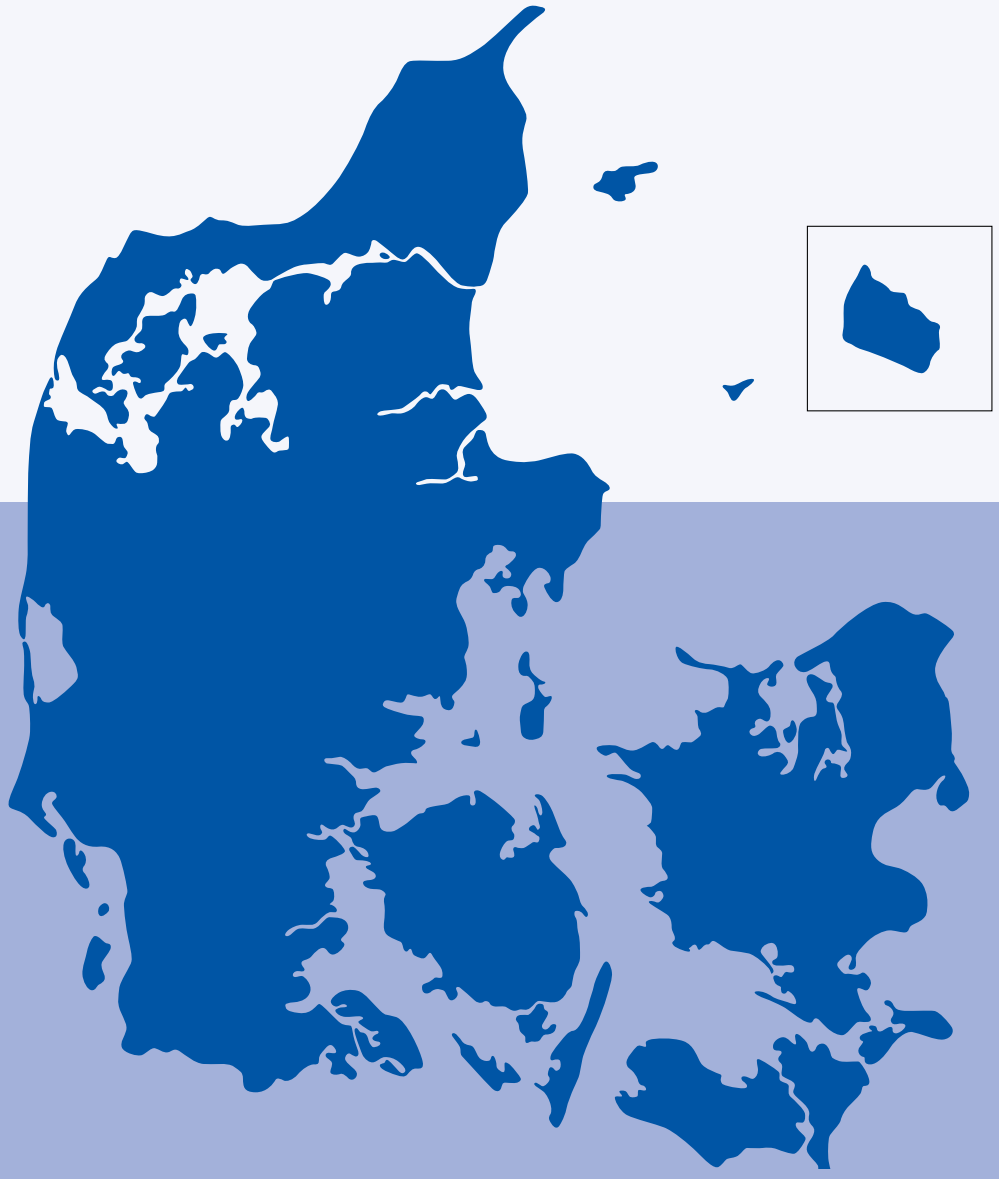
DANMAP 2024

Use of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, food and humans in Denmark



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DANMAP 2024

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DANMAP 2024

Use of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, food and humans in Denmark

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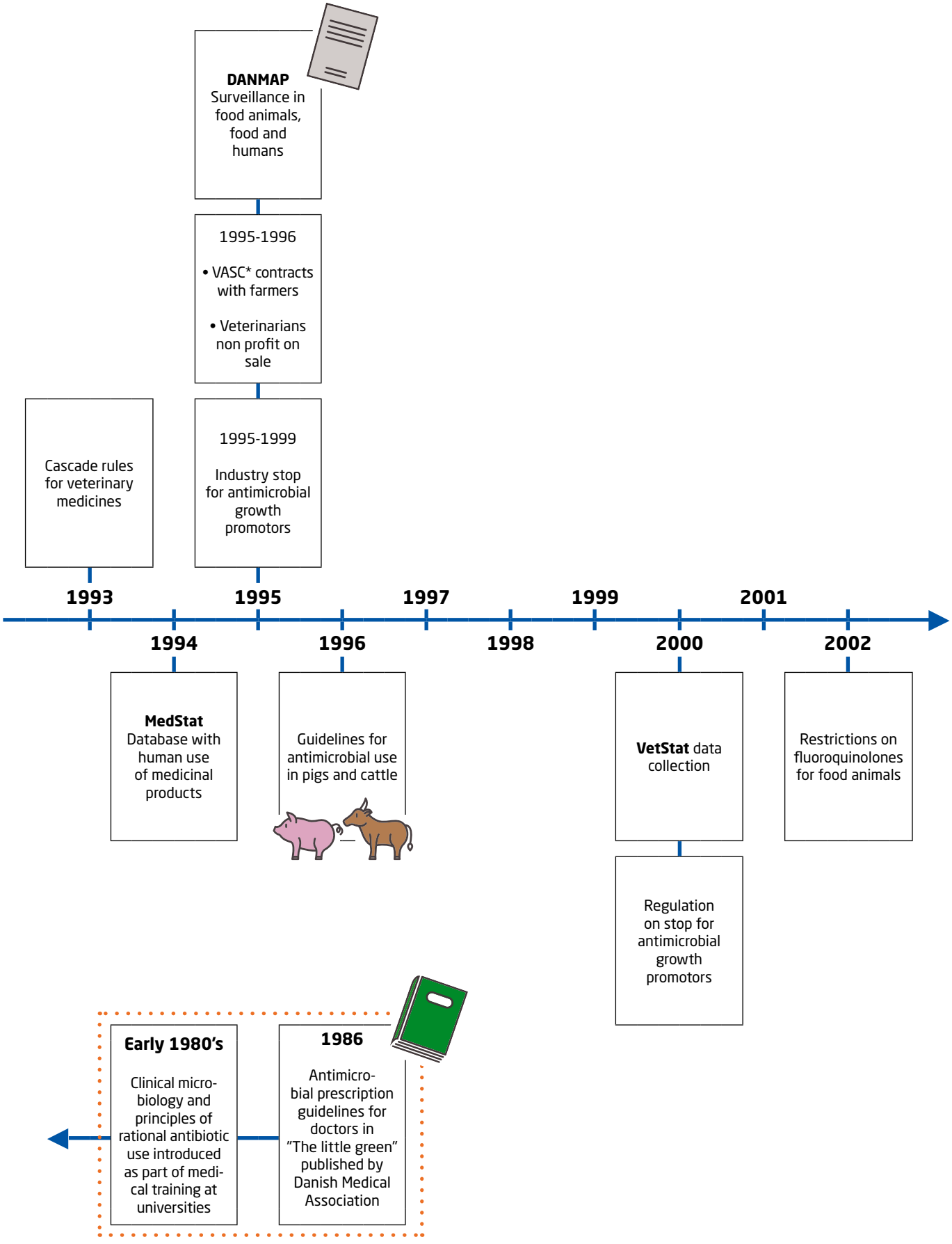

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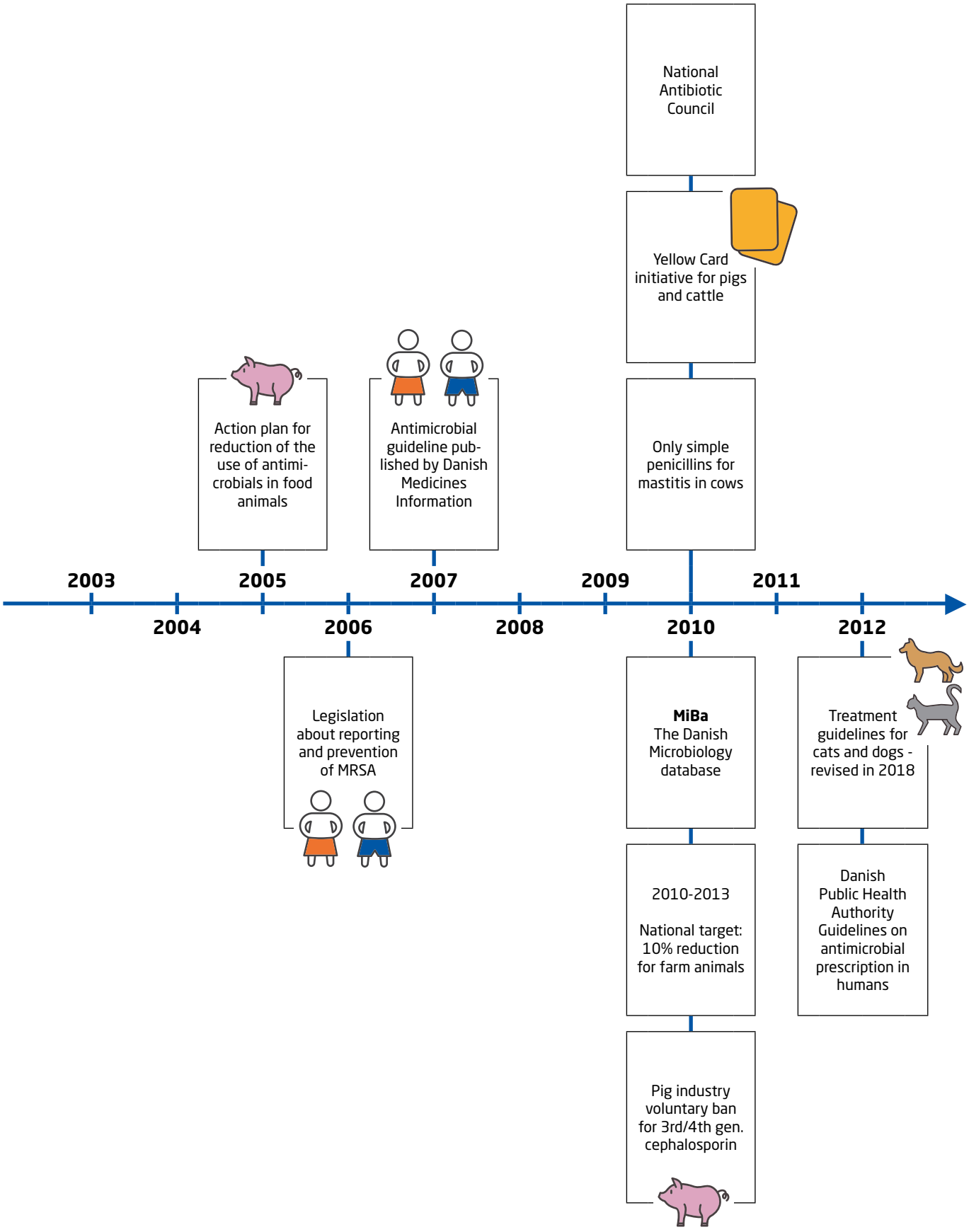
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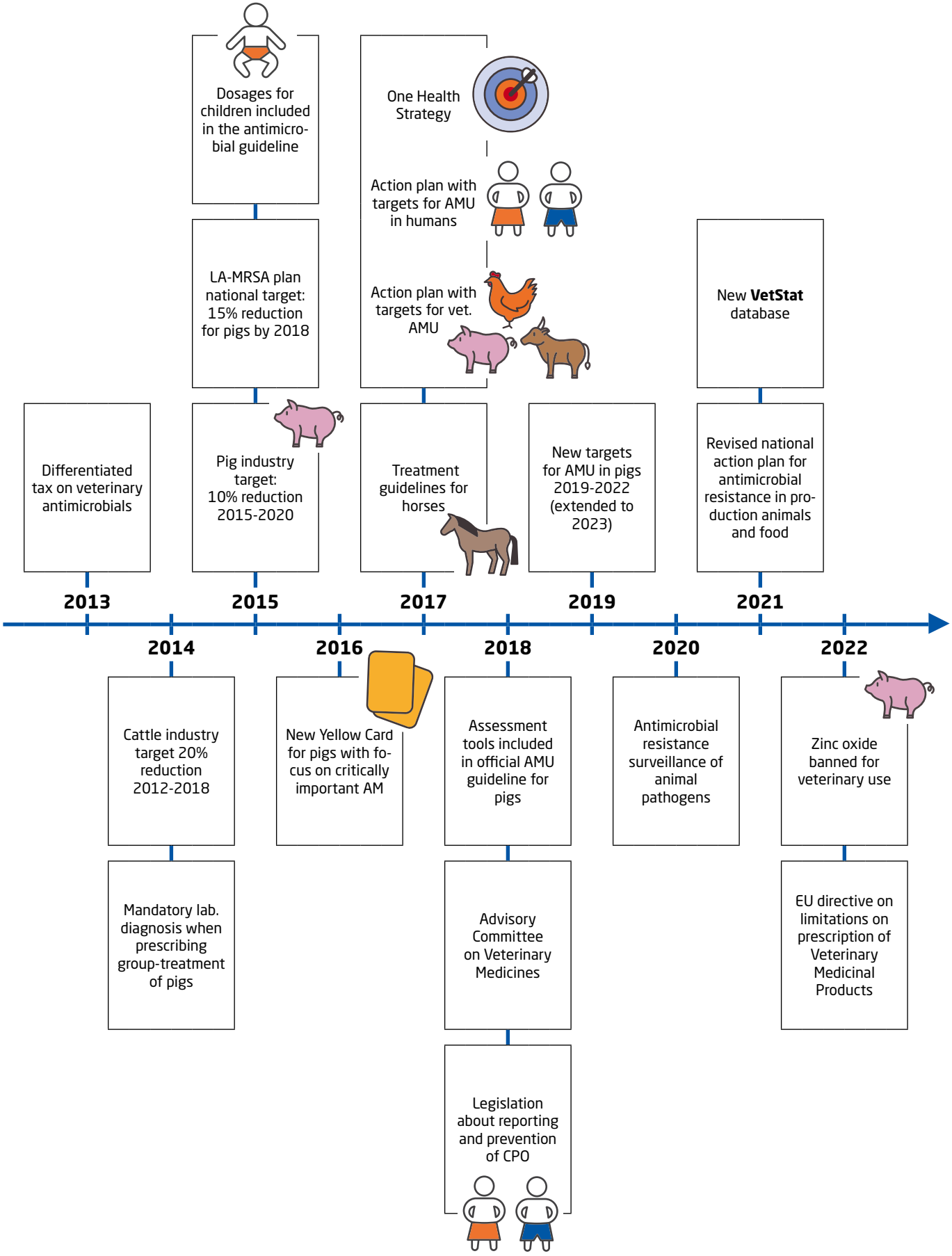
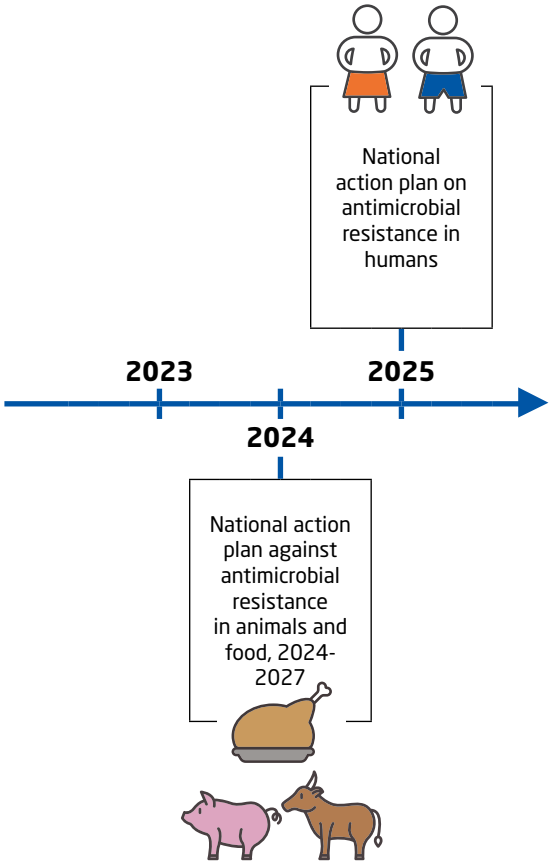



National action plan on antimicrobial resistance in humans
2023
2025
2024
National action plan against antimicrobial resistance in animals and food, 2024-2027

1. Editorial

In 2024, the UN General Assembly called for joining forces and increasing efforts in combatting antimicrobial resistance (AMR) worldwide. World leaders understood that AMR is not only one of the biggest threats to public health and economy, it is also a problem that needs to be addressed and tackled in a cross-sectoral approach - between human health, animal health and the environmental sector. In particular, it was understood that it was time to move from knowledge-gathering to implementation.

In Denmark, the Danish Veterinary and Food Administration unveiled its third National Action Plan Against AMR in Animals and Food in September 2024. The plan aligns with international frameworks such as the WHO's Global Action Plan and the EU's One Health Strategy, while also responding to Denmark's own political agreements, including the 2024 Food and Veterinary Agreement.

The action plan builds on continuing efforts from former action plans from 2017 and 2021. It is structured around four strategic pillars and describes 22 concrete actions. First, it aims at strengthening surveillance of AMR in food production systems by continued integration of whole genome sequencing (WGS), supporting evidence-based decision-making in the veterinary sector. Second, it continues promoting responsible antibiotic use in livestock through regulatory refinement, enhanced veterinary supervision, and incentives for reduced consumption. Third, it advances targeted communication strategies to support informed choices among veterinarians and producers, including updated treatment guidelines and public information campaigns. Finally, it prioritizes national and international collaboration, among these Denmark's participation in Nordic and EU joint actions and research activities, and the fostering of cross-sectoral coordination and science implementation, on a global scale.

In June 2025, the Danish Ministry of the Interior and Health published its second national action plan for the fight of antimicrobial resistance in humans. The action plan provides a broad framework for the Danish efforts to promote rational use of antimicrobials and to prevent antimicrobial resistance within four focus areas: (1) fighting and reducing AMR, (2) better access to antimicrobials, (3) infection prevention and control and (4) international engagement. For each area, overarching political objectives and monitoring indicators are set to track progress towards the objectives. In total, 21 initiatives are suggested as concrete steps to work with the action in practice. The new action plan shifts to focus on positive progress measured by specific indicators rather than reaching predefined goals. The ambition is to promote sustainable change that ultimately will strengthen rational use of antimicrobials and combat antimicrobial resistance in the long term.

Both action plans address the need for joint actions and call for the development of a new national One Health AMR strategy.

From the technical level, a wish for a cross-spanning committee to cover and follow One Health actions has been uttered but not yet fulfilled.

Denmark is fortunate in many ways. The political system is built on mutual trust and close collaboration between politicians, policy makers, and executors. The health care system is characterized by short distance to high quality treatment. The surveillance is based on long-standing registers and robust data infrastructure. Despite this and close to 30 years of surveillance, DANMAP 2024 detects and presents areas that need increased focus and awareness such as the recent development and changes in antibiotic usage in pig production and the continued high usage of combination penicillins in humans with a simultaneous rise in resistance towards piperacillin-tazobactam in the monitored invasive bacterial species.

The DANMAP monitoring programme plays a pivotal role in operationalizing the strategic pillars from both action plans. By expanding the reporting of WGS results in recent years, DANMAP has enhanced its surveillance infrastructure and supports evidence-based risk assessment. The broadened scope to expand surveillance on AMR in animal pathogens and report antimicrobial use at the active compound level and in specific subgroups provides granular insights essential for regulatory refinement and targeted interventions. DANMAP also tracks antibiotic use trends in relation to specific reduction targets and evaluates the impact of implemented control measures, thereby informing policy and practice. Furthermore, its data and expertise contribute to awareness campaigns and the development of updated treatment guidelines, reinforcing informed decision-making among prescribers and producers. Internationally, DANMAP's participation in EU, Nordic, DANIDA and Strategic Sector Collaboration (SSC) AMR-related projects, along with its integration into national intersectoral coordination mechanisms, ensures that Denmark's efforts are both globally aligned and domestically coherent, advancing the One Health agenda through collaborative, data-driven action.

Despite the efforts DANMAP has not been able to monitor antibiotic usage at production site or patient level, a necessity if the impact and results from antimicrobial stewardship-programmes are to be followed and evaluated. It should also be questioned if DANMAP properly detects and describes AMR levels in healthy individuals or in certain population groups such as inhabitants of nursing homes. On the food production side there is a wish for following development of AMR in diseased animals more closely than today.

Next year DANMAP will celebrate its 30th birthday. There is much to be proud of, but also plenty to do. Let´s keep it this way!

The DANMAP team

Textbox 1.1

National action plan on antimicrobial resistance in humans

Minister's foreword
Antimicrobials are essential for the functioning of modern healthcare systems. They allow us to treat commonly occurring infections, perform essential medical procedures and utilize advanced therapies. The emergence of antimicrobial resistance therefore poses a threat to modern healthcare.

Concerted day-to-day efforts by healthcare professionals have successfully reduced the consumption of antibiotics in Denmark. Their work has been supported by national initiatives such as DANMAP, strengthened infectious disease surveillance and preparedness in accordance with the recommendations in the *Joint action plan on antibiotics and resistance* from 2010. In 2017, three goals for antimicrobial consumption followed in the *National action plan for antibiotics for humans*. Yet, resistance rates are rising, nationally and in particular globally. Antimicrobial shortages are increasingly frequent. The situation calls for action and political leadership to curb this worrying development.

Therefore, I am proud to have presented a new Danish *National action plan on antimicrobial resistance in humans* in June 2025. The action plan is the result of an agreement between the Danish Government and all parties of the Danish parliament underlining a broad political commitment to combatting antimicrobial resistance in Denmark and allocating a total of DKK 130 million from 2025-2028 to AMR initiatives.

The national action plan broadens the scope of Danish efforts to combat antimicrobial resistance in humans by strengthening four central priority areas: (1) antimicrobial stewardship, (2) access to antimicrobials, (3) infection prevention and control and (4) international engagement. Each priority area contains an overarching political objective and a number of underlying indicators to monitor overall progress towards reaching the political objective. In total, 21 initiatives provide concrete steps to achieving the political objective of ultimately contributing to combatting the development and spread of antimicrobial resistance.

Sophie Løhde,
Minister of the Interior and Health

Antimicrobial stewardship
Inappropriate use of antimicrobial drugs is a key driver of antimicrobial resistance. Reducing and rationalizing our consumption of antimicrobials must therefore be an integrated part of any effort to hinder the development of antimicrobial resistance. We therefore commit to reducing the use of antimicrobials and prioritising antimicrobials associated with a lower risk of resistance development by:

1) Strengthening cooperation on infection prevention and control and the rational use of antibiotics between hospitals and municipalities, general practitioners and practising specialists.
2) Strengthening diagnostics through a research-based pilot project developed in a public-private partnership to generate knowledge on how rapid point-of-care diagnostics can be implemented in primary care.
3) Assessing the need for prescription requirements for topical antimicrobials currently available over the counter to promote rational use.
4) Adjusting the packaging of antimicrobials to ensure greater alignment with treatment guidelines and updated package leaflets.
5) Improving quality in general practice through a cluster package on the rational use of antimicrobials for within clusters practice.

Access to antimicrobials
Measures to ensure antimicrobial stewardship necessitates access to the appropriate antimicrobials. Limited availability and shortages may lead clinicians to resort to less suitable alternatives and hinder the proliferation of stewardship efforts. We therefore commit to working to ensure a more stable and improved supply of antimicrobials by:

6) Exploring the potential for participating in an innovative joint European procurement model to safeguard access to essential antibiotics.
7) Strengthening Nordic cooperation on the development of a joint procurement model to improve the availability of narrow-spectrum antibiotics that are particularly used in Denmark and the rest of the Nordic region.
8) Exempting antimicrobials from annual fees to the Danish Medicines Agency to remove unnecessary barriers to marketing and keep antimicrobials on the market in Denmark.

Infection prevention and control

Preventing infections reduces the underlying need to prescribe antimicrobials, thereby slowing the development of antimicrobial resistance. We already know that vaccines and basic hygiene are cost-effective infection prevention and control measures. We therefore commit to combating any upward trend and working towards a reduction in the level of infections requiring treatment by:

9) Strengthening training in hygiene and infection prevention and control by developing new educational materials on hygiene and infection prevention
10) Conducting a Health Technology Assessment (HTA) of pneumococcal vaccination to provide a well-founded basis for decisions on a potential public vaccination programme.
11) Introducing antimicrobial resistance as a parameter in the Danish Health Authority's future professional assessments of vaccine effectiveness
12) Simplifying guidance materials to streamline and support staff in their infection prevention and control efforts
13) Improving general practitioners' access to the Danish Vaccination Register (DDV) to enhance citizens' access to vaccines with conditional reimbursement.

International engagement

The fight against antimicrobial is a global issue. The movement of people and goods contribute to cross-border spread of antimicrobial resistance. Denmark have extensive experience in fighting antimicrobial resistance. We therefore commit to strengthening Denmark's international engagement and contribution to global efforts against antimicrobial resistance by:

14) Actively applying Danish knowledge and experience to support initiatives to combat AMR in both bilateral and multilateral partnerships.
15) Appointing a *High-Level Representative* to promote Danish solutions, participate in international forums and influence the global AMR agenda.
16) Providing financial support to the International Centre for Antimicrobial Resistance (ICARS) to sustain its ongoing work with low- and middle- income countries in developing evidence-based and sustainable AMR solutions adapted to local contexts.
17) Supporting the scaling up of the DTU National Food Institute's engagement as a WHO Collaborating Centre to strengthen Danish research-based advisory capacity and global capacity building.

In addition to the four priority areas, the action plan includes a number of cross-cutting initiatives aimed at supporting the national action plan's overall objective of combatting antimicrobial resistance by:

18) Establishing a national AMR advisory group where stakeholders involved in the implementation of the action plan can meet and exchange experiences to support broad societal anchoring.
19) Continuously monitoring the objectives of the action plan to provide the necessary knowledge base for future decision-making in the AMR area.
20) Promoting further research in AMR to generate new knowledge that can form an important foundation for future efforts to combat anti-microbial resistance.
21) Designing awareness and information campaigns on AMR targeting both the public and healthcare professionals.

For further information: sum@sum.dk

Textbox 1.2

National action plan against antimicrobial resistance in animals and food 2024-2027

In September 2024, a new national action plan against antimicrobial resistance (AMR) in animals and food was launched by the Danish Veterinary and Food Administration (DVFA). This is the third national action plan from the DVFA and it continues the efforts against AMR in the period 2024-2027. The vision for the action plan is to prevent the occurrence of resistant micro-organisms in animals and food in order to ensure effective treatment of microbial infections in humans and animals. This will be facilitated by a number of initiatives, under four focus areas:

- Strengthened Monitoring with a One Health Perspective
- Healthy Livestock with a Prudent and Low Consumption of Antibiotics
- Targeted Communication in order to Contribute to Informed Choices
- National and International Cooperation as High Priorities

The initiatives relate to antimicrobial consumption, antimicrobial resistance, and biosecurity:
The DVFA will continue to monitor antimicrobial use in animals and resistance in food and animals with a continuous focus on ensuring data of high quality. This will include implementation of new requirements by the EU, to report the use of antimicrobial medicines for animals at species level (Textbox 4.1).

Good biosecurity is important to keep livestock healthy. The DVFA has launched a project on biosecurity, which, amongst other things, will go through legislation in the area and make knowledge more accessible to the public.

In accordance with the Food and Veterinary Agreement, the action plan aims to support reducing the consumption of antibiotics in pigs, by 2027, to a politically agreed target of an 8% reduction based on the 2018 level.

A new focus area in the action plan is targeted communication. One of the first initiatives will be to improve and consolidate information about AMR on the DVFA website.

The DVFA continues to share experiences with other authorities and organisations, while also learning from other countries that have found good solutions in the fight against AMR. This is done through active participation in international forums on AMR.

The full list of initiatives can be found in the official National Action plan, which is available at the DVFA website (www.fvst.dk).

The joint AMR group at the Danish Veterinary and Food Administration
For further information: 15@fvst.dk

Acknowledgements

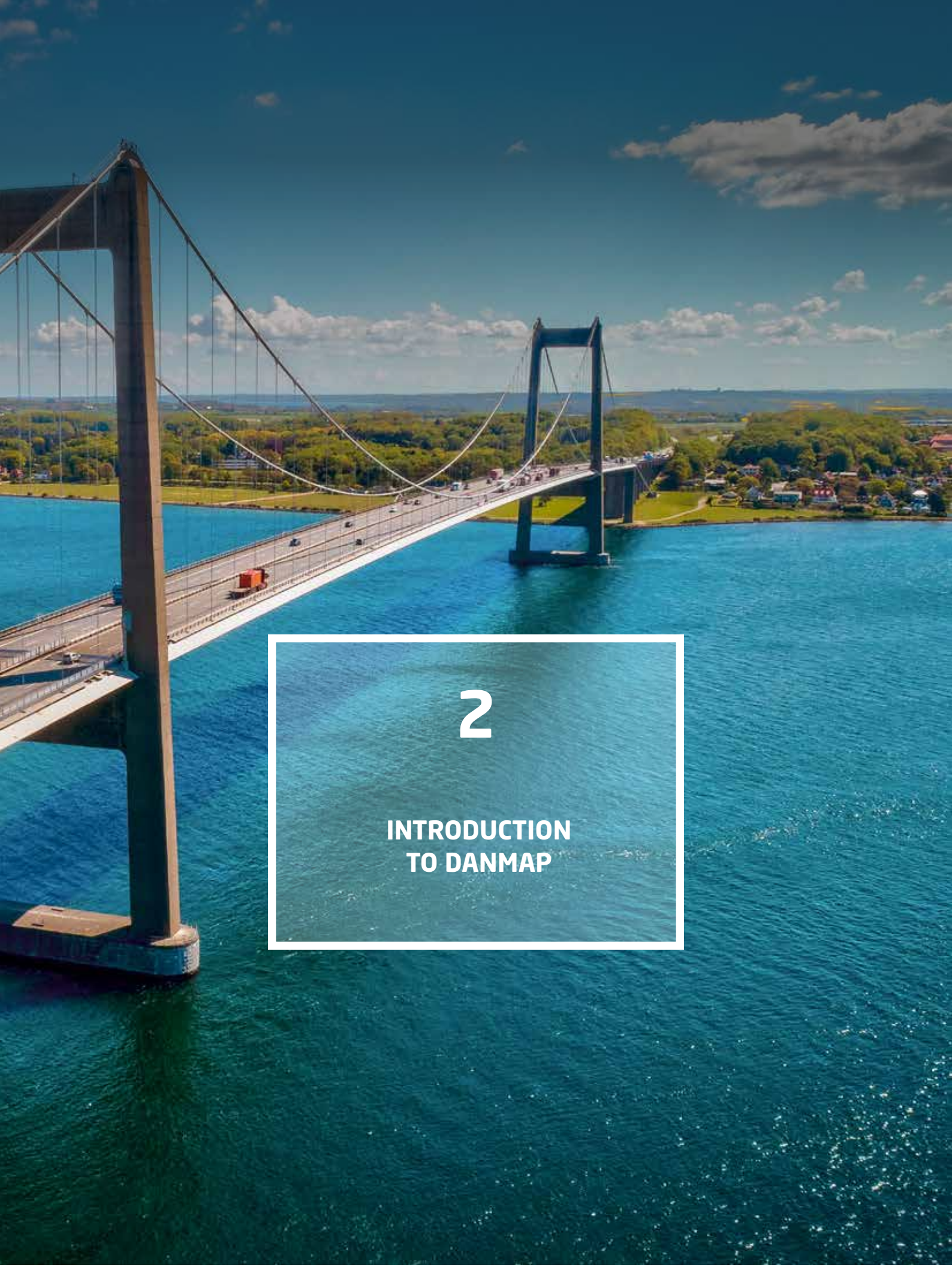
DANMAP is based on a strong collaboration between several institutions and on the contributions from highly skilled staff from many specialties and professions. Without their knowledge and engagement, there would be no DANMAP surveillance.

The DTU National Food Institute would like to thank the following:

- The meat inspection staff and company personnel at the participating slaughterhouses for collecting samples from animals at slaughter
- The staff of local Veterinary and Food inspections units for collecting food and animal samples
- The staff of the Danish Veterinary and Food Administration's Laboratory, Ringsted for analysing animal and food samples
- The Danish Veterinary and Food Administration's Food and Feed Safety Division, for collecting and transmitting data on antimicrobial resistance in food and animal samples and for discussing data interpretation
- The Danish Veterinary and Food Administration's Animal Medicine and Veterinary Trade Division, for collecting and transmitting data on veterinary consumption of antimicrobial agents from VetStat and discussing the interpretation of the data
- Colleagues at the National Food Institute, DTU, for valuable discussions on many topics related to the report
- All data providers for textboxes and textbox authors

Statens Serum Institut would like to thank the following:

- The Departments of Clinical Microbiology and the DANRES group - Danish Study Group for Antimicrobial Resistance Surveillance - for providing data on resistance in bacteria from human clinical samples and discussing many of the topics included in the report
- The staff of the Neisseria and Streptococcus Typing Unit at SSI for providing data on samples and resistance in beta-haemolytic streptococci, *H. influenzae* and *Neisseria gonorrhoeae*
- The staff of the Foodborne Pathogens Unit at SSI for providing data on resistance in *Campylobacter* and *Salmonella* from human clinical isolates
- The staff of the Staphylococcus Laboratory at SSI for providing data on invasive staphylococcal infections as well as all MRSA
- The staff of the Antimicrobial Resistance Reference Laboratory and Surveillance Unit at SSI for providing data on resistance in the referred *E. coli*, *K. pneumoniae*, *A. baumannii*, *P. aeruginosa* and vancomycin and linezolid-resistant enterococci
- The staff at the Unit of Mycology at SSI for providing resistance data for human *Candida* and *Aspergillus*
- Colleagues at the Infectious Disease Epidemiology & Prevention Unit at SSI
- Colleagues at the Data Integration and Analysis Secretariat at SSI
- The Danish Health Data Authority and the Register of Medicinal Products Statistics for providing data on antimicrobial consumption on healthcare activity
- All Danish hospital pharmacies for providing data on antimicrobials consumed at hospitals through special deliverances



2

INTRODUCTION TO DANMAP

2. Introduction to DANMAP

2.1 The DANMAP surveillance system

DANMAP is a surveillance system with five key objectives:

- To establish the state-of-nation in regards to the use of antimicrobial agents in food-producing animals and humans
- To carry out surveillance of the occurrence of antimicrobial resistance in bacteria isolated from food-producing animals, food of animal origin (meat) and humans
- To identify areas for further research, e.g. antimicrobial resistance transmission or possible associations between antimicrobial consumption and antimicrobial resistance
- To deliver data to veterinarians, medical doctors and other health professionals for the development of antibiotic treatment guidelines
- To act as a knowledge base for authorities, academia and politicians when performing risk assessment and management, thus supporting decision making in the prevention and control of resistant bacterial infections

Since 2021, DANMAP also provides an integrated analysis of resistance in bacteria from humans and food animals.

The monitoring programme was initially developed in 1995 by researchers, based on frequent discussions and exchange of knowledge and results from research. Since then, DANMAP has evolved into a governmentally supported programme.

However, much of the design of the programme, including participation of the human laboratories and referral of strains is based on a voluntary principle.

DANMAP surveillance relies on four equally important components: well-established and well-functioning diagnostic systems, well-designed and representative surveys, reliable registers as well as mutual trust and openness between all collaborators.

A positive effect of the regular meetings and exchange between stakeholders is that these prove helpful in other aspects, for example, by contributing to a common knowledge pool regarding laboratory methods. This ensures and contributes to continuous improvements and harmonisation of the laboratory work. Meetings across sectors and between different stakeholders also contribute to a better mutual understanding, facilitating development and work towards mutual goals.

Surveillance is a complex undertaking and DANMAP encompasses many different surveillance components and covers resistance in different populations and contexts.

These categories of bacteria are included in DANMAP:

- Human clinical isolates to reflect the antimicrobial resistance levels in the human population that seeks medical care
- Foodborne zoonotic bacteria along the whole farm-to-patient chain to monitor the levels of antimicrobial resistance in shared pathogens
- Indicator bacteria from healthy food-producing animals to monitor status of antimicrobial resistance in the animal reservoirs
- Clinical isolates from sick food-producing animals to monitor resistance

The National Food Institute at the Technical University of Denmark (DTU) and the National AMR reference laboratory at Statens Serum Institut (SSI) are responsible for data interpretation and output communication mainly via the annual DANMAP report and seminar. Interpretations are independent of policy, risk management and private industries.

The DANMAP programme is funded jointly by the Ministry of Health and the Ministry of Food, Agriculture and Fisheries. Support from the ministries has also helped build the databases and maintaining the registers, which the current surveillance system relies upon.

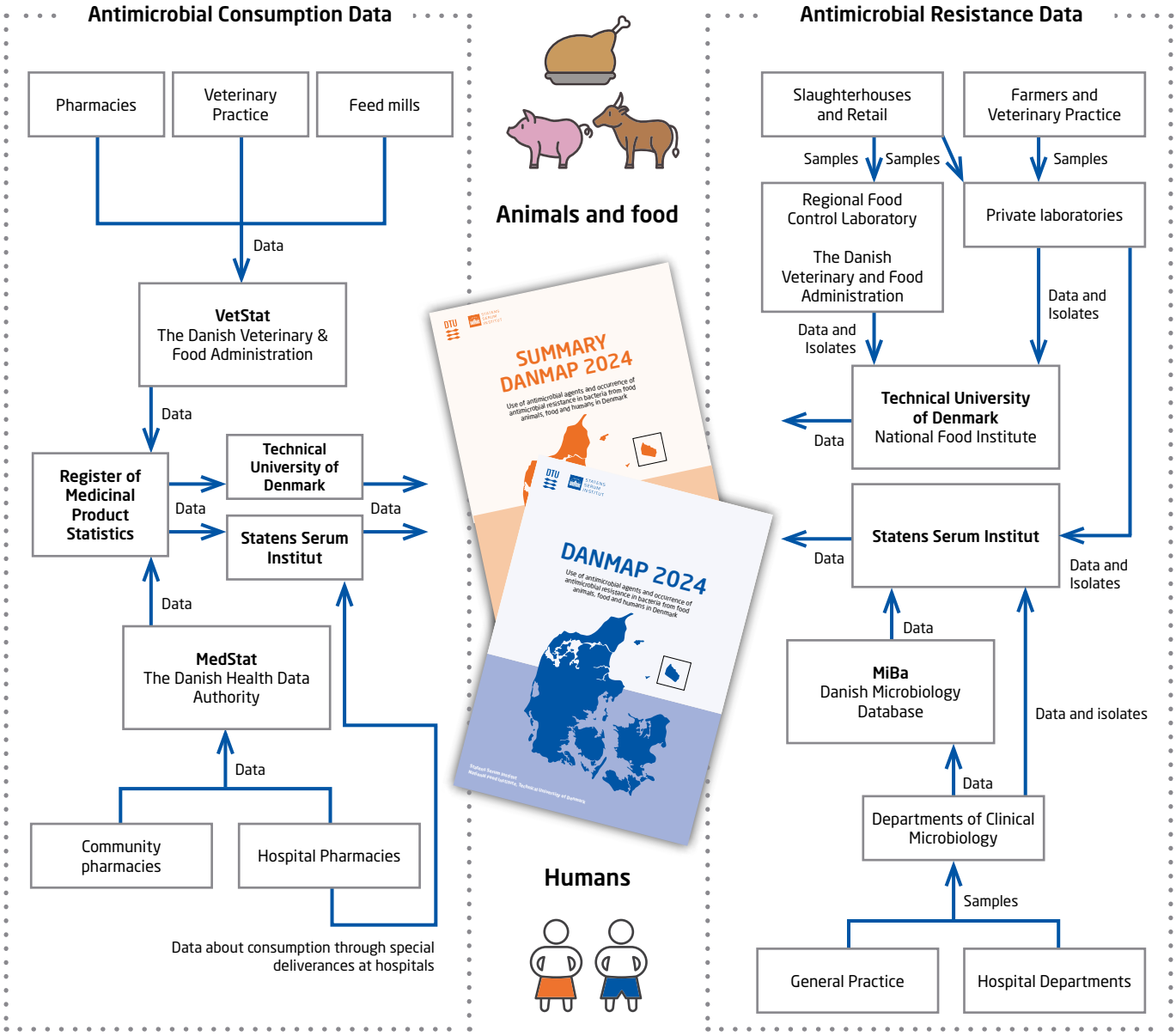
For further information on the development and history of DANMAP, please read Chapter 2, "DANMAP – A 20 year perspective" in DANMAP 2015 and Chapter 1, "DANMAP - the beginning" in DANMAP 2020.

Organisation and data flow

Since 1995, a main purpose of DANMAP has been to monitor the entire chain from farm to fork to patient. The organisation and collection of DANMAP data and the interdisciplinary collaboration between sectors and organisations is presented in Figure 2.1.

The introduction of whole genome sequencing (WGS) has been a big step forward for surveillance purposes and in outbreak situations and has become routine standard in many clinical laboratories and most reference laboratories. However, phenotypical testing is still considered relevant, more feasible, cheaper and sometimes faster, especially in a clinical setting. Phenotypical testing also continues to be used in combination with WGS to describe and determine which resistance genes are relevant to look for when using molecular analysis. Furthermore, it complies with EU regulations in food and animal testing.

Figure 2.1 Organisation DANMAP regarding data and data flow DANMAP 2024



Bacterial isolates from food, food animals and humans are submitted to the Regional Food Control Laboratory or occasionally the Technical University of Denmark and Statens Serum Institut, respectively, for further phenotypic and genotypic characterisation (Figure 2.1). The choice of the methods in surveying different bacteria and infections is described in more detail in the different chapters and sections of the report.

Figure 2.2 The five Danish healthcare regions and their respective population distributions. In addition, the ten DCMs are marked by black dots. The grey dot indicates the national reference laboratories (NRL) situated at Statens Serum Institut DANMAP 2024

North Denmark Region

No. of inhabitants	593,135
No. of inhabitants/km^2	75
No. of inhabitants/GP	1,803

Central Denmark Region

No. of inhabitants	1,365,688
No. of inhabitants/km^2	105
No. of inhabitants/GP	1,692

Capital Region of Denmark

No. of inhabitants	1,911,067
No. of inhabitants/km^2	745
No. of inhabitants/GP	1,784

Region Zealand

No. of inhabitants	852,953
No. of inhabitants/km^2	118
No. of inhabitants/GP	1,925

Region of Southern Denmark

No. of inhabitants	1,238,406
No. of inhabitants/km^2	101
No. of inhabitants/GP	4,627

GP = General Practioner
DCM = Department of Clinical Microbiology
NRL = National Reference Laboratories

Data source: Statistics Denmark [www.dst.dk] and the Danish Medical Association [www.laeger.dk]

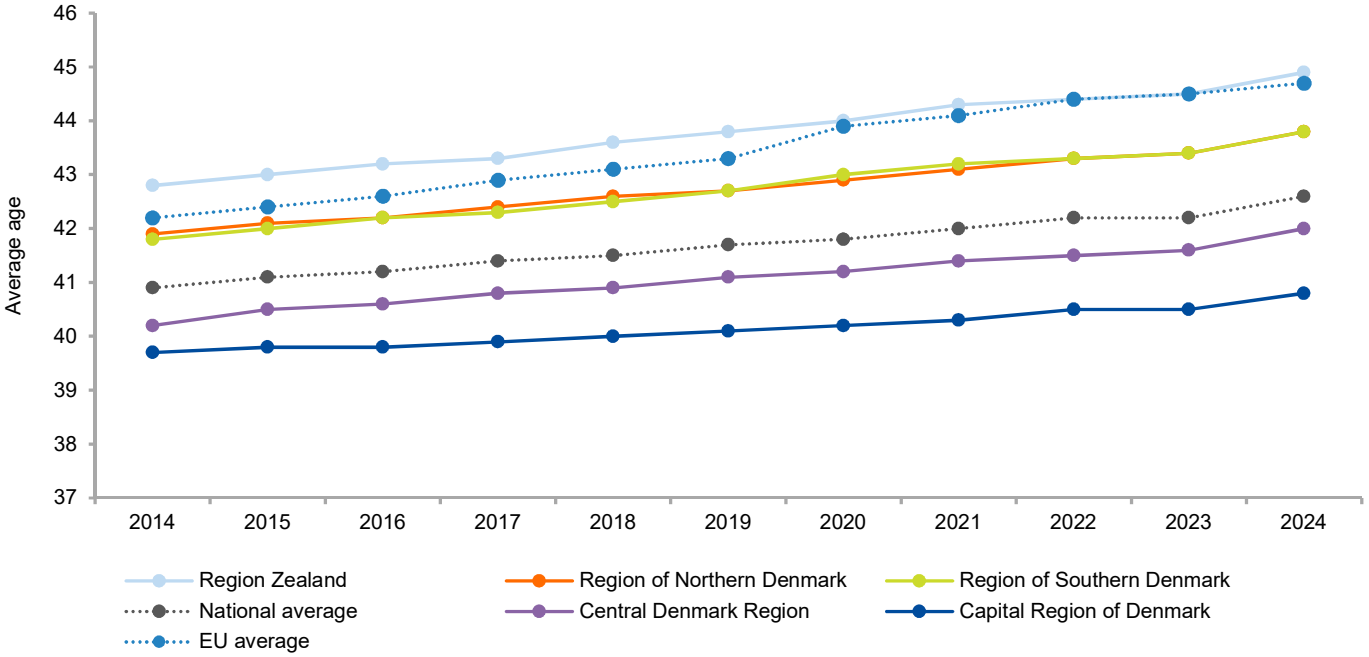
2.2 Information on demographics and health care system

During the past 29 years, the human population in Denmark has increased from approximately 5.2 million inhabitants in 1995 to 5.9 million in 2024 [www.dst.dk]. Simultaneously, the average age has increased gradually. In 2023, the national average age was 42.6 years. The population and the respective regional distribution, in 2024, is presented in Figure 2.2, while regional differences and changes in age are presented in Figure 2.3.

In Denmark, microbiological analyses are carried out by ten hospital departments of clinical microbiology (DCMs) situated at the main regional hospitals, Figure 2.2. The analyses performed cover all samples from public hospitals and most samples from general practitioners (GPs). In addition, some GPs perform culturing of urinary samples from their patients. In the Capital Region of Denmark one private laboratory also performs additional analyses for the GPs.

Data on regional and national health care activity at hospitals in 2015 and 2024 are presented in Table 2.1. Denmark has a very high bed occupancy rate at hospitals and can reach maximum capacity during winter time for example due to high influenza activity. In 2024, the number of admissions at Danish somatic hospitals was registered to be 668.894 and the number of bed-days was registered to be 2,715,304. From 2015-2024, the number of bed-days decreased by 23%, the number of admissions decreased by 7% whereas the Danish population grew by 7%.

Figure 2.3 Changes in average age, Denmark and EU, 2014-2024 DANMAP 2024



Data source: Statistics Denmark and Eurostat

Table 2.1 Activity at Danish hospitals, 2015 and 2024 DANMAP 2024

Region	Number of bed-days in somatic hospitals		Number of admission to somatic hospitals		Population	
	2015	2024	2015	2024	2015	2024
Capital Region of Denmark	1,354,297	876,497	257,193	220,471	1,768,125	1,911,067
Region Zealand	467,371	417,273	101,340	99,084	820,480	852,953
Region of Southern Denmark	699,947	548,765	153,851	137,747	1,205,728	1,238,406
Central Denmark Region	658,707	571,220	157,093	142,954	1,282,750	1,365,688
North Denmark Region	336,936	301,549	69,618	68,638	582,632	593,135
Denmark	3,517,259	2,715,304	739,095	668,894	5,659,715	5,961,249

Data: Activity at somatic hospitals
Data source: The National Patient Register

2.3 Information on animal population and food production system

Denmark is an agricultural country, with more than half of its area managed by the agricultural sector. Approximately 25% of Danish agricultural enterprises are specialized in livestock production, focusing primarily on pigs, cattle, and chickens. The agricultural sector contributed around 22% of Denmark's total goods exports in 2023. Danish Agriculture & Food Council. Denmark - a Food and Farming Country: Facts & Figures 2023. https://agricultureandfood.dk/media/m1qfuuju/lf-facts-and-figures-2023.pdf.

The production of food-producing animals as well as the production of meat and milk are presented in Table 2.2 and 2.3.

Table 2.2 Production (1,000 heads) of food animals, Denmark, 2015-2024 DANMAP 2024

	Pigs		Cattle		Poultry	
Year	Total	Exported [a]	Slaughter cattle	Dairy cows	Broilers	Turkeys [b]
2015	30874	12133	511	561	119152	1051
2016	31660	13280	540	572	120359	1095
2017	31662	14173	509	570	122854	841
2018	32571	14449	533	575	130626	602
2019	31694	14897	518	567	127642	356
2020	32018	14736	500	567	122748	455
2021	32649	14096	506	564	123189	306
2022	31681	13867	506	557	116035	443
2023	29353	14865	499	547	121968	395
2024	30706	16452	490	547	121361	394

Source: Statistics Denmark. Export data for poultry from Statistics Denmark, personal communication until 2022 and from www.dst.dk from 2023
a) Export of live pigs. These are included in total number of heads
b) Since 2006, more than 99% of the turkeys have been exported for slaughter

Table 2.3 Production (mill kg) of meat, milk and fish, Denmark, 2015-2024 DANMAP 2024

						Farmed fish [c]	
Year	Pork	Beef	Broiler meat [a]	Turkey meat	Milk [b]	Land based	Marine net ponds
2015	1954	135	197	15	5744	36	16
2016	1943	142	177	16	5892	36	12
2017	1896	135	185	13	6088	37	14
2018	1967	142	219	9	6305	38	14
2019	1864	137	205	5	6323	41	14
2020	1952	133	201	7	6394	36	11
2021	2066	134	203	4	6390	37	12
2022	1957	131	193	7	6392	32	14
2023	1663	130	203	6	6377	30	14
2024	1743	126	200	6	6325	-	-

Source: Statistics Denmark. Export data for poultry from Statistics Denmark, personal communication until 2022 and from www.dst.dk from 2023
a) Average weight after slaughter for poultry from Statistics Denmark, personal communication until 2022. In 2022, a final slaughtered weight of 1.74 kg per broiler produced and 12.93 kg per turkey produced was estimated. The same weight estimates were used in 2024
b) Conventional and organic
c) The numbers for 2024 are not final. Data are based on accounts statistics for aquaculture. The production of farmed fish includes fish transferred from one production facility to another

2.4 Registered antimicrobial agents

Table 2.4 shows the antimicrobial agents registered to treat bacterial infections in humans and animals. Some of these are listed on the highest priority list of medically important antimicrobials for the treatment of bacterial infections in humans, according to definitions made by the World Health Organization [WHO 2024]. In order to be considered critically important or highest priority critically important an antimicrobial class or subclass with authorized use in humans and animals must meet two criteria; 1) be the only - or one of a limited number of compounds available to treat serious human infections and 2) be used to treat infections caused by bacteria that are either possibly transmitted from non-human sources, or carry resistance genes from non-human sources.

Furthermore, when both criteria are met, two prioritization factors are applied: 1) the antimicrobial class contains at least one antimicrobial that is both on the WHO Essential Medicines List (EML) and is classified as Watch or Reserve on the AWaRe classification list; 2) the antimicrobial class is used to treat human infections, often invasive and life-threatening, for which there is extensive evidence of transmission of resistance from non-human sources. When both prioritization factors are met, the antimicrobial is Highest Priority Critically Important (HPCIA), otherwise it is classified as Critically Important (CIA). Thus, in the newest list revision from 2024, four drug classes were considered highest priority critically important: 3rd and 4th generation cephalosporins, quinolones, polymyxins and phosphonic acid derivatives. Additionally, three antimicrobial classes were considered critically important: aminoglycosides, macrolides and ansamycins. In Denmark, the use of HPCIA classes in food-producing animals has generally been absent or reduced through either voluntary or legislative restrictions, while there is some use of the CIA classes aminoglycosides and macrolides. See Chapter 4 for more information.

Furthermore, other antimicrobials may also be restricted due to national risk mitigation. For trends and preferred therapeutic choices in the antimicrobial treatment of humans, see Chapter 5.

Growth promoters are no longer used for animals in Denmark and are shown in parentheses in Table 2.4. Most of these influenced Gram-positive bacteria. Since 1995, the indicator enterococci from animals and meat have been used to monitor resistance towards former growth promoters.

Table 2.4 Antimicrobial agents registered for systemic and veterinary intramammary therapeutic use in animals and humans, Denmark DANMAP 2024

ATC / ATCvet codes [a]	Therapeutic group	Antimicrobial agents within the therapeutic groups	
		Animals	Humans
J01AA / QJ01AA, QJ51AA	Tetracyclines	Chlortetracycline, doxycycline, oxytetracycline, tetracycline	Doxycycline, lymecycline, tetracycline, tigecycline, eravacyclin
QJ01BA	Amphenicols	Florfenicol	
J01CA / QJ01CA, QJ1RC	Penicillins with extended spectrum	Ampicillin, amoxicillin,	Ampicillin, pivampicillin, amoxicillin, pivmecillinam, mecillinam, benzathin benzylpenicillin
J01CE / QJ01CE	Beta-lactamase sensitive penicillins	Benzylpenicillin, phenoxymethylpenicillin, procaine penicillin, penethamate hydroiodide, benzathin benzylpenicillin	Benzylpenicillin, phenoxymethylpenicillin
J01CF / QJ51CF, QJ51RC	Beta-lactamase resistant penicillins	Cloxacillin, nafcillin	Dicloxacillin, cloxacillin, flucloxacillin
J01CR / QJ01CR	Comb. of penicillins and beta-lactamase inhibitors	Amoxicillin/clavulanic acid	Amoxicillin/clavulanic acid, piperacillin/tazobactam
J01DB / QJ01DB, QJ51DB	First-generation cephalosporins	Cefalexin, cefadroxil, cefapirin	Cefalexin, cefazolin
J01DC	Second-generation cephalosporins		Cefuroxime
J01DD / QJ01DD, QJ51DD	Third-generation cephalosporins incl. comb. with beta-lactamase inhibitors	Cefoperazone, ceftiofur, cefovecin	Cefotaxime, ceftazidime, ceftriaxone, ceftazidime/avibactam
J01DE / QJ51DE, QJ01DE	Fourth-generation cephalosporins	Cefquinome	Cefepime
J01DF	Monobactams		Aztreonam
J01DH	Carbapenems		Meropenem, ertapenem, imipenem and cilastatin
J01DI	Fifth-generation cephalosporins incl. comb. with beta-lactamase inhibitors		Ceftaroline fosamil, ceftolozan/tazobactam, ceftobiprol, cefiderocol
J01EA	Trimethoprim and derivatives		Trimethoprim
J01EB / QJ01EQ	Short-acting sulfonamides	Sulfadimidine, sulfathiazole, sulfadiazine, sulfamerazine	Sulfamethizole
J01EE / QJ01EW, QJ51RE	Comb.of sulfonamides and trimethoprim, incl. derivatives	Sulfadiazine/trimethoprim, sulfadoxine/trimethoprim, sulfatroxazole/trimethoprim, sulfadimidine/trimethoprim, sulfamethoxazole/trimethoprim	Sulfamethoxazole/trimethoprim
J01FA / QJ01FA	Macrolides	Spiramycin, tylosin, tilmicosin, tylvalosin, tulathromycin, gamithromycin, tildipirocin	Erythromycine, roxithromycine, clarithromycine, azithromycine
J01FF / QJ01FF, QJ51FF	Lincosamides	Clindamycin, lincomycin, spectinomycin, pirlimycin	Clindamycin
QJ01XX [b]	Streptogramins	(Virginiamycin)	Framycetin
J01GB / QJ01RA, QJ01GB, QJ01RV, QJ51RG, QJ51RC, QJ51RF	Aminoglycosides	Dihydrostreptomycin, gentamicin, neomycin, apramycin, framycetin	Tobramycin, gentamicin, amikacin
J01MA / QJ01MA	Fluoroquinolones	Enrofloxacin, marbofloxacin, difloxacin, ibafloxacin, pradofloxacin, danofloxacin, orbifloxacin	Ciprofloxacin, levofloxacin, moxifloxacin
QJ01MB	Other quinolones	Oxolinic acid	
QJ01MQ [b]	Quinoxalines	(Carbadox, olaquindox)	
J01XA,A07AA / Not in ATCvet [b,c]	Glycopeptides	(Avoparcin)	Vancomycin, teicoplanin, dalbavancin
J01XB / QJ51RC [b]	Polypeptides incl. polymyxins	Colistin (bacitracin)	Colistin
J01XC	Steroid antibacterials		Fusidic acid
J01XD,P01AB / QJ01XD, QJ01RA [c]	Imidazole derivatives	Metronidazole	Metronidazole
J01XE	Nitrofurane derivatives		Nitrofurantoin
J01XX	Other antibacterials		Methenamine, linezolid, daptomycin, fosfomycin
QJ01XQ	Pleuromutilins	Tiamulin, valnemulin	
QP51AG04	Antiprotozoals, sulfonamides	Sulfaclozine	
Not in ATCvet [b]	Oligosaccharides	(Avilamycin)	
Not in ATCvet [b]	Flavofosfolipols	(Flavomycin)	

a) ATCvet codes start with a Q
b) Animal growth promoters used before 1999 are listed in parentheses
c) Intestinal antiinfectives (A07AA) and imidazole derivatives for protozoal diseases (P01AB) were, for the first time, included in DANMAP 2014, since their widespread use in the treatment of *Clostridium difficile* infections makes them belong to the most used antibiotics in human infections in Denmark

3

ONE HEALTH AMR

3. One Health AMR

3.1 Introduction

One Health is defined as a unified approach to optimize the health of people, animals and the environment, under which multiple sectors must collaborate at varying levels [www.who.int].

DANMAP was established with the aim of understanding the drivers of AMR in humans and in the livestock industry and their interconnectedness. The monitoring programme has always been considered an integrated approach to research and surveillance, but with integration taking place at the coordination level rather than at the level of data collection and management. Hence, data are stored in separate databases by the animal and human sectors, however interpretation of results is done in cooperation whenever possible. Moreover, integration happens when discussing resistance findings in indicator and pathogenic bacteria and using it as a basis for recommendations and treatment guidelines. Finally, DANMAP supports the development and definition of strategies and action plans to reduce AMR in a collaborative manner, by monitoring sector-specific targets and by fostering the dialogue between different actors and stakeholders across sectors.

However, there has always been the wish to get a more in-depth understanding of the possible relationship between the animal, food and human sectors concerning antimicrobial usage (AMU) and development of antimicrobial resistance (AMR). To be able to foresee if changes in one sector will have a possible significant impact on the other sector, it requires knowledge of the probable routes of transmission and the size and speed of transfer. This again calls for further harmonised data collection, to define common denominators and units and to be able to perform cross-analyses on data from both the veterinary and human sectors.

At the EU level, an attempt to perform cross-analysis has been made since 2015 in the JIACRA reports [JIACRA IV, 2019-2021, ECDC, EFSA, EMA; 2024]. At the national level, even in a country such as Denmark with a long-established detailed monitoring system based on stable delivery of high-quality data, there are a few challenges in the implementation of integrated data analysis. Data are collected in the animal, food and human sectors often under different premises - following different legislation, with varying sampling strategies and magnitudes.

Here we cross-analyse antimicrobial resistance data from monitoring in livestock animals, meat and humans in Denmark. We map the frequency of multi-locus sequence types (MLST) and resistance genes and mutations of extended spectrum beta-lactamase-producing *E. coli* (here abbreviated to ESBL Ec) recovered from livestock animals and meat and from humans with bloodstream infections. Several recent studies [Aziz, et al 2024. *Microbiology Spectrum*. 12. e0341523; Nadimpalli et al 2023, *Frontiers in Ecology and the Environment*. 21. 10.1002/fee.2639; Liu et al 2023. *One Health*, 16: 100518; Roer, et al. 2019. *J Antimicrob Chemother* 74(3):557- 560; Valcek, et al. 2019. *J Antimicrob Chemother* 74(8):2171- 2175] report possible zoonotic transmission of ESBL Ec, both in high-income and low- and middle-income countries, underlining the importance of monitoring the occurrence of these bacteria in animals and humans, and assessing the possibility of transfer across sectors. A very recent modelling study [Brinch et al. 2025. *Zoonotic Diseases* 5(1): 7] performed in Denmark including the ESBL Ec isolates that have also been reported in DANMAP, has contributed to the body of work that assesses the likelihood of zoonotic transmission of ESBL Ec (see Textbox 3.1).

The annual number of bloodstream infections in humans in Denmark caused by ESBL Ec decreased during the COVID-19 pandemic, but has since resurged (see Chapter 8, section 8.2.1). Among animal and food sources, a significant reduction in ESBL Ec has been observed in Danish broilers (see Chapter 7, section 7.3.1), cattle and pigs (see DANMAP 2023, Chapter 7, section 7.3.1), as well as among most domestic and imported meat (DANMAP 2023, 2024, Chapter 7, section 7.3.1) with the exception of imported broiler meat in 2024. In this chapter, we investigate possible relationships between ESBL Ec from different sources in Denmark.

Despite its undoubtful integrated nature, the DANMAP programme continues to fall short on the monitoring of antimicrobials and antimicrobial resistance in the environment, as recently reported (see DANMAP 2021, Chapter 3, Textbox 3.1). The 2024 revision of the Urban Waste Water Treatment Directive (UWWTD) is expected to foster new national environmental monitoring activities in the near future, which will hopefully strengthen the focus on AMR of the already existing national surveillance program for aquatic environment and nature (NOVANA) (see Textbox 3.2).

3.2 Genotypic comparison of ESBL/AmpC-producing *E. coli* from humans, animals and food

Since 2022 (DANMAP 2021, Chapter 3), DANMAP has compared the distributions of multi-locus sequence types (MLSTs or STs) and ESBL/AmpC genes and mutations among ESBL Ec from humans, food-producing animals and meat to identify any major overlaps between sectors suggesting a zoonotic link.

In the present report, we added new data from 2024; 89 isolates of animal origin and 146 isolates from humans, totaling a dataset of 2068 ESBL isolates from humans and animals from 2018 through 2024. The 1,300 human isolates were clinical isolates from bloodstream infections sent voluntarily from the departments of clinical microbiology to the SSI reference laboratory for antimicrobial susceptibility testing. The animal and meat isolates (broilers: 109, broiler meat: 164, cattle: 56, beef: 41, pigs: 219, pork: 50, and turkey meat: 129) stem from the

EU mandatory screening programme from healthy animals and meat products (see Chapter 10 for more information).

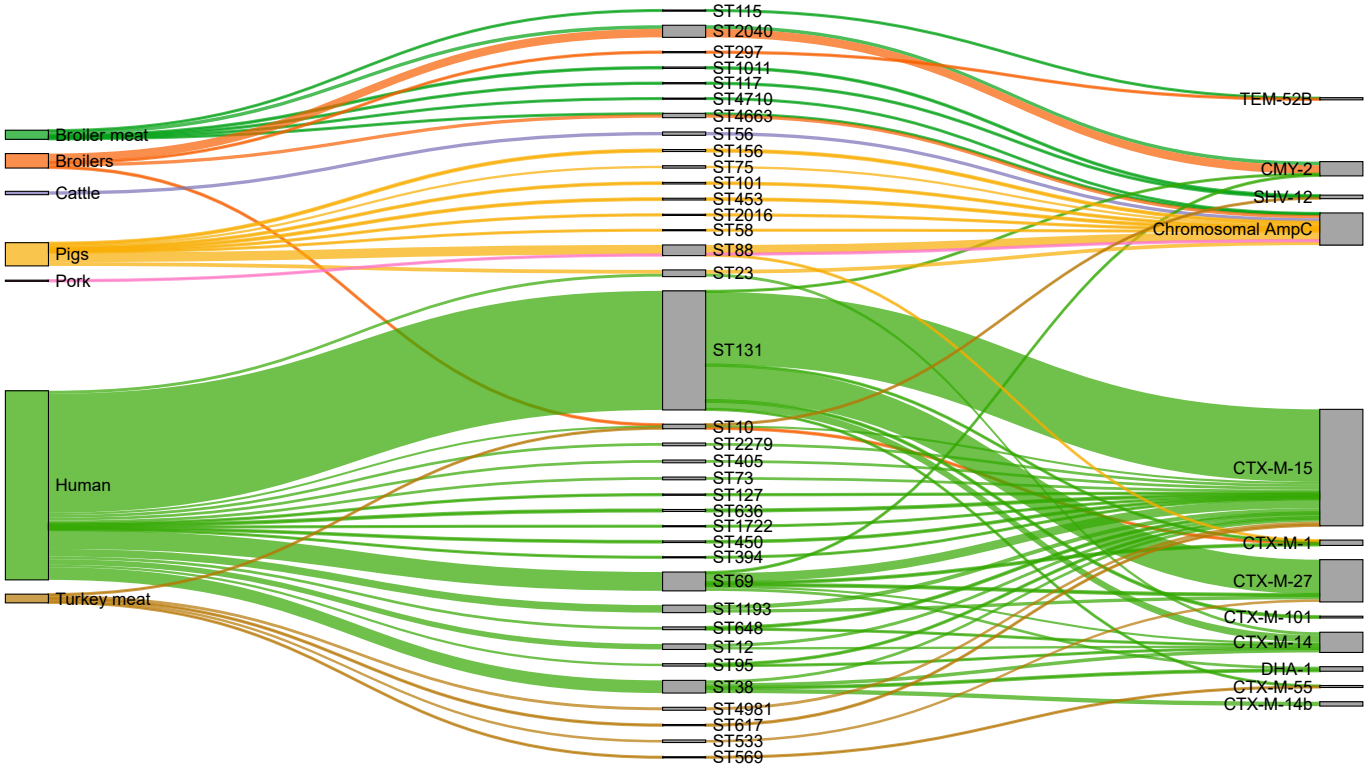
Each isolate has been sequenced as part of the surveillance activities, and the MLST and ESBL/AmpC genotype were extracted from the whole genome sequence. For an overview of sequence types and ESBL/AmpC genotypes detected in 2024 in *E. coli* from bloodstream infections, and from broilers, broiler meat and turkey meat, see Chapter 8 (Tables 8.14-16), and Chapter 7 (Table 7.3), respectively. For the purpose of the visual demonstration of the abundance of STs and resistance genes in the different reservoirs, we selected only flows of five or more isolates, thus limiting the analysis to a selection of data (Figure 3.1). The results described below refer to the selected isolates.

As in the previous years, limited overlap was found in both STs and ESBL/AmpC genes and mutations in isolates from humans vs. animals and food (Figure 3.1).

Regarding the distribution of MLSTs, one or few sequence types predominated among the isolates of each source. Isolates from humans were mostly from ST131, followed by ST69 and ST38 (see also Chapter 8, Table 8.16). The most abundant STs of animal and meat isolates were ST2040 for broilers and broiler meat, ST4981 for turkey meat, ST88 for pigs and pork, and ST56 for cattle. In accordance with former findings (see DANMAP 2015, Textbox 7.3), ST23 was found in both humans and pigs, although the ESBL/AmpC genotype differed between the human and pig strains. The pig isolates from ST23 harboured AmpC C-42T mutations, whereas the human isolates harboured the ESBL gene *CTX-M-14*. Additionally, ST10 was found in broilers, turkey meat and humans, but also harbouring different resistance mechanisms – *CTX-M-1*, *SHV-12* and *CTX-M-15*, respectively.

As observed in previous years, the AmpC plasmid-mediated gene *CMY-2*, and the ESBL genes *CTX-M-1*, *CTX-M-15*, *CTX-M-27* were found in both humans and food-producing animals or meat. Additionally, in 2024, also the ESBL genes *CTX-M-55* and *SHV-12* were detected across sectors. Interestingly, turkey meat isolates were those with the largest overlap with human isolates regarding the detected ESBL genotypes, including carriage of *CTX-M-15* and *CTX-M-27* (the two most common ESBL genes among human isolates; see also Chapter 8, Table 8.15), as well as *CTX-M-55*, although by different MLSTs.
The *CMY-2* AmpC gene was almost exclusively found among isolates from broilers and broiler meat from ST2040, but also in human isolates of ST69 and ST131. The *CTX-M-1* gene was mostly found among human isolates, but also in pig isolates of ST88 and ST10 isolates from broilers. All isolates from cattle harboured a C-42T mutation, which was not detected among the selected human isolates.

Figure 3.1 A Sankey diagram comprised of 1,272 ESBL Ec MLST-gene/mutation combinations from humans, animals and food showing the relationship between the isolates' source, sequence type and ESBL/AmpC gene or mutation DANMAP 2024



In general, sequence types seem to strongly associate with species, whereas there is more variance in combinations of STs and ESBL/AmpC genes and mutations. In the 2018 DANMAP report Textbox 7.2, Roer, et al., used whole genome sequencing on a similar, but smaller, dataset to investigate for possible zoonotic links. A possible link was found in ST69/*CTX-M-1*, but the SNP-distance was not indicative of an outbreak or a direct transmission, but rather of a clonal relationship.

In conclusion, it remains challenging to find clear evidence of zoonotic transmission of ESBL Ec between animals and humans in Denmark, within the investigated time frame of seven years, and when considering the occurrence of ESBL/AmpC genotypes in different sequence types. Further research into slow transmission over longer time spans, as well as more in-depth genomic analyses are of continued interest and on-going.

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Textbox 3.1

Understanding the spread of extended-spectrum cephalosporin-resistant *E. coli*: Insights from a dual modelling study

Background

Extended-spectrum cephalosporin-resistant *Escherichia coli* (ESC-EC) is an increasing public health concern, as it is now frequently detected not only in clinical settings but also in healthy individuals and various animal species. This study used two complementary modelling approaches to explore the spread of ESC-EC in Denmark: a compartmental model to simulate the risk of transmission in various sub-populations, and a Bayesian source attribution model to estimate the relative contribution of different sources to human infections based on genetic resistance profiles [1].

Method

The compartmental model

A compartmental model was developed to simulate ESC-EC transmission, capturing four stages of infection: susceptible, colonised, infected, and infected receiving antibiotic treatment. The Danish population was divided into three subpopulations: the general public, farmers, and pet owners, reflecting different patterns of exposure. Transmission pathways included person-to-person spread, foodborne exposure (from both domestic and imported meat), direct contact with animals such as livestock and pets, and colonisation following international travel.

Animal- and food-related exposures were quantified using an exposure indicator, which incorporated the proportion of resistant bacteria in each source, contact frequency, and the likelihood of transmission at the point of exposure, e.g., accounting for risk-reducing factors such as cooking or hygiene practices. The model estimated the total number of ESC-EC infections and evaluated the impact of individual sources by simulating scenarios in which each was removed. The additional burden of infections due to earlier antibiotic use was also assessed.

The Bayesian source attribution model

To complement the dynamic model, a Bayesian source attribution model was applied to estimate the contribution of different reservoirs to human ESC-EC infections, based on the distribution of resistance genes. The model compared the frequency of resistance gene combinations in human clinical isolates with those from isolates from various potential sources, including pets, domestic and imported food, and healthy human carriers. Data from DANMAP Chapter 3 formed the core of the dataset, supplemented with data from Swedish surveillance [2] and published literature.

Results

The compartmental model estimated a total of 61,067 ESC-EC infections annually in Denmark, with 3.2% linked to increased infection risk due to earlier antibiotic use. Human-to-human transmission was identified as the most significant pathway, and removing this route alone led to a 79% reduction in total infections. Excluding livestock sources resulted in a 59% decrease in infections, with cattle being the most influential species, responsible for 27% of the total burden. Foodborne transmission was responsible for 17% of infections; within this category, imported meat contributed more substantially than domestically produced meat. Pets, particularly dogs, accounted for 9% of infections. In contrast, colonisation via returning international travellers had only a modest impact, with their exclusion reducing total infections by just 3%.

In total, 2,696 *E. coli* isolates were included in the source attribution analysis: 1,295 from clinical cases, 265 from healthy colonised individuals, and 1,136 from non-human sources. A total of 101 distinct resistance gene combinations were identified, 21 of which were shared between infected humans and at least one of the different sources.

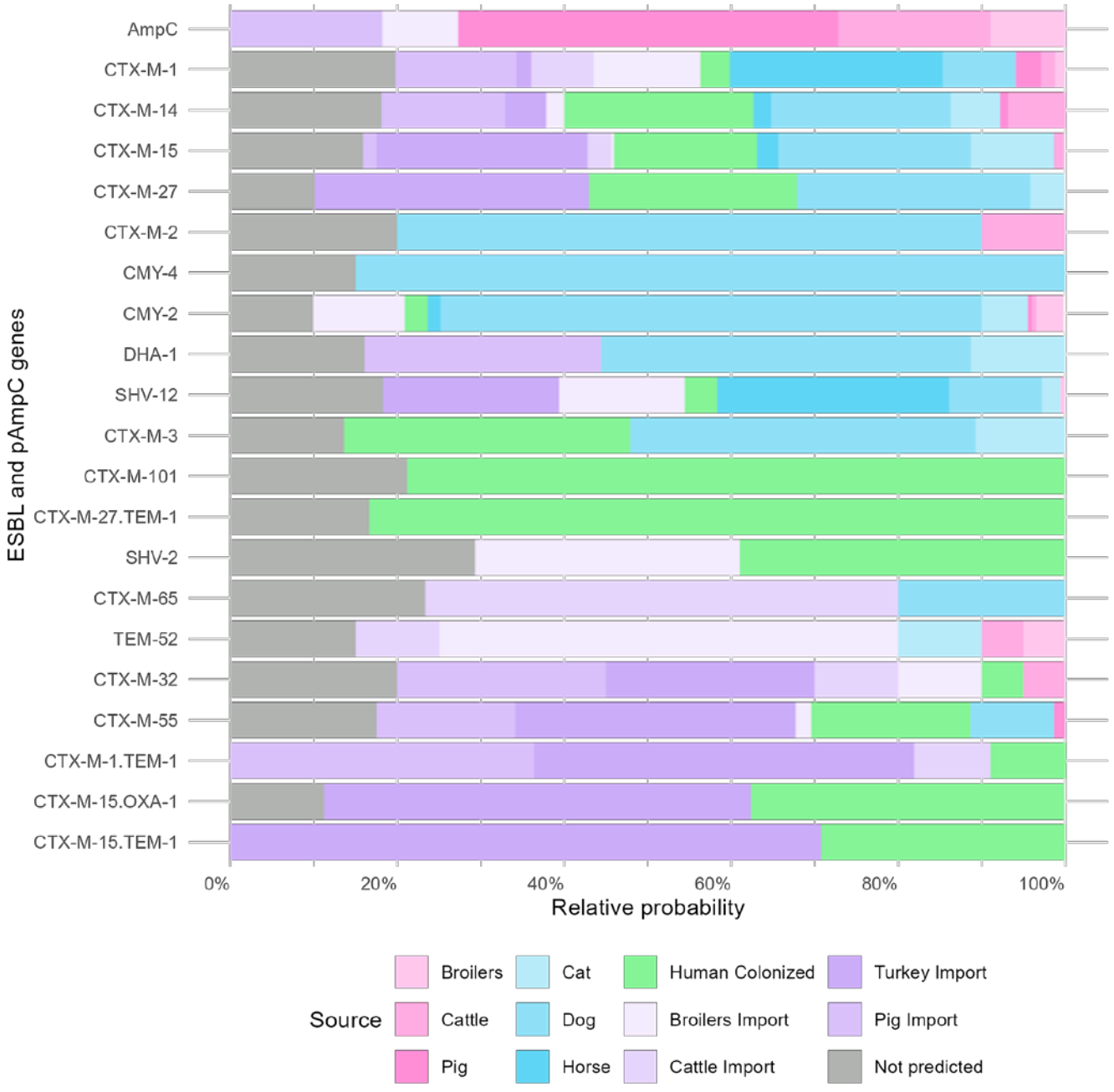
The Bayesian model estimated that dogs were the most significant contributor, accounting for 20.3% of human cases. This was followed by imported turkey meat (18.7%) and colonised humans (16.0%). Gene-specific attribution (Figure 1) revealed that pets (blue shades) and imported meat (purple shades) generally had higher attribution probabilities. For example, CMY-4 was exclusively attributed to dogs, while AmpC promoter mutations were the only resistance determinants present in infected humans and strongly linked to domestic animal sources, particularly pigs. In contrast, CTX-M-101 and CTX-M-27+TEM-1 were found only in colonised and infected humans, and not in any non-human reservoirs, suggesting possible human-adapted lineages.

continued ... Textbox 3.1

Conclusion

The findings of this study underscore the dominant role of human-to-human transmission in the spread of ESC-EC, while also highlighting the significant contributions from livestock, food, and pets. Although the impact of international travel was relatively limited in this model, it may still serve as a route for the introduction of novel resistant strains. Overall, the complexity of transmission dynamics revealed by this study supports the application of a One Health framework—integrating human, animal, and environmental health—to guide future surveillance, intervention, and policy efforts targeting antimicrobial resistance.

Figure 1 ESC gene-specific attribution in individuals infected with *E. coli*, shown as relative probabilities (%) DANMAP 2024



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[1] M. L. Brinch, A. S. R. Duarte, O. O. Apenteng, and T. Hald, 'Modeling the Transmission of ESBL and AmpC-Producing Escherichia coli in Denmark: A Compartmental and Source Attribution Approach', *Zoonotic Diseases*, vol. 5, no. 1, p. 7, Mar. 2025, doi: 10.3390/zoonoticdis5010007

[2] Swedres-Svarm 2022. Sales of antibiotics and occurrence of resistance in Sweden. Solna/Uppsala ISSN2001-7901.

Textbox 3.2

Antibiotics in wastewater and surface water

A) Current and forthcoming regulation on antibiotics in wastewater.

The Urbane Wastewater Treatment Directive
Antibiotics, as active pharmaceutical ingredients or partly degraded compounds, can be excreted to urban wastewater as a result of human consumption.

In November 2024, a revised Urban Waste Water Treatment Directive (UWWTD) was approved[1]. The directive sets the legal framework for the collection, treatment and discharge of urban wastewater.

The revised UWWTD has determined a requirement for establishment of a quaternary treatment step on wastewater treatment plants to remove micropollutants – including pharmaceuticals and thus antibiotics – from urban wastewater. All urban wastewater treatment plants of 150.000 p.e.[2] and above shall provide quaternary treatment, and for wastewater treatment plants of 10.000 -149.999 p.e. quaternary treatment must be established for wastewater treatment plants discharging effluent to areas identified as sensitive to pollution with micropollutants. The requirement of quaternary treatment shall gradually be implemented at all relevant wastewater treatment plants from 2033 to 2045.

Requirements for the quaternary treatment step is a minimum 80 percent removal of minimum six out of 13 indicator compounds all of which are pharmaceuticals. The list of indicator compounds include one antibiotic.

The additional costs related to installation of new treatment technologies at urban wastewater treatment plants has to be paid through an extended producer responsibility system. An assessment of micropollutants in urban wastewater determined that pharmaceuticals and cosmetic residues contribute to 92% of the total toxic load of untreated wastewater, of this pharmaceuticals account for 66% and cosmetic products for 26%[3]. Thus, producers of compounds from these two product categories will be included in the extended producer responsibility system in accordance with the polluter pays principle.

The UWWTD further requires monitoring of a broad number of compounds in influent and effluent from wastewater treatment plants; - minimum two samples per year for wastewater treatment plants of 150.000 p.e. and above and at least one sample every two years for wastewater treatment plants of between 10.000 p.e. and 150.000 p.e. The monitoring scheme will thus give continuous data on the content of a broad number of micropollutants expected to include antibiotics.

Current Danish regulation on wastewater
In Denmark, discharge of wastewater from wastewater treatment plants to surface water requires a discharge permit issued by the municipalities. The municipalities is also the legal authority to issue permit for discharge of wastewater from hospitals to surface water. The Danish Environmental Protection Agency issues discharge permit for wastewater directly to surface water from pharmaceutical industry. The permit must secure that discharge of micropollutants – including pharmaceuticals – to surface water does not compromise compliance with EU and nationally established environmental quality standards and criteria or other ecotoxicological threshold values (proposed no effect concentration values).

If wastewater from pharmaceutical industry or hospitals is connected to sewers leading to waste water treatment plants, this requires a connection permit issued by the municipalities, which must secure that micropollutants in the effluent does not prevent the wastewater treatment plants from complying with their discharge permits.

B) National surveillance of antibiotics in surface water and wastewater.

The national surveillance program for aquatic environment and nature (NOVANA[4]) monitors the status of the aquatic and terrestrial environments in Denmark and ensures that Denmark meets national legislation, EU directives, and international conventions. Furthermore, NOVANA provides data supporting the national action plans to support fulfillment of the water frame directive. The monitoring is carried out by the Agency for Green Transition and Aquatic Environment in Denmark.

As part of NOVANA, the presence of micropollutants in the aquatic environment is monitored. Thus, a wide range of different substances are measured in samples from streams, lakes, and marine areas. The list of substances monitored includes pharmaceuticals, such as antibiotics, metals, pesticides, plasticizers, and PFAS. The substances are monitored in water, sediment or biota (fish or mussels) depending mainly on their physical-chemical properties. Selected substances are also monitored at point sources such as wastewater treatment plants and storm water overflows, in order to identify which substances are emitted as a direct result of human consumption with wastewater.

Results

In 2017 a total of four antibiotics - trimethoprim, sulfamethiazole, sulfamethoxazole, and sulfadiazine, was included in the NOVANA surveillance program of surface water. The antibiotics are monitored in freshwater from streams as this is where the highest concentrations is expected to be found. Reviewing the collected data from 2017-24, sulfamethiazole has been found most frequently in 20% of the samples in concentrations ranging from 0.005 to 1.1 µg/L. The remaining antibiotics have been found in approximately 5% of the samples (table 1). None of the detected concentrations exceed the national environmental quality standards (EQS) for trimethoprim (100 µg/L) and sulfadiazine (4.6 µg/L).

Table 1 Overview of data from the national surveillance of antibiotics in surface water (streams) DANMAP 2024

	Parameter	CAS	Incl. in NOVANA	Number of samples	Detection frequency (%)	Range of concentrations (µg/L)
1478	Trimethoprim	738-70-5	2017-25	1297	3	0.001-0.45
912	Sulfamethiazole	144-82-1	2017-25	678	19	0.005-1.1
915	Sulfamethoxazole	723-46-6	2017-25	685	4	0.01-0.2
909	Sulfadiazine	68-35-9	2017-25	1080	3	0.0077-0.98

At point sources a total of six antibiotic (azithromycine, clarithromycine, erythromycine, sulfamethiazole, sulfamethoxazole, and trimethoprim) are monitored in samples from wastewater treatment plants and storm water overflows through NOVANA. Based on the results from the surveillance program, national mean concentrations[5] of discharges are estimated for each type of point source[6, 7]. For sulfamethiazole a national mean concentration of 0.58 µg/L is found in effluent from advanced wastewater treatment plants while a national mean concentration of 4.8 µg/L is found in effluent from mechanical treatment plants. It is, at this point, not possible to establish reliable national mean concentrations for the remaining antibiotics. Approximately 95% of the total amount of wastewater in Denmark is treated in advanced treatment plants and the remaining 5% in mechanical treatment plants.

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[1] DIRECTIVE (EU) 2024/3019 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 27 November 2024 concerning urban wastewater treatment
[2] One population equivalent' or '(1 p.e.)' means the organic biodegradable load per day, having a five-day biochemical oxygen demand (BOD5) of 60 g of oxygen per day.
[3] Feasibility of an EPR system for micropollutants. Final Report (070201/2020/837586/SFRA/ENV.C.2)
[4] https://www2.mst.dk/Udgiv/publikationer/2023/09/978-87-7038-556-5.pdf
[5] National mean concentrations signify the best estimate of the national Danish annual mean value of the concentration of a substance
[6] https://www2.mst.dk/Udgiv/publikationer/2021/03/978-87-7038-287-8.pdf
[7] https://www2.mst.dk/Udgiv/publikationer/2022/01/978-87-7038-386-8.pdf

Textbox 3.3

Infection prevention and control and prevention of antimicrobial resistance are interconnected

In Denmark there are numerous activities concerning infection prevention and control (IPC) and antimicrobial resistance (AMR) - both on the national and on the international level. Across Europe as well as globally it is increasingly stressed that controlling AMR in human health must be based on aligning efforts within surveillance, antimicrobial stewardship (AMS) and IPC.

IPC is for the first time in a Danish action plan on AMR specifically mentioned as one out of four central focus areas in the newly issued national action plan (NAP) on AMR as of 11 June 2025[1]. In June 2023, the European Union recommended to step up EU actions to combat antimicrobial resistance with a One Health approach[2]. To support the countries in stepping up the AMR actions the European Commission has invested 50 million Euros in EU-JAMRAI 2 four-year-project (2024-2027)[3] under the EU4health programme[4].

EU-JAMRAI 2 (European Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections) seeks to implement concrete actions to monitor, prevent and effectively tackle AMR across human, animal and environmental health domains through a "One-Health" approach and to make Europe a best practice region. The project focuses on multiple areas, such as AMS, surveillance, awareness raising, capacity building, IPC, behavioral science and updating NAPs on AMR with a focus on both AMR and IPC[5].

The project was launched at a kick-off meeting in Paris in February 2024 and an annual meeting took place in Bilbao in March 2025[6]. The project is progressing well and the first results will be available and presented from autumn 2025 and onwards.

Among the 10 work packages (WP) in EU-JAMRAI 2, Denmark participates in WP5 (National Action Plans), WP6 (Antimicrobial Stewardship), WP7 (Infection Prevention and Control), WP8 (One Health Surveillance) and WP9 (Access to antibiotics).

WP7 is about improving IPC actions within the human, veterinary and environmental sectors and has a general focus on behavior change strategies to support further uptake of IPC recommendations. Several subtasks are described within the human activities: Development of frameworks for implementation of IPC competencies and prioritizing EU standards in IPC programs, support the participating member states and associated countries in the implementation of IPC core components, give access to an IPC toolbox and, finally, organizing peer-to-peer activities and exchanges with IPC experts. Topics which constitute a challenge for IPC of today as e.g. lack of educated workforce, specialized care moving out of the hospitals and replaced by care at home, and IPC in the green transition will be included in the work.

As part of the EU-JAMRAI 2 project the Danish National Center for Infection Control (CEI) in close collaboration with our national IPC partners aim at improving the access to IPC knowledge and tools, strengthening IPC networking and the sharing of knowledge. A general focus is on how to improve and maintain IPC competencies. CEI follows a number of IPC implementation activities from around the country. Both municipalities, regions and projects across sectors are represented. The implementation and behavior change knowledge from these projects will later be shared. In 2025, as a part of the peer-to-peer programme, CEI has organized a national behavior change workshop and mediated a number of IPC webinars in collaboration with EUCIC (European Committee on Infection Control)[7]. CEI has launched a new site for IPC inspiration for the sharing of materials and tools among healthcare professionals working with IPC in Denmark. Read more about the Danish EU-JAMRAI 2 IPC activities at CEI SSI subsite[8].

EU-JAMRAI 2 receives funding from the European Union's EU4Health programme under grant agreement n°101127787.

EU-JAMRAI Joint Action Antimicrobial Resistance and Healthcare-Associated Infections

Funded by the European Union

Funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or the European Health and Digital Executive Agency (HADEA). Neither the European Union nor the granting authority can be held responsible for them.

The Danish IPC guidelines are in place

All healthcare professionals are expected to be familiar with and act in compliance with the national guidelines for IPC (published by the National Centre for Infection Control at SSI); in Danish "NIR Generelle forholdsregler for sundhedssektoren"[9]. The supplemental national guideline includes specific guidance on VRE, ESBL and other multidrug-resistant microorganisms (MDRO) and should be followed when being in contact with a patient, for which either clinical infection or carriage of MDRO is suspected or known; "NIR Supplerende forholdsregler ved infektioner og bærertilstand i sundhedssektoren"[10].

The Guidance on Preventing the Spread of MRSA by the Danish Health Authority was issued in 2006, the year MRSA became notifiable. The applicable 3rd edition of the guideline is from 2016; Guidance on Preventing the Spread of MRSA - The Danish Health Authority (sst.dk)[11]. The guideline represents the national recommendations and strategic framework for preventing the spread of MRSA at hospitals and in other healthcare settings and nursing homes. A 16-year MRSA surveillance report[12] has shown that the national MRSA strategy has been successful in controlling the spread of MRSA at hospitals as the primary goal of the MRSA guideline and to stabilize the spread of livestock-associated MRSA.

The first national guideline on preventing the spread of CPO by the Danish Health Authority was issued in 2018 (only in Danish); "Vejledning om forebyggelse af spredning af CPO"[13]. The guideline provides a national strategic framework for detection and management of CPO in hospitals. The main purpose of the guideline is to maintain a low prevalence of disease caused by CPO associated with certain high-risk situations. Despite this national guideline CPO is increasing in Denmark (see chapter 8.3.2, carbapenemase-producing organisms, CPO) indicating that more needs to be done in order to combat the outbreaks at hospitals and at long-term care facilities. There are a lot of challenges in controlling these outbreaks as they are long-lasting.

The purpose of both guidelines is to minimize the spread of these often highly resistant bacteria to the ill and weak patients at hospitals and in long-term care facilities, simultaneously keeping the occurrence of these bacteria on a continued low level. The guidelines contain recommendations for active screening of patients on admission to hospital, based on assessment of certain risk situations, e.g. admission to a hospital abroad during the last six months. Both guidelines are free of charge and easy to download from the Danish Health Authority website www.sst.dk.

In hospitals, nursing homes and home care, it is necessary to supplement the general precautions with transmission based (isolation) precautions in the case of an outbreak: "Infektionshygiejniske retningslinjer for MRSA"[14] and "Infektionshygiejniske retningslinjer for CPO"[15].

All IPC guidelines emphasize the importance of all healthcare staff, irrespective of profession, to contribute to the management and prevention of infections and to prescribe antibiotics with care.

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1 https://www.ism.dk/Media/638852182560099312/National%20handlingsplan%20for%20antimikrobiel%20resistens%20hos%20mennesker.pdf
2 https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32023H0622(01)
3 https://eu-jamrai.eu/
4 https://health.ec.europa.eu/funding/eu4health-programme-2021-2027-vision-healthier-european-union_en
5 https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/opportunities/projects-details/43332642/101127787/EU4H
6 https://eu-jamrai.eu/event/eu-jamrai-2-annual-meeting-2025/
7 https://www.escmid.org/science-research/eucic/
8 https://hygiejne.ssi.dk/formidling/eu-jamrai-2
9 https://hygiejne.ssi.dk/NIRgenerelle
10 https://hygiejne.ssi.dk/NIRsupplerende
11 https://www.sst.dk/en/english/publications/2022/Guidance-on-Preventing-the-Spread-of-MRSA
12 https://hygiejne.ssi.dk/overvaagning/mrsa
13 https://www.sst.dk/da/udgivelser/2018/vejledning-og-bekendtgoerelse-om-forebyggelse-mod-spredning-af-cpo
14 https://hygiejne.ssi.dk/retningslinjer/infektionshygiejniske-retningslinjer-for-mrsa
15 https://hygiejne.ssi.dk/retningslinjer/infektionshygiejniske-retningslinjer-for-cpo

4

ANTIMICROBIAL CONSUMPTION IN ANIMALS

4. Antimicrobial consumption in animals

Highlights

In 2024, the total consumption of antimicrobials in animals amounted to 87.46 tonnes of active compounds. Of this total, antimicrobial consumption in pigs accounted for 83.92%, followed by cattle at 9.46%, and poultry at 1.30%.

The Defined Animal Daily Dose (DADD) was revised for pigs and cattle in 2024, with notable changes to neomycin and procaine benzylpenicillin. These revisions significantly impacted the overall treatment proportion (DAPD) calculations, particularly for the antimicrobial classes aminoglycosides and beta-lactamase-sensitive penicillins.

In 2024, antimicrobial use in **pigs** reached 73.40 tonnes of active compounds, a 0.75% increase from 2023, while overall pig biomass rose by 0.48% due to higher exports. Overall DADD declined by 0.19%, though it rose in sows and piglets, and fell in weaners and finishers. In 2024, daily antimicrobial treatment affected 1.94% of sows and piglets, and finishers, with weaners receiving treatment most frequently (11.64%). Compared to 2023, overall DAPD increased for other penicillins (11.28%), sulfonamides with trimethoprim (6.46%), and beta-lactamase-sensitive penicillins (2.88%), while lincosamides and amphenicols declined by 32.73% and 20.80%, respectively. In sows and piglets, pleuromutilins and aminoglycosides rose by 24.14% and 8.98%, respectively while lincosamides dropped sharply by 73.51%. In weaners, sulfonamides with trimethoprim and other penicillins increased by 27.13% and 16.95%, respectively while amphenicols and tetracyclines fell by 37.32% and 5.76%, respectively. Among finishers, beta-lactamase-sensitive penicillins, tetracyclines and macrolides rose by 6.80%, 6.33% and 2.22%, respectively. Meanwhile, pleuromutilins declined by 6.57%.

In 2024, antimicrobial use in **cattle** increased to 8.28 tonnes of active compounds, representing a 4.08% rise compared to 2023, while overall cattle biomass declined by 1.8%. In 2024, daily systemic antimicrobial treatment affected 0.27% of adult cattle and 0.81% of young cattle. In adult cattle, the DAPD of other penicillins increased by 26.26%, macrolides by 22.54%, and aminoglycosides by 4.38%, while amphenicols dropped by 12.08%. Among young cattle, the use of amphenicols rose by 17.54%, macrolides by 13.30%, other penicillins by 12.59%, and sulfonamides with trimethoprim by 8.49%, while aminoglycosides declined by 4.78%. Intramammary treatments rose slightly in 2024 compared to 2023. Other penicillins were the most used for dry-cow treatment (50.00%), while beta-lactamase-sensitive penicillins dominated therapeutic intramammary treatments, accounting for 95.24% of use.

In 2024, antimicrobial consumption in **poultry** totaled 1,140.9 kg of active compounds, representing a 12.63% decrease compared to 2023.

In 2024, cephalosporins were primarily prescribed for **pets and horses** (46.0 kg) and used as intramammary treatments in cattle (35.0 kg). Fluoroquinolones (13.0 kg) were almost exclusively prescribed for horses and pets.

4.1 Introduction

The DANMAP programme has monitored national antimicrobial consumption in both humans and animals since 1995. From the early 1990s, growing political and public concern over antimicrobial use in Danish animal production led to significant changes, including the discontinuation of antimicrobials for growth promotion and the implementation of several initiatives, such as voluntary bans on the use of 3rd and 4th generation cephalosporins in pig and cattle production. Additionally, regulatory measures were introduced to govern their therapeutic use.

Figure 4.1 presents the total antimicrobial consumption in animals and humans beginning in 1990 and 1997, respectively. The increase and intensification of pig production during this period also played a significant role in shaping overall consumption trends.

The observed decline in antimicrobial consumption after 1994 was primarily attributed to the discontinuation of antimicrobials for growth promotion. Additional contributing factors likely included: 1) restrictions on veterinary practitioners' profit from sales of medicines, 2) implementation of Veterinary Advisory Service Contracts (VASCs), which introduced regular veterinary visits aimed at promoting preventive strategies and optimizing antimicrobial consumption, and 3) enforcement of the "cascade rule" [Order (DK) 142/1993], limiting the prescription of (cheaper) extemporaneously produced medicines.

Other important interventions included legislative restrictions on the use of fluoroquinolones in production animals implemented in 2002 and 2003. This was followed by a voluntary ban on the use of cephalosporins in pig production in 2010, extended to dairy cattle production in 2014.

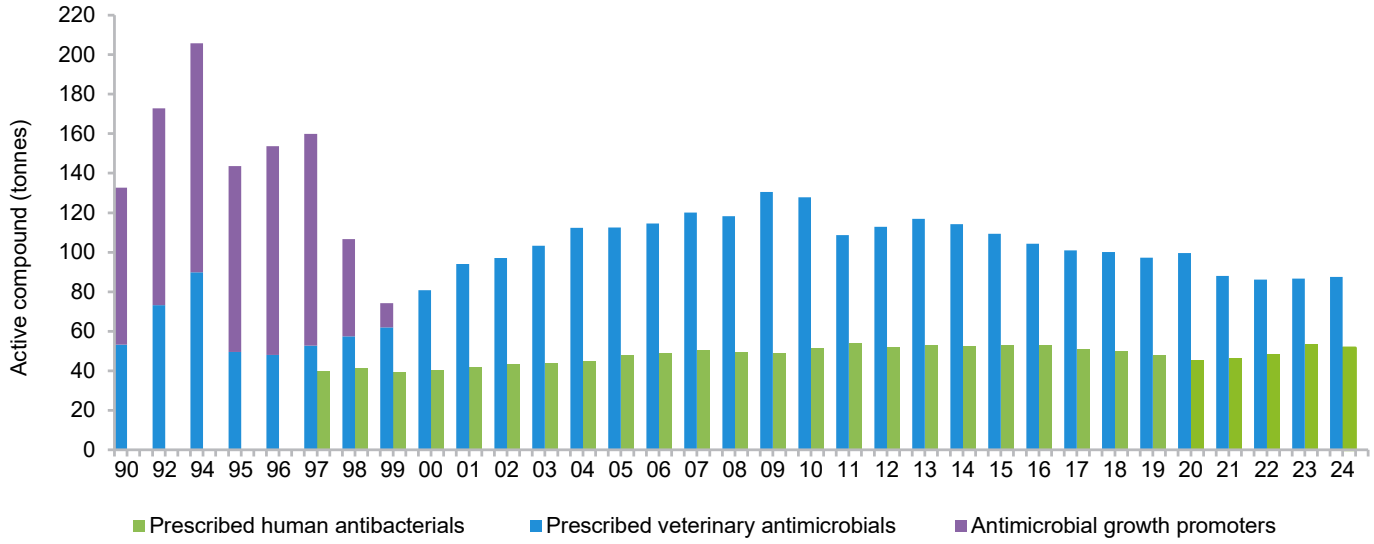
The national action plan against antimicrobial resistance has evolved over time, setting various goals to curb antimicrobial use. Initially, the plan aimed for a 10% reduction in antimicrobial consumption in production animals by 2014, using 2009 levels as the baseline. In 2015, a new objective was introduced under the national strategy to combat livestock-associated MRSA, targeting a 15% reduction in antimicrobial use in pig production between 2015 and 2018.

To support the goals outlined in the national action plan, the Yellow Card initiative was introduced in 2010, establishing herd-level surveillance of antimicrobial consumption in pig production. Under this initiative, antimicrobial use is monitored in individual herds against legally defined thresholds, enabling authorities to act against farmers with excessive usage per pig [DANMAP 2010].

The implementation of the Yellow Card system led to a noticeable reduction in antimicrobial consumption at the national level, particularly during its initial rollout from 2010 to 2011 and again following its revision between 2016 and 2018. In 2016, the initiative was updated to include multiplication factors that adjusted the weighting of specific antimicrobials in the monitoring system. Tetracyclines were initially assigned a factor of 1.2, which was increased to 1.5 in 2017. Fluoroquinolones, cephalosporins, and colistin were assigned the highest multiplication factor of 10 [DANMAP 2017], reflecting their critical importance and the need to discourage their use.

Figure 4.1 Antimicrobial consumption for humans and all animal species, tonnes of active compound, Denmark, 1990-2024

DANMAP 2024



Sources: Antimicrobials for humans: The Danish Medicines Agency. Antimicrobials for animals: Data are based on reports from the pharmaceutical industry of total annual sales (until 2001), from the Federation of Danish pig producers and slaughterhouses (1994-1995), from the Danish Medicines Agency and Danish Plant Directorate (1996-2000), and since 2001 from the VetStat. For DANMAP 2024, consumption data were extracted from the VetStat on 20 May 2025 and include all antimicrobials approved for use in animals

Other legislative measures have also likely influenced antimicrobial prescribing practices. For instance, in 2014, regulations governing group medication in pig herds were tightened [Order (DK) 534 of 27/05/2014]. These changes required more rigorous diagnostic procedures, including thorough laboratory testing, as well as more frequent veterinary visits. The aim was to ensure that antimicrobials administered orally to groups of pigs via water or feed were prescribed only when clearly justified, thereby encouraging more targeted treatments such as individual injections.

In 2017, the Ministry of Environment and Food and the Ministry of Health presented a new One Health strategy to combat antimicrobial resistance. This strategy established a comprehensive framework aimed at reducing the development and spread of AMR across both human and animal populations. In 2017, Denmark launched its first national action plan targeting antimicrobial resistance in animals, setting specific goals to further reduce antimicrobial use in animal production over the following years. This was followed by a second action plan in 2021. Most recently, in June 2024, a new national action plan against AMR in animals and food was adopted.

To help reduce the need for disposing of excess antimicrobials, a regulation introduced in 2019 [Order (DK) 1655/2018] permitted veterinarians and pharmacies to split packages of veterinary medicines. This initiative not only minimizes waste but may also improve surveillance by narrowing the gap between the quantities of antimicrobials prescribed and those actually consumed.

Official treatment guidelines for pigs and cattle have been available since 1996. Over time, the Danish Veterinary and Food Administration (DVFA) has updated the guidelines in collaboration with stakeholders and university experts [DANMAP 2010, www.foedevarestyrelsen.dk/].

In 2012, the Danish Veterinary Association (DVA) published treatment guidelines to promote the prudent use of antimicrobials in dogs and cats. These guidelines were developed by clinical specialists and experts from the Faculty of Health and Medical Sciences at the University of Copenhagen and the National Food Institute at the Technical University of Denmark. A revised edition of the guidelines for dogs and cats was published in 2018. Similarly, in 2017, the DVA released treatment guidelines for responsible use of antimicrobials in horses.

By 2020, the Danish dairy and beef producers' board had set a strategic goal to reduce antimicrobial use for mastitis and other cattle diseases by 20% compared to 2012 levels. Another objective was to lower the geometric mean bulk tank somatic cell count to 150,000 cells/ml. The strategy also promotes the use of simple penicillins (beta-lactamase-sensitive) for dry-cow therapy and mastitis treatment.

For the period 2021–2023, the board renewed its strategy for disease prevention in calves and cows, including updated udder health targets. The goals included a 10% annual reduction in antimicrobial use for cattle under 1 year old and a 3% annual reduction for cattle over 1 year old. Additionally, the strategy aimed to reduce the proportion of milk producers with somatic cell counts >200,000 cells/mL from 60% to 30%.

Since 28 January 2022, Order 2019/6 on veterinary medicinal products has been in effect in Denmark, aligning with EU Regulation 2019/6. This regulation places particular emphasis on reducing the risk of antimicrobial resistance [Order (DK) 6/2019]. It includes several key provisions regarding the prescription and use of veterinary medical products. These include limiting prescriptions to the exact quantity required for treatment, restricting the use of antimicrobials for metaphylactic or prophylactic purposes, and ensuring that all VMPs are used in accordance with their marketing authorizations (SPC). Furthermore, the regulation prohibits the routine use of antimicrobials to compensate for poor hygiene or management practices and designates certain critically important antimicrobials listed in Order 2022/1255 as being used exclusively for the treatment of specific infections in humans [DANMAP 2022, Textbox 4.1]

In line with recommendations from the European Medicines Agency (EMA) and a subsequent decision by the European Commission in 2017, Denmark along with all EU Member States was required to phase out the use of veterinary medicinal products (VMPs) containing zinc oxide in food-producing animals by June 2022. As a result, the use of prescribed zinc oxide in pig production has been banned in Denmark since that date [DANMAP 2022, Textbox 4.2].

Data sources

In Denmark, antimicrobials are available by prescription only, and data on antimicrobial consumption have been systematically collected since 1990.

Since 2001, data on all medicines prescribed for animal use have been systematically recorded in the national database VetStat. Since 2010, VetStat has been hosted and maintained by DVFA. In June 2021, DVFA launched an updated version of the VetStat platform.

The 2024 data presented in this report were extracted from this new VetStat on 20 May 2025. Data extraction, analysis, and interpretation were carried out by the National Food Institute at the Technical University of Denmark on behalf of DANMAP.

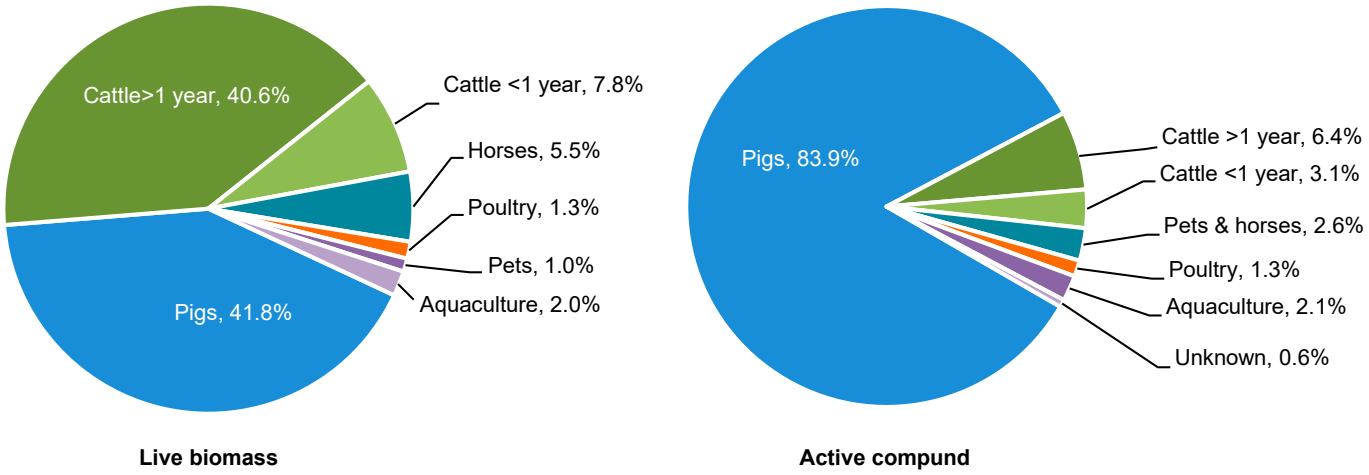
4.2 Total antimicrobial consumption in animals

In 2024, the total consumption of antimicrobials in all animals amounted to 87.46 tonnes of active compound, representing a 0.89% (775.60 kg) increase compared to 2023 (Figure 4.1). Of this total, antimicrobial consumption in pigs accounted for 83.92%, followed by cattle at 9.46%, and poultry at 1.30% (Figure 4.2, Table 4.1). By comparison, total antimicrobial consumption in human health care amounted to 51.57 tonnes.

Pig production is the primary driver of antimicrobial consumption in animals in Denmark. While cattle represent the largest share of live biomass, most of this biomass consists of dairy cows, which have significantly lower antimicrobial usage compared to growing animals such as those in slaughter pig production.

Between 2000 (the start of VetStat) and 2009, the total amount of antimicrobial active compounds used in animals increased by 61.7% (Figure 4.1). During this period, both the number of finishers produced, and the proportion of live pigs exported at approximately 30 kg rose. From 2009 to 2021, antimicrobial consumption declined, while the proportion of exported pigs increased. Between 2022 and 2024, there was a modest 1.5% increase in overall antimicrobial usage. Notably, the number of finishers produced fell by 20.00% compared to 2022, while the export of live pigs increased by 18.63%.

Figure 4.2 Distribution of live biomass and antimicrobial consumption in main animal species, tonnes, Denmark, 2024 DANMAP 2024



The live biomass is estimated from census data (pigs, cattle and pet animals) and production data (poultry, fur animals, aquaculture). The live biomass estimates for poultry (turkeys and broilers), aquaculture, horses and pet animals are based on 2012 data and may well be underestimated. The estimation procedures are described in Chapter 10, Section 10.2

Table 4.1 Antimicrobial consumption by animal species and age group, kg active compound, Denmark, 2023-2024 DANMAP 2024

	Aminoglycosides	Amphenicols	Cephalosporins [a]	Fluoroquinolones	Lincosamides	Macrolides	Other antimicrobials [b]	Other quinolones	Penicillins, b-lactamase sensitive	Penicillins, others	Pleuromutilins	Sulfonamides and trimethoprim	Tetracyclines	2023	2024
Pigs	19174.1	472.6	-	-	1219.4	11022.3	-	-	11488.5	8148.3	6225.6	5208.8	10435.6	72851.6	73395.3
Sows, piglets, gilts and boars	2212.9	247.1	-	-	1,28.7	366.1	-	-	6067.9	2123.6	743.8	3729.1	1044.3	16470.9	16663.5
Weaners, =<30kg	16829.4	203.1	-	-	1,033.9	7481.5	-	-	1681.4	5338.6	2245.0	1429.7	6754.7	42067.1	42997.3
Finishers and polts	131.9	22.3	-	-	56.8	3174.8	-	-	3739.1	686.0	3236.9	50.0	2636.7	14313.6	13734.5
Cattle	774.8	1072.0	35.2	-	5.1	230.4	5.0	-	4352.1	655.8	0.0	391.5	754.7	7952.4	8276.6
Intramammaries	23.6	-	35.0	-	4.5	-	-	-	229.7	176.7	-	-	-	457.3	469.6
Cows, bulls, heifers and steers >24 months	188.1	7.8	0.1	-	0.5	79.0	0.1	-	3542.9	348.9	0.0	285.5	481.8	4761.2	4934.8
Calves <12 months	546.1	1,051.8	0.0	-	0.1	146.8	4.9	-	474.4	119.7	-	104.5	258.3	2596.2	2706.6
Young cattle btw 12 and 24 months	17.0	12.4	0.0	-	0.0	4.6	0.0	-	105.0	10.5	-	1.5	14.6	137.7	165.7
Poultry	51.1	-	-	-	21.6	232.9	-	-	155.7	302.8	14.4	72.6	289.8	1305.8	1140.9
Broilers	32.1	-	-	-	16.0	76.5	-	-	44.2	154.4	-	71.4	154.2	697.2	548.7
Layer hens	-	-	-	-	-	148.5	-	-	45.8	14.2	14.4	-	24.4	191.3	247.2
Turkeys	12.7	-	-	-	5.3	.	-	-	65.3	123.5	-	-	79.0	378.9	285.8
Other poultry	6.4	-	-	-	0.3	8.0	-	-	0.3	10.7	-	1.2	32.2	38.4	59.2
Other production animals	10.2	134.9	-	-	0.7	0.2	0.0	316.8	0.6	9.6	-	1356.3	2.8	1588.2	1832.0
Aquaculture	8.4	134.8	-	-	-	-	-	316.8	-	.	-	1352.1	-	1580.6	1812.1
Fur animals	1.3	-	-	-	0.7	-	-	-	-	9.0	-	4.2	2.5	3.1	17.7
Other	0.5	0.0	-	-	-	0.2	0.0	-	0.6	0.5	-	0.0	0.3	4.5	2.2
Companion animals	2.9	0.5	46.0	13.0	75.5	0.4	51.2	-	15.5	476.3	0.1	1576.9	38.1	2353.6	2296.3
Horses	0.6	-	0.0	0.0	0.0	0.0	0.1	-	7.1	0.2	-	167.3	6.9	181.8	182.2
Pets	1.4	0.1	16.7	4.2	16.9	0.4	18.1	-	8.4	89.2	0.1	206.6	18.3	383.0	380.4
Unspecified	0.9	0.4	29.3	8.8	58.6	-	32.9	-	-	386.9	-	1203.0	12.9	1788.8	1733.7
Unknown [c]	71.6	11.5	0.4	0.1	-1.2	7.0	0.4	-3.0	282.7	69.4	2.8	15.3	65.6	636.4	522.6
Total	20084.8	1691.4	81.6	13.0	1321.1	11,493.2	56.6	313.8	16295.1	9662.1	6243.0	8621.4	11586.5	86688.0	87463.6

Data for 2024 were extracted from VetStat on 20 May 2025
Combination products are split into active compounds
A dash (-) indicates no antimicrobial usage
a) In 2024, 3rd generation cephalosporins were used in companion animals (0.76 kg), and cattle (0.14 kg)
b) Including other antiinfectives, dermatologicals, ontological, opthalmologicals, polymyxin, quinolones, and sulfonamides, plain
c) Including data with no information on animal species/age group, or mismatch between animal species and age group

4.3 Antimicrobial consumption by animal species

4.3.1 Antimicrobial consumption in pigs

In 2024, a total of 73.40 tonnes of antimicrobials were used in pig production, marking an increase of 0.75% (543.66 kg) compared to 2023 (Table 4.1). During the same period, the estimated live biomass of pigs increased by 0.48%, primarily due to an increase in the number of exported pigs.

Of this amount, approximately 16.66, 43.00 and 13.73 tonnes were used for sow and piglets, weaners, and finishers, respectively (Table 4.1).

With the launch of the new VetStat platform, minor adjustments were made to the recorded strength of active compounds of certain products. These updates influenced the Defined Animal Daily Dose (DADD), and subsequently the DAPD, prompting a revision of veterinary antimicrobial products for pigs and cattle covering the period from 2010 to 2024, as reflected in this year's DANMAP report. The revision was guided by the Summary of Product Characteristics (SPCs), which serve as the gold standard for veterinary medicinal products. In cases where SPCs were unavailable searching the internet, the previously established DADD values were retained.

The **treatment proportion** (DAPD) of the total population serves as an indicator of antimicrobial selection pressure within the population. Figures 4.3, 4.4, and 4.5 illustrate DAPD values for the overall population of pigs, as well as for specific age groups of pigs and cattle.

This year, all figures showing the measured DAPD are presented with the revised DADD values.

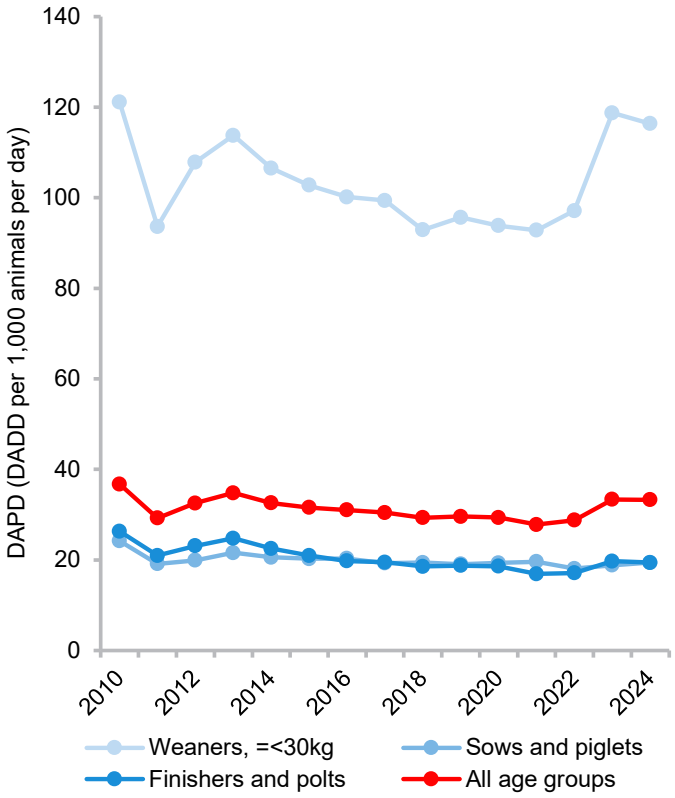
From 2004 to 2009, the DAPD showed a steady increase across all age groups. This was followed by a marked decline in 2010 and 2011, coinciding with the introduction of the Yellow Card initiative. Between 2013 and 2021, a slight but consistent downward trend in treatment proportion was observed (Figure 4.3).

In contrast to the decreasing trend in DAPD observed from 2013 to 2021, a substantial increase of approximately 20% was observed from 2021 to 2023. This was particularly due to increased usage in weaners.

In 2024, the overall DAPD decreased by 0.19 percent. However, trends varied across age groups: DAPD increased by 2.98 percent in sows and piglets, while it declined by 2.00 percent in weaners and by 1.53 percent in finishers (Figures 4.3).

In 2024, it is estimated that on any given day, approximately 1.94% of sows, piglets, and finishers, and 11.63% of weaners were treated with antimicrobials.

Figure 4.3 Total antimicrobial consumption in the pig production, DAPD, Denmark, 2010-2024 DANMAP 2024



The category "Sows and piglets" also includes boars, which make up approximately 4-5% of the estimated live biomass for this age group
Data for 2024 were extracted from VetStat on 20 May 2025

Compared to 2023, antimicrobial consumption in 2024 in the overall population, increased for other penicillins (11.28%), sulfonamides with trimethoprim (6.46%), and beta-lactamase-sensitive penicillins (2.88%). In contrast, usage declined for lincosamides (32.73%), amphenicols (20.80%), and pleuromutilins 4.64%). For aminoglycosides, macrolides, sulfonamides with trimethoprim, and tetracyclines, the year-on-year variation was less than 1% (Figure 4.4).

Among sows and piglets, the change from 2023 to 2024 in DAPD values showed increased usage of pleuromutilins (24.14%), aminoglycosides (8.98%), beta-lactamase-sensitive penicillins (5.39%), sulfonamides with trimethoprim (4.47%), and tetracyclines (1.98%). In contrast, lincosamide usage declined markedly by 73.51%, and amphenicol use decreased by 6.77% (Figure 4.4).

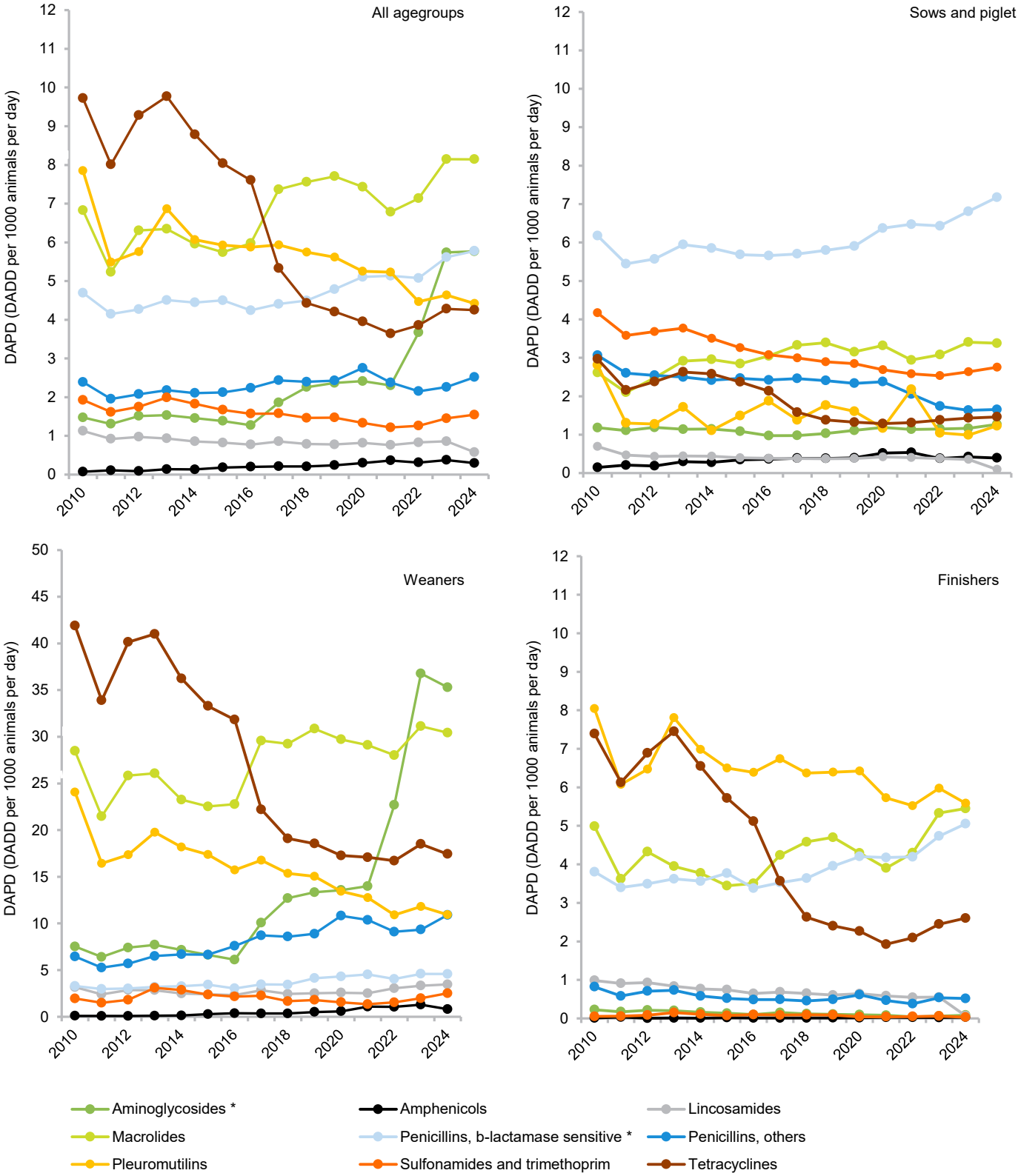
Following the ban on prescribed zinc oxide in pig production (effective June 2022), the discontinuation of colistin, and the enforcement of Regulation (EU) 2019/6 on veterinary medicinal products (effective 28 January 2022), the use of aminoglycosides, primarily neomycin and apramycin, in weaners increased significantly. The DAPD values of aminoglycosides rose from 13.99 in 2021 to 36.78 in 2023. In 2024, usage declined slightly to 35.29 DAPD, representing a 4.05% decrease compared to the previous year (Figure 4.4). Additional changes in weaners from 2023 to 2024 included a 27.13% increase in the DAPD of sulfonamides with trimethoprim and a 16.95% increase in other penicillins. In contrast, reductions were observed in the DAPD of amphenicols (37.32%), pleuromutilins (7.46%), tetracyclines (5.76%), and macrolides (2.22%) (Figure 4.4).

In finishers, the change from 2023 to 2024 showed that the DAPD for beta-lactamase-sensitive penicillins, tetracyclines and macrolides increased by 6.80%, 6.33% and 2.22%, respectively. Meanwhile, pleuromutilins declined by 6.57% (Figure 4.4).

In 2024, the three most commonly used active compounds in sows and piglets were procaine benzylpenicillin, tulathromycin, and sulfadoxine. Among weaners, the most frequently used compounds were tylosin, apramycin, and neomycin. For finishers, tiamulin, procaine benzylpenicillin, and tylosin were the predominant choices (Table 4.2).

Figure 4.4 Antimicrobial consumption in the total pig production and in each age group at antimicrobial class level, DAPD, Denmark, 2010-2024

DANMAP 2024



* Please note that the reported level differs noticeably from previous DANMAP reports due to DADD revisions
The category “Sows and piglets” also includes boars, which make up approximately 4-5% of the estimated live biomass for this age group
DAPDs are calculated as the number of standard doses for one kg animal divided by the estimated live biomass in the age group or the total population (in tonnes)
Data for 2024 were extracted from VetStat on 20 May 2025
Combination products are split into active compounds

Table 4.2 Antimicrobial consumption in each age group of pig production at antimicrobial class and active compound level, DAPD, using new DADD, Denmark, 2015-2024 **DANMAP 2024**

Antimicrobial class	Active compound	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Sows, piglets, gilts and boars											
Aminoglycosides	Apramycin	0.12	0.13	0.08	0.08	0.15	0.15	0.16	0.14	0.15	0.15
	Dihydrostreptomycin	0.75	0.60	0.51	0.51	0.53	0.59	0.59	0.64	0.67	0.71
	Gentamicin	0.00	0.02	0.03	0.04	0.03	0.03	0.01	0.01	0.03	0.00
	Neomycin	-	-	0.10	0.17	0.15	0.13	0.11	0.10	0.08	0.11
	Paromomycin	0.01	0.01	0.01	0.02	0.03	0.05	0.09	0.10	0.09	0.16
	Spectinomycin	0.20	0.21	0.24	0.23	0.22	0.23	0.18	0.16	0.14	0.14
Amphenicols	Florfenicol	0.34	0.36	0.39	0.38	0.40	0.52	0.54	0.38	0.42	0.39
Cephalosporins	Cefquinom	0.00	-	0.00	0.00	-	-	-	-	-	-
	Ceftiofur	0.00	0.00	0.00	0.00	-	-	-	-	-	-
Lincosamides	Lincomycin	0.40	0.38	0.38	0.37	0.38	0.42	0.40	0.38	0.35	0.09
Macrolides	Gamithromycin	-	0.51	1.19	1.32	1.35	1.40	1.01	0.86	0.73	0.51
	Spiramycin	0.03	0.00	-	-	-	-	-	-	-	-
	Tildipirosin	0.35	0.28	0.19	0.19	0.15	0.13	0.10	0.07	0.08	0.06
	Tilmicosin	0.14	0.14	0.14	0.16	0.09	0.08	0.06	0.04	0.03	0.02
	Tulathromycin	2.09	1.88	1.61	1.50	1.32	1.38	1.38	1.71	2.20	2.47
	Tylosin	0.23	0.23	0.20	0.17	0.19	0.31	0.39	0.39	0.37	0.32
	Tylvalosin	0.01	0.00	0.01	0.06	0.05	0.02	0.00	0.00	0.00	0.00
Other antimicrobials	Colistin	0.32	0.36	0.12	0.00	0.00	0.00	-	-	-	-
Penicillins, b-lactamase sensitive	Benzylpenicillin	0.16	0.04	0.00	-	-	-	-	-	-	-
	Penethamathydroiodid	-	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	Procaine benzylpenicillin	5.53	5.62	5.70	5.80	5.90	6.37	6.47	6.43	6.81	7.18
Penicillins, others	Amoxicillin	2.37	2.33	2.40	2.32	2.25	2.27	1.97	1.64	1.58	1.61
	Amoxicillin (beta-lactamase inhibitor)	0.09	0.09	0.06	0.09	0.08	0.11	0.09	0.10	0.06	0.05
	Ampicillin	0.01	-	-	-	-	-	-	-	-	-
Pleuromutilins	Tiamulin	1.50	1.87	1.38	1.76	1.61	1.17	2.18	1.05	0.99	1.23
	Valnemulin	-	-	0.00	-	-	-	-	-	-	-
Sulfonamides and trimethoprim	Sulfadiazine	2.06	1.93	1.83	1.65	1.64	0.66	-	-	0.00	0.53
	Sulfadoxine	0.65	0.63	0.65	0.74	0.72	1.57	2.15	2.11	2.19	1.76
	Sulfamethoxazole	0.01	0.00	0.01	0.03	0.01	0.01	0.00	0.00	0.00	0.00
	Trimethoprim	0.54	0.51	0.50	0.48	0.47	0.45	0.43	0.42	0.44	0.46
Tetracyclines	Chlortetracycline	0.04	0.04	0.03	0.04	0.03	0.03	0.06	0.03	0.03	0.03
	Doxycycline	0.33	0.22	0.13	0.15	0.11	0.08	0.07	0.14	0.14	0.06
	Oxytetracycline	2.00	1.88	1.42	1.20	1.17	1.18	1.18	1.21	1.27	1.37
Weaners, =<30kg											
Aminoglycosides	Apramycin	0.82	0.69	0.66	0.61	0.89	1.27	1.63	3.64	13.85	13.45
	Dihydrostreptomycin	1.35	1.07	1.07	1.04	1.25	1.41	1.42	1.28	1.51	1.48
	Gentamicin	-	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01
	Neomycin	-	-	2.69	6.19	6.18	5.79	5.88	11.63	14.66	13.21
	Paromomycin	0.12	0.07	0.04	0.06	0.08	0.08	0.12	0.15	0.18	0.20
	Spectinomycin	4.34	4.29	5.61	4.80	4.94	5.02	4.93	6.00	6.58	6.95
Amphenicols	Florfenicol	0.27	0.37	0.35	0.35	0.51	0.58	1.08	1.05	1.29	0.81
Cephalosporins	Cefquinom	0.00	0.00	0.00	-	-	-	-	-	-	-
	Ceftiofur	0.01	0.00	-	0.00	0.00	0.00	-	-	-	-
Lincosamides	Lincomycin	2.40	2.33	2.84	2.45	2.52	2.57	2.52	3.05	3.33	3.47
Macrolides	Gamithromycin	-	0.41	0.98	0.91	1.30	1.69	1.21	0.90	0.68	0.65
	Spiramycin	0.00	-	-	-	-	-	-	-	-	-
	Tildipirosin	0.47	0.35	0.26	0.22	0.23	0.24	0.20	0.14	0.13	0.11
	Tilmicosin	5.46	4.97	5.29	5.06	5.88	6.41	6.48	5.32	5.54	5.05
	Tulathromycin	1.23	1.04	1.08	0.89	0.89	1.00	1.14	1.33	2.07	2.60
	Tylosin	14.60	14.75	18.90	17.81	18.05	16.40	16.50	16.00	17.19	16.72
	Tylvalosin	0.78	1.25	3.07	4.34	4.49	3.97	3.56	4.33	5.51	5.30

The category “Sows and piglets” also includes boars, which make up approximately 4-5% of the estimated live biomass for this age group
DAPDs are calculated as the number of standard doses for one kg animal divided by the estimated live biomass in the age group or the total population (in tonnes)
Data for 2024 were extracted from VetStat on 20 May 2025
Combination products are split into active compounds
A dash (-) indicates no antimicrobial usage

continued ... Table 4.2 Antimicrobial consumption in each age group of pig production at antimicrobial class and active compound level, DAPD, using new DADD, Denmark, 2015-2024 DANMAP 2024

Antimicrobial class	Active compound	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
continued ... Weaners, =<30kg											
Other antimicrobials	Colistin	7.78	8.21	3.14	0.01	-	-	-	-	-	-
Penicillins, b-lactamase sensitive	Benzylpenicillin	0.30	0.07	0.00	-	-	-	-	-	-	-
	Penethamathydroiodid	-	0.00		0.00	-	-	-	-	-	-
	Procaine benzylpenicillin	3.14	2.96	3.46	3.45	4.13	4.31	4.54	4.04	4.59	4.59
Penicillins, others	Amoxicillin	5.48	6.81	8.25	8.37	8.65	10.28	9.70	8.15	8.50	9.93
	Amoxicillin (beta-lactamase inhibitor)	1.16	0.77	0.47	0.21	0.24	0.54	0.67	0.95	0.84	0.98
	Ampicillin	0.01	0.00	-	-	-	-	-	-	-	-
Pleuromutilins	Tiamulin	17.38	15.65	16.12	14.99	14.86	13.29	12.76	10.91	11.80	10.92
	Valnemulin	-	0.09	0.65	0.37	0.20	0.15	0.01	-	-	
Sulfonamides and trimethoprim	Sulfadiazine	1.23	0.88	0.99	0.57	0.63	0.24	0.01	-	-	0.65
	Sulfadoxine	0.21	0.23	0.24	0.28	0.36	0.61	0.87	1.10	1.48	1.30
	Sulfamethoxazole	0.53	0.69	0.65	0.54	0.51	0.45	0.25	0.19	0.17	0.15
	Trimethoprim	0.39	0.36	0.38	0.28	0.30	0.26	0.22	0.26	0.33	0.42
Tetracyclines	Chlortetracycline	5.71	5.28	4.07	3.47	3.29	2.66	2.06	1.16	0.98	0.82
	Doxycycline	23.17	22.26	14.02	12.07	11.55	11.44	11.97	12.49	14.04	13.08
	Oxytetracycline	4.41	4.29	4.13	3.55	3.71	3.17	3.05	3.07	3.48	3.54
Finishers and polts											
Aminoglycosides	Apramycin	-	-	0.00	-	0.00	0.00	0.00	0.00	0.00	0.00
	Dihydrostreptomycin	0.04	0.02	0.03	0.02	0.03	0.03	0.03	0.02	0.02	0.02
	Gentamicin	-	-	-	-	-	0.00	-	-	-	0.00
	Neomycin	-	-	0.00	0.01	0.02	0.03	0.03	0.01	0.02	0.03
	Paromomycin	0.00	-	0.00	-	0.00	0.00	-	-	0.00	-
	Spectinomycin	0.10	0.08	0.12	0.08	0.06	0.04	0.03	0.02	0.02	0.03
Amphenicols	Florfenicol	0.02	0.01	0.01	0.01	0.01	0.02	0.03	0.02	0.02	0.03
Cephalosporins	Ceftiofur	0.00	0.00	0.00	0.00	0.00	0.00	-	-	-	-
Lincosamides	Lincomycin	0.74	0.65	0.69	0.65	0.60	0.64	0.59	0.55	0.55	0.07
Macrolides	Gamithromycin	-	0.01	0.02	0.02	0.03	0.03	0.02	0.01	0.01	0.02
	Spiramycin	0.00	-	-	-	-	-	-	-	-	-
	Tildipirosin	0.03	0.01	0.02	0.00	0.01	0.00	0.00	0.00	0.00	0.00
	Tilmicosin	0.08	0.05	0.06	0.06	0.07	0.07	0.05	0.05	0.01	0.01
	Tulathromycin	0.03	0.02	0.03	0.02	0.02	0.04	0.02	0.02	0.03	0.06
	Tylosin	3.18	3.05	3.39	3.56	3.48	3.17	2.99	3.03	3.36	3.37
	Tylvalosin	0.13	0.37	0.73	0.92	1.10	0.98	0.82	1.18	1.92	1.98
Other antimicrobials	Colistin	0.06	0.03	0.01	-	-	-	-	-	-	-
Penicillins, b-lactamase sensitive	Benzylpenicillin	0.01	0.00	-	-	-	-	-	-	-	-
	Penethamathydroiodid	-	-	-	0.00	-	-	-	-	-	-
	Procaine benzylpenicillin	3.76	3.38	3.52	3.64	3.96	4.20	4.18	4.19	4.73	5.05
Penicillins, others	Amoxicillin	0.51	0.48	0.49	0.45	0.49	0.61	0.46	0.37	0.53	0.51
	Amoxicillin (beta-lactamase inhibitor)	0.01	0.01	0.00	0.00	0.00	0.00	0.01	0.00	0.01	0.00
	Ampicillin	0.00	-	-	-	-	-	-	-	-	-
Pleuromutilins	Tiamulin	6.50	6.38	6.68	6.25	6.26	6.35	5.72	5.52	5.98	5.58
	Valnemulin	-	0.01	0.07	0.12	0.14	0.07	0.00	-	-	-
Sulfonamides and trimethoprim	Sulfadiazine	0.02	0.03	0.02	0.02	0.03	0.01	-	0.00	-	0.00
	Sulfadoxine	0.01	0.01	0.00	0.01	0.01	0.01	0.02	0.02	0.02	0.01
	Sulfamethoxazole	0.03	0.04	0.04	0.05	0.04	0.02	0.02	0.02	0.03	0.01
	Trimethoprim	0.01	0.02	0.01	0.02	0.01	0.01	0.01	0.01	0.01	0.01
Tetracyclines	Chlortetracycline	0.84	0.80	0.59	0.46	0.43	0.34	0.22	0.14	0.08	0.09
	Doxycycline	3.45	3.10	1.88	1.37	1.15	1.18	1.09	1.30	1.57	1.70
	Oxytetracycline	1.44	1.22	1.10	0.80	0.83	0.74	0.62	0.66	0.79	0.81

The category “Sows and piglets” also includes boars, which make up approximately 4-5% of the estimated live biomass for this age group
DAPDs are calculated as the number of standard doses for one kg animal divided by the estimated live biomass in the age group or the total population (in tonnes)
Data for 2024 were extracted from VetStat on 20 May 2025
Combination products are split into active compounds
A dash (-) indicates no antimicrobial usage

4.3.2 Antimicrobial consumption in cattle

In 2024, approximately 8.28 tonnes of active antimicrobial compounds were recorded for use in cattle, representing an increase of 4.08% compared to 2023 (Table 4.1). During the same period, the estimated live biomass of cattle decreased by 1.80%.

Of this amount, approximately 0.46 tonnes were used for intramammary therapeutic purposes or dry-cow treatment. Around 5.10 tonnes of antimicrobials were administered systemically to young cattle (under 12 months of age), with the remaining proportion used in adult cattle (over 12 months) (Table 4.1).

Except for 2024, systemic antimicrobial consumption in adult cattle declined over the past decade: it was 3.52 DAPD in 2015 and 2.58 DAPD in 2023. In 2024, the DAPD was 2.74 (Figure 4.5). During the same period, systemic antimicrobial consumption in young cattle increased significantly. In 2015, the treatment proportions were 5.93 DAPD. By 2024, this value had risen to 8.13 DAPD (Figure 4.5). Notably, during the same period, the biomass of young cattle declined by 9.14%.

In 2024, it is estimated that on any given day, approximately 0.27% of adult cattle, and 0.81% of young cattle were treated with systemic antimicrobials.

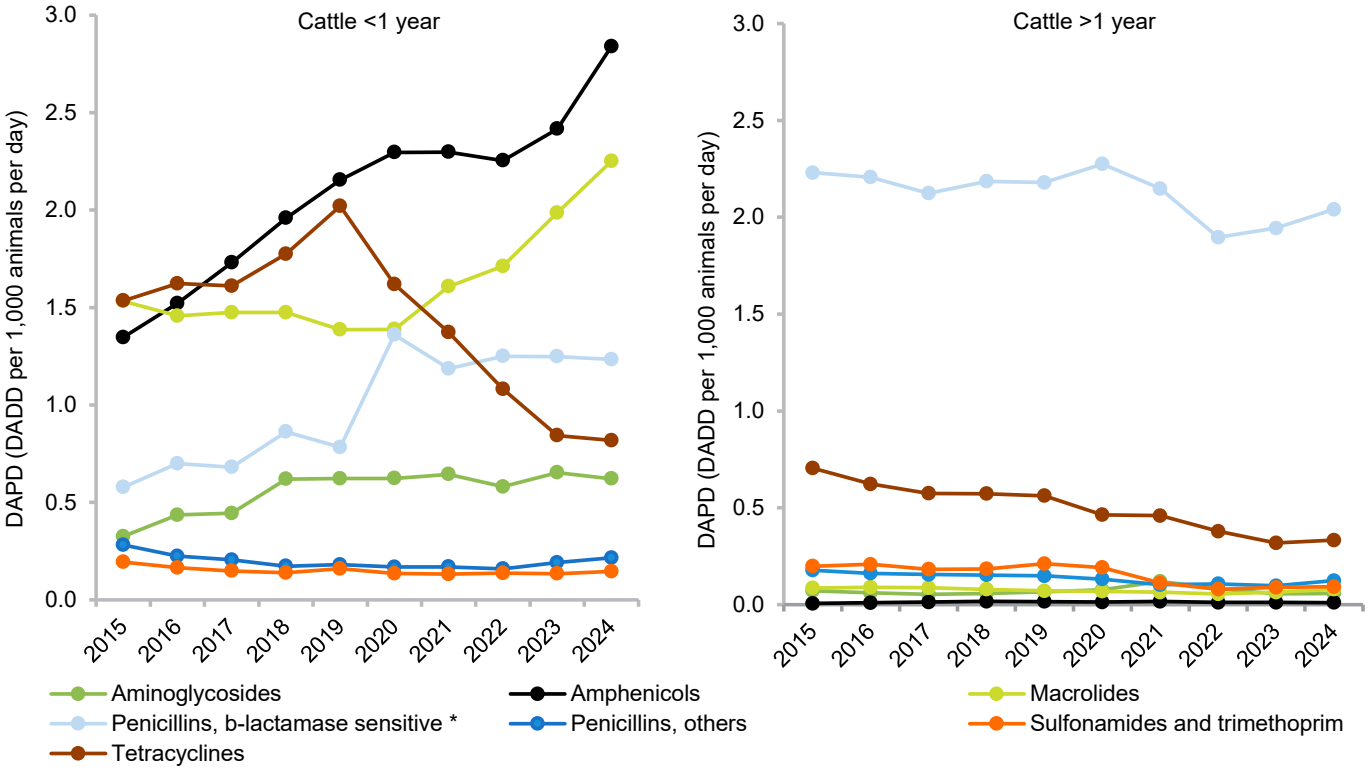
In young cattle, change from 2023 to 2024 in DAPD values showed increased usage of amphenicols (17.54%), macrolides (13.30%), other penicillins (12.59%), and sulfonamides with trimethoprim (8.49%), and decreased usage of aminoglycosides (4.78%). Subsequently, the increase observed in 2024 is primarily attributed to the use of amphenicols, which remains the most frequently used antimicrobial class in young cattle (Figure 4.5).

Among adult cattle, change from 2023 to 2024 in DAPD values showed increased usage of other penicillins (26.26%), macrolides (22.54%), beta-lactamase-sensitive penicillins (5.00%), aminoglycosides (4.38%), and tetracyclines (4.55%). In contrast, amphenicol use decreased by 12.08%. In 2024, treatments with beta-lactamase-sensitive penicillins accounted for 74.55% based on the new DADD (Figure 4.5).

In 2024, the most frequently used active compounds for systemic treatments in young cattle were florfenicol, tulathromycin, and procaine benzylpenicillin. Among adult cattle, the most frequently used compounds were procaine benzylpenicillin, and oxytetracycline (Table 4.3).

Figure 4.5 Antimicrobial consumption in cattle production by age groups at antimicrobial class level, DAPD, Denmark, 2015-2024

DANMAP 2024



* Please note that the reported level differs noticeably from previous DANMAP reports due to DADD revisions
DAPDs are calculated as the number of standard doses for one kg animal divided by the estimated live biomass in the age group or the total population (in tonnes)
Intramammary applications are not included (doses needed for calculating DAPD not available)
The DAPDs of amphenicols in cattle <1 year differ from previous reports, due to missing data in the old VetStat
Data for 2024 were extracted from VetStat on 20 May 2025
Combination products are split into active compound

Table 4.3 Antimicrobial consumption in each age group of cattle production at antimicrobial class and active compound level, DAPD, using new DADD, Denmark, 2015-2024 DANMAP 2024

Antimicrobial class	Active compound	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Cattle <1 year											
Aminoglycosides	Apramycin	0.02	0.02	0.01	0.01	0.01	0.01	0.01	0.01	0.04	0.01
	Dihydrostreptomycin	0.18	0.17	0.15	0.22	0.20	0.18	0.16	0.16	0.23	0.20
	Neomycin	0.00	-	0.01	0.00	0.00	0.01	0.00	0.00	-	0.00
	Paromomycin	0.12	0.25	0.28	0.38	0.41	0.42	0.47	0.41	0.39	0.41
	Spectinomycin	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Amphenicols	Florfenicol	1.35	1.52	1.73	1.96	2.15	2.30	2.30	2.25	2.42	2.84
Cephalosporins	Cefquinom	0.01	0.01	0.01	0.01	0.01	0.00	0.00	-	-	-
	Ceftiofur	0.01	0.01	0.01	0.01	0.00	0.00	-	-	-	0.00
Fluoroquinolones	Enrofloxacin	0.00	-	-	-	-	-	-	-	-	
Lincosamides	Lincomycin	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Macrolides	Gamithromycin	0.08	0.11	0.13	0.12	0.10	0.12	0.12	0.06	0.05	0.04
	Spiramycin	0.00	0.00	0.00	-	0.00	-	-	-	-	-
	Tildipirosin	0.46	0.41	0.43	0.46	0.43	0.39	0.34	0.20	0.07	0.04
	Tilmicosin	0.08	0.14	0.13	0.14	0.10	0.14	0.17	0.14	0.08	0.11
	Tulathromycin	0.81	0.73	0.73	0.69	0.69	0.69	0.94	1.27	1.69	1.99
	Tylosin	0.10	0.07	0.05	0.06	0.06	0.05	0.04	0.05	0.10	0.06
Other antimicrobials	Colistin	0.11	0.07	0.03	0.02	0.01	-	-	-	-	-
Penicillins, b-lactamase sensitive	Benzylpenicillin	0.06	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	Penethamathydroiodid	0.00	0.00	0.00	0.00	0.00	0.01	0.01	0.00	0.01	0.00
	Procaine benzylpenicillin	0.51	0.68	0.68	0.86	0.78	1.35	1.18	1.25	1.24	1.23
Penicillins, others	Amoxicillin	0.25	0.21	0.20	0.17	0.18	0.17	0.17	0.16	0.19	0.22
	Amoxicillin (beta-lactamase inhibitor)	0.03	0.01	0.00	0.00	0.00	0.00	0.00	0.00	-	-
	Ampicillin	0.00	0.00	-	-	0.00	-	-	-	-	-
Sulfonamides and trimethoprim	Sulfadiazine	0.14	0.12	0.11	0.10	0.12	0.06	0.01	0.00	0.00	0.03
	Sulfadoxine	0.02	0.02	0.01	0.02	0.02	0.05	0.10	0.11	0.11	0.09
	Sulfamethoxazole	-	-	-	-	0.00	-	-	-	-	-
	Trimethoprim	0.03	0.03	0.02	0.02	0.03	0.02	0.02	0.02	0.02	0.02
Tetracyclines	Chlortetracycline	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	Doxycycline	0.27	0.25	0.27	0.31	0.47	0.37	0.27	0.18	0.10	0.12
	Oxytetracycline	1.26	1.37	1.34	1.47	1.55	1.25	1.10	0.90	0.74	0.70
Cattle >1 year											
Aminoglycosides	Apramycin	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	Dihydrostreptomycin	0.07	0.06	0.05	0.06	0.06	0.07	0.12	0.08	0.05	0.06
	Gentamicin	-	-	-	-	-	0.00	-	-	-	-
	Neomycin	0.00	-	-	-	0.00	0.00	0.00	0.00	-	-
	Paromomycin	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	Spectinomycin	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Amphenicols	Florfenicol	0.01	0.01	0.01	0.02	0.02	0.01	0.02	0.01	0.01	0.01
Cephalosporins	Cefquinom	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-	-	-
	Ceftiofur	0.04	0.04	0.04	0.04	0.03	0.00	0.00	-	-	0.00
Fluoroquinolones	Enrofloxacin	0.00	-	-	-	-	-	-	-	-	-
Lincosamides	Lincomycin	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Macrolides	Gamithromycin	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	Spiramycin	0.00	0.00	0.00	0.00	-	-	-	-	-	-
	Tildipirosin	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	Tilmicosin	-	-	0.00	-	0.00	0.00	0.00	-	-	-
	Tulathromycin	0.00	0.00	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
	Tylosin	0.08	0.08	0.07	0.07	0.06	0.06	0.05	0.05	0.06	0.06
Other antimicrobials	Colistin	0.00	0.00	0.00	0.00	0.00	-	-	-	-	-
Penicillins, b-lactamase sensitive	Benzylpenicillin	0.03	0.01	0.00	0.00	0.00	0.00	0.01	0.01	0.01	0.01
	Penethamathydroiodid	0.00	0.10	0.15	0.17	0.18	0.18	0.17	0.18	0.20	0.21
	Procaine benzylpenicillin	2.20	2.10	1.97	2.01	2.00	2.09	1.97	1.70	1.73	1.82

DAPDs are calculated as the number of standard doses for one kg animal divided by the estimated live biomass in the age group or the total population (in tonnes)
Data for 2024 were extracted from VetStat on 20 May 2025
Combination products are split into active compounds
A dash (-) indicates no antimicrobial usage

continued ... Table 4.3 Antimicrobial consumption in each age group of cattle production at antimicrobial class and active compound level, DAPD, using new DADD, Denmark, 2015-2024 DANMAP 2024

Antimicrobial class	Active compound	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
continued ... Cattle <1 year											
Penicillins, others	Amoxicillin	0.18	0.16	0.16	0.15	0.15	0.13	0.10	0.11	0.10	0.12
	Amoxicillin (beta-lactamase inhibitor)	0.00	0.00	0.00	0.00	0.00	0.00	-	-	-	-
	Ampicillin	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-	-	-
Pleuromutilins	Tiamulin	-	-	-	-	-	-	-	-	-	0.00
Sulfonamides and trimethoprim	Sulfadiazine	0.15	0.16	0.14	0.14	0.16	0.06	0.00	0.00	0.00	0.02
	Sulfadoxine	0.02	0.02	0.02	0.02	0.02	0.10	0.09	0.07	0.07	0.06
	Trimethoprim	0.03	0.03	0.03	0.03	0.04	0.03	0.02	0.01	0.01	0.02
Tetracyclines	Chlortetracycline	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	Doxycycline	0.00	0.00	0.00	0.01	0.01	0.00	0.00	0.00	0.00	-
	Oxytetracycline	0.70	0.62	0.57	0.56	0.55	0.46	0.45	0.38	0.32	0.33

DAPDs are calculated as the number of standard doses for one kg animal divided by the estimated live biomass in the age group or the total population (in tonnes)
Data for 2024 were extracted from VetStat on 20 May 2025
Combination products are split into active compounds
A dash (-) indicates no antimicrobial usag

The consumption of intramammary treatments, measured as doses per cow per year, is presented in Figure 4.6. From 2015 to 2023, usage declined by 17.24%. However, in 2024, there was a 2.67% increase compared to the previous year.

In 2019, a notable shift occurred in dry-cow treatments: the use of beta-lactamase-sensitive penicillins for this purpose almost ceased, while the use of other penicillins, particularly cloxacillin, increased substantially. This shift resulted from a product shortage in which the primary beta-lactamase-sensitive penicillins for dry-cow treatment was unavailable for extended periods during 2019. Consequently, other penicillins, especially products containing cloxacillin, had to be used as alternatives [Personal communication; Michael Farre, Danish Agriculture and Food Council] (Figure 4.6).

In 2024, other penicillins remained the most frequently used antimicrobials for dry-cow treatment, accounting for 50.00% of total usage, followed by beta-lactamase-sensitive penicillins at 24.94%. Cephalosporins were used exclusively for dry-cow treatments in 2024 (Figure 4.6).

For therapeutic intramammary treatments, beta-lactamase-sensitive penicillins remained the dominant antimicrobial class from 2015 to 2023, and in 2024, they accounted for 97.18% of all therapeutic intramammary treatments.

4.3.3 Antimicrobial consumption in poultry

Poultry production in Denmark comprises broiler chickens, laying hens, and turkeys, supplemented by smaller-scale operations involving ducks, geese, and game birds. Among these sectors, conventional broiler production is characterized by stringent biosecurity protocols, which contribute to comparatively low levels of antimicrobial usage relative to other livestock sectors. However, due to the overall low baseline usage, disease outbreaks in a limited number of farms can exert a substantial influence on national antimicrobial consumption statistics (Table 4.4).

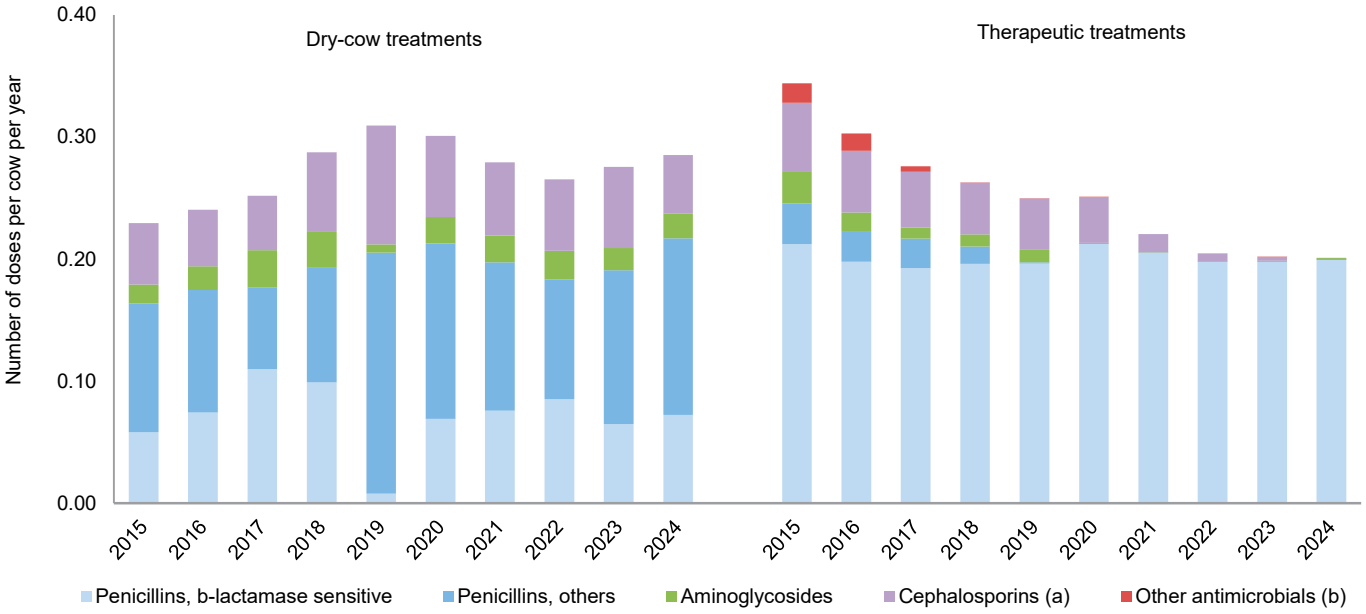
Marked fluctuations in antimicrobial usage, both increases and decreases, are frequently attributable to disease outbreaks affecting multiple flocks within a single production unit [personal communication, Susanne Kabel, Danish Agriculture and Food Council].

Historically, the Danish VetStat surveillance system lacked the resolution to disaggregate antimicrobial usage data by specific poultry production types. This limitation was addressed through the revised VetStat system, which has enabled more granular reporting since June 2021. As longitudinal data accumulates, this enhancement will facilitate more precise monitoring of antimicrobial usage trends across distinct poultry production categories.

In 2024, total antimicrobial consumption in the poultry sector declined by 12.63% in terms of kilograms of active compound compared to 2023. Despite this overall reduction, usage of certain antimicrobial classes increased: other penicillins by 99.69 kg, macrolides by 56.60 kg, and sulfonamides in combination with trimethoprim by 41.40 kg. In contrast, the use of beta-lactamase-sensitive penicillins and tetracyclines decreased by 160.23 kg and 207.14 kg, respectively (Table 4.4).

Figure 4.6 Consumption of antimicrobials for intramammary application in cattle, treatments per cow per year, Denmark, 2015-2024

DANMAP 2024



For intramammary treatment, the consumption has been estimated as the number of doses divided by the estimated live biomass in the age group
Data for 2024 were extracted from VetStat on 20 May 2025
Combination products are split into active compounds
a) 1st generation cephalosporins only
b) Includes lincomycin for dry-cow treatments. For therapeutic treatment, mainly sulfonamides-trimethoprim, but also lincomycin and bacitracin

Table 4.4 Consumption of antimicrobials in poultry, kg active compound, Denmark, 2015-2024

DANMAP 2024

	Aminoglycosides	Amphenicols	Fluoroquinolones	Lincosamides	Macrolides	Other antimicrobials[a]	Other quinolones	Penicillins, b-lactamase sensitive	Penicillins, others	Pleuromutilins	Sulfonamides and trimethoprim	Tetracyclines	Total
2015	258.47	4.37	1.00	129.12	133.31	9.96	-	204.43	565.96	0.63	445.46	818.09	2570.78
2016	60.19	4.83	-	23.77	175.58	8.00	-	264.55	257.65	0.38	111.00	764.56	1670.51
2017	64.87	5.06	-	31.75	244.87	-	1.00	355.55	334.77	0.45	84.60	487.45	1610.37
2018	50.56	-	-	25.28	194.95	-	-	357.83	242.58	0.83	36.60	521.12	1429.73
2019	54.80	0.23	0.01	27.36	274.83	-	-	368.37	234.30	0.64	64.25	694.27	1719.07
2020	58.19	-	-	29.01	156.91	-	-	334.10	237.34	0.23	54.60	1590.93	2461.31
2021	58.87	-	-	27.69	168.64	-	-	115.38	204.10	0.38	34.80	656.61	1266.46
2022	50.42	-	-	14.98	433.96	-	-	232.70	139.88	19.38	12.60	442.43	1346.35
2023	50.23	-	-	15.28	176.34	-	-	315.90	203.06	16.88	31.20	496.92	1305.80
2024	51.15	-	-	21.65	232.94	-	-	155.68	302.75	14.38	72.60	289.78	1140.92

Data for 2024 were extracted from VetStat on 20 May 2025
Combination drugs are divided into active compounds
a) Other antimicrobials also include polymyxins
A dash (-) indicates no antimicrobial usage

4.3.4 Antimicrobial consumption in aquaculture, fur animals, and companion animals

Aquaculture

Antimicrobial consumption in aquaculture is mainly driven by the summer air temperatures and hours of summer sunlight because bacterial diseases are more likely to occur when water temperatures are high [Villumsen and Bojesen, 2022. Microbiol Spectr. 10(5):e0175222]. Although the aquaculture production continues to focus on developing improved vaccination strategies to reduce the risk of bacterial diseases that may require treatment with antimicrobials, the antimicrobial consumption varies significantly from year to year. In 2024 the antimicrobial consumption decreased by 12.01% compared to the average consumption in the previous five years. The decrease was primarily due to decreased usage of combination products of sulfonamides and trimethoprim (Table 4.5).

In 2024, three antimicrobial classes accounted for the majority of treatments for bacterial infections in aquaculture: sulfonamides with trimethoprim made up 74.61% of total use, followed by other quinolones (oxolinic acid) at 14.48%, and amphenicols (florfenicol) at 7.44% (Table 4.5).

Companion animals - horses and pets

The information available on antimicrobial consumption in companion animals is not as accurate as for production animals, since VetStat allows registration of antimicrobials for companion animals without defining animal species. Table 4.6 shows the antimicrobial consumption registered for companion animals in three categories: horses, pets, and "unspecified".

The total amount of antimicrobials estimated for consumption in companion animals in 2024 was 2296.33 kg (Table 4.6). As in previous years, a substantial amount of sulfonamide/trimethoprim registered as used for pets or unspecified is oral paste, a product normally used for horses. Thus, a substantial amount of sulfonamide/trimethoprim included in Table 4.6 is likely to have been used for horses (1202.96 kg in 2024).

A large proportion of antimicrobials for dogs and cats are prescribed for the treatment of chronic or recurrent disease, mainly dermatitis. Due to the close contact between owners and their pets, repeated use of critically important antimicrobials may pose a risk to the owners, and the use of these antimicrobials is therefore monitored carefully.

Since the treatment guidelines by DVA were published in 2012 (revised in 2018), the use of cephalosporins has been reduced from 272.70 kg in 2012 to 45.98 kg of active compound in 2024. The pets accounted for 56.37% of all the cephalosporins consumed in animals (Table 4.1 and 4.6).

In 2024, the consumption of fluoroquinolones in companion animals, mainly dogs and cats, was 12.98 kg active compound (Table 4.1 and 4.6).

Table 4.5 Consumption of antimicrobials in aquaculture, kg active compound, Denmark, 2015-2024 DANMAP 2024

	Aminoglycosides	Amphenicols	Other antibacterials[a]	Other quinolones	Penicillins, b-lactamase sensitive	Penicillins, others	Sulfonamides and trimethoprim	Tetracyclines	Total
2015	-	311.09	-	1004.50	-	5.05	1655.01	0.72	2976.36
2016	-	315.34	0.00	893.07	-	13.55	1085.88	0.40	2308.24
2017	-	350.26	-	636.81	0.04	35.03	679.34	0.10	1701.57
2018	-	323.47	-	899.34	-	51.58	2292.56	0.50	3567.45
2019	-	292.56	-	446.88	-	43.90	1720.93	22.01	2526.28
2020	-	341.19	-	565.26	-	27.05	1030.20	1.00	1964.70
2021	-	295.42	0.12	366.33	1.71	19.50	1088.90	1.42	1773.39
2022	-	143.85	-	366.53	-	-	1940.76	0.60	2451.74
2023	-	124.93	-	523.98	-	-	931.70	-	1580.61
2024	8.40	134.83	-	316.78	-	-	1352.08	-	1812.09

Data for 2024 were extracted from VetStat on 20 May 2025
Combination products are split into active compounds
a) Other antibacterials also includes lincosamides
A dash (-) indicates no antimicrobial usage

Table 4.6 Estimated consumption of antimicrobials for horses, pets and unspecified animals, kg active compound, Denmark, 2015-2024

DANMAP 2024

	Aminoglycosides	Amphenicols	Cephalosporins	Fluoroquinolones	Lincosamides	Macrolides	Other antimicrobials[a]	Other quinolones	Penicillins, b-lacta-mase sensitive	Penicillins, others	Pleuromutilins	Sulfonamides and trimethoprim	Tetracyclines	Total
Horses														
2015	2.82	-	0.43	0.00	0.01	0.06	0.02	-	6.88	0.05	-	114.58	4.75	129.61
2016	0.78	-	0.13	0.01	-	-	0.03	-	5.21	0.02	-	108.02	5.30	119.50
2017	0.86	0.09	0.11	0.00	-	-	0.04	-	5.38	0.06	-	106.44	2.98	115.95
2018	0.70	0.05	0.15	-	-	0.08	0.04	-	5.96	0.01	-	100.56	3.78	111.33
2019	0.95	-	0.08	0.00	-	0.02	0.02	-	4.92	0.09	-	94.19	3.82	104.09
2020	1.71	-	0.00	0.00	0.00	-	0.02	-	5.32	0.03	-	111.46	3.52	122.06
2021	0.20	-	0.01	0.00	0.00	0.02	0.06	-	5.20	0.13	-	106.03	1.99	113.65
2022	0.35	0.00	0.04	0.00	0.02	1.00	0.16	-	5.07	0.39	-	137.09	7.32	151.45
2023	0.30	0.00	0.01	0.03	0.01	-	0.26	-	5.91	0.57	-	167.02	7.67	181.77
2024	0.61	-	0.02	0.00	0.00	0.02	0.12	-	7.08	0.17	-	167.32	6.88	182.20
Pets														
2015	4.80	0.12	61.76	5.60	21.78	3.31	6.83	-	13.18	123.44	1.75	226.16	20.46	489.20
2016	3.39	0.43	55.31	5.38	21.78	2.31	7.38	0.06	9.81	131.16	0.25	269.09	21.49	527.84
2017	3.80	0.70	41.70	5.22	18.38	1.66	8.32	-	9.16	125.79	0.13	272.44	19.34	506.63
2018	3.93	0.28	35.86	4.94	17.51	1.66	14.34	1.00	10.00	113.72	0.50	253.22	21.12	478.08
2019	3.73	0.26	32.33	4.45	17.19	7.35	15.02	0.00	10.35	108.43	0.63	236.83	14.79	451.35
2020	4.34	0.56	30.68	5.06	19.07	3.84	17.61	-	12.88	103.42	0.50	262.32	17.75	478.01
2021	3.20	0.67	27.98	4.74	19.25	2.16	20.82	-	11.46	100.15	0.13	270.77	23.66	484.99
2022	1.69	0.01	22.30	3.87	16.48	0.23	24.39	-	9.39	79.53	0.13	165.50	22.26	345.77
2023	2.21	0.64	21.56	4.31	17.72	2.19	24.46	-	10.02	86.54	0.16	194.37	18.81	383.00
2024	1.38	0.12	16.67	4.15	16.88	0.36	18.12	-	8.45	89.17	0.13	206.62	18.34	380.39
Unspecfied														
2015	41.28	0.33	95.87	8.73	46.84	0.04	25.13	1.00	1.50	429.17	-	946.83	17.02	1613.73
2016	37.45	0.38	81.64	9.71	48.91	0.27	26.31	-	2.21	468.68	-	1015.35	17.02	1707.93
2017	33.22	0.21	69.14	9.27	50.12	0.00	28.25	-	1.94	469.78	-	1071.67	14.71	1748.31
2018	31.84	1.32	61.41	9.76	45.80	-	34.83	-	1.84	452.95	-	1136.63	12.96	1789.33
2019	29.24	0.23	60.64	9.87	48.83	0.13	36.80	-	1.90	442.56	0.13	1140.68	16.04	1787.07
2020	22.62	0.42	56.90	10.70	52.24	0.06	40.17	-	2.90	446.94	-	1221.66	15.65	1870.25
2021	17.26	0.39	49.36	10.11	57.52	-	47.35	-	0.79	457.54	-	1284.34	14.46	1939.13
2022	1.28	0.40	38.82	8.76	54.31	-	51.89	-	-	395.35	-	1100.12	11.94	1662.86
2023	1.04	0.41	36.93	8.73	55.63	-	49.24	-	-	390.36	-	1233.67	12.82	1788.82
2024	0.91	0.39	29.31	8.83	58.61	-	32.92	-	-	386.95	-	1202.96	12.85	1733.74

Data for 2024 were extracted from VetStat 20 May 2025
Combination products are split into active compounds
The estimates include all veterinary approved antimicrobials, for use in horses, pets, as well as products without a specified animal species (unknown)
a) Other antimicrobials also include other otologicals, pleuromutilins, polymyxins and sulfonamides, plain
A dash (-) indicates no antimicrobial usage

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Textbox 4.1

The effect of the discontinued use of zinc oxide on antimicrobial usage in Danish pig farms

Background

On June 26, 2022, Denmark implemented a ban on veterinary medicinal products containing zinc oxide, generally used for prevention of *E. coli*-related post-weaning diarrhoea in pigs. The decision followed an EU directive issued in 2017 driven by environmental concerns. A five year phase-out period allowed farms the time to gradually discontinue the use of zinc oxide. In the year the ban was enforced, a national increase in antimicrobial usage (AMU) in pigs – primarily driven by an increase in the peroral use of neomycin in weaners – was observed by DANMAP.

Method

In this study, the farm-level effect of the discontinued use of zinc oxide on AMU in weaners and finishers in Denmark was assessed [1]. The study included 4020 conventional, organic, free-range and breeding farms in Denmark supervised by 146 veterinarians from January 2018 to December 2023. Data was extracted from two national databases: farm characteristics from the Central Husbandry Register (CHR) and antimicrobial prescription records from the Danish Veterinary Medicine Statistic Program database (VetStat). Separate datasets were compiled for weaners and finishers, using only data from the longest period under one veterinarian. The monthly within-farm AMU was standardized by converting the amount of antimicrobials prescribed into number of Defined Animal Daily Doses (ADDkg) administered per pig, on the respective farm, per day, in the respective study month (ADDkg/pig-day). The VetStat data showed that each month before the ban, ~75% of farms with weaners used zinc oxide and that a gradual decline in usage began about a year before the ban was enforced (Figure 1). Farms discontinuing zinc oxide use within that year were classified as zinc-using prior to the ban. Additionally, a farm-level time variable marked AMU before, 1-5 months after, or >5 months after zinc discontinuation (for zinc-using weaner farms) or the legal ban (for other farms). The three level data (AMU in a study month, on a farm, supervised by a veterinarian) was analysed using a linear mixed-effect model including time-dependent and farm-specific fixed effects as well as the random effects of the individual farms and veterinarians.

Results

Figure 2 presents the estimated percentage changes in AMU (ADDkg/pig-day) on the individual farms 1-5 and >5 months after the implementation of the ban or the within-farm discontinuation of zinc oxide. The most significant effect was seen in zinc-using farms, where AMU for weaners increased by ~5% on average 1-5 months after the within-farm discontinuation of zinc oxide, followed by a ~17% increase after >5 months. In contrast, the AMU for finishers initially decreased by ~5% on average 1-5 months after the ban – likely a collateral effect of the increased AMU in weaners – but returned to pre-ban levels thereafter. An effect was also seen >5 months after the ban in non-zinc-using farms, where AMU in weaners increased by ~19% on average – however, this increase occurred from a ~14% lower average pre-ban AMU compared to zinc-using farms, indicating that non-zinc-using farms generally had a lower disease frequency. The rise in AMU among non-zinc-using farms may be attributed to a national increased disease frequency or shifts in veterinary prescribing practices in response to the ban.

The effect of the zinc oxide ban resembles that of the antimicrobial growth promoter (AGP) ban in 2000, where antimicrobial treatment for diarrhoea doubled in the first year [2]. However, this increase declined again as producers adapted to the change and the Danish pig production was not negatively impacted long-term [3]. A similar adjustment may follow the zinc oxide ban but has yet to emerge. While the average zinc-using farm increased AMU in weaners following the discontinuation of zinc oxide, some farms faced substantial increases, whereas others had few or no problems maintaining gut health in weaners during the transition – a pattern that was similarly observed after the discontinued use of AGPs. This between-farm variation indicated that the effect of the absence of zinc oxide on the prevalence of post-weaning diarrhoea was significantly influenced by individual farm management practices.

Figure 1 The proportion of farms with weaners using zinc oxide (vertical axis) each study month throughout the study period (horizontal axis), estimated from the extracted VetStat data. Horizontal dashed lines mark the year preceding the enforcement of the ban

DANMAP 2024

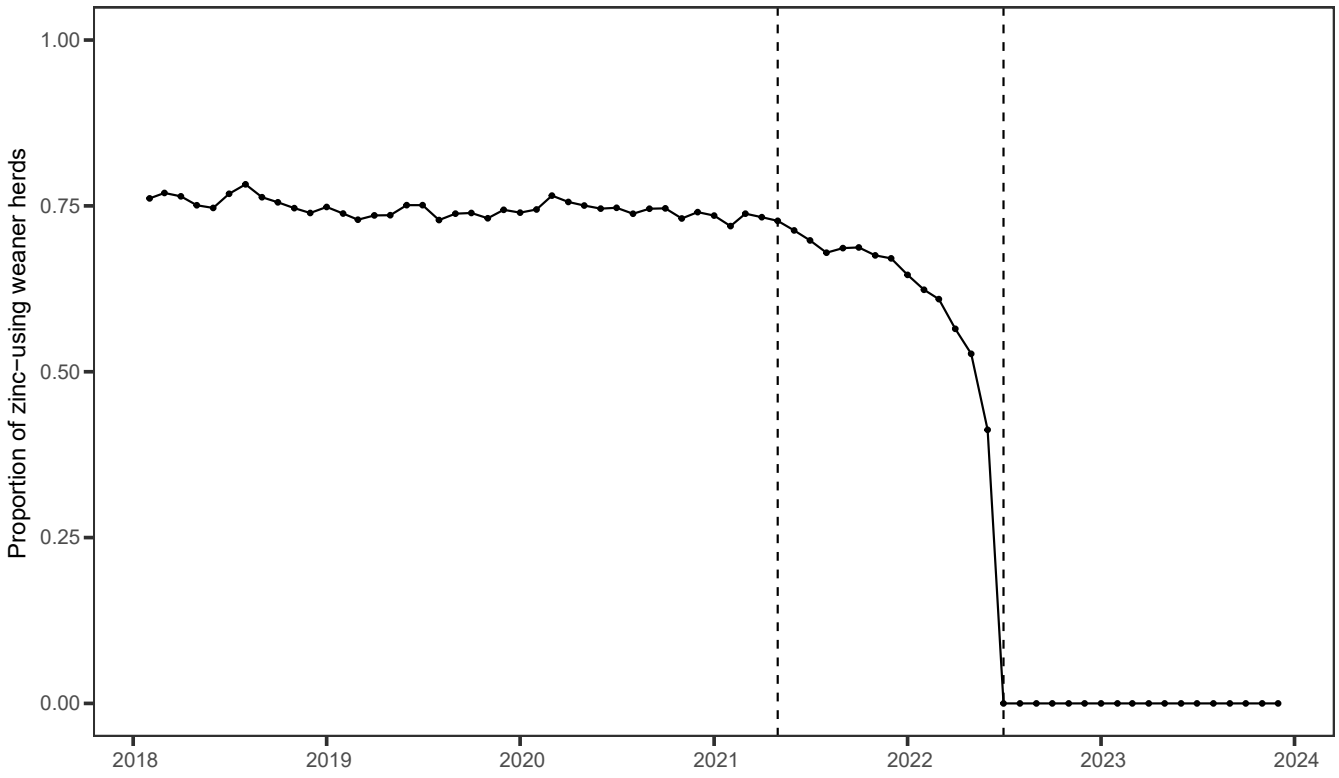
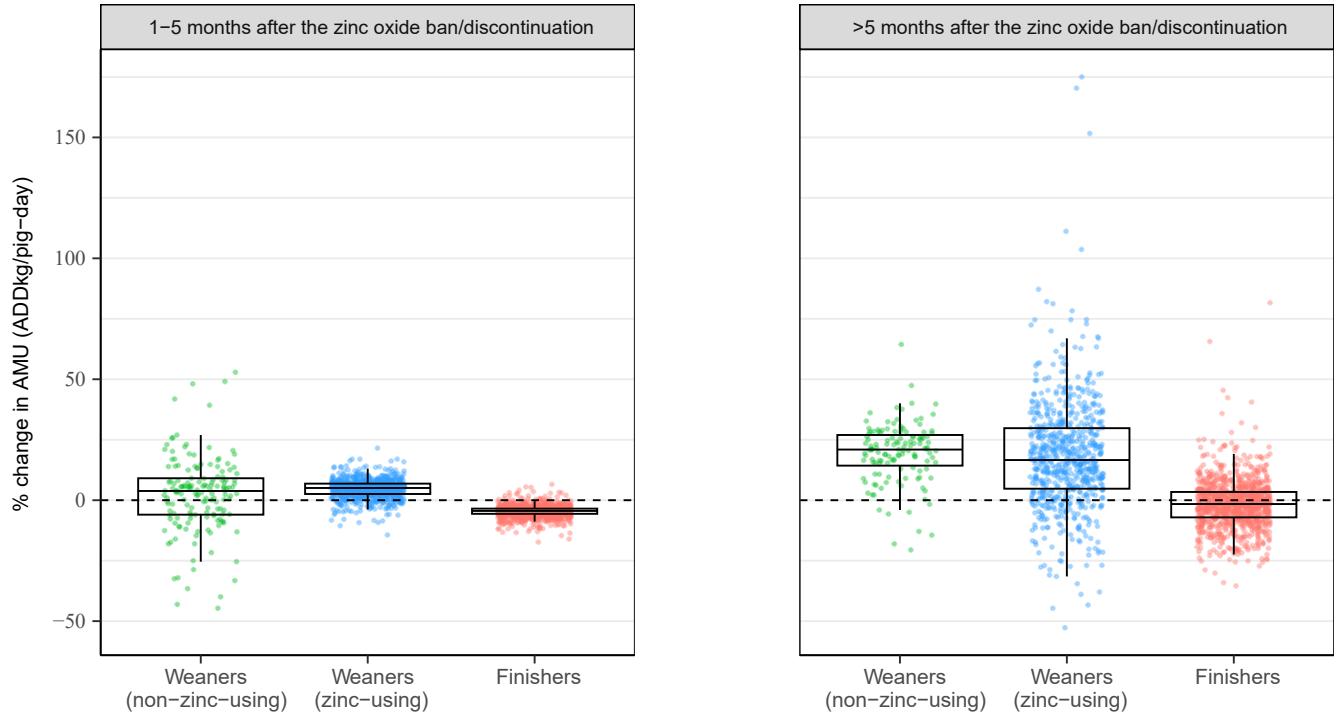


Figure 2 The effect of the zinc oxide ban, estimated as the predicted percentage change in AMU (ADDkg/pig-day) in weaners and finishers in the individual farms *1-5 months* and *>5 months* after the zinc oxide ban/discontinuation, compared to before the zinc oxide ban/discontinuation. The effect was predicted for the individual farms in the study where data was available both before and after the ban/discontinuation (number of farms from left to right: 158, 840, 1268, 131, 689, 1028)

DANMAP 2024



continued ... Textbox 4.1

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Textbox 4.2

The european sales and use of antimicrobials for veterinary medicine (ESUAvet): 2023 surveillance report

The European Sales and Use of Antimicrobials for Veterinary Medicine (ESUAvet) annual surveillance report is a new initiative launched by the European Medicines Agency aimed at addressing the critical challenge of antimicrobial resistance in veterinary medicine across the European Union. In March 2025, the first ESUAvet report was published, summarizing data reported from 2023 by all EU member states, as well as Iceland and Norway.

Data is reported by participating countries via the *Antimicrobial Sales and Use* (ASU) Platform, which was strategically developed to support the EU's commitment to mandatory data collection and transparent reporting on the sales and use of antimicrobial medicinal products across all animal sectors throughout the EU and European Economic Area. In this first year of ESUAvet reporting, countries were required to report sales data for all animals and use of antimicrobials for cattle, pigs, chickens, and turkeys. The reporting will be expanded in 2027 to include additional production animal species, such as horses, and in 2030 to encompass companion animals including cats, dogs, and fur animals.

Results of the 2023 ESUAvet Report and data comparisons
According to the 2023 ESUAvet report, 71.1 tonnes of antimicrobial active compounds were sold for treatment of animals in Denmark, corresponding to 20.1 mg/kg animal biomass. This places Denmark in the mid-range compared to the other countries in the report.

Only sales results were presented in the 2023 ESUAvet report, as the data on antimicrobial use across all participating countries was not considered complete and accurate enough for quantitative analysis. Many countries are still in the process of developing or refining systems for collecting data on antimicrobial use.

For Denmark, sales data was reported by the Danish Medicines Agency, based on pharmacy sales records. Use data was reported by the Danish Veterinary and Food Administration (DVFA), using data from *VetStat*, the national database for veterinary prescription medicine use, based on reports from veterinarians, feed mills, and pharmacies. Because sales and use data are derived from different sources and reflect different levels of the supply chain, they should not be directly compared.

It is also important to acknowledge that differences in data processing methods and analytical approaches can impact the results. For this reason, the ESUAvet report includes a disclaimer noting that the country-level results presented may differ from those published in national reports. In Denmark, the DVFA and DANMAP have jointly identified challenges related to data harmonization between the antimicrobial use determined in the reporting process to the ASU platform and DANMAP respectively. The primary discrepancy in methodology concerns classification and quantification of antimicrobial products, including the use of different International Units and derivative conversion factors. These differences highlight the continued strategic importance of thorough methodologies and established national surveillance systems like DANMAP.

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5

ANTIMICROBIAL CONSUMPTION IN HUMANS

5. Antimicrobial consumption in humans

Highlights

Antimicrobial consumption in Denmark was 16.27 DID in 2024, 7.3% lower than consumption in 2015 (17.56 DID) and almost similar to 2023 (16.47 DID). This may indicate stabilization of consumption since the COVID-19 related marked decreases in 2020 and 2021 followed by sharp increases in 2022 and 2023.

In primary health care, total antimicrobial consumption was 14.35 DID in 2024, comparable to the 14.56 DID in 2023 and 8.4% lower than in 2015 (15.66 DID). The four groups of penicillins constituted 64% of the consumption and beta-lactamase sensitive penicillins were the most used group of antimicrobials (accounting for 24% of total consumption in primary health care).

Antimicrobials prescribed for respiratory tract infections in 2024 decreased by 7% compared to 2023. In 2022 and 2023, antimicrobial consumption had been characterized by notable winter peaks compared to the pre-pandemic years of 2018-2019. These were most likely due to high rates of viral infections, in particular early and more severe RSV and influenza seasons, as well as an outbreak of Group A streptococci and a prolonged period of infections with *Mycoplasma pneumoniae* in children.

Antimicrobials prescribed to children decreased in 2024: among the 0-4 year olds, consumption in 2024 was on average 230 treated patients per 1,000 inhabitants, a 23% decrease compared to 298 treated patients per 1,000 inhabitants in 2023. For the 5-9 year olds, 172 patients per 1,000 inhabitants were treated in 2024 compared to 197 patients per 1,000 inhabitants in 2023 (13% decrease).

Elderly inhabitants living at care homes during 2024 received 93% more antimicrobials than elderly inhabitants living in their own homes (1,813 prescriptions per 1,000 inhabitants at long-term care facilities compared to 937 prescriptions per 1,000 inhabitants in their own homes). Urinary tract infections remained the main cause of the observed difference in the treatment frequency. After decreasing antimicrobial consumption for elderly since 2016, the consumption was unchanged for the first time in 2024 compared to the previous year of 2023.

Antimicrobial consumption in hospital care measured in DID (i.e. not accounting for hospital activity) was 1.92 DID in 2024, similar to 2023 (1.91 DID). When measuring in DDD per 100 bed-days (DBD), the consumption in 2024 (146.17 DBD) was 2.6% higher than in 2023 (142.51 DBD) and 33% higher than in 2015 (110.23 DBD).

Product shortages are of increasing concern in antimicrobial supply. In 2023, nitrofurantoin was unavailable in several months due to product shortage and in parts of 2024 metronidazole was unavailable. Simultaneously, the supply through special deliveries increased to cover the need.

AWaRe classification of antimicrobials used in Denmark showed that 82% consisted of access antimicrobials (WHO's goal is 60% access antimicrobials).

5.1 Introduction

In Denmark, antimicrobials are available by prescription from medical doctors, veterinarians and dentists. Sale is restricted to licensed pharmacies who have exclusive rights to sell prescription-only medicines. Thus, no over-the-counter sale takes place. All consumption of medicinal products for humans is recorded through the Register of Medicinal Product Statistics at the Danish Health Data Authority (Figure 2.1). This includes sales data from all public and private healthcare providers. Antimicrobial sales data have been submitted from the primary care sector since 1994 and from the hospital sector since 1997.

Registration of medicine consumption in the primary care sector covers sales from pharmacies to individuals and private clinics. Sales data contain an identifier of the prescriber and the patient in addition to information about the prescribed antimicrobial, including ATC code, formulation, package size and number of packages sold. Since 2004, the Register of Medicinal Product Statistics also receive information on the indication for prescribing. This allow a very detailed and near-complete surveillance of all systemic antimicrobials used in Denmark in primary health care.

For the hospital sector, antimicrobial consumption data from all public somatic hospitals with acute care function (referred to as somatic hospitals) are included in the report. Data from psychiatric hospitals, private hospitals and hospices are excluded, since they only account for a minor share of the consumption and no reliable denominator for measuring antimicrobial consumption in these facilities is available.

In this chapter, the term 'antimicrobials' covers all systemic antibacterial agents for human use listed in the Anatomical Therapeutic Chemical (ATC) Classification under the code J01. In addition, since 2014 metronidazole (ATC code P01AB01) and for hospitals vancomycin (ATC code A07AA09) have been included. Consumption of tuberculostica, antifungal drugs and antivirals are not included in this chapter.

The Danish Healthcare system has undergone changes in recent years, which led to functions being reassigned from hospitals to ambulatory care and further on to smaller health units, rehabilitation centers and general practice. Based on the recommendations from The Danish Resilience Commission, September 2023, future changes will include the establishment of regional and local health councils and the merge of the Capital Region and the Region Zealand as from January 2027. Such changes in organization are expected to impact the overall consumption per healthcare sector but also demonstrate changing trends in commonly used ways of reporting, e.g. number of DDD per bed days or per admission.

Antimicrobial stewardship has been an integrated part of the daily work at Danish Clinical Microbiology Departments for more than 30 years. In primary care, the Danish Research Center for General Medicine has, together with the Association of General Practitioners, undertaken important research on implementation of actions that support a more rational use of antibiotics in General practice. During the last decade, many of the bigger hospitals established antibiotic committees and the Danish Regions developed criteria for reduction of bacterial infections at hospitals including focus on better use of critically important antibiotics via the Danish Learning and Quality Teams. In addition, Infectious Disease specialists have in recent years enrolled in educational programs and established antimicrobial stewardship teams at some of the bigger hospitals.

The new Danish National Action Plan against antimicrobial resistance in humans from June 2025 aims to further strengthen the work.

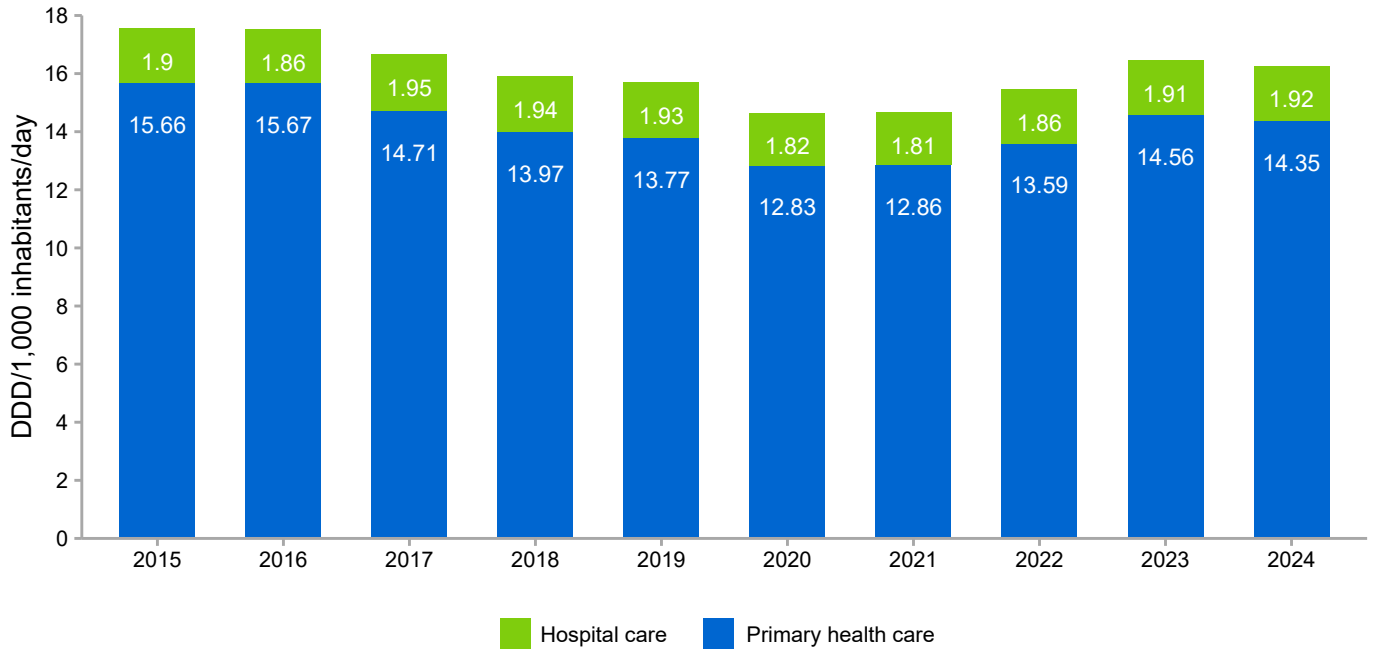
5.2 Total antimicrobial consumption in the Danish healthcare system

During the first five years of surveillance from 1996 to 2000, the consumption of systemic antimicrobials in Denmark showed no significant changes and consumption was estimated to be between 13 to 14 Defined Daily Doses per 1,000 inhabitants per day (DID). These first years of reporting are not fully comparable to later years due to changes in reporting methods and data systems. Between 2001 and 2011, consumption of antimicrobials increased steadily and peaked at a total of 18.95 DID in 2011 (not shown). From 2011 to 2021, consumption decreased markedly, with a further marked drop during the COVID-19 pandemic (Figure 5.1). However, from 2022 to 2023, the consumption increased by 6.6% from 15.45 DID to 16.47 DID, and in 2024 the consumption was 16.27 DID. The primary care sector accounts for the majority of the consumption in Denmark (88%).

The decrease in total antimicrobial consumption since 2013 was driven by reduced prescribing in primary health care. Measured in DID and not adjusted for hospital activity, antimicrobial consumption at hospitals fluctuated over the years, moving between the lowest levels of 1.86 DID in 2016 to highest levels of 1.95 DID in 2017. The notably lower levels in 2020 and 2021 are considered exceptions due to the COVID-19 pandemic.

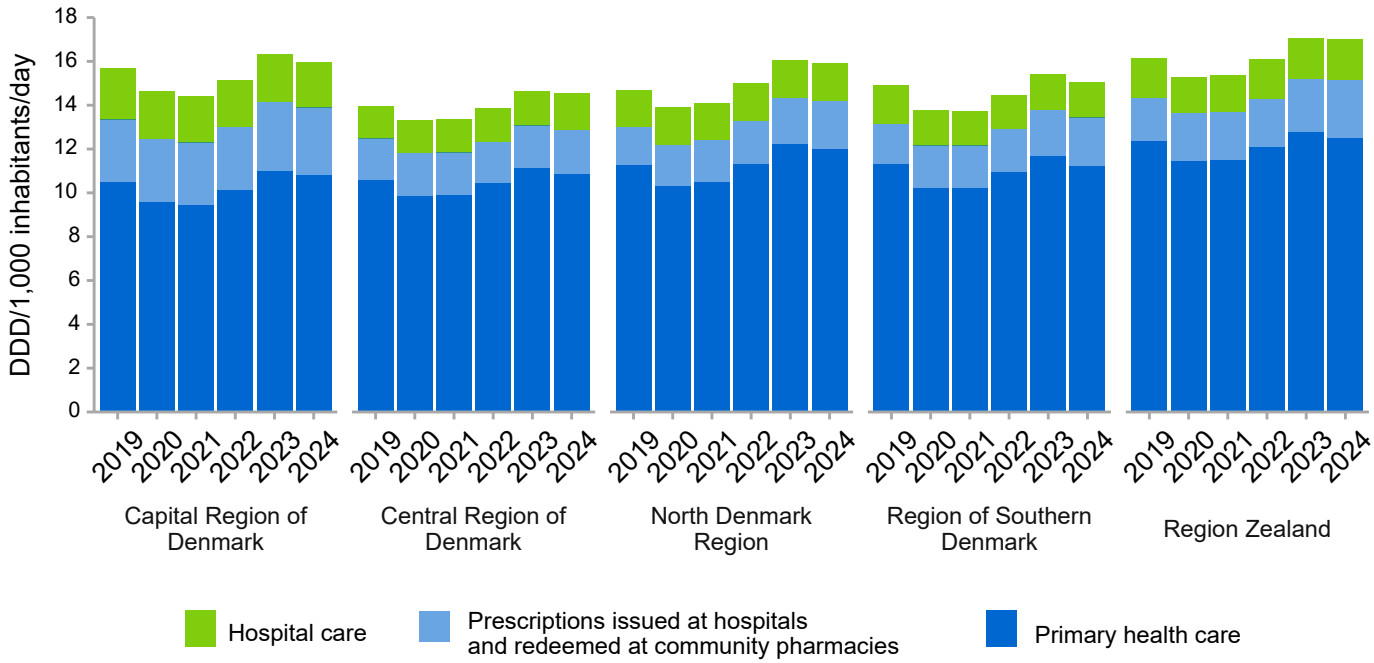
The total consumption of antimicrobials for both primary health care and somatic hospitals in the five Danish health regions is presented in Figure 5.2. The trends in consumption are similar for all five regions. Region Zealand showed the highest total consumption of 17.00 DID in 2024, whereas Central Region of Denmark had the lowest total consumption of 14.54 DID. Figure 5.3 presents the main drug classes used in primary health care and at hospitals; both sectors show a high share of penicillins in their usage patterns. Hospitals prescribe the majority of cephalosporins, aminoglycosides and carbapenems used, as well as other broadspectrum antibiotics (Figure 5.4). Assessed by WHO's AWaRe classification system, "access antimicrobials" constituted at least 80% since 2014 and 82% in 2024.

Figure 5.1 Total consumption of systemic antimicrobial agents in humans, DDD per 1,000 inhabitants per day, Denmark, 2015-2024
DANMAP 2024



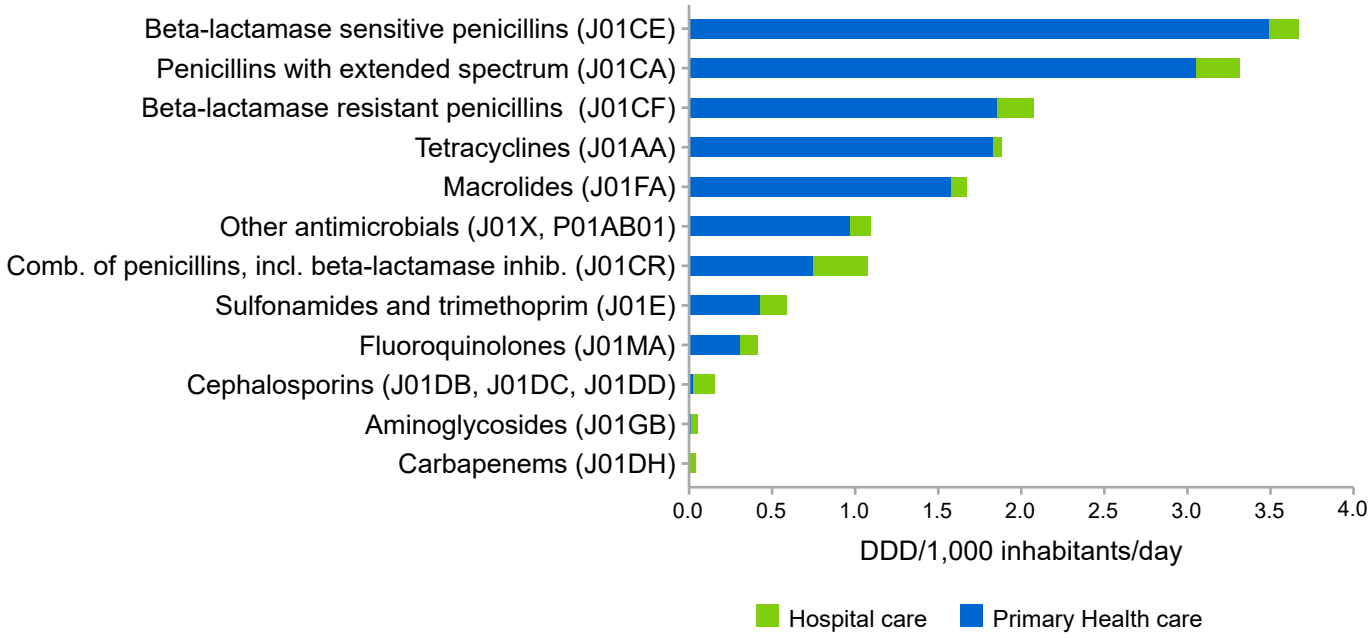
Data: Sales of antimicrobials in Denmark
Data source: Register of Medicinal Product Statistics and the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system

Figure 5.2 Consumption of systemic antimicrobial agents in primary health care and somatic hospitals, DDD per 1,000 inhabitants per day, Danish regions, 2019-2024
DANMAP 2024



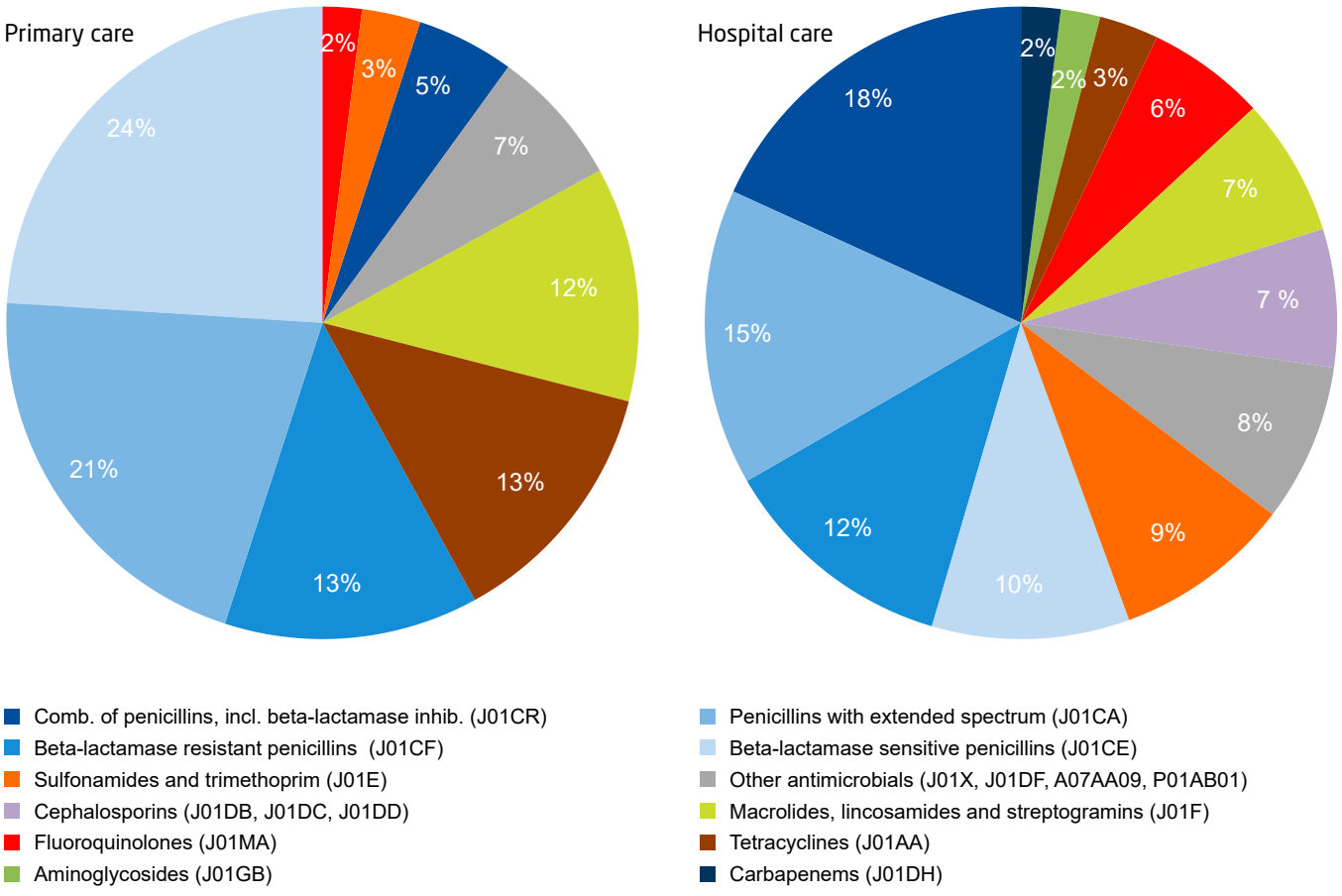
Data: Registered sales of antimicrobials to individuals and antimicrobial consumption at somatic hospitals
Data source: Register of Medicinal Product Statistics and the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system

Figure 5.3 Distribution of main antimicrobial classes used for humans in primary and hospital care, DDD per 1,000 inhabitants per day, Denmark, 2024
DANMAP 2024



Data: Registered sales of antimicrobials to individuals and antimicrobial consumption at somatic hospitals
Data source: Register of Medicinal Product Statistics and the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system

Figure 5.4 Percentage distribution of antimicrobial agents in primary health care and hospital care measured in, DDD, Denmark, 2024
DANMAP 2024



Data: Registered sales of antimicrobials to individuals and antimicrobial consumption at somatic hospitals
Data source: Register of Medicinal Product Statistics and the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system

5.3 Antimicrobial consumption in primary health care

In the following sections, the consumption of antimicrobials in primary health care is described by the units DDD per 1,000 inhabitants per day, number of prescriptions per 1,000 inhabitants and number of treated patients per 1,000 inhabitants. Data are based on sales to individuals and do not include the approximately 4% of antimicrobials, mainly penicillins, sold to clinics and doctors on call.

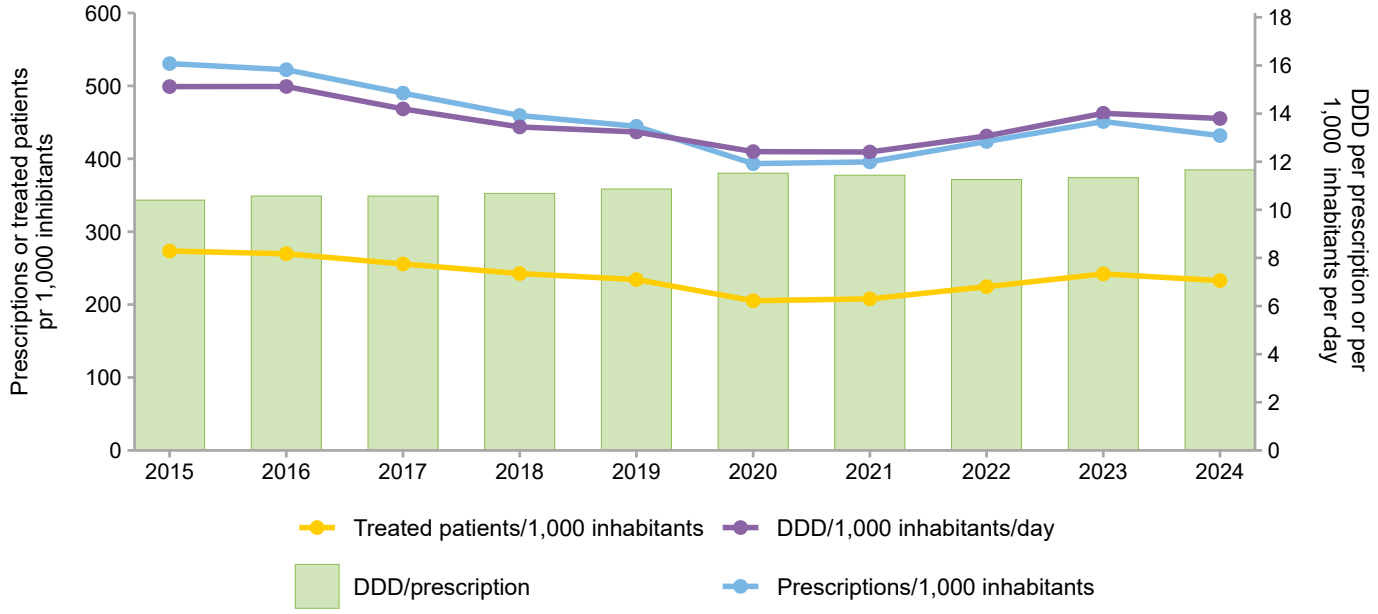
5.3.1 Overall antimicrobial consumption in primary health care

Comparison of trends over time by different indicators showed decreased consumption from 2014-2020, no change from 2020-2021 and increased consumption from 2021-2023 (Figure 5.5). In 2024, an average of 233 patients per 1,000 inhabitants were treated and 432 prescriptions per 1,000 inhabitants were issued (4% more than in 2023). The number of DDD per 1,000 inhabitants was 13.80 (1.5% lower than in 2023).

A decade earlier, in 2015, the number of treated patients per 1,000 inhabitants was 273, the number of prescriptions per 1,000 inhabitants was 531, and the number of DDD per 1,000 inhabitants was 15.12 (Table 5.1, Table 5.2 and Table 5.3).

The decreases in the number of treated patients and prescriptions over the decade are significant, a reduction of 15% and 19%, respectively. However, doses per prescription have increased, primarily due to switch to antibiotics that contribute with more DDDs per treatment, e.g. the switch to pivmecillinam as the drug of choice in the treatment of urinary tract infections and the switch to tetracycline as drug of choice in the treatment of chlamydia.

Figure 5.5 Consumption of systemic antimicrobial agents in primary health care, Denmark, 2015-2024 DANMAP 2024



Data: Registered sales of antimicrobials to individuals
Data source: Register of Medicinal Product Statistics and the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system

Table 5.1 Consumption of antimicrobial agents for systemic use in primary health care, DDD per 1,000 inhabitants per day, Denmark, 2005 and 2015-2024

DANMAP 2024

ATC group	Therapeutic group	Year										
		2005	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
J01AA	Tetracyclines	1.26	1.59	1.60	1.41	1.38	1.46	1.68	1.63	1.68	1.72	1.81
J01CA	Penicillins with extended spectrum	2.30	3.16	3.20	3.23	3.21	3.14	3.08	3.05	3.13	3.16	2.93
J01CE	Beta-lactamase sensitive penicillins	5.01	4.14	3.98	3.71	3.44	3.28	2.74	2.78	3.10	3.81	3.37
J01CF	Beta-lactamase resistant penicillins	0.96	1.35	1.44	1.52	1.57	1.59	1.55	1.58	1.68	1.74	1.82
J01CR	Combinations of penicillins, including beta-lactamase inhibitors	0.05	0.91	0.91	0.77	0.64	0.62	0.51	0.54	0.62	0.69	0.73
J01D	Cephalosporins and other betalactam antibiotics	0.03	0.03	0.03	0.03	0.03	0.02	0.02	0.02	0.02	0.02	0.02
J01EA	Trimethoprim and derivates	0.44	0.55	0.56	0.56	0.53	0.45	0.43	0.42	0.39	0.41	0.35
J01EB	Short-acting sulfonamides	0.33	0.17	0.16	0.14	0.13	0.12	0.11	0.09	0.08	0.08	0.06
J01EE	Combination of sulfonamides and trimethoprim, including derivates	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
J01FA	Macrolides	2.34	1.72	1.77	1.57	1.41	1.36	1.11	1.08	1.13	1.27	1.53
J01FF	Lincosamides	0.01	0.05	0.05	0.06	0.05	0.06	0.06	0.07	0.07	0.08	0.09
J01GB	Aminoglycosides											
J01MA	Fluroquinolones	0.32	0.49	0.47	0.44	0.41	0.36	0.32	0.31	0.33	0.32	0.30
J01XC	Steroid antibacterials (combination fusidic acid)	0.01	0.01	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00
J01XE	Nitrofuran derivates (nitrofurantoin)	0.45	0.45	0.43	0.26	0.15	0.27	0.27	0.28	0.27	0.12	0.19
J01XX	Other antibacterials (metheamine >99%)	0.24	0.20	0.21	0.22	0.22	0.23	0.25	0.28	0.29	0.33	0.37
P01AB01	Metronidazole	0.19	0.28	0.27	0.24	0.23	0.23	0.23	0.24	0.24	0.24	0.20
J01 and P01AB01	Antibacterial agents for systemic use (total)	13.96	15.12	15.13	14.19	13.44	13.24	12.42	12.40	13.07	14.01	13.80

Data: Registered sales of antimicrobials to individuals
Data source: Register of Medicinal Product Statistics and the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system

Table 5.2 Number of treated patients per 1,000 inhabitants for leading antimicrobial agents in primary health care, Denmark, 2005 and 2015-2024

DANMAP 2024

ATC group	Therapeutic group	Year										
		2005	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
J01AA	Tetracyclines	11.96	11.32	11.04	10.35	9.69	10.10	14.43	12.99	13.64	14.06	13.42
J01CA	Penicillins with extended spectrum	73.00	74.87	74.05	74.04	73.56	71.97	67.14	68.60	71.45	72.42	66.04
J01CE	Beta-lactamase sensitive penicillins	170.17	130.06	125.69	119.32	110.90	104.70	84.93	87.69	100.09	116.67	105.69
J01CF	Beta-lactamase resistant penicillins	27.78	28.85	29.70	29.96	31.10	31.06	30.52	30.89	32.92	33.77	33.42
J01CR	Combinations of penicillins, including betalctamase inhibitors	1.52	22.03	22.17	19.89	17.73	17.33	14.43	15.50	17.90	20.28	21.16
J01E	Sulphonamides and trimethoprim	36.12	22.45	21.17	19.87	18.42	16.63	15.04	13.66	12.67	12.47	10.50
J01FA	Macrolides	70.73	51.75	53.21	46.01	40.11	38.45	25.13	24.97	27.16	30.06	38.55
J01MA	Fluoroquinolones	12.19	15.04	14.37	13.36	12.26	10.74	9.01	8.52	9.10	8.87	8.01
J01X	Other antibacterials (methenamine >99%)	7.41	7.35	7.47	5.01	3.62	5.66	5.80	5.95	5.91	2.65	5.17
P01AB01	Metronidazole	13.22	16.47	16.03	14.84	14.05	13.57	13.36	13.77	13.94	14.11	11.88
J01 and P01AB01	Antibacterial agents for systemic use (total)	311	273	270	256	243	234	205	208	225	242	233

Data: Registered sales of antimicrobials to individuals
Data source: Register of Medicinal Product Statistics and the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system

Table 5.3 Number of prescriptions per 1,000 inhabitants for leading antimicrobial agents in primary health care, Denmark, 2005 and 2015-2024

DANMAP 2024

ATC group	Therapeutic group	Year										
		2005	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
J01AA	Tetracyclines	20.00	17.90	17.18	15.89	14.63	15.11	20.19	18.25	18.71	19.11	17.84
J01CA	Penicillins with extended spectrum	106.07	113.53	113.16	114.37	114.31	112.19	105.93	107.97	112.19	114.05	103.92
J01CE	Beta-lactamase sensitive penicillins	224.20	163.09	157.13	148.52	136.81	128.77	104.07	107.28	122.87	145.45	129.58
J01CF	Beta-lactamase resistant penicillins	39.56	40.81	41.87	41.87	43.35	43.16	42.87	43.17	45.66	47.05	46.42
J01CR	Combinations of penicillins, including betalctamase inhibitors	2.31	30.73	31.13	27.09	23.71	23.07	19.14	20.36	23.45	26.32	27.36
J01E	Sulphonamides and trimethoprim	55.30	38.39	36.41	34.29	31.74	28.14	25.59	23.07	21.26	21.30	18.31
J01FA	Macrolides	96.24	68.00	68.85	60.00	52.64	50.71	33.66	33.80	36.94	40.32	49.77
J01MA	Fluoroquinolones	15.74	19.50	18.74	17.37	15.97	13.99	12.07	11.41	11.96	11.57	10.48
J01X	Other antibacterials (methenamine >99%)	16.15	16.28	15.82	10.18	6.76	10.29	10.62	10.70	10.72	5.47	9.88
P01AB01	Metronidazole	15.44	19.15	18.63	17.26	16.31	15.78	15.62	16.00	16.17	16.25	13.55
J01 and P01AB01	Antibacterial agents for systemic use (total)	592.36	530.56	522.19	490.08	459.39	444.53	393.34	395.76	423.70	451.09	431.77

Data: Registered sales of antimicrobials to individuals
Data source: Register of Medicinal Product Statistics and the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system

Table 5.4 Consumption of antimicrobial agents for systemic use in primary health care at regional level, Denmark, 2020-2024

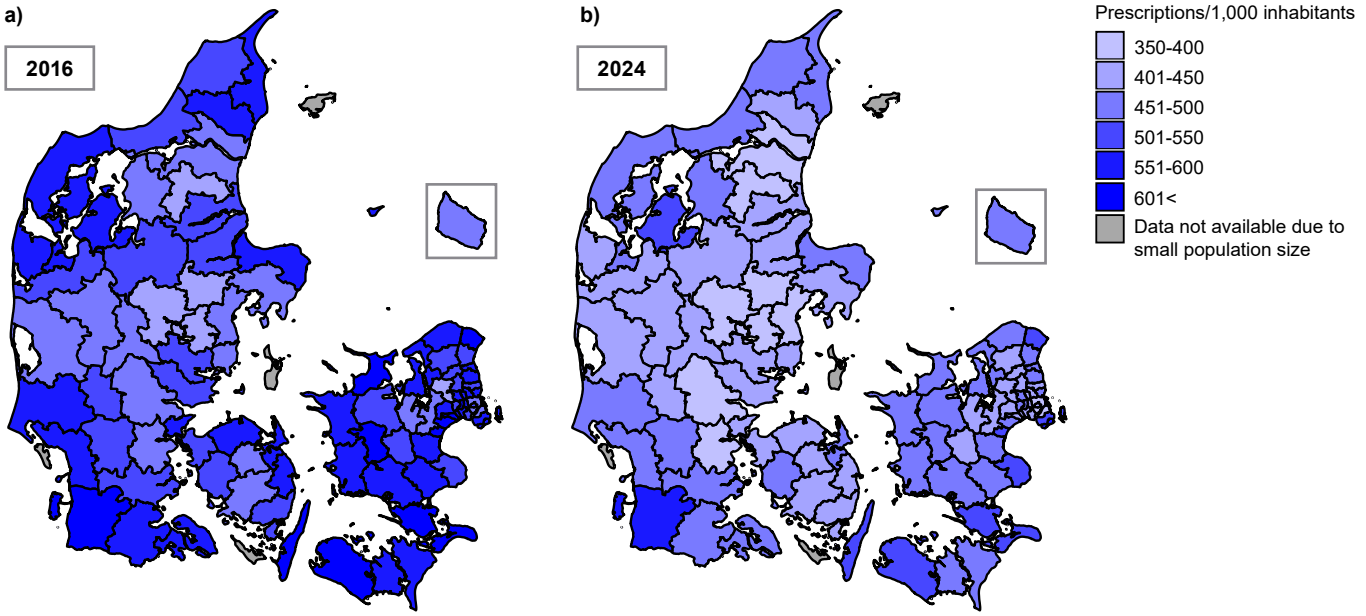
DANMAP 2024

Region	Indicator	Year				
		2020	2021	2022	2023	2024
Capital Region	DDD/1,000 inhabitants/day	12.47	12.32	13.03	14.14	13.90
	Prescriptions/1000 inhabitants	382	378	409	443	423
Region Zealand	DDD/1,000 inhabitants/day	13.65	13.71	14.31	15.21	15.14
	Prescriptions/1,000 inhabitants	436	440	466	489	470
Region of Southern Denmark	DDD/1,000 inhabitants/day	12.17	12.17	12.91	13.78	13.44
	Prescriptions/1,000 inhabitants	401	405	434	460	440
Central Denmark Region	DDD/1,000 inhabitants/day	11.82	11.83	12.32	13.07	12.86
	Prescriptions/1,000 inhabitants	374	380	402	425	408
North Denmark Region	DDD/1,000 inhabitants/day	12.20	12.42	13.27	14.33	14.23
	Prescriptions/1000 inhabitants	390	400	431	458	438
Denmark (total)	DDD/1,000 inhabitants/day	12.42	12.40	13.07	14.01	13.80
	Prescriptions/1,000 inhabitants	393	396	424	451	432

Data: Registered sales of antimicrobials to individuals
Data source: Register of Medicinal Product Statistics and the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system

Figure 5.6 Number of prescriptions in primary health care per 1,000 inhabitants in Danish municipalities in a) 2016 and b) 2024

DANMAP 2024



Data: Registered sales of antimicrobials to individuals
Data source: Register of Medicinal Product Statistics and the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system

Interregional differences in the levels of prescribing have been described in DANMAP since 2017 (Table 5.4). In general, the Danish population is relatively homogeneous and health care is of standardized quality, which, combined with several initiatives to educate GPs in appropriate prescribing, diminish potential differences in prescribing trends. However, observed variations in prescribing may owe to differences in population density (distance to nearest general practitioner), differences in age and comorbidity of the population (younger populations in bigger cities and in the Capital Region) as well as behavioral differences between urban and rural populations.

Figure 5.6 shows the number of prescriptions per 1,000 inhabitants at municipality level in 2016 and 2024, respectively. In 2024, the consumption ranged from 365 to 573 prescriptions per 1,000 inhabitants. In 2016, the range was 434-727 prescriptions per 1,000 inhabitants. 2016 was the baseline year for the first Danish action plan on reducing antimicrobial use in human health care (see Textbox 5.1 in DANMAP2021). Of note is that prescribers in all municipalities reduced their prescribing activities in the shown period. Demographic differences might impact the range of prescribing. Distribution of elderly inhabitants above 60 years in the municipalities closely follows the distribution of prescriptions per 1,000 inhabitants with higher prescription rates in municipalities with larger populations of elderly inhabitants above 60 years (data not shown).

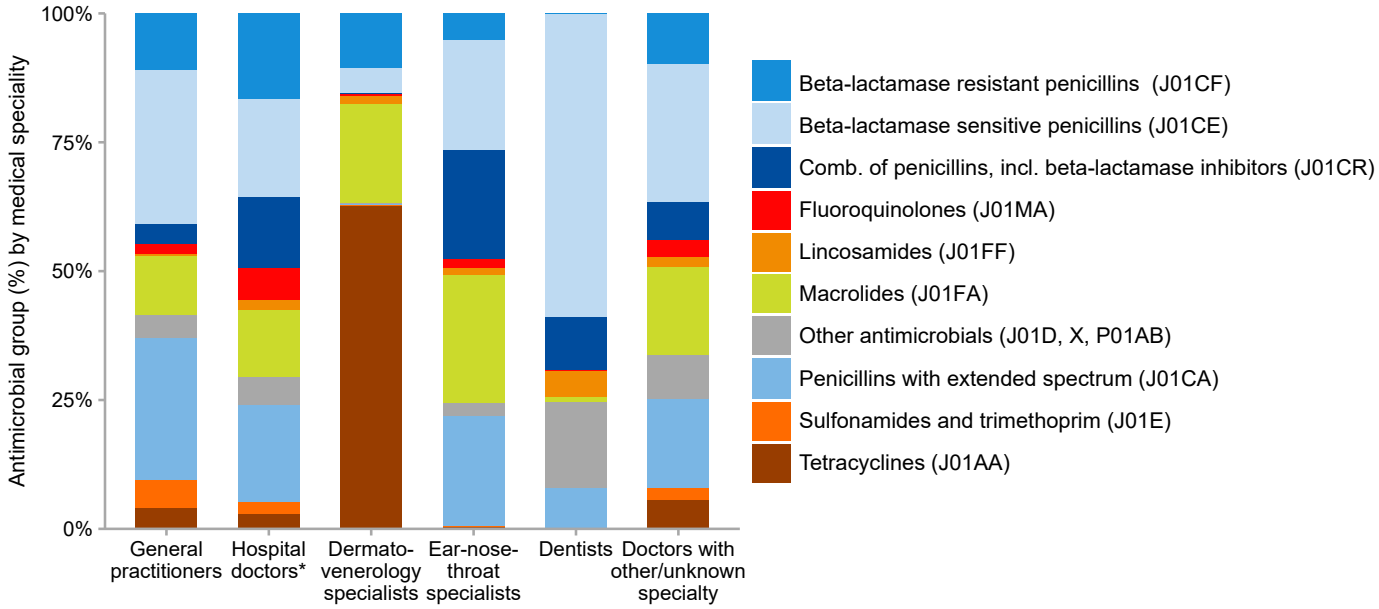
5.3.2 Antimicrobial consumption by prescriber

Prescribing trends in primary health care clearly differ by prescriber's specialty. Table 5.5 shows an overview of number of prescriptions issued by different specialists, including hospital doctors issuing prescriptions for patients at hospitals, which then are then redeemed at a community pharmacy. Figure 5.7 shows the main antimicrobial groups prescribed by medical specialty in primary health care in 2024. In general practice, beta-lactamase sensitive penicillins were the most prescribed (30%) indicating adherence to the guidelines recommending beta-lactamase sensitive penicillins as the drug of choice in many common infections. In 2024, 63% of antimicrobial prescriptions from dermato-venerology specialists were tetracyclines, which are indicated for treatment of severe acne and sexually transmitted chlamydia/mycoplasma infections.

The majority of prescriptions by dentists were narrow-spectrum beta-lactamase sensitive penicillins (59%) reflecting adherence to the recommended first-line treatment for common dental infections in primary health care.

General practitioners have access to their own prescribing data through ordiprax+, an online dashboard with personal log-in visualising prescription data and enabling comparisons with other practices on regional level (DANMAP 2020 Textbox 5.2). Additionally, general practitioners are organized in quality clusters where improvement of antimicrobial prescribing is discussed among other topics.

Figure 5.7 Antimicrobial groups prescribed by main medical specialities in primary health care, Denmark, 2024 DANMAP 2024



*Hospital doctors issuing prescriptions for patients in ambulatory care or upon discharge from hospital
Data: Registered sales of antimicrobials to individuals
Data source: Register of Medicinal Product Statistics and the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system

Table 5.5 Number of prescriptions per 1,000 inhabitants by main medical specialties, Denmark, 2020-2024 DANMAP 2024

Prescriber		Year				
		2020	2021	2022	2023	2024
General practitioners	Prescriptions per 1,000 inhabitants	280.4	279.0	300.9	323.1	305.5
	DDD per prescription	11.1	11.0	10.8	10.9	11.2
Hospital doctors*	Prescriptions per 1,000 inhabitants	64.6	63.5	62.0	65.6	64.3
	DDD per prescription	13.0	13.2	13.6	13.7	14.4
Ear-nose-throat specialists	Prescriptions per 1,000 inhabitants	6.1	6.9	8.1	8.5	8.1
	DDD per prescription	8.9	8.3	8.1	8.0	8.1
Dermato-venerology specialists	Prescriptions per 1,000 inhabitants	5.3	5.0	4.6	4.4	4.4
	DDD per prescription	33.8	35.4	35.0	34.6	37.1
Dentists	Prescriptions per 1,000 inhabitants	25.6	28.9	34.4	33.1	32.8
	DDD per prescription	7.9	7.7	7.7	8.2	8.2

*Hospital doctors issuing prescriptions for patients in ambulatory care or upon discharge from hospital
Data: Registered sales of antimicrobials to individuals
Data source: Register of Medicinal Product Statistics and the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system

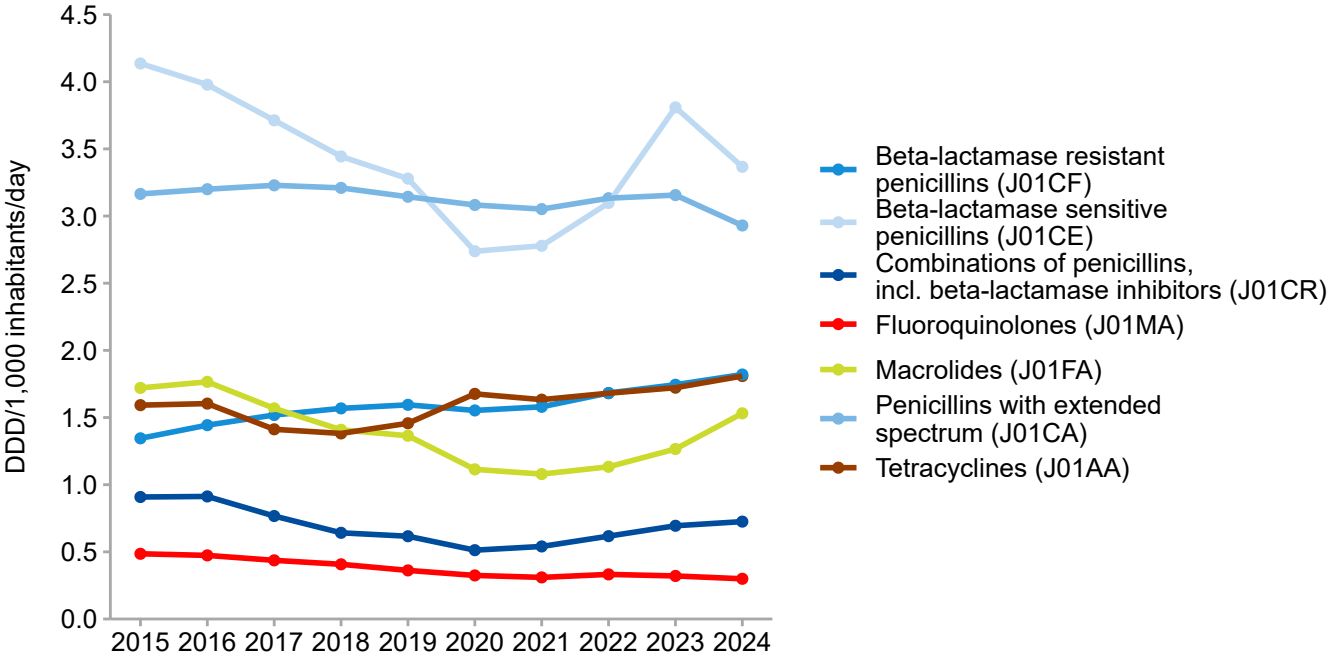
5.3.3 Consumption of antimicrobial groups

In compliance with treatment guidelines, beta-lactamase sensitive penicillins have been the most used antimicrobials in primary health care in Denmark for decades (Figure 5.8). In 2024, beta-lactamase sensitive penicillins accounted for 24% of total consumption in primary health care. The steep increase of these penicillins, observed post COVID-19 and attributed to a renormalized circulation of airway infections, discontinued in 2024, (-11.6% from 2023 to 2024).

Altogether, the four penicillin groups (penicillins with extended spectrum; beta-lactamase sensitive penicillins; beta-lactamase resistant penicillins; combinations of penicillins, including beta-lactamase inhibitors) accounted for 8.84 DID corresponding to 64% of antimicrobials consumed in primary health care in 2024. Other beta-lactams such as cephalosporins, monobactams and carbapenems were either used at extremely low level or restricted to hospital use only.

In contrast, consumption of macrolides increased by 21% from 2023 to 2024. This is attributed to the Group A streptococcal pandemic that circulated at high rates in 2023 to 2024, mainly among children and their parents.

Figure 5.8 Consumption of leading antimicrobial groups for systemic use in primary health care, DDD per 1,000 inhabitants per day, Denmark, 2015-2024
DANMAP 2024



Data: Registered sales of antimicrobials to individuals
Data source: Register of Medicinal Product Statistics and the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system

5.3.4 Antimicrobial consumption by patient case mix

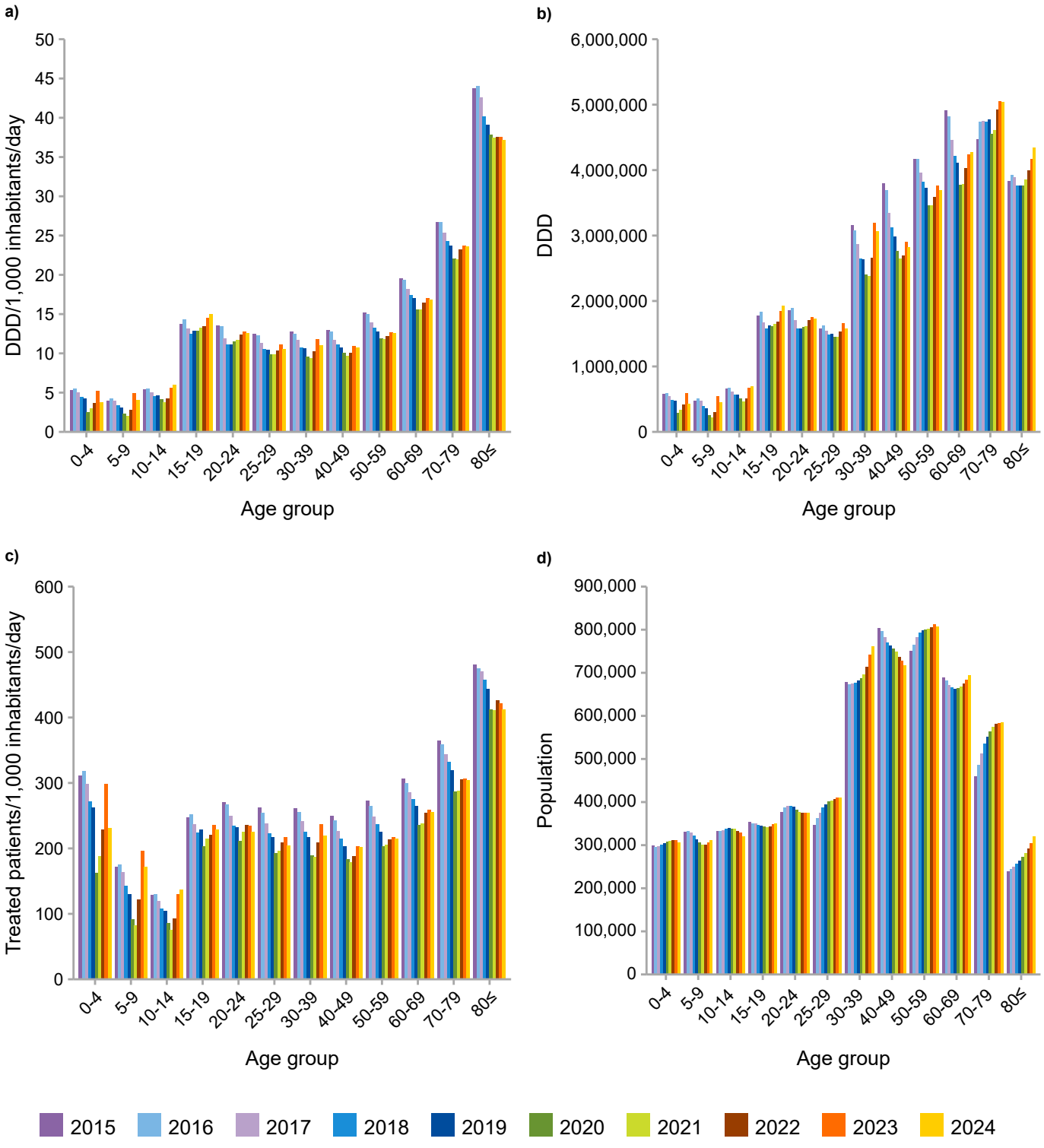
Antimicrobial consumption is highly affected by patient case mix. The need for antimicrobials differs throughout life and for the two genders. Antimicrobial consumption is also affected by sociodemographic factors such as civil status, educational level, employment status and country of birth (DANMAP 2022, Textbox 5.2). Figure 5.9a-c presents consumption of antimicrobials by age group based on different denominators: Figure 5.9a presents consumption in DDD per 1,000 inhabitants per day; Figure 5.9b in crude DDD, i.e. not corrected for population size; Figure 5.9c presents the number of patients treated per 1,000 inhabitants; Figure 5.9d presents population size by age group. Children and adolescents are presented in five-year age groups, while adults are clustered in 10-year age groups.

Estimates of antimicrobial consumption for children based on DDD should be interpreted with caution since the DDD is defined as "maintenance dose per day for its main indication in adults". The maintenance dose per day for children may differ from the one for adults due to different pharmacodynamics and -kinetics. Furthermore, infants and young children in the same age group might be treated with different doses based on body weight. Therefore, other units of measurement might be more suitable to monitor consumption in children, e.g. number of treated patients per 1,000 inhabitants and number of prescriptions per 1,000 inhabitants.

Macrolides play an important role in the treatment of bacterial respiratory tract infections in children and adolescents (Figure 5.10). Macrolides were also used as first-line treatment for chlamydia infections until the change in guidance (described in DANMAP2020), which may be the reason for the relatively high, but in recent years decreasing, consumption of macrolides in the 15-24 year olds. However, penicillins continued to be the most used antimicrobial agents for children and adolescents, constituting between 63% and 86% of all antimicrobials prescribed depending on age group (Figure 5.10).

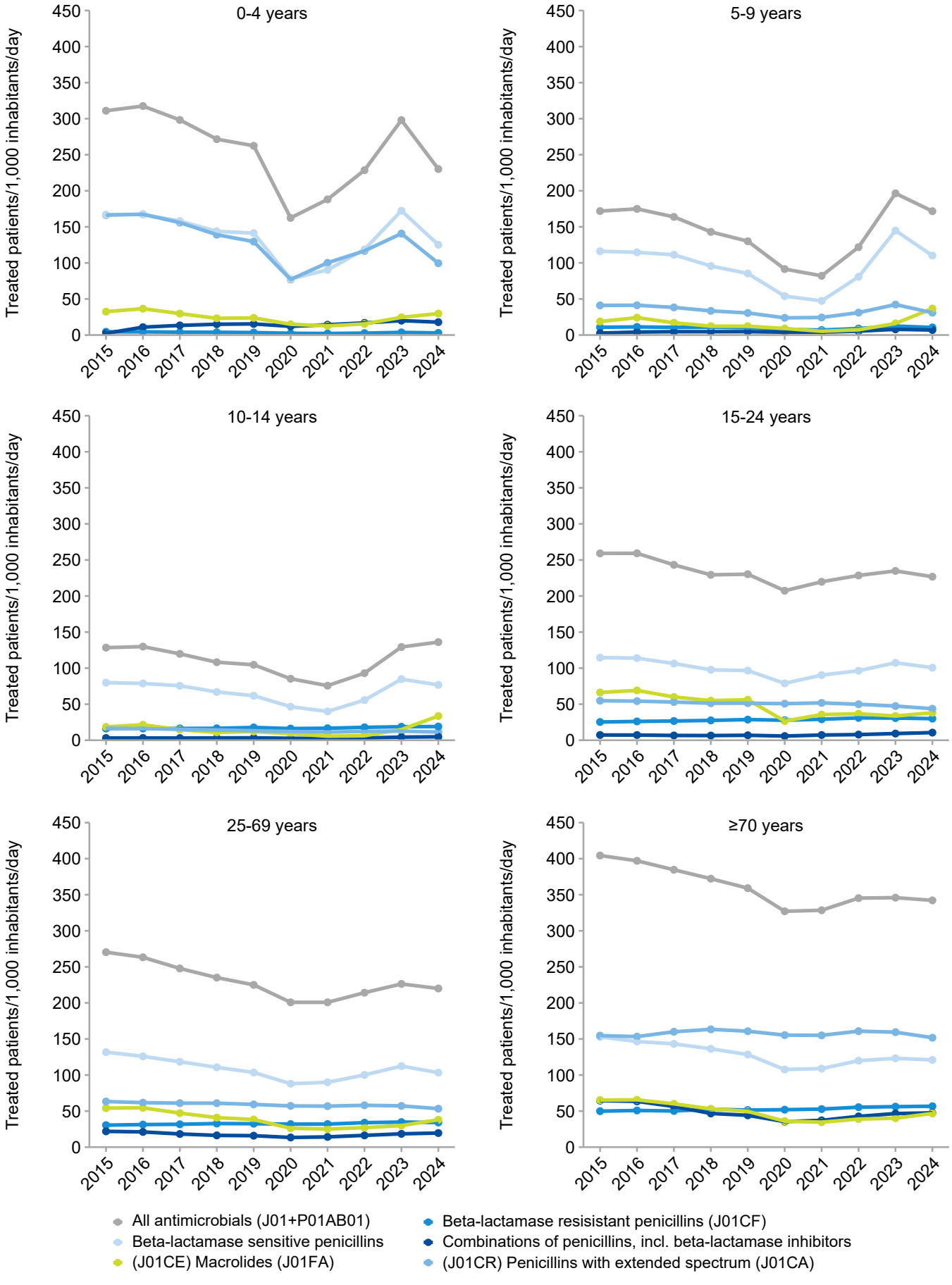
Differences in antimicrobial consumption between genders are well known – a trend driven by higher incidence of urinary tract infections and different healthcare seeking behavior. In 2024, the number of treated females (all age groups) was 271 per 1,000 inhabitants and the number of treated males was 195 per 1,000 inhabitants. Particularly the consumption of pivmecillinam, sulfonamides, trimethoprim and nitrofurantoin, all indicated for treatment of urinary tract infections, was approximately three times higher for females than for males (Figure 5.11). Decreasing trends were primarily observed in the number of prescriptions for elderly women (80+ years), who were the most frequently treated (559 prescriptions per 1,000 females above 80 years).

Figure 5.9 Consumption of systemic antimicrobial agents in primary health care by age group, measured in a) DDD per 1,000 inhabitants per day, b) DDD, c) treated patients per 1,000 inhabitants and d) population size, Denmark, 2015-2024 DANMAP 2024



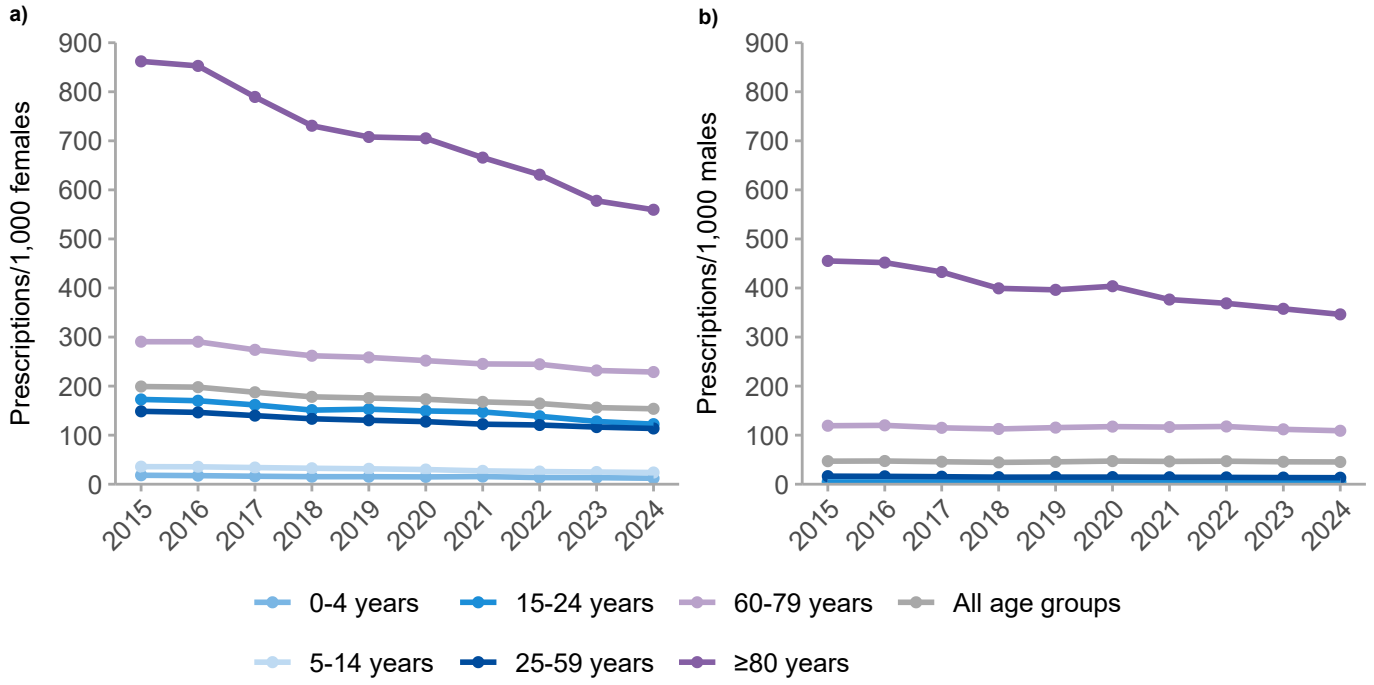
Data: Registered sales of antimicrobials to individuals
Data source: Register of Medicinal Product Statistics, the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system and Statistics Denmark
Children and adolescents are presented in five-year age groups, while adults are clustered in 10-year age groups

Figure 5.10 Consumption of main antimicrobial agents by age group, treated patients/1,000 inhabitants, Denmark, 2015-2024 DANMAP 2024



Data: Registered sales of antimicrobials to individuals
Data source: Register of Medicinal Product Statistics and the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system

Figure 5.11 Consumption of antimicrobials primarily used for treatment of urinary tract infections* in primary health care for a) females and b) males, prescriptions per 1,000 inhabitants, Denmark, 2015-2024 DANMAP 2024



* Pivmecillinam, sulfonamides, trimethoprim and nitrofurantoin
Data: Registered sales of antimicrobials to individuals
Data source: Register of Medicinal Product Statistics and the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system

5.3.5 Antimicrobial consumption for treatment of respiratory tract infections

One of the main indications provided by general practitioners in primary health care for prescribing antimicrobials is upper and/ or lower respiratory tract infections. In 2024, an abrupt drop in the number of prescriptions per 1,000 inhabitants for respiratory infections was observed compared to 2023, from 116 to 108 (-7%), Figure 5.12. The years before, in 2020 antimicrobial consumption had set out slightly lower, then demonstrated a sharp drop from April 2020 to July 2021. This coincided with a marked decreases in the number of laboratory confirmed influenza and RSV infections, most likely due to the societal restrictions implemented in March 2020 due to the COVID-19 pandemic. However, from August 2021 the consumption went back to levels similar to the corresponding pre-pandemic months in 2019, again coinciding with the Respiratory Syncytial Virus (RSV) summer epidemic in 2021. Antimicrobial consumption during the winter 2022-2023 reached a higher level than observed in 2018-2019. This coincided with an early RSV and influenza season as well as an outbreak of Group A streptococci, as also observed in other European countries.

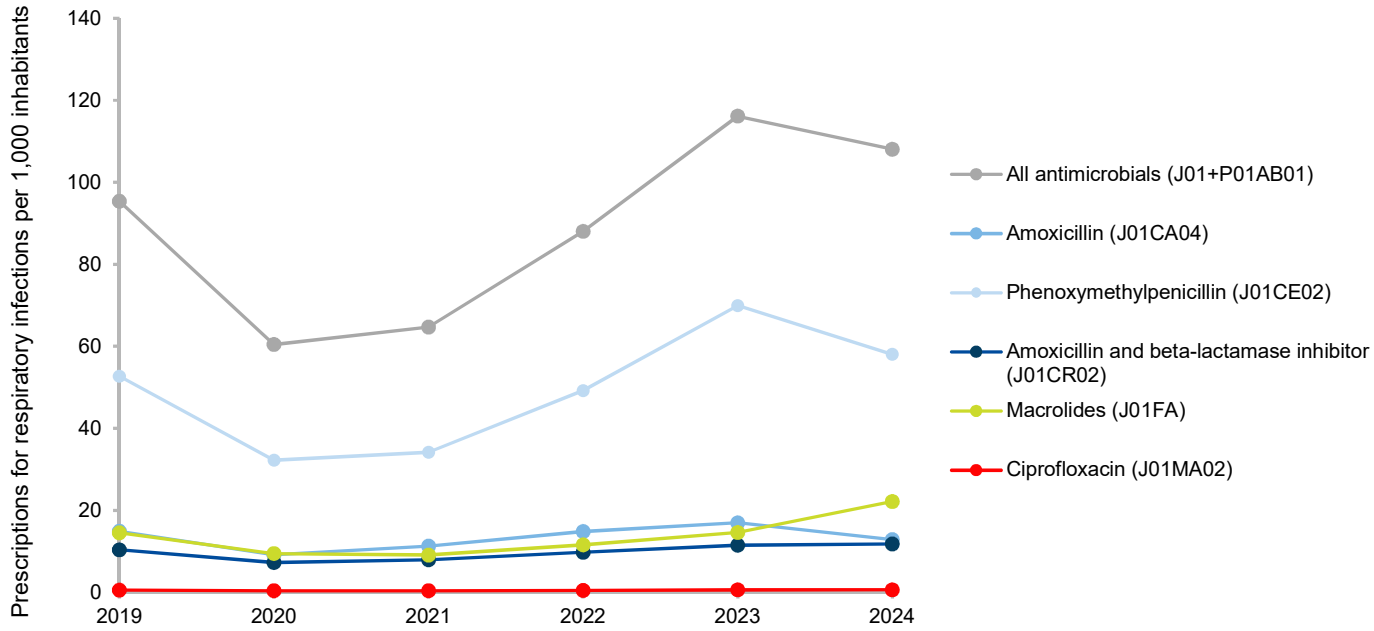
5.3.6 Antimicrobial consumption for elderly inhabitants

One of the more recent additions to the DANMAP program is surveillance of antimicrobial consumption in elderly inhabitants aged 65 years and above. Close monitoring of infections in this population is necessary, as it is one of the most fragile populations in society. Surveillance of antimicrobial consumption contributes to high-quality treatment of infections and thereby prevents emergence of antimicrobial resistant pathogens. Data are based on the Danish Care Home Register and the Danish Civil Registry. By combining these registries, it is possible to divide elderly inhabitants into two populations; elderly living in their own homes and elderly living at long-term care facilities.

Figure 5.13 shows antimicrobial consumption for elderly inhabitants aged 65 years and above in 2016-2024. Elderly inhabitants living at care homes received 93% more antimicrobials than elderly inhabitants living in their own homes in 2024. The consumption for the elderly has been decreasing since 2016, with a steeper decrease in consumption for elderly living at care homes. However, in 2024 the consumption was unchanged for the first time when comparing the consumption in the previous year of 2023. The figure also compares trends in prescription codes for different infectious entities.

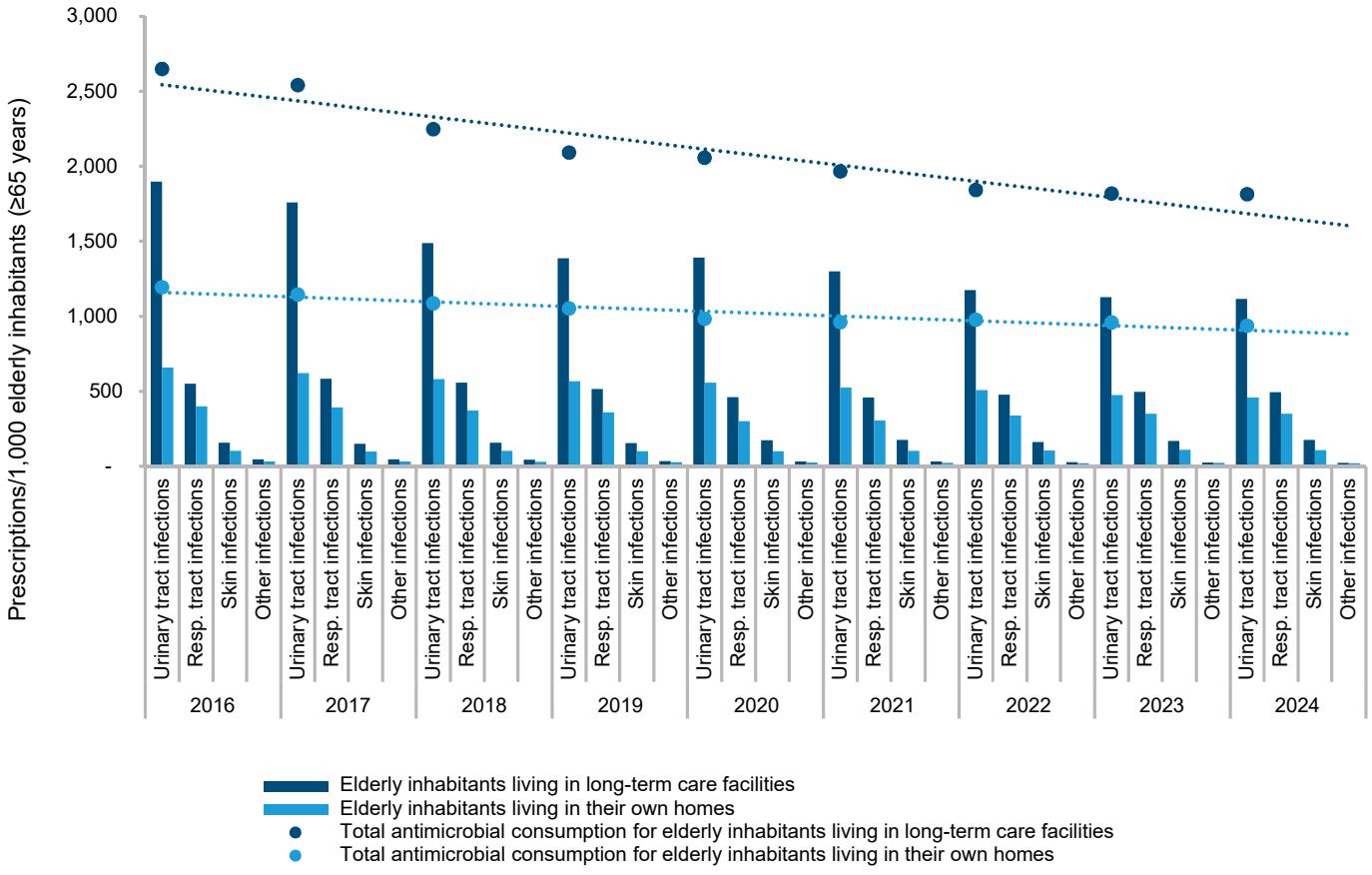
One of the main actions of the new Danish national action plan about antimicrobial resistance in human health, is to improve knowledge and awareness about infection prevention and control at long-term care facilities, but also among the elderly in general.

Figure 5.12 Antimicrobial prescriptions indicated for treatment of respiratory tract infections in primary health care, prescriptions per 1,000 inhabitants, Denmark, 2019-2024
DANMAP 2024



Data: Registered sales of antimicrobials to individuals
Data source: Register of Medicinal Product Statistics and the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system

Figure 5.13 Consumption of antimicrobials in primary health care for elderly inhabitants (≥65 years) living in long-term care facilities or in their own homes, Denmark, 2016-2024
DANMAP 2024



Data: Registered sales of antimicrobials to individuals
Data source: Register of Medicinal Product Statistics, and the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system, Care Home Register and Danish Civil Registry

5.4 Antimicrobial consumption in hospital care

Surveillance of antimicrobial consumption in hospital care is based on sale of systemic antimicrobials (ATC code J01, P01AB01 and A07AA09) from Danish hospital pharmacies to hospitals, excluding private hospitals and psychiatric departments (approximately 2-3% of the total hospital consumption). Antimicrobial consumption data are presented as DDD per 100 occupied bed-days (DBD) and per 100 admissions (DAD) to account for hospital activity. The consumption is also presented as DDD per 1,000 inhabitants per day to enable comparison with consumption in primary health care and to correct for changes in consumption data based on changes in hospital activity, the background population being a more stable denominator.

Hospital activity has changed over the years with decreasing number of bed-days and admissions, although at differing rates (Figure 5.14). Earlier discharge of patients, increasing ambulatory care functions in the community as well as in care homes and changed workflow due to new electronic systems all affect the activity and need to be considered when interpreting antimicrobial consumption trends in hospitals (see Table 2.1 in Chapter 2 'Introduction').

Information on consumption at patient level is currently not available to DANMAP for the hospital sector. This information is expected to become available to DANMAP through the "Hospital Medicine Register" in coming years.

5.4.1 Antimicrobial consumption at public somatic hospitals accounting for hospital activity

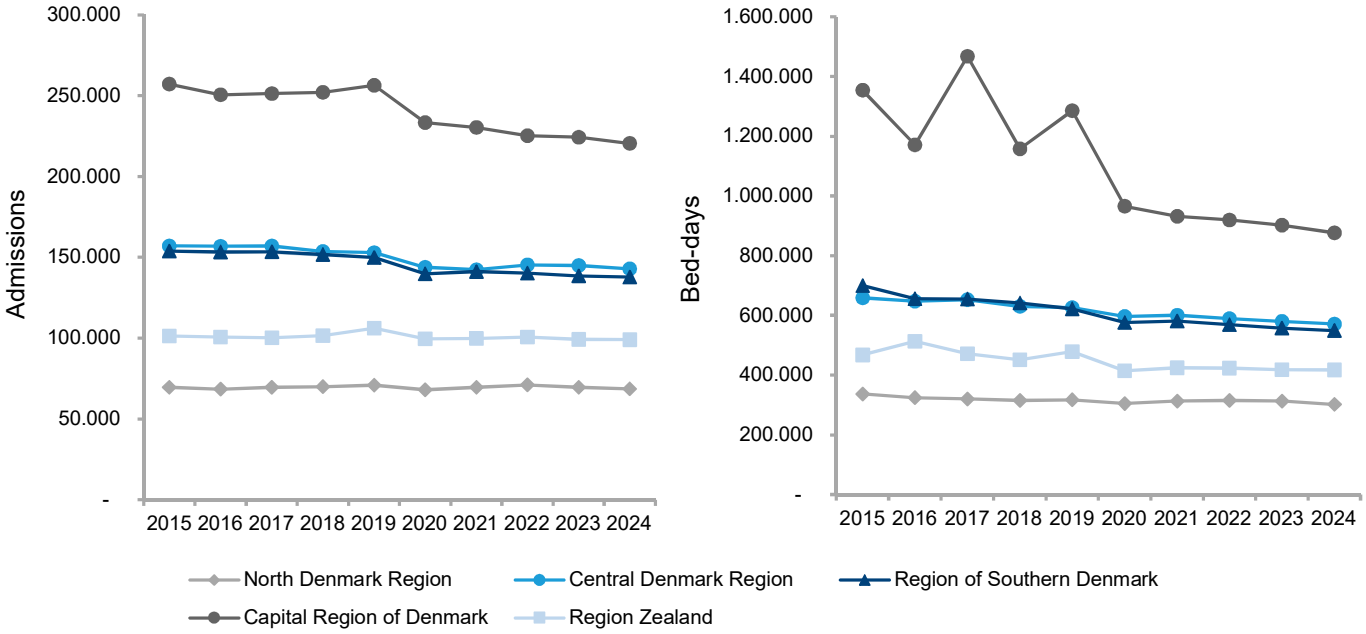
In 2024, the consumption of antimicrobial agents at somatic hospitals was 146.17 DBD. This is comparable (+2.5%) to 2023 (142.51 DBD) and 33% higher than a decade ago (110.23 DBD in 2015) (Table 5.6). The four penicillin groups (penicillins with extended spectrum, beta-lactamase sensitive penicillins, beta-lactamase resistant penicillins and combinations of penicillins, including beta-lactamase inhibitors) accounted for 80.83 DBD, corresponding to 55% of the total consumption of antimicrobials at somatic hospitals in Denmark in 2024. The main group of antimicrobials in 2024; combinations of penicillins, including beta-lactamase inhibitors increased by 56% since 2015.

Much has changed within choice and usage of antimicrobials at Danish hospitals, an example being the increase of combination penicillins as an attempt to reduce the usage of cephalosporins, while recent initiatives now include the combination penicillins among the broad-spectrum antimicrobials that should be closely monitored and, whenever possible, replaced by narrow-spectrum penicillins. These initiatives were included in the latter and the new Danish national action plan against antimicrobial resistance (DANMAP2021, Textbox 5.1 and DANMAP2024, Textbox 1.1).

Linezolid consumption has increased to 0.72 DBD in 2024 which is the highest level observed the last decade. Over the past decade, the consumption of linezolid increased by 38% (0.52 DBD in 2015). Consumption of daptomycin peaked in 2018 (0.18 DBD), and has since been fluctuating over the years reaching 0.12 DBD in 2024 (Table 5.6). Although the overall consumption of both antimicrobials is low, these changes are of concern due to the high risk of resistance in enterococci and staphylococci. The consumption is concentrated at the highest specialised tertiary care hospitals in Denmark, which can result in local selection pressure for resistant bacteria.

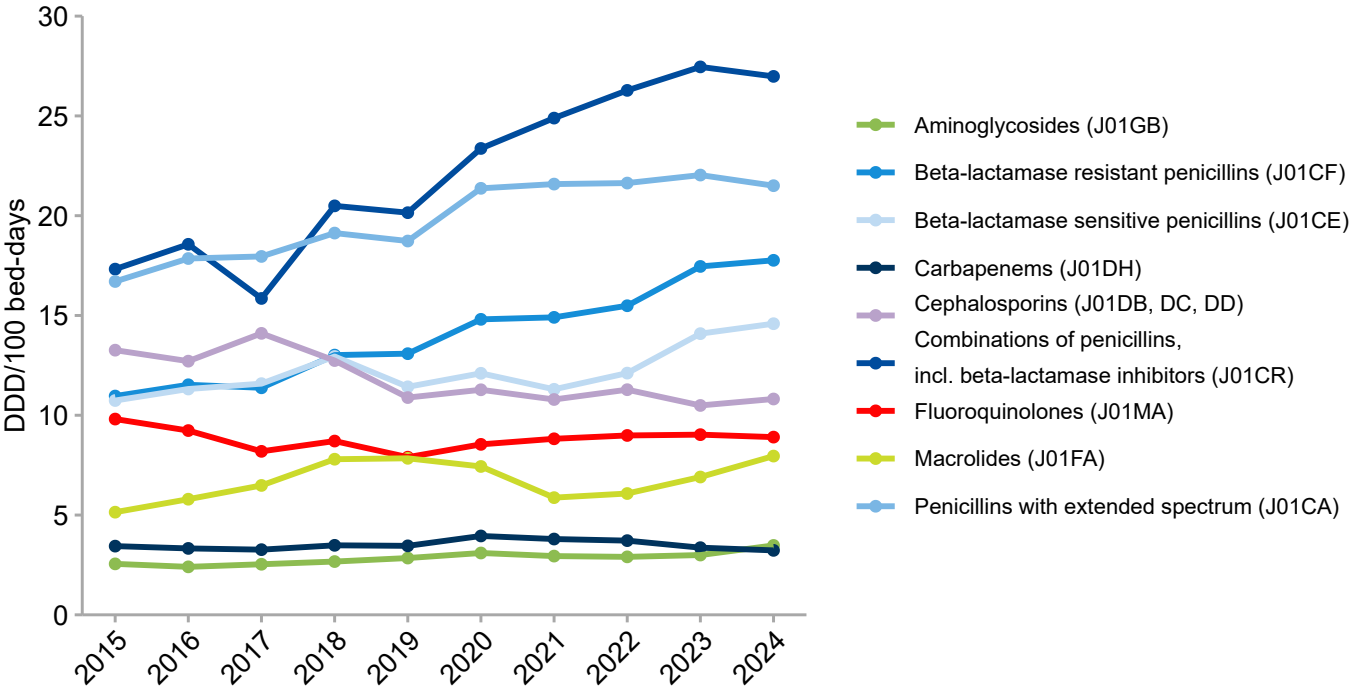
The consumption of antimicrobials at hospitals when measured in DDD per 100 patients admitted to hospitals is presented in Table 5.7.

Figure 5.14 Activity at somatic hospitals, bed-days and admissions, Denmark, 2015-2024 DANMAP 2024



Data source: National Patient Register
Data from the National Patient Register are subject to change due to continous development of the new National Patient Register. This means that data will be continously updated, both prospectively and retrospectively

Figure 5.15 Consumption of leading groups of antimicrobial agents at somatic hospitals, DDD per 100 bed-days, Denmark, 2015-2024 DANMAP 2024



Data: Antimicrobial consumption at somatic hospitals
Data source: Register of Medicinal Product Statistics, the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system and The National Patient Register

Table 5.6 Consumption of antimicrobial agents for systemic use in somatic hospitals, DDD per 100 bed-days, Denmark, 2015-2024

DANMAP 2024

ATC group	Therapeutic group	Year									
		2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
J01AA	Tetracyclines	2.14	2.59	2.32	2.95	3.67	3.29	3.42	3.72	4.2	4.46
J01CA	Penicillins with extended spectrum	16.7	17.85	17.96	19.13	18.73	21.37	21.58	21.64	22.04	21.5
J01CE	Beta-lactamase sensitive penicillins	10.74	11.32	11.58	12.94	11.42	12.1	11.3	12.11	14.09	14.59
J01CF	Beta-lactamase resistant penicillins	10.96	11.53	11.38	13.01	13.09	14.81	14.91	15.49	17.46	17.76
J01CR	Comb. of penicillins. incl. beta-lactamase inhibitors	17.32	18.57	15.85	20.49	20.15	23.37	24.89	26.28	27.45	26.98
J01DB	First-generation cephalosporins	0.05	0.05	0.05	0.05	0.03	0.04	0.04	0.03	0.03	0.01
J01DC	Second-generation cephalosporins	11.98	11.39	12.54	11.2	9.47	9.79	9.3	9.64	8.93	9.24
J01DD	Third-generation cephalosporins	1.23	1.27	1.51	1.49	1.39	1.45	1.45	1.61	1.53	1.56
J01DF	Monobactams	0.03	0.01	0.01	0.01	0.01	0.01	0.01	0.02	0.01	0.03
J01DH	Carbapenems	3.44	3.33	3.27	3.48	3.46	3.95	3.8	3.72	3.36	3.23
J01EA	Trimethoprim and derivatives	0.47	0.46	0.47	0.54	0.47	0.55	0.51	0.48	0.45	0.4
J01EB	Short-acting sulfonamides	0.14	0.12	0.12	0.12	0.1	0.08	0.08	0.06	0.05	0.05
J01EE	Comb. of sulfonamides and trimethoprim. incl. derivatives	6.17	6.61	6.36	7.45	7.77	8.85	9.76	10.13	11.18	12
J01FA	Macrolides	5.14	5.79	6.48	7.8	7.84	7.43	5.87	6.08	6.91	7.96
J01FF	Lincosamides	0.67	0.77	0.73	0.95	0.86	0.88	0.83	0.86	1.58	2.66
J01GB	Aminoglycosides	2.55	2.4	2.53	2.67	2.85	3.1	2.94	2.9	3	3.48
J01MA	Fluoroquinolones	9.81	9.23	8.19	8.71	7.9	8.54	8.82	8.99	9.03	8.91
J01XA	Glycopeptides	1.37	1.34	1.49	1.58	1.56	1.82	1.83	1.79	1.66	1.88
J01XB	Polymyxins	0.23	0.24	0.22	0.28	0.26	0.29	0.29	0.3	0.36	0.47
J01XC	Steroid antibacterials (fusidic acid)	0.19	0.14	0.08	0.08	0.07	0.06	0.07	0.05	0.06	0.05
J01XD	Imidazole derivatives	4.98	5.56	5.28	5.39	4.79	5.19	4.81	4.68	4.56	4.42
J01XE	Nitrofuran derivatives (nitrofurantoin)	0.32	0.29	0.29	0.33	0.33	0.42	0.38	0.39	0.46	0.38
J01XX05	Methenamine	0.11	0.1	0.08	0.13	0.09	0.1	0.14	0.13	0.15	0.13
J01XX08	Linezolid	0.52	0.45	0.42	0.65	0.62	0.6	0.61	0.68	0.68	0.72
J01XX09	Daptomycin	0.05	0.06	0.09	0.18	0.08	0.12	0.15	0.14	0.13	0.12
A07AA09	Vancomycin	0.55	0.6	0.59	0.62	0.64	0.81	0.71	0.83	0.87	0.91
P01AB01	Metronidazole	2.37	2.69	2.31	2.42	2.23	2.42	2.34	2.28	2.28	2.27
J01, P01AB01, A07AA09	Antimicrobial agents for systemic use, incl. metronidazole and vancomycin	110.23	114.76	112.2	124.65	119.88	131.44	130.84	135.03	142.51	146.17

Data: Antimicrobial consumption at somatic hospitals
Data source: The Register of Medicinal Product Statistics, the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system and National Patient Register

Table 5.7 Consumption of antimicrobial agents for systemic use in somatic hospitals, DDD per 100 admissions, Denmark, 2015-2024
DANMAP 2024

ATC group	Therapeutic group	Year									
		2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
J01AA	Tetracyclines	10.2	11.74	11.33	12.94	16.58	13.74	14.26	15.34	17.2	18.09
J01CA	Penicillins with extended spectrum	79.49	81.01	87.56	83.85	84.67	89.16	90.04	89.29	90.25	87.29
J01CE	Beta-lactamase sensitive penicillins	51.1	51.35	56.48	56.74	51.64	50.49	47.14	49.98	57.7	59.21
J01CF	Beta-lactamase resistant penicillins	52.17	52.3	55.47	57.05	59.15	61.77	62.18	63.91	71.5	72.11
J01CR	Comb. of penicillins. incl. beta-lactamase inhibitors	82.43	84.25	77.3	89.83	91.09	97.5	103.83	108.45	112.44	109.52
J01DB	First-generation cephalosporins	0.25	0.24	0.23	0.21	0.14	0.16	0.15	0.14	0.11	0.05
J01DC	Second-generation cephalosporins	57.02	51.68	61.17	49.1	42.79	40.83	38.8	39.78	36.57	37.5
J01DD	Third-generation cephalosporins	5.84	5.76	7.37	6.54	6.28	6.06	6.06	6.63	6.28	6.35
J01DF	Monobactams	0.15	0.06	0.04	0.03	0.05	0.04	0.03	0.07	0.03	0.13
J01DH	Carbapenems	16.38	15.1	15.92	15.27	15.63	16.49	15.84	15.34	13.78	13.11
J01EA	Trimethoprim and derivatives	2.23	2.09	2.29	2.38	2.1	2.28	2.14	1.99	1.85	1.63
J01EB	Short-acting sulfonamides	0.68	0.56	0.56	0.54	0.46	0.32	0.32	0.25	0.19	0.2
J01EE	Comb. of sulfonamides and trimethoprim. incl. derivatives	29.37	29.99	31.01	32.67	35.13	36.93	40.7	41.79	45.8	48.7
J01FA	Macrolides	24.47	26.29	31.61	34.18	35.46	31.01	24.5	25.09	28.28	32.29
J01FF	Lincosamides	3.21	3.5	3.58	4.16	3.91	3.65	3.47	3.54	6.48	10.81
J01GB	Aminoglycosides	12.15	10.91	12.36	11.7	12.86	12.92	12.28	11.99	12.27	14.12
J01MA	Fluoroquinolones	46.68	41.89	39.94	38.17	35.71	35.63	36.79	37.09	36.98	36.15
J01XA	Glycopeptides	6.5	6.07	7.27	6.91	7.04	7.59	7.65	7.39	6.8	7.63
J01XB	Polymyxins	1.08	1.08	1.07	1.24	1.16	1.21	1.19	1.23	1.46	1.89
J01XC	Steroid antibacterials (fusidic acid)	0.92	0.64	0.37	0.34	0.3	0.27	0.29	0.22	0.23	0.19
J01XD	Imidazole derivatives	23.72	25.25	25.76	23.61	21.66	21.63	20.05	19.31	18.7	17.94
J01XE	Nitrofuran derivatives (nitrofurantoin)	1.51	1.33	1.4	1.47	1.48	1.77	1.57	1.59	1.88	1.53
J01XX05	Methenamine	0.5	0.45	0.4	0.57	0.41	0.43	0.58	0.54	0.63	0.54
J01XX08	Linezolid	2.46	2.04	2.06	2.85	2.8	2.48	2.55	2.81	2.78	2.93
J01XX09	Daptomycin	0.22	0.28	0.45	0.78	0.34	0.49	0.63	0.56	0.54	0.5
A07AA09	Vancomycin	2.64	2.72	2.88	2.7	2.87	3.38	2.95	3.42	3.56	3.68
P01AB01	Metronidazole	11.28	12.2	11.28	10.61	10.1	10.1	9.74	9.4	9.32	9.22
J01, P01AB01, A07AA09	Antimicrobial agents for systemic use, incl. metronidazole and vancomycin	524.65	520.78	547.16	546.44	541.81	548.33	545.73	557.14	583.61	593.31

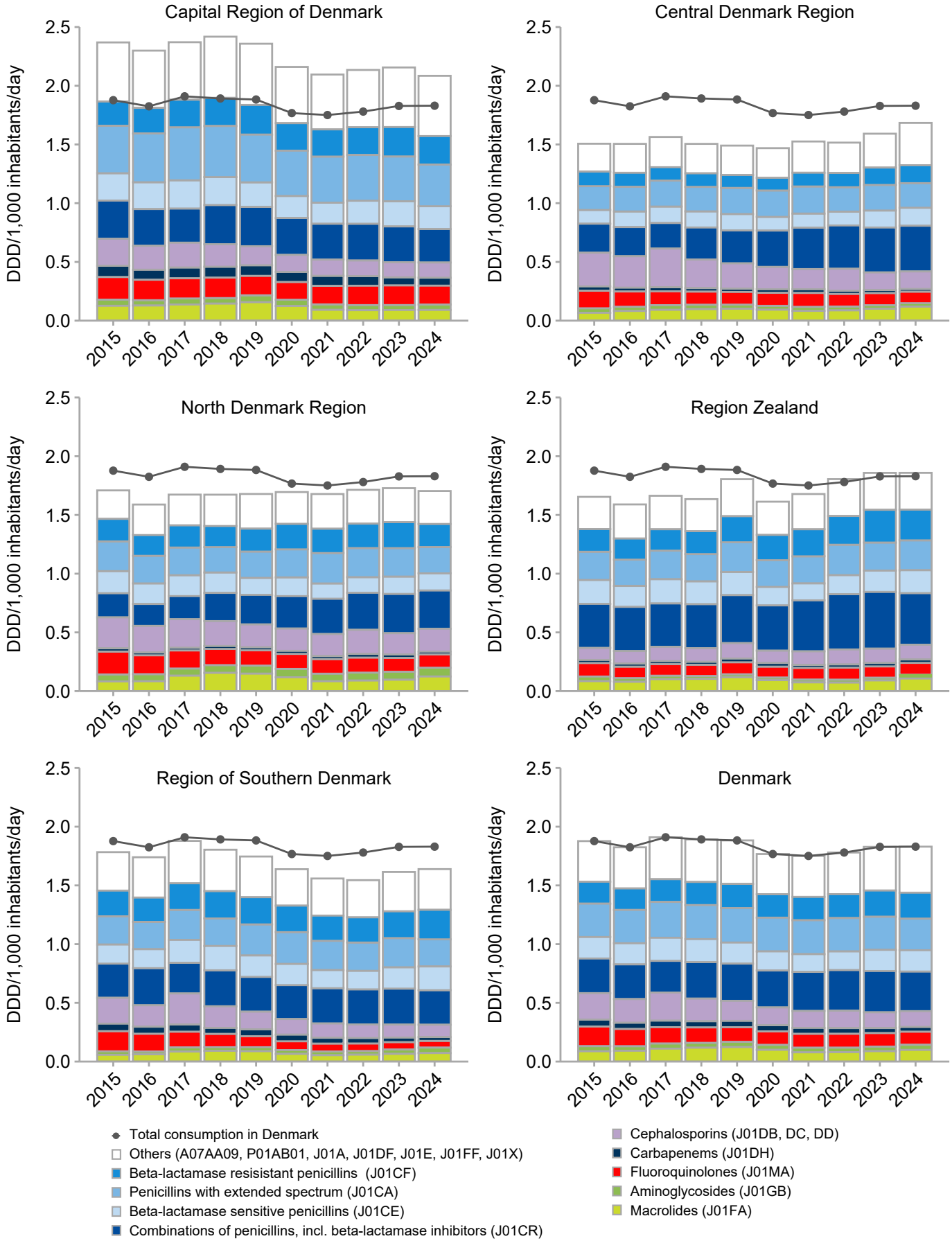
Data: Antimicrobial consumption at somatic hospitals
Data source: The Register of Medicinal Product Statistics, the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system and National Patient Register

5.4.2 Antimicrobial consumption at regional level at public somatic hospitals

Trends in hospital consumption at regional level measured in DDD per 100 bed-days are presented in Figure 5.17. The Capital Region of Denmark shows the highest level of consumption when compared to the other regions in 2024. It is also notable that consumption increased for each region over the last decade when measured in DBD (Figure 5.17) but remains almost unchanged over the same period when measured in DID (Figure 5.16). This reflects that hospital activity changed during the years, where more patients are treated in the hospitals, but for shorter time of stay. Thus more antimicrobials were used in relation to hospital patients' bed-days.

Figure 5.16 Consumption of antimicrobial agents for systemic use at hospitals in the five health regions, DDD per 1,000 inhabitants per day, Denmark, 2015-2024

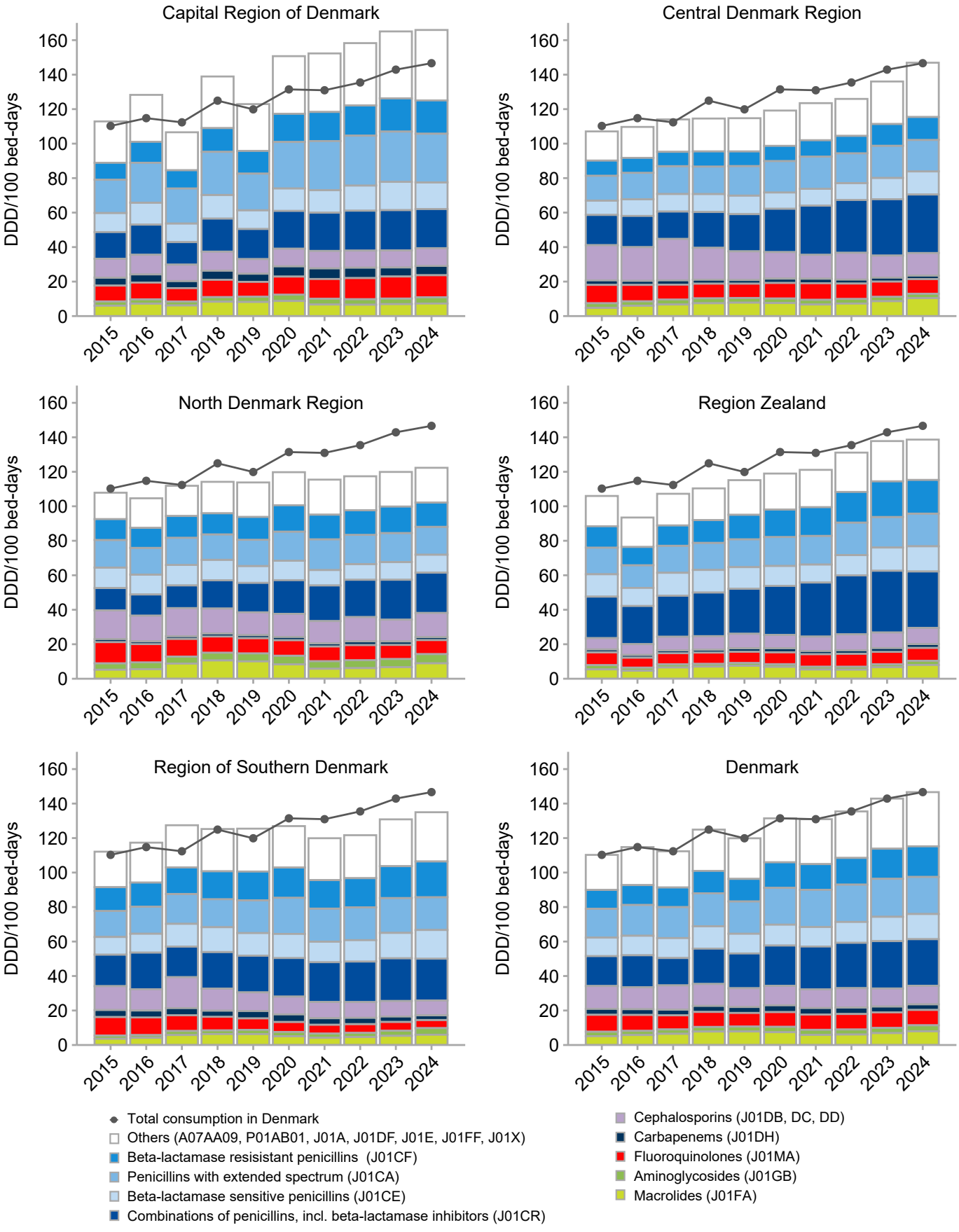
DANMAP 2024



Data: Antimicrobial consumption at somatic hospitals
Data source: Register of Medicinal Product Statistics, and the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system

Figure 5.17 Consumption of antimicrobial agents for systemic use at hospitals in the five health regions, DDD per 100 bed-days, Denmark, 2015-2024

DANMAP 2024



Data: Antimicrobial consumption at somatic hospitals
Data source: Register of Medicinal Product Statistics, and the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system and National Patient Register

5.4.3 AWaRe classification of antimicrobials at Danish somatic hospitals

The World Health Organization (WHO) has developed the AWaRe classification system as a tool to assist antibiotic stewardship and to reduce antimicrobial resistance. Antibiotics are classified into three groups to emphasise the importance of their appropriate use:

- Access: Antibiotics used to treat common susceptible pathogens with lower resistance potential than antibiotics in the other groups. 60% of total antimicrobial consumption should consist of access agents.
- Watch: Antibiotics that have higher resistance potential, including most of the highest priority agents. These antibiotics should be prioritised as key targets of stewardship programs and monitoring.
- Reserve: Antibiotics reserved for treatment of confirmed or suspected infections due to multi-drug resistant organisms. These antibiotics should be considered as "last resort" options.

Antimicrobial consumption at Danish somatic hospitals has consisted of more than 60% "access antimicrobials" since 2016, and in 2024 the share was 66%. "Reserve antimicrobials" constituted 1% in all years (Figure 5.18).

Several hospitals work with stricter classification of antimicrobials and have set up local criteria for use of certain antimicrobials associated with observed increasing levels of resistance. For instance, amoxicillin and beta-lactamase inhibitor are moved from the access group to watch, and meropenem from watch group to reserve.

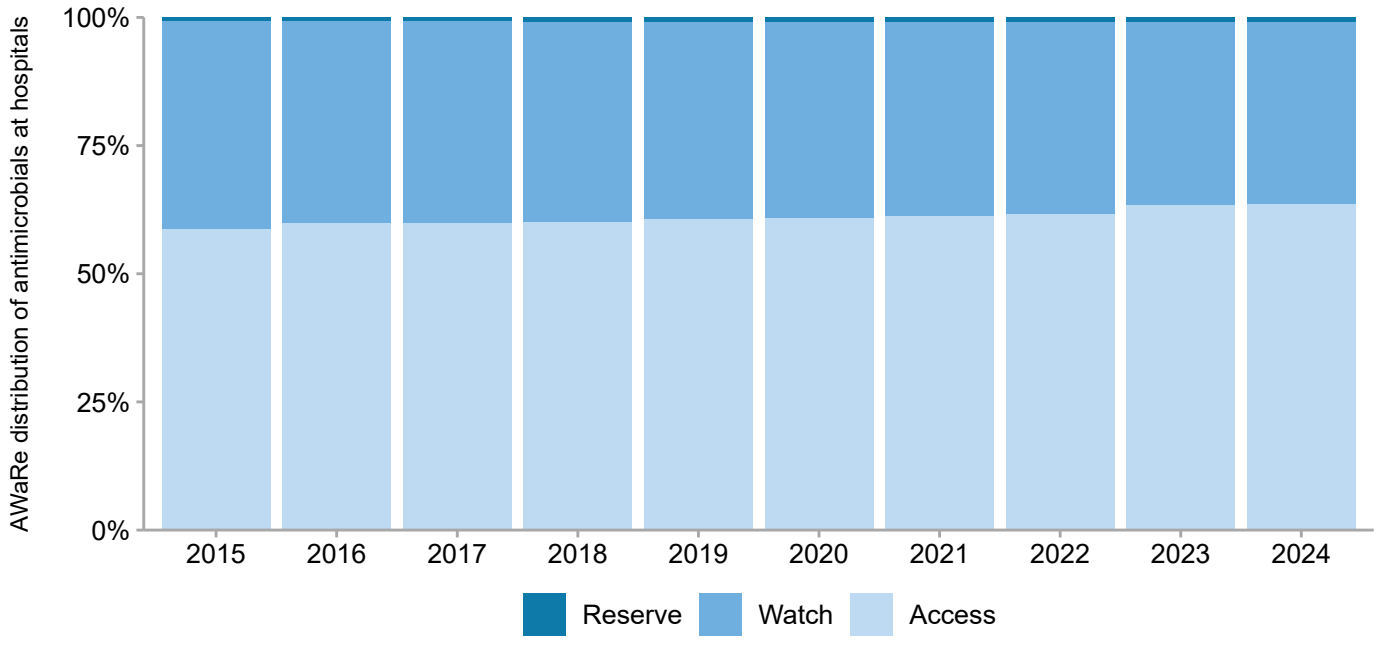
5.4.4 Shortage of antimicrobials

Issues with supply chains of antimicrobials can lead to product shortages. Some shortages do not reach the patient due to the substitution rules in Denmark. Shortages can also be solved by using non-marketed antimicrobials on special delivery, which requires permission from the Danish Medicines Agency.

Consumption of the main antimicrobial groups for treatment of critically ill patients at hospitals from 2015 to 2024 is shown in Figures 5.19. In 2022, penicillin/betalactamase inhibitor combinations decreased sharply in July and August due to product shortages (not shown). However, prescribers had access to penicillin/beta-lactamase inhibitor combinations via special deliveries. Approximately 70,000 DDD penicillin/beta-lactamase inhibitor combinations were purchased through special delivery in 2022, whereas in 2019-2021 the number was approximately 4,000 DDD (not shown).

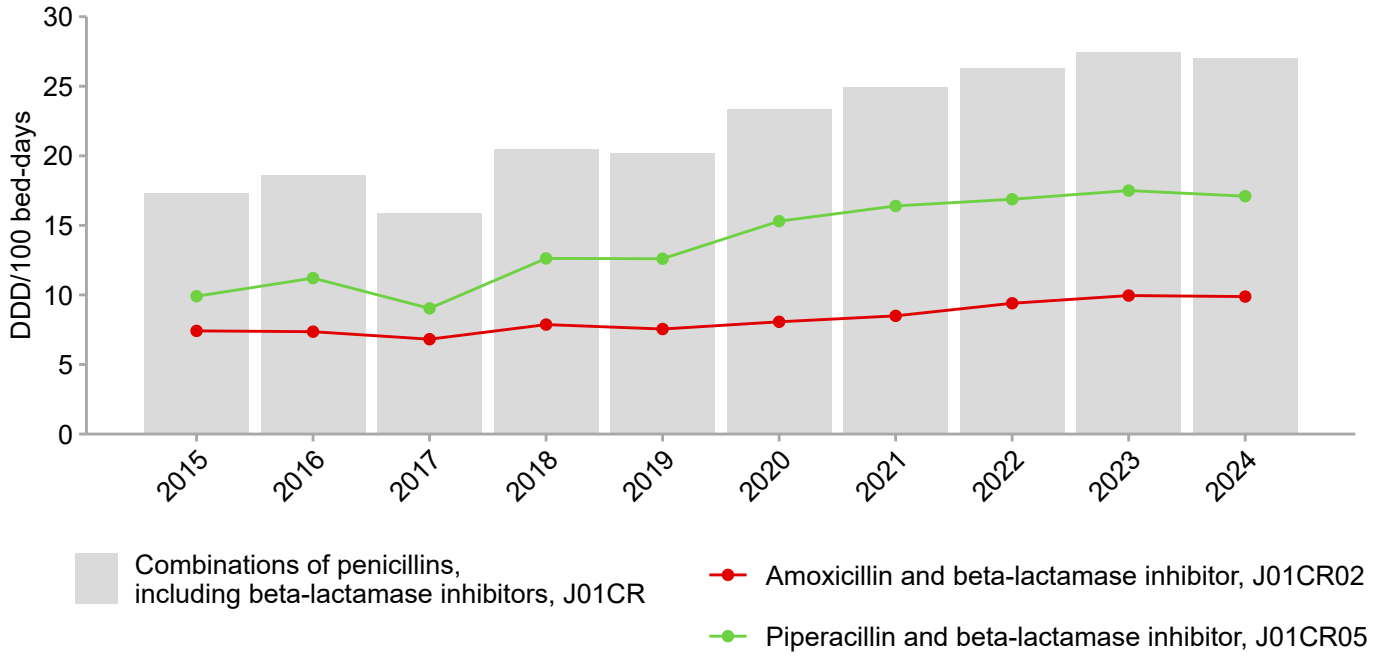
Special deliveries could not solve the shortage of penicillin/beta-lactamase inhibitor combinations in 2017, which led to a significant decrease in consumption that year (Figure 5.19). Simultaneously, an increase in consumption of cephalosporins was observed (Figure 5.15). In 2023, nitrofurantoin was hit by a shortage and even with increased supply via special deliveries, it was not possible to cover the whole need, why other antimicrobials were chosen for treatment. In 2024, metronidazole was one of the most purchased antimicrobials via special deliveries (Table 5.8).

Figure 5.18 Percentage distribution of antimicrobials at somatic hospitals according to WHO AWaRe classification, DDD, Denmark, 2015-2024
DANMAP 2024



Data: Antimicrobial consumption at somatic hospitals
Data source: Register of Medicinal Product Statistics and the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system

Figure 5.19 Consumption of combination penicillins at somatic hospitals, DDD per 100 bed-days, Denmark, 2015-2024 DANMAP 2024



Data: Antimicrobial consumption at somatic hospitals
Data source: Register of Medicinal Product Statistics, the 2025 edition of the Anatomical Therapeutic Chemical (ATC) classification system and National Patient Register

Table 5.8 Consumption of selected antimicrobials on special delivery to hospitals, DDD, 2015-2024 DANMAP 2024

Antimicrobial	Year									
	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
J01MA12 Levofloxacin	7,240	8,080	8,180	6,710	7,360	20,370	44,200	41,530	45,360	41,875
P01AB01 Metronidazole		175	200		8	80	32	94	10	12,833
J01FA09 Clarithromycin	624	414	1,084							3,022
J01GB01 Tobramycin					6,895	6,840	4,790	3,850	2,620	2,780
J01EE01 Sulfamethoxazole and trimethoprim	6,590	6,703.75	8,188	7,596	7,136	3,094	7,985	2,610	3,760	2,502
J01CF05 Flucloxacillin	2,312	2,275	2,200	1,782	1,790	1,665	1,872	2,540	2,232	2,208
J01MA02 Ciprofloxacin	1,155	1,195	690	766	726	1,028	908	935	890	985
J01FG01 Pristinamycin	60	160	160	200	425	390	466	1,067	533	856
J01AA02 Doxycycline	700	801	252	286	312	227	449	444	341	723
J01AA08 Minocycline					125	500	225	325	275	700

Data: Consumption of antimicrobials on special delivery
Data source: Danish Hospital Pharmacies

We would like to acknowledge Maja Laursen from the National Health Data Authority in Denmark for data on antimicrobial consumption and activity in hospital care. We would also like to acknowledge all hospital pharmacies in Denmark for data on special delivery of antimicrobials to the hospitals. Finally, we would like to acknowledge the panel of experts from clinical microbiology laboratories and from research centers for general practice for their valuable input to this chapter.

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Textbox 5.1

Maintaining access to antimicrobials in a time of increasing product shortages

Access to antimicrobials, especially the narrow spectrum, is crucial to promote rationale use of antimicrobials and thus to combat antimicrobial resistance. In a time of increasing supply issues, antimicrobials risk to disappear from the markets which in turn may push the treatment of infections towards more broad-spectrum antimicrobials.

In Denmark, national stakeholders work to promote and maintain access to antimicrobials in collaboration with national and international experts. We have invited three of them to present their point of views on this matter. Below, you can read the contributions from The Danish Medicines Agency, the pharmaceutical wholesaler Nomeco and the procurement organization for hospital medicines Amgros.

Joint Nordic Initiative to ensure access to critical antibiotics

The consumption of antibiotics in Denmark and other Nordic countries is characterized by a high proportion of older, narrow-spectrum antibiotics[1] – not least due to the focused national efforts in antibiotic stewardship. The national authorities are very aware of the risk of supply failures for these generics and have under the auspices of the Nordic Council of Ministers initiated joint work on the development of common models to ensure access to critical antibiotics to the Nordic countries.

From the Danish side, the initiative is an element of the national action plan for antimicrobial resistance in humans[2], which includes a number of initiatives regarding resistance control with a focus on the use of antibiotics that lead to a lower risk of resistance development, as well as a focus on a more stable and improved supply of antibiotics.

One of the joint Nordic initiatives is to develop and implement a revenue guarantee model for antibiotics in the primary sector. The companies involved will receive a revenue guarantee combined with a fixed participation award, if they commit to having no registered shortages of the product up to a maximum guaranteed package volume.

The model will ideally cover the entire Nordic market for important formulations of narrow-spectrum antibiotics in the primary sector, thereby ensuring larger and more attractive volumes for companies. This may require system and legal changes in all countries, so the initiative starts with a proof of concept (POC) for a single formulation of an antibiotic substance and separate service contracts with the manufacturers for each country. The aim is to test whether a revenue guarantee actually can improve the availability of an important antibiotic and to gain experience on possible adjustments for such a model to possibly be effective.

The proposed antibiotic substance to test in the POC is **phenoxymethylpenicillin 50mg/ml oral suspension**, which is 1st line treatment in most of the Nordic countries primarily for neonates and toddlers. The product is provided to the Nordic market by four companies.

Status: In 2025H2 the medical, legal and commercial challenges and solution options will be identified in each country, along with a preparation of a proposal for a cooperation model and a process plan for implementing the model. This must be approved by the Nordic Council of Ministers in early 2026, after which the POC can be initiated.

[1] The Nordic countries have the highest proportion of narrow-spectrum consumption in Europe. The consumption of narrow spectrum penicillins, cephalosporins and erythromycin in the Nordic countries was 2.5-10 times the consumption of broad-spectrum penicillins, cephalosporins, macrolides (except erythromycin) and fluoroquinolones in 2023. For the EU as a whole the proportion was only around 0,2 times. Source: *Antimicrobial consumption in the EU/EEA (ESAC-Net) - Annual Epidemiological Report for 2023*

[2] Danmark opruster i kampen mod antibiotikaresistens med ny handlingsplan | Indenrigs- og Sundhedsministeriet

By working with this model, Nordic cooperation in this area will be significantly strengthened on several levels. The experience, the structures and the processes that need to be built up to develop and implement the model will strengthen future joint initiatives in this area. Collaboration on reimbursement models also connects to other Nordic collaborations in the area, such as joint purchasing, joint electronic package leaflets, treatment recommendations, and possibly joint stockpiling.

Danish Medicines Agency
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Nomeco's proposed initiatives for an improved robustness of the supply-chain of narrow-spectrum antibiotics
Nomeco is Denmark's largest pharmaceutical wholesaler handling approximately ¾ of all pharmaceuticals in the pharmacy sector and more than half of the pharmaceuticals used in the hospital sector – including antibiotics. Nomeco is a full-line and product neutral wholesaler meaning, that we keep stock of all registered pharmaceuticals, regardless of manufacturer, brand, type, price etc. Nomeco's stock and purchasing profile and algorithms are based on current pharmacy legislation and advanced forecasting – and obviously product availability from our suppliers

With the aim to improve the availability of all critical pharmaceuticals – not least antibiotics, Nomeco has put forward several concrete proposals on how to strengthen the supply security of narrow-spectrum antibiotics in Denmark.

The first set of proposals concerns a *redistribution model* aimed at better utilization of existing stocks. Often back-orders are short and regional or even local. So, to avoid reaching out for the broad-spectrum antibiotics in cases were the narrow-spectrum products are unavailable locally or temporarily, Nomeco suggest looking into alternative and more dynamic distribution models – including elements like consignment stocks at pharmacy level or models enabling redistribution of individual products between pharmacies facilitated by the wholesalers. Financing of the costs resulting from alternative and dynamic distribution models could be made via a tiny fee on all pharmaceuticals going into a fund controlled by the authorities. Such a fund should of course also cover other costs throughout the pharmaceutical supply chain resulting from increasing shortage, instability and risk in general.

The second set of proposals focuses on economic incentives to ensure stable production and attract new manufactures. This includes elements like attractive pricing and a national tender model with at least two winning suppliers and long-term agreements. Other elements to consider include guaranteed minimum purchase volumes etc.

Nomeco is of course fully aware that the above-mentioned initiatives do not solve the underlying problem concerning lack of sufficient supplies of narrow-spectrum antibiotics. Nevertheless, initiatives like these are crucial to ensuring a more stable supply of critical pharmaceuticals and thus also contributing to the fight against antibiotic resistance.

Nomeco, pharmaceutical wholesaler
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continued ... Textbox 5.1

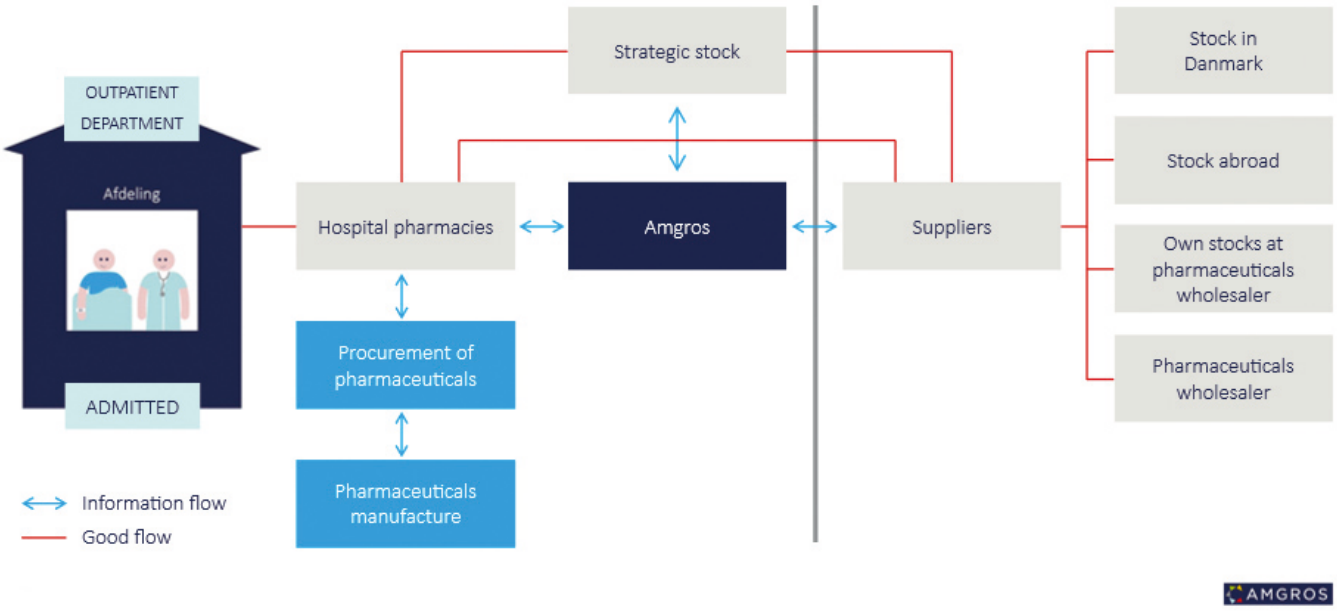
Amgros' Backorder Management of Medicines for Public Hospitals

Amgros is the procurement organization for hospital medicines and hearing aids on behalf of the Danish healthcare regions. Together with the country's hospital pharmacies, Amgros ensures that essential medicines are available to patients in public hospitals - at the right time, in the right place, at the right price - and with environmental considerations in mind. This is achieved through strategic planning and execution of tenders and procurement, ensuring supply security, and systematic follow-up on backorders. In 2024, Amgros achieved savings of DKK 9.9 billion, corresponding to approximately 49% of total expenditure. Around 98% of the medicines used in public hospitals are supplied through Amgros contracts.

National Backorder Management in the Hospital Sector

Amgros and hospital pharmacies continuously monitor orders and registers backorders to manage supply disruptions by standardized escalation model. The model is outlined below.

Figure 1 Amgros': How medicine meets hospital patients in Denmark DANMAP 2024



Escalation Model – Steps 0-5

Step 0: Prevention: In collaboration with hospital pharmacies Amgros is incorporating preventive measures into contracts to ensure supply security

Step 1: Standard Backorder Handling: Amgros' IT system ensures structured and transparent handling of backorders, including registration, monitoring, and coordination with relevant stakeholders. Most backorders are resolved at this stage.

Step 2: Assessment of Compounding: The possibility of in-house compounding at hospital pharmacies is assessed.

Step 3: Procurement of IRS Medicines: Evaluation of the possibility of purchasing alternative medicines without Danish marketing authorization (IRS medicines).

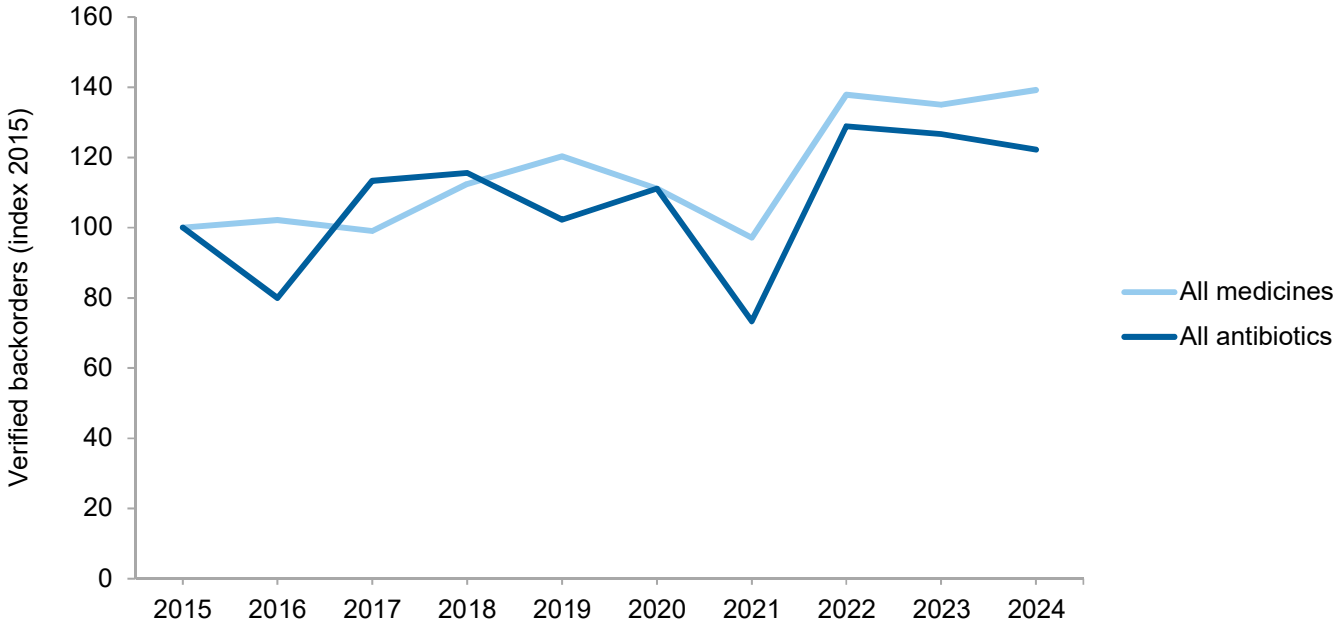
Step 4: Alternative Treatment Regimens: Clinical experts assess analog treatments, patient prioritization, or alternative handling. A cross-regional working group ensures broad implementation of the solution.

Step 5: Initiation of Production: In very rare cases, production is initiated at a hospital pharmacy or an external supplier if APIs, raw materials, and packaging are available.

Supply Situation for Antibiotics in the Hospital Sector

Antibiotics are particularly challenging due to treatment criticality, seasonal variation, and low prices over many years, which have made the market less attractive and reduced the number of suppliers. The backorder index for antibiotics was 120 in 2024 compared to 100 in 2015 meaning a 20% increase in backorders for antibiotics, compared to a 40% increase for all medicines. In almost all cases, alternatives were found based on the backorder management system and flexible procurement options.

Figure 2 Verified backorders of all medicines and of antimicrobials at hospitals, Denmark, 2015-2024 DANMAP 2024



Strategic Measures by Amgros to Improve Supply Security

Creating an Attractive Market: Amgros has a strategic approach to tenders, which includes market analysis, outreach to attract more suppliers to Denmark, and adjustment of tender criteria aimed at supply security.

Strategic Medicine Stock: Amgros and hospital pharmacies operate a national stockpile of treatment-critical medicines and medicines with low supply security. This provides a buffer in case of delivery failures and helps prevent disruptions from affecting patients.

Use of Forecasts: Amgros systematically collects consumption data and prepares forecasts as an integral part of the tender process. Once the contract is signed, the expected consumption is shared with the supplier, enabling them to adjust production and logistics to anticipated demand. Suppliers are also informed in case of significant changes during the contract period, allowing them to adjust production.

International Cooperation: Amgros participates actively in the Nordic Pharmaceutical Forum working for a more attractive Nordic market. Several joint Nordic tenders, including selected antibiotics, have been carried out by Denmark, Norway, and Iceland. In addition, the Nordic Pharmaceutical Forum collaborate with the Nordic medicines agencies to promote registration of joint Nordic packages.

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6

RESISTANCE IN ZOONOTIC BACTERIA

6. Resistance in zoonotic bacteria

Highlights: In 2024, resistance in ***Campylobacter jejuni*** isolates from humans remained lower in domestically acquired cases (ciprofloxacin 44%, tetracycline 22%) than in travel-associated cases (ciprofloxacin 85%, tetracycline 62%), but higher than in isolates recovered from broilers (ciprofloxacin 29%, tetracycline 17%) and cattle (ciprofloxacin 26%, tetracycline 1%). This is similar to previous years, albeit with some fluctuations. The proportion of fully susceptible *C. jejuni* has remained stable over time (69% in broilers, 73% in cattle and 46% in human cases for 2024). Erythromycin resistance remained rare in *C. jejuni* from cattle and was not observed in isolates from broilers and humans.

Campylobacter coli showed higher levels of resistance in human and broiler isolates compared to *C. jejuni*, with particularly high levels of resistance to ciprofloxacin (83% in travel-related cases, 66% in domestic cases and 54% in broilers) and tetracycline (75% in travel-related human cases, 72% in domestic human cases and 58% in broilers). Resistance to erythromycin was observed in 14% of human isolates and in 17% of isolates from broilers. This is an important finding as macrolides are used for the treatment of human patients in severe cases.

Phenotypic resistance in ***Salmonella* Typhimurium** and **monophasic *S*. Typhimurium** isolates remained overall higher in domestic pork than in humans. In addition to results from phenotypic resistance testing, DANMAP 2024 presents results from whole-genome sequencing of all isolates, representing the two *Salmonella* serovars, isolated the most between 2020 and 2024.

In 2024, two large **human outbreaks** caused by *S.* Typhimurium and monophasic *S.* Typhimurium affected the overall levels of phenotypic resistance in human isolates. The monophasic outbreak was caused by an atypical fully susceptible clone. In all 823 human isolates tested, resistance to third-generation cephalosporins remained low, and no resistance to meropenem was observed. Six human isolates (1%) were simultaneously resistant to azithromycin, third-generation cephalosporins and ciprofloxacin. Genetic determinants conferring resistance to quinolones, azithromycin, gentamicin, and third-generation cephalosporins were detected sporadically from 2020 to 2024. The yearly occurrence of commonly found resistance determinants, *blaCARB-2*, *blaTEM-1*, *floR*, *sul1*, *sul2*, *tet(A)*, *tet(B)*, *tet(G)*, was influenced by outbreak-associated clones.

Among *Salmonella* **isolates from pork**, the level of full susceptibility in *S.* Typhimurium and monophasic *S.* Typhimurium increased compared to 2023. Phenotypic ampicillin-, sulfamethoxazole-, and tetracycline resistance (ASuT) remained common in monophasic S. Typhimurium isolates and the most common genetic profile conferring ASuT resistance was reported. Phenotypic fluoroquinolone (ciprofloxacin) resistance remained undetected. Unlike in 2023, phenotypic azithromycin resistance was detected in two monophasic *S.* Typhimurium isolates from pork. The occurrence of phenotypic resistance to gentamicin remained similar to that in 2022 and 2023. Genes conferring resistance to amikacin and gentamicin were detected in monophasic *S.* Typhimurium, and the *aac(3)-IVa* gene, conferring resistance to gentamicin and apramycin, was found in three *S.* Typhimurium isolates.

6.1 Introduction

6.1.1 Introduction to resistance in zoonotic bacteria

Zoonoses are infectious diseases transmitted between animals and humans through direct contact or indirectly via contaminated food, water or environment. In DANMAP, information on antimicrobial resistance (AMR) in zoonotic bacteria is collected from the national programme for monitoring and control on zoonoses. For more information see the Annual Report on Zoonoses in Denmark 2024 [www.food.dtu.dk].

In humans, AMR is monitored in clinical *Salmonella* isolates. For *Campylobacter jejuni* and *C. coli*, a geographically stratified selection of clinical isolates is tested. The testing is performed in accordance with the ECDC recommendations (see Chapter 10, section 10.9). Travel histories of the patients are collected when possible.

In Denmark, antimicrobials are generally not recommended for treating human patients with diarrhoea apart from prolonged or severely ill cases. When necessary, macrolides (azithromycin) may be used for *Campylobacter* infections. In cases of prolonged or recurrent *Salmonella* infection, treatment with ciprofloxacin or trimethoprim-sulfamethoxazole may be considered, based on antimicrobial susceptibility testing. Information regarding concrete antimicrobial usage in diarrheal patients on patient level is currently not available.

In animals, *Salmonella* isolates were obtained from carcasses of healthy pigs at slaughter, while *Campylobacter* isolates were obtained from caecal samples from healthy broilers and cattle at slaughter. Antimicrobial susceptibility testing of *Campylobacter* and *Salmonella* from animals and meat is done in accordance with the Commission Implementing Decision 2020/1729/EU of 17 November 2020 (see Chapter 10 for further details).

In Danish food-producing animals, macrolides are often used to treat infections, particularly in pigs. Fluoroquinolones and 3rd and 4th generation cephalosporins are not used in production animals. The use of antimicrobials in the Danish poultry sector is low and limited to a few antimicrobial classes, primarily tetracyclines (see Chapter 4, Table 4.1).

6.2 *Campylobacter* spp.

A total of 200 human isolates of *C. jejuni* (158 domestic, 39 travel-associated, 3 unknown) and 44 isolates of *C. coli* (29 domestic, 12 travel-associated, 3 unknown) were tested for antimicrobial susceptibility.

In animals, all *C. jejuni* isolates recovered from broilers (202) and cattle (93), as well as all *C. coli* isolates from broilers (52) and cattle (4), were also tested for antimicrobial susceptibility. Due to the low number of isolates recovered, resistance data for *C. coli* from cattle are not reported.

6.2.1 Resistance in *Campylobacter jejuni*

The resistance levels recorded in *C. jejuni* isolates from humans, Danish broilers and cattle at slaughter in 2024 are shown in Table 6.1. The ten-year trends in resistance to selected antimicrobials are shown in Figure 6.1.
In 2024, 69% of *C. jejuni* from broilers, 73% from cattle and 46% from human cases (54% from domestically acquired and 13% from travel-related cases) were fully susceptible to all tested antimicrobials. The percentage of fully susceptible *C. jejuni* isolates from broilers, cattle and human cases has remained stable over the past decade (Figure 6.1).

Overall, resistance levels in *C. jejuni* from human isolates remained stable over the last ten years, with notably higher resistance levels in isolates from travel-associated cases compared to domestic. Human isolates also have generally higher levels of resistance than isolates from broilers and cattle.

Resistance to ciprofloxacin and tetracycline remained common in *C. jejuni* from both humans and food-producing animals, except in cattle, where tetracycline resistance was only observed in one isolate.

As in previous years, combined resistance to ciprofloxacin and tetracycline in *C. jejuni* isolates was common; 27% from human cases (54% in travel-related and 20% in domestically acquired cases) and 16% from broilers (Table 6.1 and Figure 6.1). Over the last 10 years, the prevalence of isolates with this resistance profile has fluctuated slightly in domestic human cases and in broilers, but remained stable for travel-related cases and in cattle (Figure 6.1).

Macrolide (erythromycin) resistance in *C. jejuni* is rare. In 2024, it was not observed in human and broiler isolates and was found in only one isolate from cattle. Resistance to chloramphenicol and gentamicin is also rare and in 2024, no resistance to chloramphenicol was detected. Similarly, no gentamicin resistance was recorded in isolates from humans and cattle, but two resistant *C. jejuni* isolates from broilers were reported (1%).

Ertapenem resistance has been monitored in *Campylobacter* since 2021. However, the European Committee on Antimicrobial Susceptibility Testing (EUCAST) has not proposed an epidemiological cut-off (ECOFF) or clinical breakpoint for ertapenem resistance, which is crucial for correctly identifying whether an isolate is susceptible or resistant. Therefore, the clinical relevance of human strains resistant to ertapenem is unclear. The EU Reference Laboratory for AMR (EURL-AMR) and the European Food Safety Authority (EFSA) have established a provisional ECOFF of 0.5 mg/L (EFSA, 2024), adopted in DANMAP.

Among *C. jejuni* isolates from broilers, 7% were resistant to ertapenem - an increase of 5% from the previous year. No ertapenem resistance was found in cattle isolates.

Table 6.1 Resistance (%) in *Campylobacter jejuni* isolates from broilers, cattle and human cases, Denmark, 2024 DANMAP 2024

	Broilers	Cattle	Human	
	Danish	Danish	Domestically acquired	Travel abroad reported
Antimicrobial agent	%	%	%	%
Chloramphenicol	0	0	0	0
Ciprofloxacin	29	26	44	85
Ertapenem	7	0	4	5
Erythromycin	0	1	0	0
Gentamicin	1	0	0	0
Tetracycline	17	1	22	62
CIP-TET	16	0	20	54
Fully susceptible	69	73	54	13
Number of isolates	202	93	158	39

An isolate is categorised as domestically acquired if the patient did not travel outside Denmark one week prior to the onset of disease
The threshold for resistance to ertapenem in *Campylobacter* has not been validated by the European Committee on Antimicrobial Susceptibility Testing (EUCAST)
CIP TET: all isolates with both ciprofloxacin and tetracycline resistance. Fully susceptible: isolates sensitive to all antimicrobial agents included in the test panel (See Chapter 10, Table 10.3)

6.2.2 Resistance in *Campylobacter coli*

The resistance data for *C. coli* isolates from humans and Danish broilers at slaughter in 2024 are presented in Table 6.2.

Historically, AMR in *C. coli* from these sources has not been a focus of DANMAP, limiting longitudinal comparisons, particularly for broiler isolates. However, comparisons with 2023 data are possible for human isolates. The data from humans indicate high levels of resistance in *C. coli*. In travel-related cases resistance to ciprofloxacin was 83% and to tetracycline 75%, in domestic cases it was 75% to ciprofloxacin and 72% to tetracycline. The levels are comparable to those observed in 2023, the first year of reporting human data, and higher than the levels observed in human *C. jejuni* isolates.

Resistance in *C. coli* from broilers was also high, with 54% and 58% of the isolates resistant to ciprofloxacin and tetracycline, respectively.These resistance levels are higher than those observed in *C. jejuni* isolates from broilers and humans (Tables 6.1 and 6.2).

Resistance to erythromycin was observed in 14% of human isolates, and in 17% of isolates from broilers. This is important as macrolides are frequently used for the treatment of severely ill patients.

Gentamicin resistance was low, detected in only 8% of the travel-related and none of the domestic human cases, and it was not detected in broilers. Similarly, no resistance to chloramphenicol was observed in any of the human and broiler isolates.

While in 2023, no resistance to ertapenem was reported in *C. coli* from pigs, in 2024, it was commonly observed in isolates from broilers (37%).

Overall, the comparably high levels of resistance in *C. coli* from human isolates and isolates from broilers point towards broilers being a probable source of infection with *C. coli* in humans.

Table 6.2 Resistance (%) in *Campylobacter coli* isolates from broilers and human cases, Denmark, 2024 DANMAP 2024

	Broilers	Human	
	Danish	Domestically acquired	Travel abroad reported
Antimicrobial agent	%	%	%
Chloramphenicol	0	0	0
Ciprofloxacin	54	66	83
Ertapenem	37	28	25
Erythromycin	17	7	25
Gentamicin	0	0	8
Tetracycline	58	72	75
Fully susceptible	21	14	8
Number of isolates	52	29	12

An isolate is categorised as domestically acquired if the patient did not travel outside Denmark one week prior to the onset of disease. The threshold for resistance to ertapenem in *Campylobacter* has not been validated by the European Committee on Antimicrobial Susceptibility Testing (EUCAST)

Figure 6.1 Resistance to ciprofloxacin, tetracycline, erythromycin, combined ciprofloxacin and tetracycline resistance and full susceptibility (%) among *Campylobacter jejuni* from broilers, cattle and human cases, Denmark, 2015-2024 DANMAP 2024

An isolate is categorised as domestically acquired if the patient did not travel outside Denmark one week prior to the onset of disease
CIP TET: all isolates with both ciprofloxacin and tetracycline resistance. Fully susceptible: isolates sensitive to all antimicrobial agents included in the test panel. All data shown result from a minimum of 15 tested isolates (see Chapter 10 for more details)

6.3 *Salmonella* spp.

In 2024, a total of 823 human clinical *Salmonella* spp. isolates, representing 102 different serotypes, were tested for antimicrobial susceptibility. The predominant serotypes were *S.* Typhimurium (178), monophasic *S.* Typhimurium with the antigenic formula 4,[5], 12:i:- (133), and *S.* Enteritidis (44). Except for *S.* Enteritidis, the tested isolates represented all clinical Danish isolates and included outbreak isolates.

Two large *Salmonella* outbreaks took place in 2024. One involved 70 cases of *S.* Typhimurium resistant to sulfamethoxazole and tetracycline, and the other involved 66 cases of fully susceptible monophasic *S.* Typhimurium. Two other outbreaks encompassed 22 fully susceptible *S.* Umbillo cases and 11 cases of *S.* Typhimurium, which were resistant to ampicillin, chloramphenicol, sulfamethoxazole and tetracycline.

The resistance data for *S.* Typhimurium and monophasic *S.* Typhimurium, and for other serotypes from humans from 2024 are presented in Tables 6.3 and 6.4, respectively.

Also in 2024, a total of 96 *Salmonella* spp. isolates from domestic pork were tested for antimicrobial susceptibility. The most common serotypes reported in pork were monophasic *S.* Typhimurium variant 4,[5], 12:i:- (40), *S.* Derby (28), and *S.* Typhimurium (15). The resistance data from domestic pork isolates are presented in Table 6.3 for *S.* Typhimurium and monophasic *S.* Typhimurium and in Figure 6.5 for *S.* Derby.

Table 6.3 Resistance (%) in *Salmonella* Typhimurium and monophasic *S.* Typhimurium isolates from domestic pork and humans, Denmark, 2024

DANMAP 2024

	Pork		Human					
	S. Typhimurium	Monophasic *S.* Typhimurium	*S.* Typhimurium			Monophasic *S.* Typhimurium		
	Danish	Danish	Domestically acquired	Travel abroad reported	Total	Domestically acquired	Travel abroad reported	Total
Antimicrobial agent	%	%	%	%	%	%	%	%
Amikacin	0	3	0	0	0	0	0	0
Ampicillin	80	80	12	22	13	39	81	46
Azithromycin	0	5	0	0	0	1	14	3
Cefotaxime	0	0	0	0	0	2	10	3
Ceftazidime	0	0	0	0	0	2	10	3
Chloramphenicol	47	5	10	22	12	6	29	8
Ciprofloxacin	0	0	2	26	6	2	33	7
Colistin	0	0	1	0	1	1	10	2
Gentamicin	20	8	0	0	0	1	5	2
Meropenem	0	0	0	0	0	0	0	0
Nalidixic acid	0	0	2	19	4	3	33	8
Sulfamethoxazole	73	85	69	44	62	35	71	41
Tetracycline	47	80	66	44	60	32	81	41
Tigecycline	0	3	10	0	8	7	5	7
Trimethoprim	47	25	2	19	4	8	38	12
Fully susceptible	7	10	27	52	34	55	10	46
Number of isolates	15	40	124	27	178	88	21	133

Results are shown separately for *S.* Typhimurium and monophasic *S.* Typhimurium with antigenic formula *S.* 4,[5],12:i:-. Isolates from Danish pork were recovered from carcass swabs collected at slaughter. An isolate is categorised as domestically acquired if the patient did not travel outside Denmark one week prior to the onset of disease. Total number of human cases includes travel cases and infections of unknown origin. An isolate is considered fully susceptible if sensitive to all antimicrobial agents included in the test panel (Chapter 10, Table 10.3)

6.3.1 Resistance in *S.* Typhimurium, monophasic *S.* Typhimurium and other selected *Salmonella* serovars

DANMAP has historically focused on phenotypic resistance in *S.* Typhimurium and the related monophasic variant 4,[5],12:i:-, as these serotypes are prevalent in clinical human isolates and isolates from food-producing animals and derived products.

The current report only presents available data from human clinical isolates and domestic pork isolates. The lack of availability of AMR results from isolates from a wider variety of sources limits the options for comparison of resistance levels in animals at slaughter, food, and humans. It is known that there are other sources of human salmonellosis infections than domestic pork, and clonal dissemination plays an important role in the occurrence of antimicrobial resistance among *S.* Typhimurium and monophasic *S.* Typhimurium.

The resistance levels recorded in *S.* Typhimurium and monophasic *S.* Typhimurium isolates from pigs and humans in 2024 are shown in Table 6.3. Figure 6.2 presents the relative distribution (%) of AMR profiles for *S.* Typhimurium and monophasic *S.* Typhimurium from pigs, domestic pork and human domestic- and travel-related cases from 2020 to 2024. The ten-year trends in resistance to selected antimicrobials among *S.* Typhimurium combined with monophasic *S.* Typhimurium from pigs, domestic pork and human cases are shown in Figure 6.3. In addition, Table 6.4 shows resistance levels in other *Salmonella* serovars from human cases in 2024, and Figure 6.5 shows trends of resistance among *S.* Derby isolates from domestic pork in 2015-2024.

Resistance in human isolates

The resistance profile of the human outbreak related isolates affected the levels of resistance reported in 2024 for monophasic *S.* Typhimurium and *S.* Typhimurium which makes it difficult to compare the levels of resistance with the previous years. However, if the outbreak related isolates are disregarded, the resistance levels and AMR profiles, are overall similar to the last five years.

Most of the human *Salmonella* spp. isolates, 58%, were susceptible to all antimicrobial tested. Resistance to third generation cephalosporins, (cefotaxime and ceftazidime) was recorded in 2% of the total of 823 clinical *Salmonella* spp. isolates from humans and azithromycin resistance was observed in 1% of the isolates. Ciprofloxacin resistance was observed in 6% of *S.* Typhimurium, 7% of monophasic *S.* Typhimurium, and in 15% of other serotypes (Tables 6.3 and 6.4). Same sentence is at the end of this paragraph. Generally, resistance to third-generation cephalosporins, azithromycin and ciprofloxacin were higher in isolates from travel-associated cases than from domestically acquired cases. Meropenem resistance was not recorded in 2024 in human isolates.

Six human isolates (1%) were simultaneously resistant to azithromycin, third generation cephalosporins and ciprofloxacin and thereby resistant towards antimicrobials that frequently are used for empirical treatment of human infections. The infections in the six cases were caused by monophasic *S.* Typhimurium (3), *S.* Muenster (1) and *S.* Saintpaul (2). Three of the six cases were associated with travel and three cases were acquired domestically.

The level of gentamicin resistance remained at a low level, with three isolates being resistant in 2024, two monophasic *S.* Typhimurium isolates and one *S.* Corvallis isolate (Table 6.3 and Figure 6.2).

Table 6.4 Resistance (%) in other *Salmonella* serovars from humans, Denmark, 2024 DANMAP 2024

	Other *Salmonella* serovars		
	Human		
	Domestically acquired	Travel abroad reported	Total
Antimicrobial agent	%	%	%
Amikacin	0	0	0
Ampicillin	5	12	8
Azithromycin	2	1	1
Cefotaxime	2	3	2
Ceftazidime	2	3	2
Chloramphenicol	4	4	4
Ciprofloxacin	8	22	15
Colistin	2	3	4
Gentamicin	0	0	0
Meropenem	0	0	0
Nalidixic acid	7	19	13
Sulfamethoxazole	5	7	6
Tetracycline	10	12	10
Tigecycline	10	8	10
Trimethoprim	4	3	4
Fully susceptible (%)	76	67	69
Number of isolates	183	233	512

Other *Salmonella* serovars exclude isolates verified as *S.* Typhimurium and monophasic variants of *S.* Typhimurium with antigenic formula *S.* 4,[5],12:i:-. An isolate is categorised as domestically acquired if the patient did not travel outside Denmark one week prior to the onset of disease. Total number of human cases includes travel cases and infections of unknown origin. An isolate susceptible to all antimicrobial agents included in the test panel is considered fully susceptible (Chapter 10, Table 10.3)

Polymyxin (colistin) resistance is mainly seen in *S.* Dublin and *S.* Enteritidis isolates. Both serotypes, in particular *S.* Dublin, are regarded as intrinsically resistant towards polymyxins.

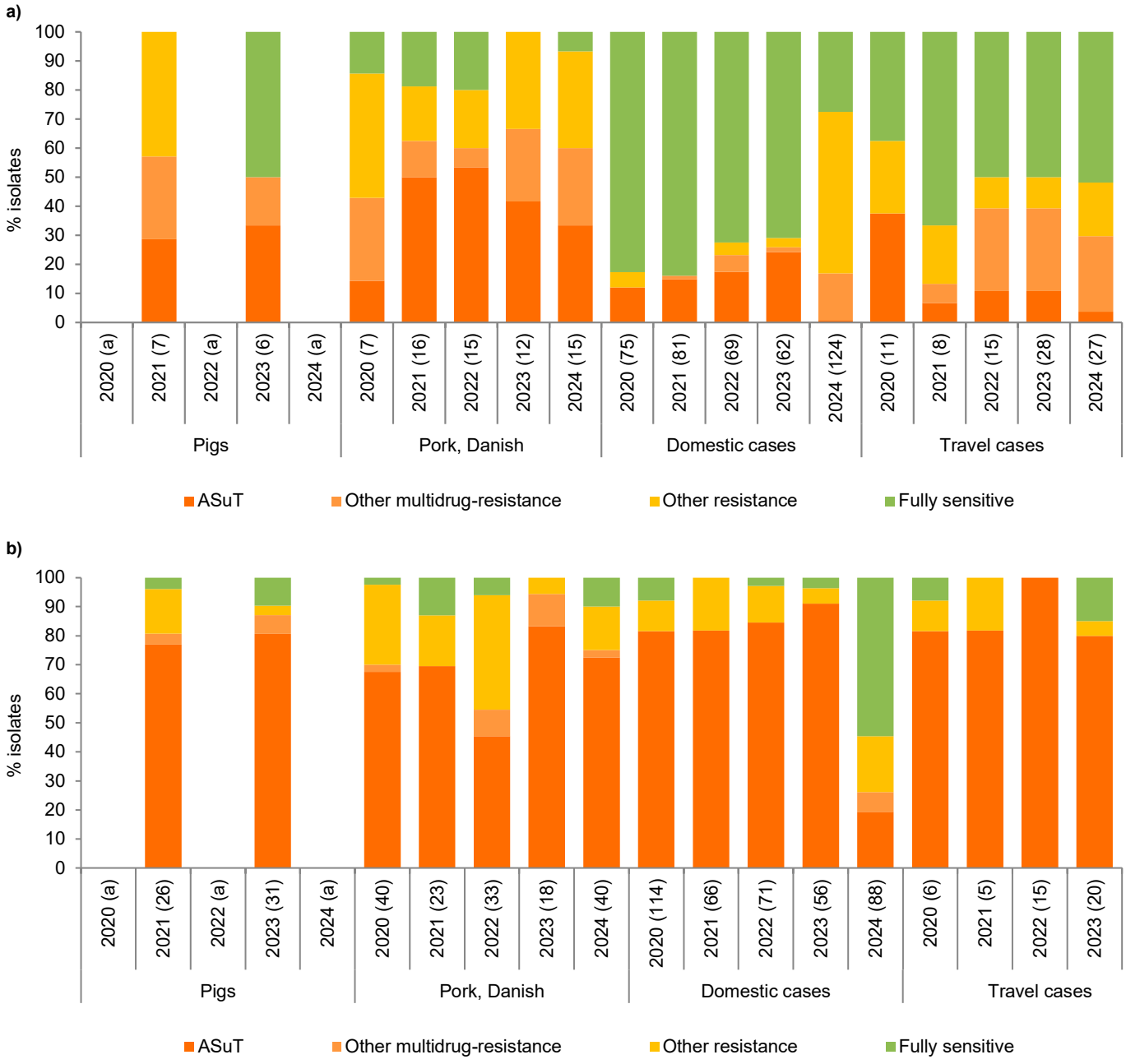
Resistance in pork isolates

As in previous years, the occurrence of resistance continued to be overall higher in isolates from domestic pork than in isolates from humans.

The level of full susceptibility in *S.* Typhimurium (7%) and monophasic *S.* Typhimurium (10%) from pork showed an increase when compared to 2023 (Figure 6.3A and B).

As in previous years, resistance to third generation cephalosporins, (cefotaxime and ceftazidime) was not observed in *S.* Typhimurium and monophasic *S.* Typhimurium isolates from domestic pork (Table 6.3).

Figure 6.2 Relative distributions (%) of AMR profiles among *Salmonella* Typhimurium (a) and monophasic *S.* Typhimurium (b) from pigs, pork and human cases, Denmark, 2020-2024
DANMAP 2024



Number of isolates included each year is presented in parentheses. Includes isolates verified as monophasic variants of *S.* Typhimurium with antigenic formula S. 4,[5],12:i:-. An isolate is considered fully susceptible if sensitive to all antimicrobial agents included in the test panel, and multidrug-resistant if resistant to three or more of all antimicrobial classes included in the test panel (See Chapter 10, Table 10.3). ASuT are multidrug-resistant isolates resistant to ampicillin, sulfamethoxazole and tetracycline. Caution in data interpretation should be taken in years with small numbers (n <15) of isolates from domestic pork, pigs and travel-associated cases
(a) No data

The occurrence of resistance to tetracycline in monophasic *S.* Typhimurium from Danish pork remained high (80%) with similar levels as those found in 2023 (89%). Resistance to tetracycline in *S.* Typhimurium isolates was lower (47%).

Genomic islands conferring resistance to ampicillin, sulfamethoxazole and tetracycline (the ASuT multidrug-resistance profile) among monophasic *S.* Typhimurium contribute to a high level of multidrug-resistance (MDR) (Figure 6.2).

Most *S.* Typhimurium isolates recovered from domestic pork were resistant to several antimicrobials, with MDR levels reaching 60%. The ASuT MDR profile was found in the majority of the MDR *S.* Typhimurium isolates from pork (33%).

When looking at monophasic *S.* Typhimurium, MDR was found at higher levels, with 75% of isolates from domestic pork resistant to three or more antimicrobial classes and ASuT the most found MDR profile (73%).

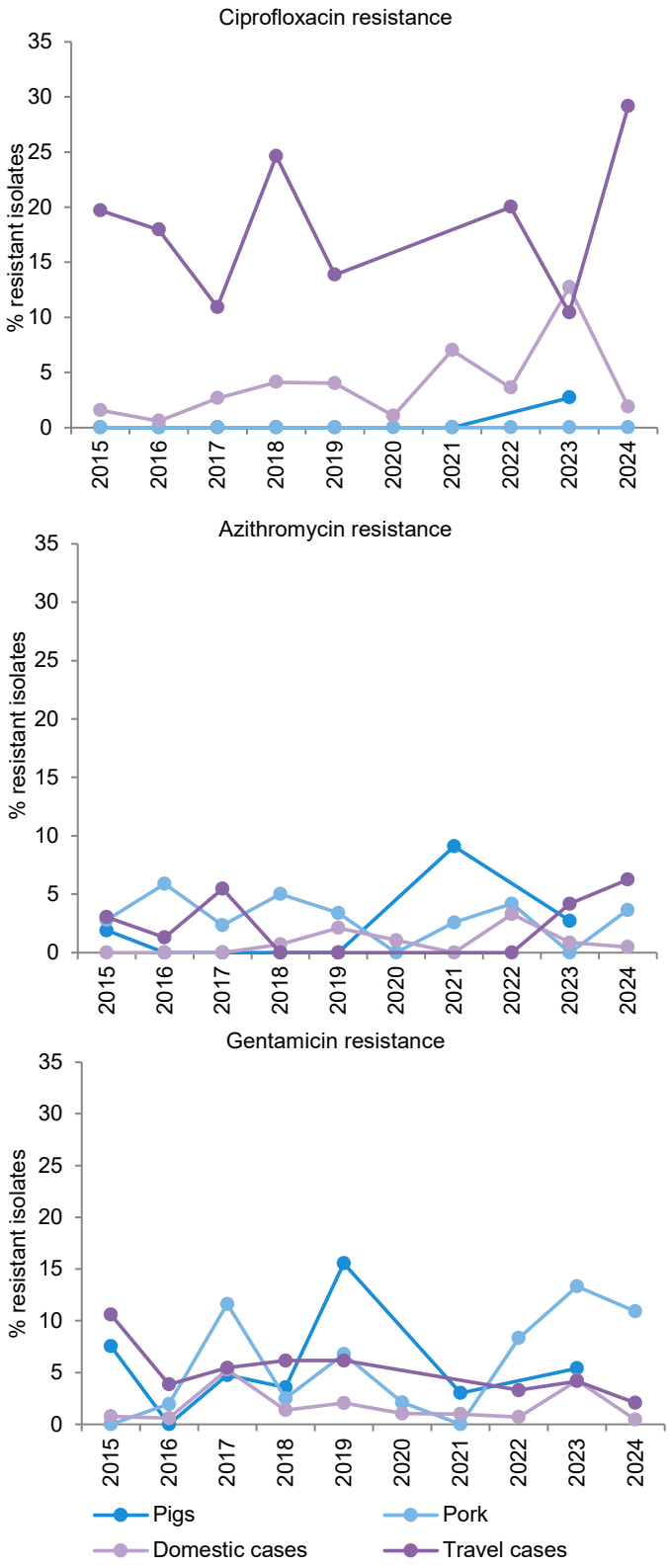
Analysing *S.* Typhimurium and monophasic *S.* Typhimurium separately reveals marked differences in their levels of MDR and especially ASuT. These are most evident in human isolates (Figure 6.2). However, caution in data interpretation should be taken in years when a small number of isolates were recovered from domestic pork, pigs and travel-associated cases.

Ciprofloxacin resistance has not been found among isolates from domestic pork since 2015 (Figure 6.3). Unlike in 2023, azithromycin resistance was detected in pork, with all resistant isolates belonging to the monophasic *S.* Typhimurium serotype (Figure 6.3).

In domestic pork, the occurrence of resistance to gentamicin (11%) remained similar to that in 2022 and 2023 (8% and 13%, respectively) (Figure 6.3).

Figure 6.3 Ciprofloxacin, azithromycin and gentamicin resistance (%) among *S.* Typhimurium and its monophasic variants from pigs, domestic pork and human cases, Denmark, 2015-2024

DANMAP 2024



Includes isolates of *S.* Typhimurium and monophasic *S.* Typhimurium with antigenic formula S. 4,[5],12:i:-. An isolate is categorised as domestically acquired if the patient did not travel outside Denmark one week prior to the onset of disease. Due to the low number of isolates (n <15), travel-associated cases are not shown separately for 2020 and 2021. No data available for pigs in 2020, 2022 and 2024

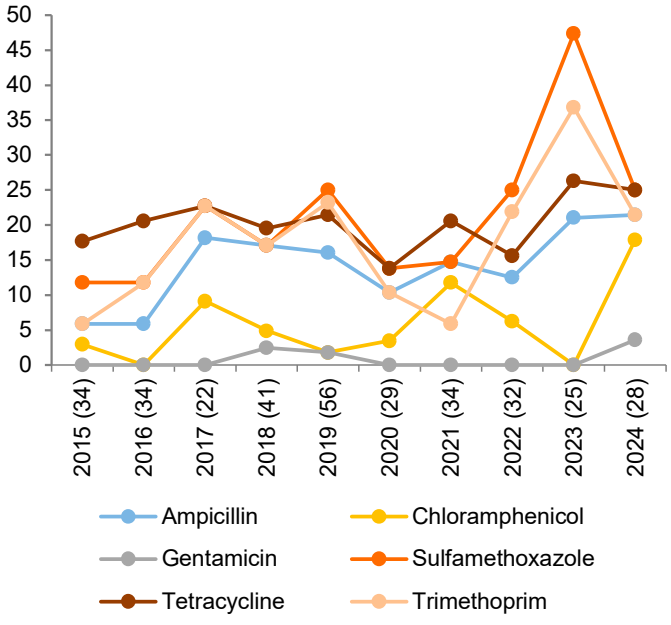
Resistance in other *Salmonella* serotypes from pork

S. Derby was the second most prevalent serotype in domestic pork, with 28 isolates recovered. The occurrence of resistance in *S.* Derby is generally lower than in *S.* Typhimurium and monophasic *S.* Typhimurium. In 2024, 64% of *S.* Derby isolates from domestic pork were fully susceptible to all tested antimicrobials. After a decrease in 2023 (to 52%), full susceptibility levels are again comparable to what was seen in 2022 (69%). After an increase in resistance to ampicillin, tetracycline, sulfamethoxazole, and trimethoprim in 2023, this year, resistance levels to ampicillin and tetracycline remained similar, while a decrease in sulfamethoxazole and trimethoprim was detected (Figure 6.5).

Resistance to critically important antimicrobials remained rare in 2024 in *S.* Derby isolates from domestic pork. Resistance to azithromycin and tigecycline was observed in 4% and 7% of pork isolates, respectively. Unlike the previous four years, resistance to gentamicin was detected (4%), but at a low level.

Additionally, *S.* Derby isolates from domestic pork showed no resistance to amikacin, 3rd generation cephalosporins, colistin, meropenem, or fluoroquinolones.

Figure 6.5 Resistance (%) among *Salmonella* Derby from domestic pork, Denmark, 2015-2024 DANMAP 2024



6.3.2 Genotypic resistance in *S.* Typhimurium and monophasic *S.* Typhimurium

Whole Genome Sequencing (WGS) can be used to complement antimicrobial susceptibility tests by identifying the genetic resistance mechanisms behind phenotypically expressed antimicrobial resistance. These mechanisms can be either induced by the specific genes or combination of genes, and/or point mutations. WGS makes it possible to investigate the dissemination of different genotypes across reservoirs.

S. Typhimurium and monophasic *S.* Typhimurium from domestic pork and human clinical isolates collected from 2020 to 2024 were investigated for genetic AMR determinants. A detailed description of the selection of isolates and methods used is included in Chapter 10.

In total, 466 *S.* Typhimurium isolates (379 domestic, 87 travel-associated) and 408 monophasic *S.* Typhimurium (341 domestic, 67 travel-associated) obtained from human cases in the period from 2020 to 2024, were included in the analysis of genetic AMR determinants. Overall, 61 and 76 unique genetic AMR determinants were identified in *S.* Typhimurium and monophasic *S.* Typhimurium isolates from humans, respectively.

All the sequenced *S.* Typhimurium (57) and monophasic *S.* Typhimurium (145) isolates from Danish pork collected from 2020 to 2024 in accordance with the EU rules for AMR monitoring were included.

The occurrence of selected AMR genes and point mutations (%) among *S.* Typhimurium and monophasic *S.* Typhimurium from domestic pork and human cases from 2020 to 2024 is presented in Figure 6.4. Only the most commonly occurring genetic AMR determinants conferring resistance to antimicrobials included in phenotypic testing (see Chapter 10, Table 10.3) are shown.

Resistance determinants in human *S.* Typhimurium isolates

In both domestic and travel-associated *S.* Typhimurium isolates from humans, *blaTEM-1*, *sul1*, *sul2* and *tet(A)* genes were the most frequently detected AMR determinants. Overall, the occurrence of these genes remained fairly stable over the years, albeit with some exceptions. In 2024, domestic isolates showed a marked increase in *sul2* and *tet(A)*, driven by an outbreak-associated *S.* Typhimurium clone with a specific AMR profile *aph(3")-Ib/aph(6)-Id/sul2/tet(A)*.

An increase of a few other genes (*floR*, *sul1*, *blaCARB-2*, and *tet(G)* was seen in domestic isolates in the period from 2022 to 2024 (Figure 6.4 A). In 2024, the increase was due to the outbreak-associated clone with a specific genetic profile *aadA2/blaCARB-2/floR/qacEdelta1/sul1/tet(G)* (n=11), and in 2022 and in 2023 due to a clone with a similar genetic profile *aadA2/blaCARB-2/floR/gyrA_D87N/qacEdelta1/sul1/tet(G)*.

An increase of *blaTEM-1* and *floR* observed in travel-associated isolates was not related to any specific *S.* Typhimurium clone (Figure 6.4a).

Resistance determinants to quinolones included five variants of the *qnr* gene (*qnrS1, qnrB19, qnrB2, qnrS13, qnrVC*), five different mutations in *gyrA* (D87N, S83Y, S83F, D87G, D87Y), and one mutation in *parC* (S80I). Over the five-year period, these determinants were detected infrequently, with only few (1-5) isolates identified per year.

The *gyrA* mutation D87N and *qnrS1* were dominating in domestic human isolates and in travel-associated isolates, respectively. *gyrA* mutations D87G, D87Y, S83F, *parC* mutation S80I, *qnrB2* and *qnrVC* were exclusively found in travel-associated isolates, whereas *gyrA* mutation S83Y was present only in domestic isolates. *qnrB19* and *qnrS13* were present in similar frequency.

Gentamicin resistance determinants, *aac(3)-IVa* and *aac(3)-IId* were detected in one domestic human isolate in 2023 and in one travel-associated isolate in 2024, respectively.

Azithromycin resistance determinants were detected in period from 2021 to 2023: *mph(A)* was detected in two travel-associated isolates, one in 2021 and one in 2022; and the *acrB* mutation R717 was detected in two travel-associated isolates in 2023.

One isolate from a domestic human case in 2021 carried *blaCMY-2* gene, conferring resistance to third-generation cephalosporins. Determinants conferring resistance to colistin and carbapenems were not detected.

Resistance determinants in pork *S.* Typhimurium isolates

Overall, in *S.* Typhimurium isolates from pork collected from 2020 to 2024, genes conferring resistance to beta-lactams (penicillins; *blaTEM-1*), sulfamethoxazole (*sul2*, *sul1* and *sul3*), tetracycline (*tet(A), tet(B)* and *tet(G)*), and trimethoprim (*dfrA12* and *dfrA1*) were the most commonly detected, matching with findings from phenotypical testing (Figure 6.4A). *aac(3)-IVa*, which confers resistance to aminoglycosides (gentamicin and apramycin), was first detected in 2022 and was found in three *S.* Typhimurium isolates in 2024 (Figure 6.4A).

The ASuT MDR genotypic profile was the most identified, present in 25 pork isolates. However, 16 different gene combinations were found, with *aph(3")-Ib/aph(6)-Id/blaTEM-1/sul2/tet(A)* found in five isolates, and *aph(3")-Ib/aph(6)-Id/blaTEM-1/sul2/tet(B)* and *aadA2/floR/blaCARB-2/sul1/tet(G)* in three isolates each.

Consistent also with the phenotypical findings, resistance genes conferring resistance towards carbapenems, 3rd, 4th and 5th generation cephalosporins, fluoroquinolones and polymyxins were not detected in *S.* Typhimurium from pork (Figure 6.5A and Table 6.3).

Resistance determinants in human monophasic *S.* Typhimurium isolates

blaTEM-1, *sul2*, and *tet(B)* were the most common genes detected in both domestic and travel-associated human isolates of monophasic *S.* Typhimurium over the five-year period in association with the genetic AMR profile *aph(3)-Ib/aph(6)-Id/blaTEM-1/sul2/tet(B)*. A combination of these genes is typically included in the epidemic monophasic *S.* Typhimurium (ST34) circulating among human cases in the EU. A notable decrease of these three genes was observed in domestic human isolates in 2024 due to the large outbreak caused by a fully susceptible monophasic *S.* Typhimurium clone.

A few AMR determinants showed higher occurrence in travel-associated human isolates than in the domestic isolates: *floR* conferring resistance to chloramphenicol and florfenicol; *qnrS1* and *qnrB19* conferring resistance to quinolones; and *tet(A)* conferring resistance to tetracycline (Figure 6.4b).

Seven unique quinolone resistance determinants distributed among 32 human isolates in the period from 2020 to 2024 were detected. *qnrS1* and *qnrB19* were the most frequent determinants with *qnrS1* detected in five domestic and eight travel-associated isolates, and *qnrB19* in six domestic and four travel-associated isolates. Other quinolone resistance determinants, *gyrA* mutations D87N, D87Y, S83F, *parE* H462Y and *qnrB2* were detected in one domestic and one travel-associated isolate each, *gyrA* mutation in 1-2 isolates each.

Among the five genes conferring resistance to gentamicin, *acc(3)*-IId was detected in four domestic and four travel-associated isolates, *aac(3)-IIe* in two domestic and two travel-associated isolates, *aac(3)-IVa* in three domestic and in one travel-associated isolate, *aac(3)-IIg* and *aac(6)-IIc* each in one domestic isolate.

Four unique genes conferring resistance to third-generation cephalosporins were detected, *blaCTX-M-55* was detected in four travel-associated isolates, *blaCTX-M-14* in one domestic and two travel-associated isolates, *blaCTX-M-1* and *blaSHV-12* each in two domestic isolates.

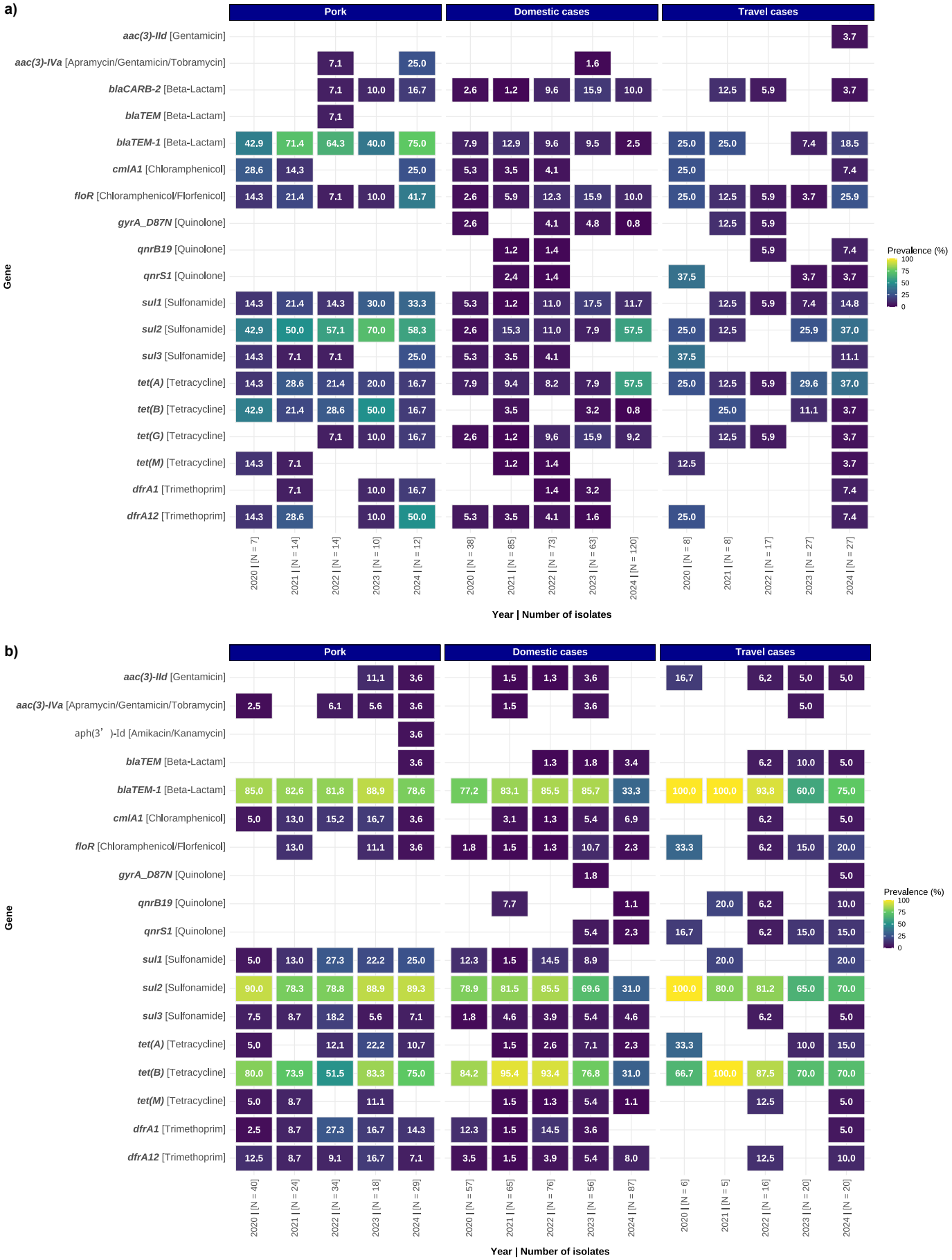
Two domestic and two travel-associated isolates carried *mph(A)* gene conferring resistance to azithromycin.

In 2022 and in 2024, single isolates carried colistin resistance genes *mcr-1* and *mcr-3*. Determinants conferring resistance to carbapenems were not detected.

In summary, the occurrence of AMR determinants differed between *S.* Typhimurium and monophasic *S.* Typhimurium isolates from humans. The differences in the most frequently detected genes were largely driven by the abundance of certain clones. Quinolone resistance determinants showed greater diversity in *S.* Typhimurium isolates - particularly those from travel-associated cases-than in monophasic *S.* Typhimurium. Moreover, the occurrence of certain quinolone resistance determinants differed between the two serotypes.

Figure 6.4 Presence (%) of genetic determinants of antimicrobial resistance among *S.* Typhimurium (a) and its monophasic variant (b) from domestic pork and human cases, Denmark, 2020-2024

DANMAP 2024



An isolate is categorised as domestically acquired if the patient did not travel outside Denmark one week prior to the onset of disease

Resistance determinants in pork monophasic *S.* Typhimurium isolates

From 2020 to 2024, monophasic *S.* Typhimurium isolates from Danish pork showed markedly high presence of resistance genes conferring resistance to beta-lactams (penicillins; *blaTEM-1*), sulfamethoxazole, predominantly carrying the *sul2* gene, and tetracycline, with the *tet(B)* gene found most (Figure 6.4B). This is a known characteristic of the most frequent monophasic *S.* Typhimurium clone (ST34) circulating within the EU. The ASuT MDR profile was identified in 105 monophasic *S.* Typhimurium isolates, showing equal results from phenotypic and WGS analysis. The most commonly found gene combination was *aph(3'')/lb-aph(6)-Id/aph(3')-Ia/**blaTEM-1**/**sul2**/**tet(B)***, present in 41 pork isolates.

Several genes were found that confer resistance to amikacin and gentamicin (aminoglycosides), such as the *aac(3)-IId, aac(3)-IVa I and aph(3')-Id* (Figure 6.4B). Resistance genes associated with macrolide resistance were rare. In 2024, one monophasic *S.* Typhimurium isolate from pork carried the *mph(A)* gene and another harbored the *mef(C)-mef(G)* tandem genes. Both resistant determinants are associated with azithromycin resistance.

In 2020 and 2023, no resistance genes conferring macrolide resistance were found. While in 2021 and 2022, two monophasic *S.* Typhimurium isolates carried the *acrB_R717Q/L* substitution.

Genes conferring resistance to high-priority or last-resort antimicrobials were not detected in monophasic *S.* Typhimurium from pork, consistent with phenotypical testing (Figure 6.4B and Table 6.3).

Conclusions and future perspectives

WGS-based analysis enabled the identification of AMR determinants not only for phenotypically tested antimicrobials but also for those not tested routinely. In addition, it allowed detection of co-occurring AMR determinants within the same isolate and their association with circulating *Salmonella* clones. Future efforts should focus on assessing concordance between phenotypic and genotypic testing to support the potential replacement of phenotypic testing with WGS.

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7

RESISTANCE IN INDICATOR BACTERIA

7. Resistance in indicator bacteria

Highlights

Over the last 5-year monitoring period, there have been no statistically significant trends in the occurrence of **fully-susceptible indicator *E. coli*** from broilers, pigs or cattle. Notably, in 2024 compared to 2023, full-susceptibility occurrence increased by 11% in isolates from cattle and decreased by 8% in isolates from pigs.

The occurrence of **multidrug-resistant indicator *E. coli*** compared to the previous year remained relatively constant in broilers and pigs and visibly decreased in cattle, in a clear shift from the increasing trend observed in recent years. Combined resistance to ampicillin, sulfamethoxazole, and tetracycline (ASuT) continued to be the most common multidrug-resistance profile among *E. coli* from pigs, however the relative occurrence of other profiles increased in 2024.

Compared to 2023, the **occurrence of resistance** to most antimicrobials in the test panel suffered a decrease in isolates from broilers and cattle, and an increase in isolates from pigs. The fluctuations between the two years were minor among isolates from broilers and pigs (1-5%), and more pronounced for cattle isolates (5-12%). Among pig isolates (although by a limited magnitude), there was an increase in occurrence of resistance to aminoglycosides (amikacin and gentamicin) and macrolides (azithromycin).

As in previous years, no colistin, meropenem or tigecycline resistance were detected in indicator *E. coli*. Resistance to amikacin, gentamicin, third generation cephalosporins and azithromycin were either absent or detected at low levels. Resistance to ciprofloxacin continued to be low in isolates from cattle and pigs and continued decreasing in broiler isolates.

As in previous years, samples from broilers, broiler meat and turkey meat examined for **carbapenemase-producing (CP) *E. coli*** (including OXA-48) were found negative. The occurrence of **ESBL- or AmpC- producing *E. coli*** remained constant below 5% in samples from broilers and domestic broiler meat, while it increased in samples from imported broiler meat and decreased in samples from imported turkey meat, by approximately 20%, compared to 2022.

7.1 Introduction

Escherichia coli and *Enterococcus* are included in the DANMAP programme to monitor the occurrence of antimicrobial resistance (AMR) in different reservoirs throughout the food chain for the following reasons: i) they are present as commensals in the gut microbiota of healthy animals and humans, ii) they can acquire antimicrobial resistance both via mutations in chromosomal genes and horizontal transfer of antimicrobial resistance genes, and iii) they have the potential to cause infections in both animals and humans, and to transfer antimicrobial resistance to pathogenic bacteria of the same or other species.

E. coli exhibiting resistance to third generation cephalosporins via the production of extended-spectrum beta-lactamases (ESBLs) and AmpC beta-lactamases (AmpCs) is among the fastest spreading antimicrobial resistance mechanisms in both humans and food-producing animals worldwide.

Carbapenemase-producing *Enterobacteriaceae* (CPE) pose a great threat to human health, as carbapenems are last-line antimicrobial drugs for the treatment of infections caused by multidrug-resistant Gram-negative bacteria.

Isolation and antimicrobial susceptibility testing of indicator *E. coli*, indicator enterococci and extended-spectrum cephalosporinase (ESC)- and carbapenemase (CP)-producing *E. coli* are performed in accordance with the rules for the EU harmonised monitoring of antimicrobial resistance [Decision 2020/1729/EU].

In 2024, isolates were obtained from randomly selected caecal samples collected from healthy broilers, cattle (calves under one year of age), and fattening pigs at slaughter. Additionally, for the specific monitoring of ESC- and CP-producing *E. coli*, fresh meat from broilers and turkeys was collected at retail. Details on sampling, analysis, susceptibility testing and interpretation of results are presented in Chapter 10.

7.2 Indicator *Escherichia coli*

Indicator *E. coli* isolates were obtained from 97%of caecal samples from broiler flocks 173/178, 90% of samples from pigs 184/205 and 93% of samples from cattle 154/166.

7.2.1 Indicator *Escherichia coli* from broilers, cattle and pigs

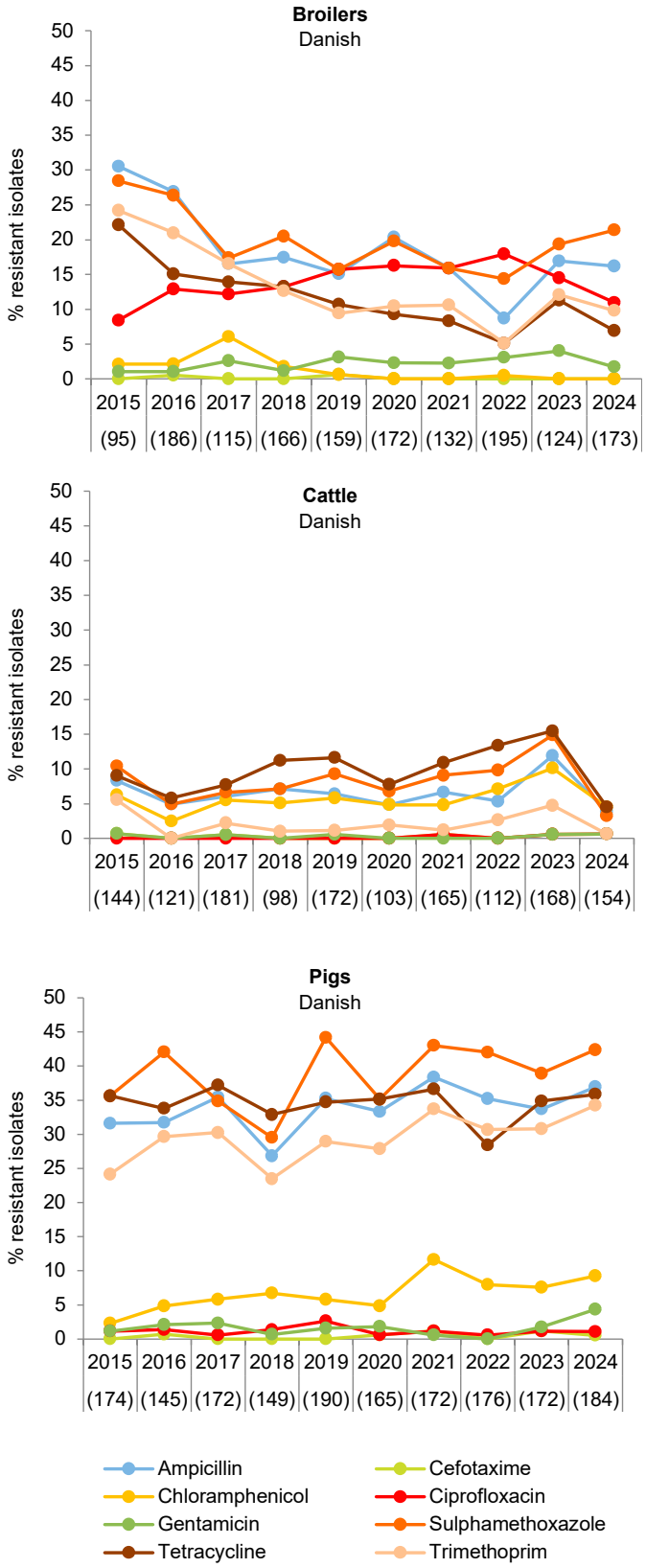
There has been no statistically significant increasing or decreasing trend in the annual prevalence of fully susceptible *E. coli* isolates from broilers, cattle or pigs during the past five years of monitoring (Figure 7.2) (p-values of 0.22 for broilers, 0.28 for pigs and 0.48 for cattle). Compared to 2023, the percentage of broiler isolates sensitive to all antimicrobials in the test panel increased by 4% in 2024, reaching the same value observed back in 2021 (64%). After the significant 5-year decrease in the proportion of fully susceptible *E. coli* in cattle, in 2024 it increased to 93% (similar to the level observed in 2020). Among isolates from pigs, the occurrence of full-susceptibility continued to decrease, and was at 40% in 2024, 8% lower than in 2023 (Table 7.1).

Table 7.1 Resistance (%) in *Escherichia coli* isolates from broilers, cattle and pigs, Denmark, 2024 DANMAP 2024

	Broilers	Cattle	Pigs
	Danish %	Danish %	Danish %
Amikacin	1	0	2
Ampicillin	16	4	37
Azithromycin	<1	<1	4
Cefotaxime	0	<1	<1
Ceftazidime	0	<1	<1
Chloramphenicol	0	5	9
Ciprofloxacin	11	<1	1
Colistin	0	0	0
Gentamicin	2	<1	4
Meropenem	0	0	0
Nalidixic acid	10	0	1
Sulphamethoxazole	21	3	42
Tetracycline	7	5	36
Tigecycline	0	0	0
Trimethoprim	10	<1	34
Fully susceptible (%)	64	93	40
Number of isolates	173	154	184

An isolate is considered fully susceptible if sensitive to all antimicrobial agents included in the test panel (Chapter 10, Table 10.3)

Figure 7.1 Resistance (%) among *Escherichia coli* isolates from broilers, cattle and pigs, Denmark, 2015-2024 DANMAP 2024



The number of isolates included each year is shown in the parentheses

Compared to 2023, the occurrence of resistance to most antimicrobials in the test panel showed an overall decrease in isolates from broilers and cattle, and an overall increase in isolates from pigs. The fluctuations between the two consecutive years were minor for broiler- and pig isolates (2-5% and 1-3%, respectively), and more pronounced for cattle isolates (5-12%) (Figure 7.1).

Remarkably, in *E. coli* from cattle, after an ongoing increase since 2021 in the occurrence of resistance to several tested antimicrobials, in 2024 the resistance levels markedly decreased, specifically for ampicillin (from 12% to 4%), chloramphenicol (from 10% to 5%), sulfamethoxazole (from 15% to 3%), tetracycline (from 15% to 5%) and trimethoprim (from 5% to <1%). While a shift in trend of tetracycline resistance could be explained by an ongoing decrease in consumption of tetracyclines in cattle, on the other hand, the consumption of amphenicols in calves continued to increase in 2024 (Chapter 4, Figure 4.5).

Also, the occurrence of resistance to ciprofloxacin in *E. coli* from broilers continued decreasing in 2024, after the decrease also observed in 2023, with fluoroquinolone resistance reaching levels similar to those of 2017 (11%). The results of 2023 and 2024 could represent a shift in the significant increasing trend observed in the decade leading to 2022.

Notably, in pig isolates (although by a limited magnitude), an increase in occurrence of resistance was observed from 2023 to 2024 for aminoglycosides (amikacin:<1% to 2%; gentamicin: 2% to 4%) and macrolides (azithromycin: 3% to 4%). These findings agree with the increases in antimicrobial consumption observed in recent years for aminoglycosides in weaners and macrolides in finishers (Chapter 4, Figure 4.4).

As in previous years, no isolates resistant to colistin, meropenem or tigecycline were detected. In 2024, amikacin resistance was detected in two isolates from broilers and three isolates from pigs. Azithromycin resistance was detected in seven isolates from pigs, and in single isolates from broilers and cattle. Resistance to third generation cephalosporins was not detected (for broilers) or detected at very low levels (up to 1%; for cattle and pigs) in indicator *E. coli* using non-selective methods. Resistance to fluoroquinolones continues to be very low (up to 1%) in isolates from cattle and pigs, and higher (11%) among broiler isolates (Table 7.1).

In 2024, the occurrence of multidrug-resistance (MDR) in *E. coli* from broilers, including combined resistance to ampicillin, sulfamethoxazole and tetracycline (ASuT) and other MDR profiles, returned to an overall level (12%) similar to that prior to 2023. In pigs, occurrence of MDR and other resistance profiles continues to appear relatively stable, although with a 4% increase in the percentage of isolates resistant to less than three antimicrobial classes, and a 5% increase in MDR profiles other than ASuT in 2024 compared to 2023.

Hence, ASuT resistance continued to be the predominant MDR profile in isolates from pigs (18%), although in 2024 its occurrence was only higher than the occurrence of other MDR profiles by 1%. Notably, in cattle, there was a clear shift in the ongoing increasing trend in the occurrence of MDR *E. coli*, and in 2024 the overall MDR level decreased to 4% (2% ASuT and 2% other MDR profiles) (Figure 4.2).

Among indicator *E. coli* isolated with a non-selective procedure, presumptive ESBL/AmpC-producing isolates were found in single samples from pigs and cattle (Table 7.1) After testing with the second antibiotic panel for confirmation of ESBL/AmpC-producing phenotype, both isolates showed resistance to third- and fourth-generation cephalosporins (cefotaxime, ceftazidime and cefepime).

Figure 7.2 Relative distributions (%) of fully susceptible, resistant and multidrug-resistant *Escherichia coli* isolates from broilers, cattle and pigs, Denmark, 2020-2024
DANMAP 2024

The number of isolates included each year is shown in parentheses. An isolate is considered fully susceptible if sensitive to all antimicrobial agents included in the test panel, and multidrug-resistant if resistant to 3 or more of the 12 antimicrobial classes included in the test panel (Chapter 10, Table 10.3). ASuT are the multidrug-resistant isolates resistant to ampicillin, sulphamethoxazole and tetracycline

7.3 ESBL/AmpC- and carbapenemase-producing *E. coli*

In 2024, caecal samples collected from broilers at slaughter, and from packages of fresh, chilled broiler- and turkey meat collected from Danish wholesale and retail outlets were subject to the specific monitoring of ESBL/AmpC- and carbapenemase (CP)-producing *E. coli*.

Among the samples randomly collected at retail, 14% (41 out of 301) of broiler meat and 100% of turkey meat were imported products. The distribution of the country of origin of the sampled imported turkey meat did not change considerably compared to 2022, with a single country representing 93% of all samples in 2024 (previously 98%). Contrarily, the distribution of the country of origin of the sampled imported broiler meat changed compared to the previous reporting year. In 2022, the collected samples originated from three producing countries, with a predominating country (A) representing 80% of the sampled imported broiler meat. In 2024, the distribution shifted, and a different predominating country (B) of origin was observed representing 56% of all samples collected (an increase of 38% compared to 2022).

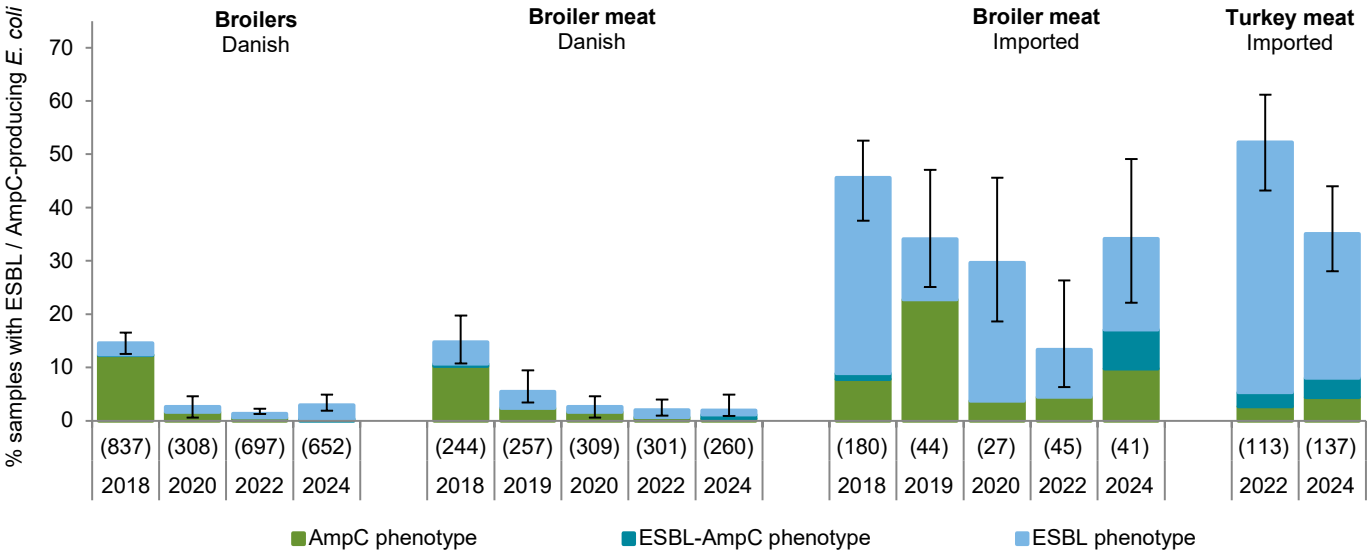
As in previous years, the selective procedures for detection of CP-producing *E. coli* (including oxacillinase-producing OXA-48-like enzymes), recovered no isolates.

7.3.1 Prevalence of ESBL/AmpC-producing *E. coli* in broilers, and broiler- and turkey- meat

Following selective enrichment, ESBL/AmpC-producing isolates, i.e. *E. coli* resistant to third generation cephalosporins (cefotaxime and/or ceftazidime), here abbreviated as ESBL/AmpC *E. coli*, were obtained from 19/652 samples from broilers (3%; CI 95%: 2-5%), 5/260 samples from Danish broiler meat (2%; CI 95%: 1-5%), 14/41 samples from imported broiler meat (34%; CI 95%: 22-49%), and 48/137 samples from imported turkey meat (35%; CI 95%: 27-43%) (Table 7.2, Figure 7.3).

In 2024, in comparison to 2022, the prevalence of ESBL/AmpC *E. coli* has increased marginally in Danish broilers (from 1% to 3%) and remained the same in domestic broiler meat (2%). Notably, it increased markedly in imported broiler meat (from 13% to 34%) and decreased in the same magnitude in imported turkey meat (from 52% to 35%) (Figure 7.3, Table 7.2). ESBL/AmpC *E. coli* continued to show higher occurrence in imported broiler meat compared to Danish broiler meat.

Figure 7.3 Occurrence (%) of samples with phenotypic ESBL- or AmpC-producing *E. coli* from animals and meat recovered by selective enrichment, Denmark 2018-2024 DANMAP 2024



Number of samples tested per year is presented in the parentheses. Confidence intervals for total proportion of samples positive for phenotypic ESBL and/or AmpC producing *E. coli* - calculated as 95% binomial proportion Wilson intervals. Classification of ESBL and AmpC phenotypes according to the scheme provided by EFSA (Chapter 10, Section 10.7.2)

After a sharp decrease from 2018 to 2020 on the occurrence of ESBL/AmpC *E. coli* in domestic broilers and broiler meat, the levels seemed to have stabilized below 5% since then. On the contrary, in imported broiler meat, after the decrease observed in the previous four monitoring years, the occurrence of ESBL/AmpC *E. coli* increased markedly in 2024, returning to the level observed in 2019. This increase in ESBL/AmpC *E. coli* prevalence can likely be explained by the shift in the origin of the imported broiler products observed in 2024. In previous years, the sampled imported broiler meat originated predominantly from a country (A) with low occurrence of ESBL/ AmpC *E. coli* in broiler products. In 2024, most sampled imported broiler meat originated from a country (B) with a considerably higher prevalence of ESBL/ AmpC *E. coli* in broiler products. The presence of ESBL/AmpC Ec in imported turkey meat in Denmark has been monitored in 2022 and 2024, according to EU Decision 2020/1729. While the level was manifestly higher in imported turkey compared to imported broiler in 2022, in 2024 a similar prevalence was observed in both meat categories (Figure 7.3).

7.3.2 Phenotypic resistance in ESBL/AmpC-producing *E. coli*

In 2024, the relative frequency of ESBL-producing and/or AmpC-producing phenotypes remained mostly unchanged in comparison to previous years, except among isolates from imported broiler meat, which showed an increase in the relative occurrence of the AmpC-producing phenotype (10% of samples; 29% of ESBL/AmpC *E. coli* isolates) and of the combined ESBL-AmpC-producing phenotype (7% of samples; 21% of ESBL/AmpC *E. coli* isolates). In isolates recovered from imported turkey meat, the ESBL-producing phenotype continued to be predominant (27% of samples; 79% of ESBL/AmpC *E. coli* isolates) (Figure 7.3, Table 7.2).

As in previous years, all the recovered ESBL/AmpC *E. coli* isolates from broilers and Danish broiler meat were resistant to both third generation cephalosporins (cefotaxime and ceftazidime) and ampicillin. In 2024, those isolates were also all resistant to fourth generation cephalosporins (cefepime). Resistance to cefotaxime, ceftazidime and ampicillin was also very high (93% to 100%) in isolates from imported broiler- and turkey meat. Unlike previous years, cefepime resistance was found at a higher prevalence among the isolates recovered from domestic broiler meat (100%) than among those from imported broiler meat (71%) and imported turkey meat (90%) (Table 7.2).

A 17% increase in the occurrence of cefepime resistance among isolates from domestic broilers and broiler meat was already observed in 2022. Again in 2024, an increase of 33% was observed compared to the previous monitoring year. On the contrary, the occurrence of cefepime resistance has decreased in 2022 (by 17%) and in 2024 (by 12%) among ESBL/AmpC *E. coli* from imported broiler meat. Note that these results are based on a very low number of isolates recovered from domestic meat (six in 2022 and five in 2024).

In the same two monitoring years, the observed resistance to fluoroquinolones (ciprofloxacin) has markedly decreased in ESBL/AmpC *E. coli* from Danish broilers (from 44% in 2022 to 0% in 2024) and remained at a similar level in Danish broiler meat (17% in 2022 and 20% in 2024). In contrast to what was observed in 2022, in 2024 ciprofloxacin resistance also decreased in isolates from imported broiler meat (from 100% to 86%), as well as in isolates from imported turkey meat (from 83% to 69%).

Unlike the previous monitoring year, in 2024 ertapenem resistance was not observed in isolates from broilers. Among isolates from imported turkey meat, two out of 48 isolates (4%) were ertapenem-resistant, and as in 2022, no resistance to meropenem or imipenem was observed. ESBL-producing *E. coli* may present ertapanem-resistant, meropenem-sensitive phenotypes [Black, et al. 2024. *Antibiotics* 13(2), 185]. Such isolates rarely encode carbapenemase genes and show distinct clinical and microbiological characteristics compared to CP-producing *E. coli* [Adelman, et al. 2021. *Open Forum Infectious Diseases*, 9(1)].

The occurrence of colistin-resistant ESBL/AmpC *E. coli* among imported turkey meat decreased from 7% in 2022 to 4% in 2024.

Azithromycin resistance was observed in two out of 14 isolates from imported broiler meat (14%, 3% lower than in 2022) and in a single isolate from imported turkey meat (2%, as in 2022). Notably, the occurrence of gentamicin resistance decreased from 10% in 2022 to 4% in ESBL/AmpC *E. coli* from imported turkey meat, but it increased from 0% to 29% in isolates from imported broiler meat.

As in 2022, resistance to tigecycline, temocillin, meropenem and imipenem was not observed among the isolates collected in 2024, and no resistance to colistin was observed in ESBL/AmpC *E. coli* from broilers and broiler meat (Table 7.2).

Table 7.2 Resistance (%) and ESC resistance phenotypes in specific monitoring of ESC-producing *Escherichia coli* from animals and meat recovered by selective enrichment, Denmark, 2024 DANMAP 2024

	Broilers	Broiler meat		Turkey meat
Antimicrobial agent	Danish %	Danish %	Import %	Import %
Amikacin	0	0	0	0
Ampicillin	100	100	100	100
Azithromycin	0	0	14	2
Cefepime	100	100	71	90
Cefotaxime	100	100	100	100
Cefotaxime/clavulansyre	0	20	29	13
Cefoxitin	11	60	50	23
Ceftazidime	100	100	93	100
Ceftazidime/clavulansyre	0	20	29	13
Chloramphenicol	0	20	64	60
Ciprofloxacin	0	20	86	69
Colistin	0	0	0	4
Ertapenem	0	0	0	4
Gentamicin	0	0	29	4
Imipenem	0	0	0	0
Meropenem	0	0	0	0
Nalidixic acid	0	20	86	58
Sulfonamide	0	0	57	73
Temocillin	0	0	0	0
Tetracycline	16	20	57	81
Tigecycline	0	0	0	0
Trimethoprim	0	0	57	40
Number of AmpC phenotypes	0	1	4	6
Number of ESBL phenotypes	17	2	7	37
Number of ESBL+AmpC phenotypes	2	2	3	5
Number of ESC isolates (%)	19 (3%)	5 (2%)	14 (34%)	48 (35%)
Number of samples	652	260	41	137

Classification of ESBL-, AmpC- and AmpC+ESBL phenotypes is based on the MIC results (Chapter 10, Section 10.7.2). AmpC, ESBL and AmpC+ESBL phenotypes indicate the number of isolates expressing each specific phenotype

7.3.3 Genotypic resistance in ESBL/AmpC-producing *E. coli*

The genetic basis for ESBL and AmpC enzymes was detected in all isolates recovered by selective enrichment. The detected enzymes corresponded to the phenotypes derived from the susceptibility testing for most isolates, except 12 (two from broilers, two from domestic broiler meat, three from imported broiler meat and five from imported turkey meat). In those isolates, susceptibility testing revealed an ESBL- and AmpC-producing phenotype, while whole genome sequencing only revealed the presence of genes encoding for ESBL enzymes. The ESBL genotypes in those isolates were mostly due to single ESBL-encoding genes (CTX-M-1, CTX-M-15, CTX-M-27, CTX-M-55 and TEM-52B). However, two isolates from imported turkey meat showed the presence of more than one gene, including less frequent variants and also genes with unknown ESBL predicted phenotypes (Tables 7.2 and 7.3).

Among the AmpC-producing isolates recovered in 2024, resistance was, as observed in previous years, conferred by upregulated AmpC promotor C-42T mutations (seven isolates), followed by the CMY-2 plasmid-mediated AmpC enzyme (four isolates) (Table 7.3).

Among all ESBL-producing isolates, 10 different ESBL-encoding genes were detected. Overall, the most commonly observed gene across all categories of animals and meat sampled in 2024 was CTX-M-1, as observed in the previous reporting year. CTX-M-55 and CTX-M-15 were the following most abundant genes. As observed in 2022, among isolates from imported turkey meat, the encoding gene CTX-M-27 was considerably frequent, all ten different detected enzymes were observed, and seven isolates (15% of all ESBL Ec from imported turkey meat) had more than one ESBL-encoding gene (Table 7.3).

In total, 36 MLSTs were observed among all ESBL/AmpC-producing *E. coli* isolates. The most common MLSTs were ST10 and ST297 in Danish broilers, ST69 and ST162 in imported broiler meat, and ST10 and ST569 in imported turkey meat.

Table 7.3 Number of ESBL and AmpC enzymes detected in beta-lactamase-producing *E. coli* isolates from animals and meat recovered by selective enrichment, Denmark, 2024 DANMAP 2024

	Broilers	Broiler meat		Turkey meat
Enzymes	Danish	Danish	Import	Import
CTX-M-1	9	2	2	11
CTX-M-15			4	6
CTX-M-27				8
CTX-M-32				1
CTX-M-55			3	10
SHV-12			1	4
TEM-106				5
TEM-126				5
TEM-207				2
TEM-52B	10	2		2
CMY-2		1	2	1
Chromossomal AmpC (C-42T)			2	5
Number of AmpC genotypes		1	4	6
Number of ESBL genotypes (two or more enzymes)	19	4	10	42 (7)
Number (%) positive samples	19 (3%)	5 (2%)	14 (34%)	48 (35%)
Number of tested samples	652	260	41	137

Number (%) positive samples are isolates recovered by selective enrichment methods for monitoring of beta-lactamase-producing *E. coli* ESBL/AmpC enzymes were determined by whole genome sequencing of the recovered isolates (Chapter 10, Section 10.6)

7.4 Indicator *Enterococci*

Enterococci were obtained from 296 (98%) out of 303 faecal samples taken from broilers at slaughter, and antimicrobial susceptibility testing was subsequently performed on all 17 *E. faecalis* isolates and on 278 *E. faecium* isolates.

7.4.1 *E. faecalis* and *E. faecium* from broilers

Overall, 29% of the *E. faecalis* isolates and 85% of the *E. faecium* isolates were susceptible to all antimicrobials in the test panel. While the level decreased by 10% compared to 2022 for *E. faecalis*, it increased by 33% for *E. faecium* in the same period (Table 7.4).

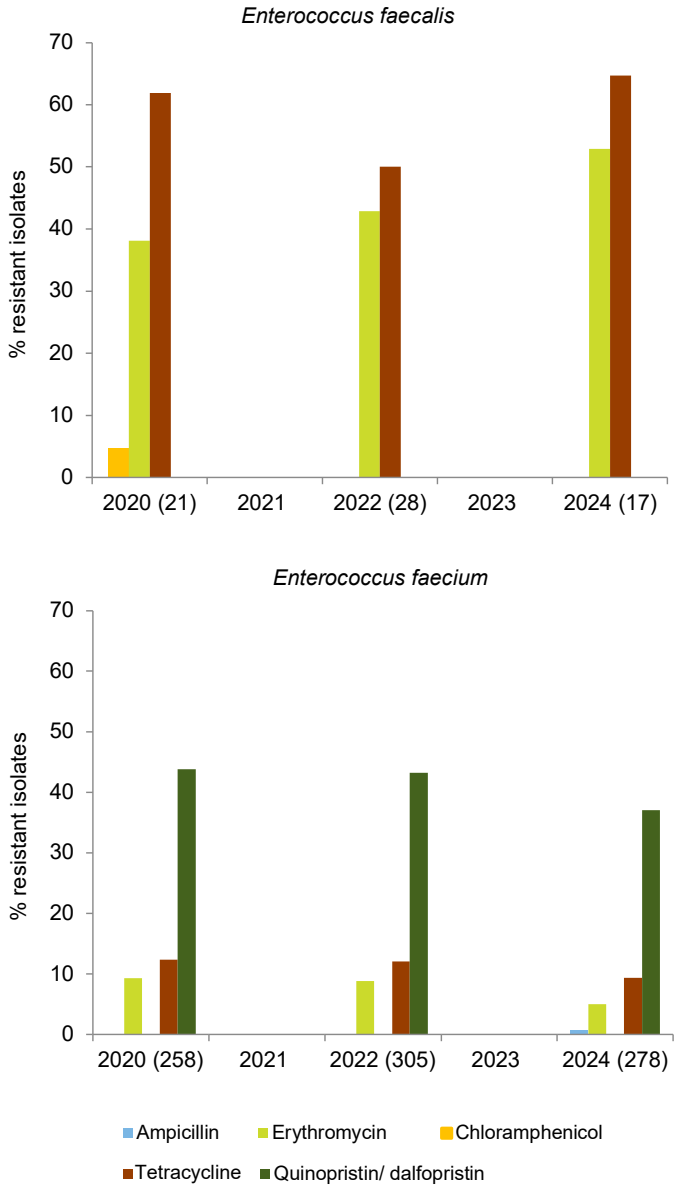
As in 2022, the previous year of monitoring in broilers, no enterococci isolates showed resistance to chloramphenicol, daptomycin, linezolid, gentamicin, teicoplanin, tigecycline or vancomycin. In 2024, ampicillin resistance was not observed in *E. faecalis*, but occurred in 1% of the *E. faecium* isolates. Resistance to erythromycin and tetracycline continued to be the most common. Compared to 2022, in 2024 resistance to these antibiotics showed an increase among *E. faecalis* (10% and 15%) and a decrease among *E. faecium* (4% and 3%). The increase in erythromycin resistance observed among *E. faecalis* isolates, follows a previous increase already observed in 2022 compared to 2020 (from 38% to 43%). The occurrence of ciprofloxacin resistance in *E. faecium* isolates was at the same level as in previous years (3%) (Table 7.4 and Figure 7.4).

Table 7.4 Resistance (%) in Enterococci isolates from broilers, Denmark, 2024 DANMAP 2024

Antimicrobial agent	*Enterococcus faecalis* %	*Enterococcus faecium* %
Ampicillin	0	1
Chloramphenicol	0	0
Ciprofloxacin	0	3
Daptomycin	0	0
Erythromycin	53	5
Gentamicin	0	0
Linezolid	0	0
Quinopristin/dalfopristin	-	37
Teicoplanin	0	0
Tetracycline	65	9
Tigecycline	0	0
Vancomycin	0	0
Fully susceptible (%)	29	85
Number of isolates	17	278

E. faecalis are assumed inherently resistant to streptogramins (Quinopristin/Dalfopristin)
An isolate is considered fully susceptible if sensitive to all antimicrobial agents included in the test panel (Chapter 10, Table 10.3)

Figure 7.4 Resistance (%) among Enterococci isolates from broilers, Denmark, 2020-2024 DANMAP 2024



Number of isolates included each year is presented in the parentheses

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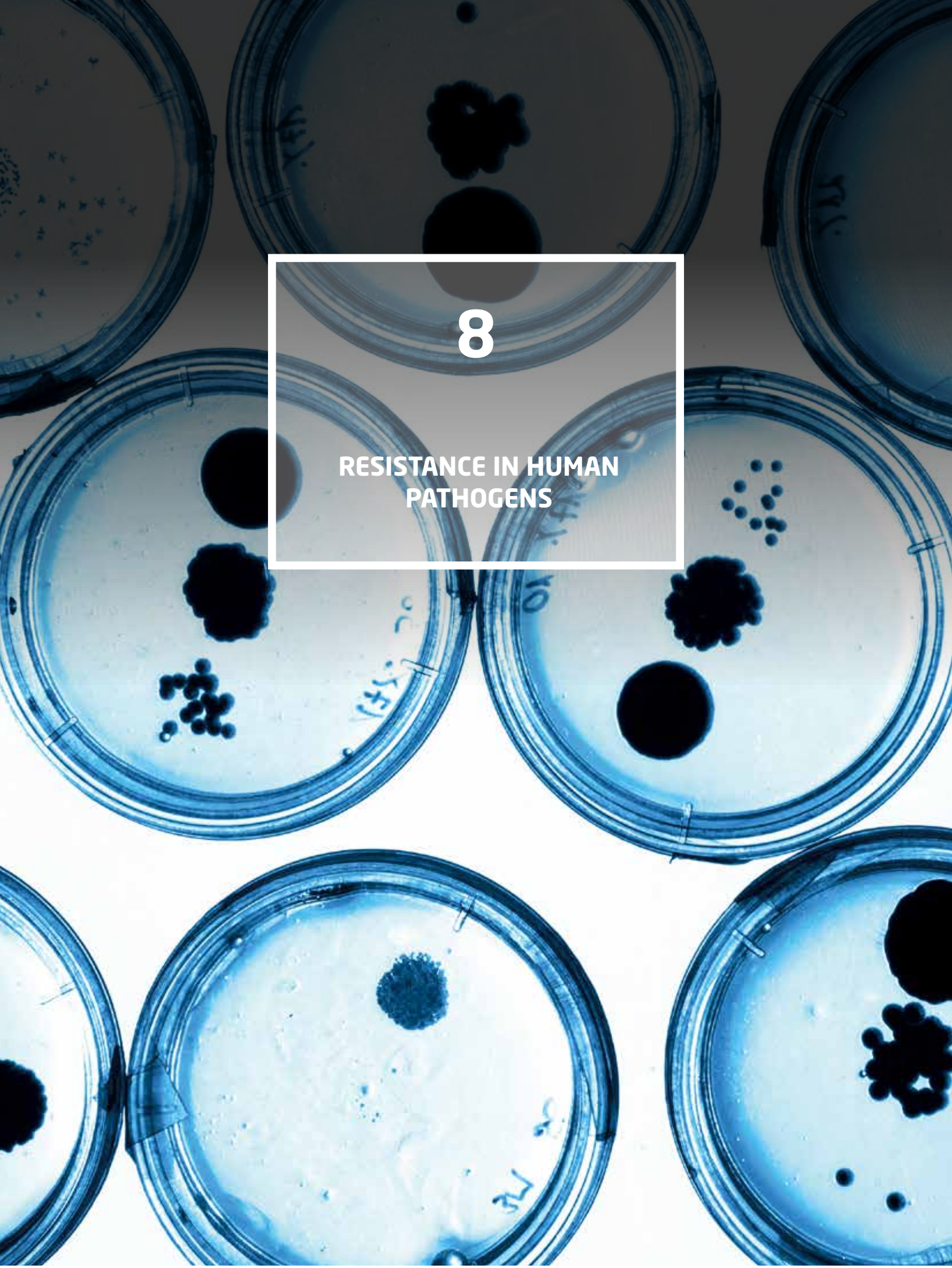


8

RESISTANCE IN HUMAN PATHOGENS

8. Resistance in human pathogens

Highlights: The **incidence of positive blood cultures** with pathogenic species increased overall from 474 per 100,000 inhabitants in 2015 to 612 per 100,000 inhabitants in 2024 (an increase of 29%). The number of individual registered invasive cases per year for the decade increased for *E. coli* from 4,597 cases to 5,957 cases, for *S. aureus* from 1,876 to 2,442 cases, for *K. pneumoniae* from 939 to 1,457 cases and for *P. aeruginosa* from 441 to 488 cases. Decreasing numbers were observed for *S. pneumoniae* from 747 to 600 annual cases, for *E. faecium* from 693 to 584 cases and for *E. faecalis* from 610 to 594 cases.

Resistance levels for invasive ***E. coli*** showed decreasing or stagnating trends for most antimicrobials, including for combined resistance to ciprofloxacin, cephalosporin and gentamicin (2.3% in 2015 to 1.0% in 2024) and combined resistance to ampicillin and gentamicin (6.3% in 2015 to 4.0% in 2024). Resistance to piperacillin-tazobactam increased in three of the five healthcare regions, leading to an overall increase from 4.9% in 2015 to 6.5% in 2024. Resistance to carbapenems remained below 1%.

In invasive ***K. pneumoniae*** **the resistance level** for piperacillin/tazobactam has been increasing steadily since 2021 and has now reached 10.9% (7.5% in 2021). However, combined resistance to 3rd generation cephalosporins, ciprofloxacin and gentamicin remains low at 1.4%. Additionally, resistance to carbapenem remained below 1%. For *K. pneumoniae* from hospital urine, resistance to piperacillin/tazobactam is now also at 10.9% mirroring the increasing resistance levels in invasive infections.

Carbapenemase-producing organisms/Enterobacterales (CPO/CPE). CPE were increasingly spreading in Danish hospitals, with cases increasing by 14% from 2023 to 2024, reaching 497 individual cases. CPE, historically linked to travel, are now increasingly found domestically. CPE outbreaks increased in hospitals despite extensive screening and cleaning efforts. 166 new CPO patients were associated with outbreaks in Denmark in 2024. Although bloodstream infections remained rare, the rise in hospital-acquired CPE indicates the emergence of domestic reservoirs. For non-outbreak related cases, 101 patients reported travelling outside Nordic countries, however, the number of cases with no travel information reported was high (142 cases). Additionally, 41 cases were patients from Ukraine.

Staphylococcus aureus. The number of *S. aureus* bacteraemia cases was 2,461 in 2024 and at the same level as in 2023. Of these, 47 cases (1.9%) were caused by methicillinresistant *S. aureus* (MRSA) with seven being livestock-associated-MRSA (LA-MRSA). Resistance to penicillin appears stable and was 68% in 2024. There were 3,372 cases of MRSA from both screening (41% of cases) and infections (59%), which was an 8% decrease compared to 2023. Thirty-eight MRSA outbreaks were registered at hospitals, nursing homes and other institutions for a total of 191 cases with 86 being infections.

Neiserria gonorrhoeae. Over the decade the number of received isolates and of reported cases increased significantly. In 2024, the reference laboratory at SSI received 1,852 isolates from 1,803 individual cases. Ciprofloxacin resistance was at 61%. Azithromycin-resistance was found in 3.5% of tested isolates in 2023 compared to 6.0% of tested isolates in 2022.

8.1 Introduction

The Danish national surveillance programme of antimicrobial resistance in human clinical bacteria collects data on routine diagnostics from all of Denmark. It is an active digital catchment system collecting results from all clinical and screening samples from patients. Data coverage is high and microbiology data from all hospitals and the majority of general practitioners feed into the system. Primarily included are data from invasive infections and urines, and in selected cases data from other specimen or sample sites.

In addition, the programme includes phenotypic resistance and typing results from the reference laboratories at SSI. Isolates are submitted to SSI either as part of the programme on mandatory notifiable diseases or based on voluntary submission of bacterial species carrying resistance mechanisms of concern. Table 8.1 gives an overview of inclusion criteria for data from the digital surveillance system and the reference laboratories.

Table 8.1 Inclusion criteria for bacterial species and types in the national antimicrobial resistance surveillance in humans, Denmark, 2024 DANMAP 2024

Routine diagnostics from all 10 DCM in Denmark. All data are extracted from EpiMiBa	
Species	**Inclusion criteria**
Escherichia coli *Klebsiella pneumoniae*	First isolate per patient per year from blood or cerebrospinal fluid, from urine in hospitalised patients and from urine from primary health care
Pseudomonas aeruginosa *Acinetobacter* species *Enterococcus faecalis* *Enterococcus faecium*	First isolate per patient per year from blood or cerebrospinal fluid
Voluntary submissions of isolates to the reference laboratories at SSI	
Species or type	**Inclusion criteria**
Staphylococcus aureus Beta-haemolytic streptococci	One isolate per patient per episode from blood or cerebrospinal fluid
Neisseria gonorrhoeae	One isolate per patient per episode from any sample site
3rd generation cephalosporin-resistant *Escherichia coli*	First isolate per patient within 12 months from blood
Vancomycin-resistant enterococci	First isolate per patient within 12 months from any sample site (excluding screening samples)
Enterococci with specific phenotype of concern (e.g. linezolid, daptomycin and tigecycline R)	First isolate per patient within 12 months from any sample site (clinical and screening samples)
All bacterial species with other exceptional phenotypes (e.g. acquired colistin resistance)	One isolate per patient per episode from any sample site
Mandatory submissions of isolates to the reference laboratories at SSI	
Species or type	**Inclusion criteria**
Carbapenemase-producing organisms	First isolate per patient within 12 months from any sample site (clinical and screening samples)
Methicillin-resistant *Staphylococcus aureus*	First isolate from all new cases of MRSA postive patients from any sample site (clinical and screening samples)
Streptococcus pneumoniae	One isolate per patient per episode from blood or cerebrospinal fluid
Haemophilus influenzae serotype b, Hib	All invasive isolates

Irrespective of number of isolates analysed per patient, only one isolate per given bacterial species per patient is included

8.1.1 Surveillance based on data from the Danish Microbiology Database (MiBa)

An important part of the national surveillance programme consists of systematically extracted data from a register (EpiMiBa) linking to the Danish Microbiology Database (MiBa). MiBa was established in 2010 with the aim of building a cross-national database that included and made available all microbiology analyses performed by the individual DCM. MiBa simultaneously delivers real time patient data to the DCM for clinical use and data to SSI for national surveillance. Until the establishment of MiBa, surveillance was based on voluntary manual reporting from the individual DCM, in the beginning including data from just two DCM in 1995, but quickly expanding to cover more than fifty percent of the DCM. Since 2015, all DCM have contributed to the program resulting in a 100% coverage of hospitalised patients and – since the DCM perform microbiology analyses for GPs and private specialists as well – also a very high coverage of results from the primary sector.

A description of MiBa and the usage and validation of data from the associated database EpiMiBa can be found on the following homepage [https://mibaen.ssi.dk/] and in DANMAP 2018, Textbox 8.1.

The MiBa-based surveillance includes all invasive isolates of *Escherichia coli, Klebsiella pneumoniae, Enterococcus faecalis, Enterococcus faecium, Pseudomonas aeruginosa* and *Acinetobacter* species and all urine isolates of *E. coli* and *K. pneumoniae*. For inclusion, the following case definition applies: The first sample of each given bacterial species per individual patient per year, by date of sample collection; an approach identical to the surveillance performed by the European Antimicrobial Resistance Surveillance Network (EARS-Net). All duplicates, patient-related or sample-related within the year of observation, are excluded.

Materials and methods are further described in paragraph 10.10 in Chapter 10.

8.1.2 Surveillance based on data from the reference laboratories

Antimicrobial resistance is also monitored in isolates submitted to the reference laboratories at SSI.

Submission of isolates began in 1957 with the voluntary referral of *S. aureus* from bloodstream infections. Still today, many isolates are sent as part of voluntary programmes; however, the majority of isolates are referred as part of surveillance programmes for notifiable diseases.

The mandatory programme includes methicillin-resistant *S. aureus* (MRSA) and carbapenemase-producing organisms (CPO) from clinical and screening samples, *S. pneumoniae* and *Haemophilus influenzae* serotype b (Hib) from invasive infections and *Nesseria gonorrhoeae* from all clinical samples. The latter three irrespective of findings of antimicrobial resistance, but resistance mechanisms are investigated both locally and at SSI (Table 8.1).

The voluntary programme includes day-to-day referral of vancomycin-resistant enterococci and monthly or periodically reporting of ESBL-positive invasive *E. coli*, invasive beta-haemolytic streptococci and invasive *S. aureus*.

In addition, the reference laboratory for antimicrobial resistance at SSI receives highly resistant strains or strains carrying atypical antimicrobial resistance mechanisms of specific concern irrespective of bacterial species.

Since 2015/2016, characterisation of antimicrobial resistance mechanisms in bacteria has been performed primarily by whole genome sequencing (WGS).

8.1.3 Number of invasive cases

The total numbers of invasive cases of the monitored bacterial species included in the surveillance programmes for both DANMAP and EARS-Net from 2015 to 2024 are presented in Figure 8.1. Invasive cases caused by *Acinetobacter* species are not shown in the figure due to the small numbers of isolates (ranging from 55 to 97 cases/year between 2015 and 2024).

Between 2015 and 2024, the number of registered individual invasive cases increased by 22% from 9,975 to 12,214 cases in Denmark: *E. coli* 4,597 to 5,957 cases (30% increase), *S. aureus* 1,876 to 2,442 cases (30%) and *K. pneumoniae* 939 to 1,457 cases (55%).

Figure 8.1 Number of invasive cases for bacterial species under surveillance, Denmark, 2015-2024 DANMAP 2024

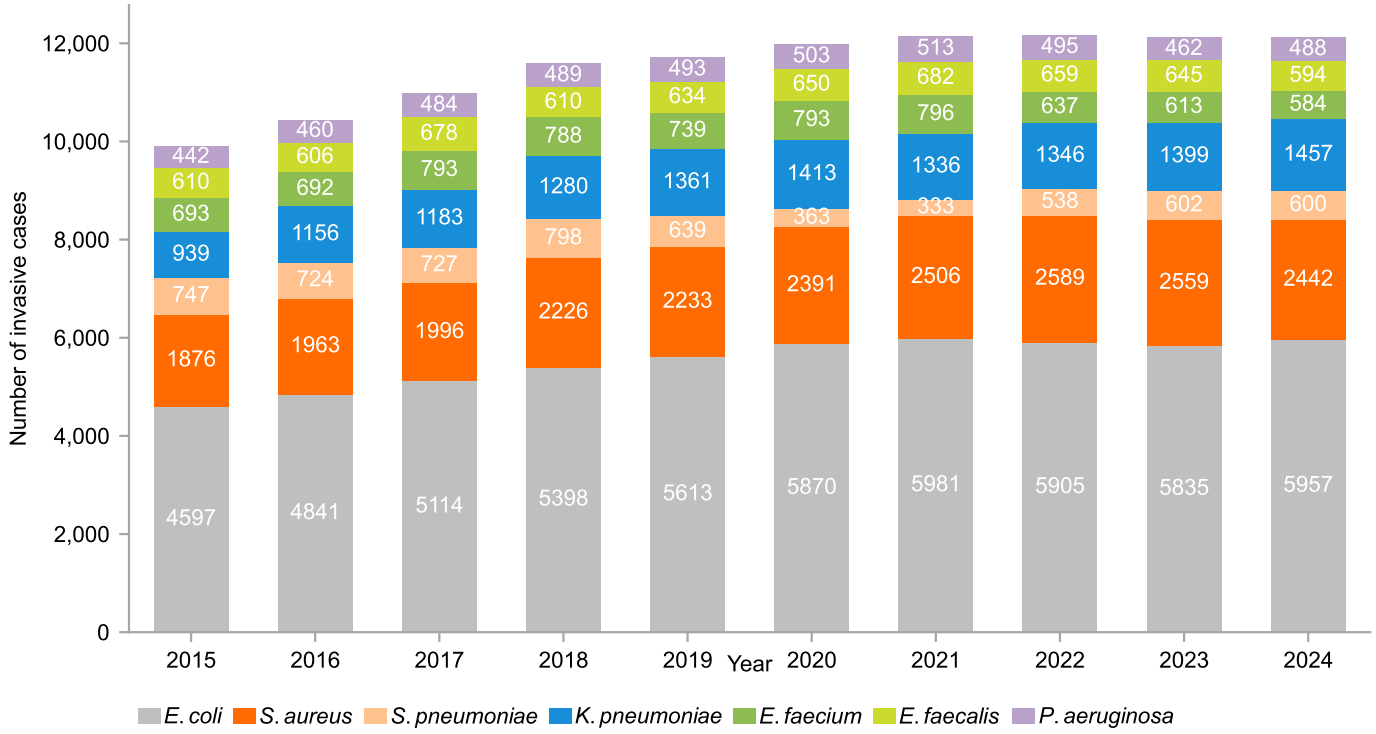
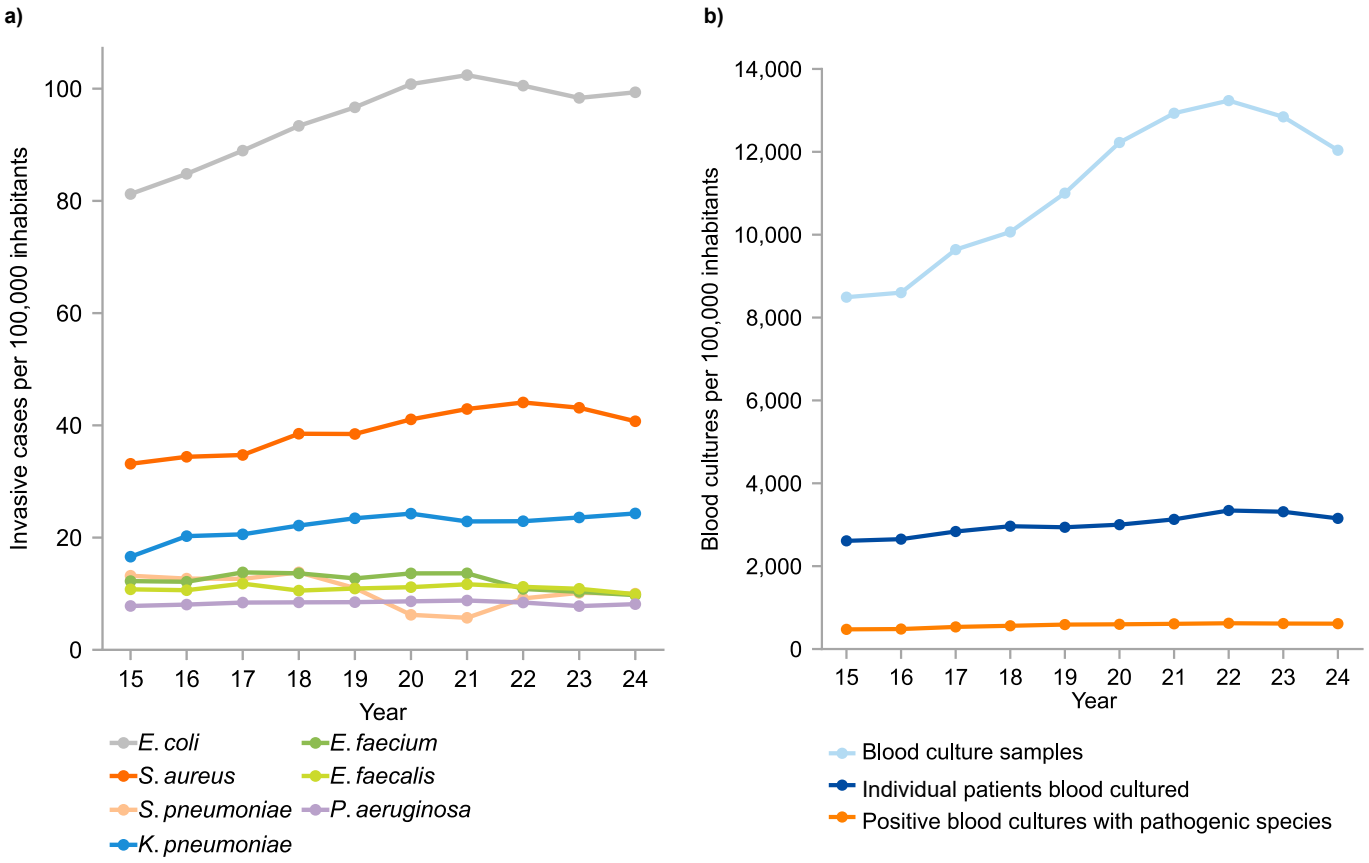


Figure 8.2a shows the incidence of invasive cases of the seven monitored species per 100,000 inhabitants in Denmark per year from 2015 to 2024. During this period, the Danish population increased by 5.9% (from 5,659,715 inhabitants in 2015 to 5,995,628 inhabitants in 2024).

For comparison, Figure 8.2b shows the total number of blood cultures taken per 100,000 inhabitants per year and the number of individual patients with minimum one blood culture taken per 100,000 inhabitants per year, for the same period. The total number of blood samples taken per 100,000 inhabitants increased by 42% and the number of individual patients with at least one blood culture taken by 21% (from 2,611 patients per 100,000 inhabitants in 2015 to 3,153 patients per 100,000 inhabitants in 2024). The incidence of positive blood cultures with pathogenic species increased from 474 per 100,000 inhabitants in 2015 to 612 per 100,000 inhabitants in 2024.

The following sections present results of resistance monitoring in Denmark for the individual bacterial species and/or resistance types under surveillance.

Figure 8.2 a) Invasive cases and b) blood cultures taken per 100,000 inhabitants, Denmark, 2015-2024 DANMAP 2024



8.2 Results from MiBa data surveillance

8.2.1 *Escherichia coli*

Escherichia coli is by far the most frequent cause of community and hospital acquired bacteraemia and urinary tract infections (UTI) in Denmark. The pathogen is part of the normal intestinal flora in both animals and humans, where it comes into close proximity to many other bacterial species. Transferable resistance mechanisms are frequently seen in these gut bacteria as well as resistance conferred by mutations. Since *E. coli* is the most frequent cause of UTI and bacteraemia, it is also responsible for a large proportion of the antimicrobials used to treat these conditions.

The percentages of resistance in invasive *E. coli* isolates for each key antimicrobial are presented in Table 8.2, as are urine samples from hospitals and primary health care (see details in later paragraphs).

Invasive cases from hospital patients

In 2024, a total of 5,957 individual patients with invasive *E. coli* isolates were identified in EpiMiBa. Antimicrobial susceptibility test results for key antimicrobials were also extracted for these isolates (See Chapter 10 'Material and methods').

Figure 8.3 and Table 8.3 show the total annual number of invasive isolates and proportion of resistant isolates by region between 2015 and 2024. Most resistance levels decreased or stagnated over the last decade, apart from resistance to piperacillin-tazobactam, which increased in three of the five healthcare regions, leading to an overall increase from 4.9% in 2015 to 6.5% in 2024.

Resistance to carbapenems remained below 1%. The percentages of multidrug resistant invasive isolates are presented in Table 8.4. Combined resistance to ciprofloxacin, cephalosporins and gentamicin decreased from 2.3% in 2015 to 1.0% in 2024 and combined resistance to ampicillin and gentamicin decreased from 6.3% to 4.0%.

Urinary cases from hospitals

In 2024, *E. coli* was isolated from urine samples of 40,624 individual hospital patients. As for invasive *E. coli* increasing resistance to piperacillin-tazobactam was observed (5,6% in 2024). In Table 8.2 summarized antimicrobial susceptibility results for *E. coli* isolates (invasive and urine specimen) are shown. In Figure 8.4 and Table 8.5, resistance for *E. coli* urine isolates from hospitalised patients are shown for 2015-2024.

Urinary cases from primary health care

In 2024, *E. coli* were isolated from urine samples from 93,436 individual patients in primary health care, a notable decrease compared to 2023. This is due to changes in workflow at one of the DCMs in the Capital Region causing data from that DCM to be excluded from the analysis. Susceptibility results for all tested antimicrobials are shown in Table 8.2. In Figure 8.5 and Table 8.6, resistance for *E. coli* urine isolates from primary health care are shown for the past decade.

Conclusion

The number of invasive cases of *E. coli* appears to have reached a plateau. Resistance levels are generally stable for all specimen types, however, the slow rise in piperacillin-tazobactam resistance in *E. coli* from invasive infections and hospital urines are cause for concern.

Table 8.2 *Escherichia coli*. Resistance (%) in isolates from humans, Denmark, 2024 DANMAP 2024

Substance	Invasive isolates, hospitals %	Urine isolates, hospitals %	Urine isolates, primary health care %
Ampicillin	42	40	34
Mecillinam	6.1	6.7	3.9
Piperacillin/tazobactam	6.5	5.6	3.6 (1)
Amoxicillin/clavulanic acid	31 (6)	10.3	6.5
Sulfonamide		30 (5)	23.7
Trimethoprim		22	19.4
Nitrofuratoin		0.8	0.5
Gentamicin	4.4	4.9	3.2 (1)
Ciprofloxacin	10.9	10.2	7.7
Cefuroxime	9.9	8.1	6.7 (3)
3rd generation cephalosporins	6.5	6.9	5.6
Carbapenem	0.1	0.0	0.0 (1)
Max. number of isolates tested for resistance to the presented antibiotics	5,950	40,624	93,436

Included are results from all DCMs where >75% of the isolates in each antibiotic/sample group were susceptibility tested
Numbers in parantheses indicate the number of DCMs included if less than six

Figure 8.3 Antimicrobial resistance in invasive *Escherichia coli* isolates from humans by region, Denmark, 2015-2024 DANMAP 2024

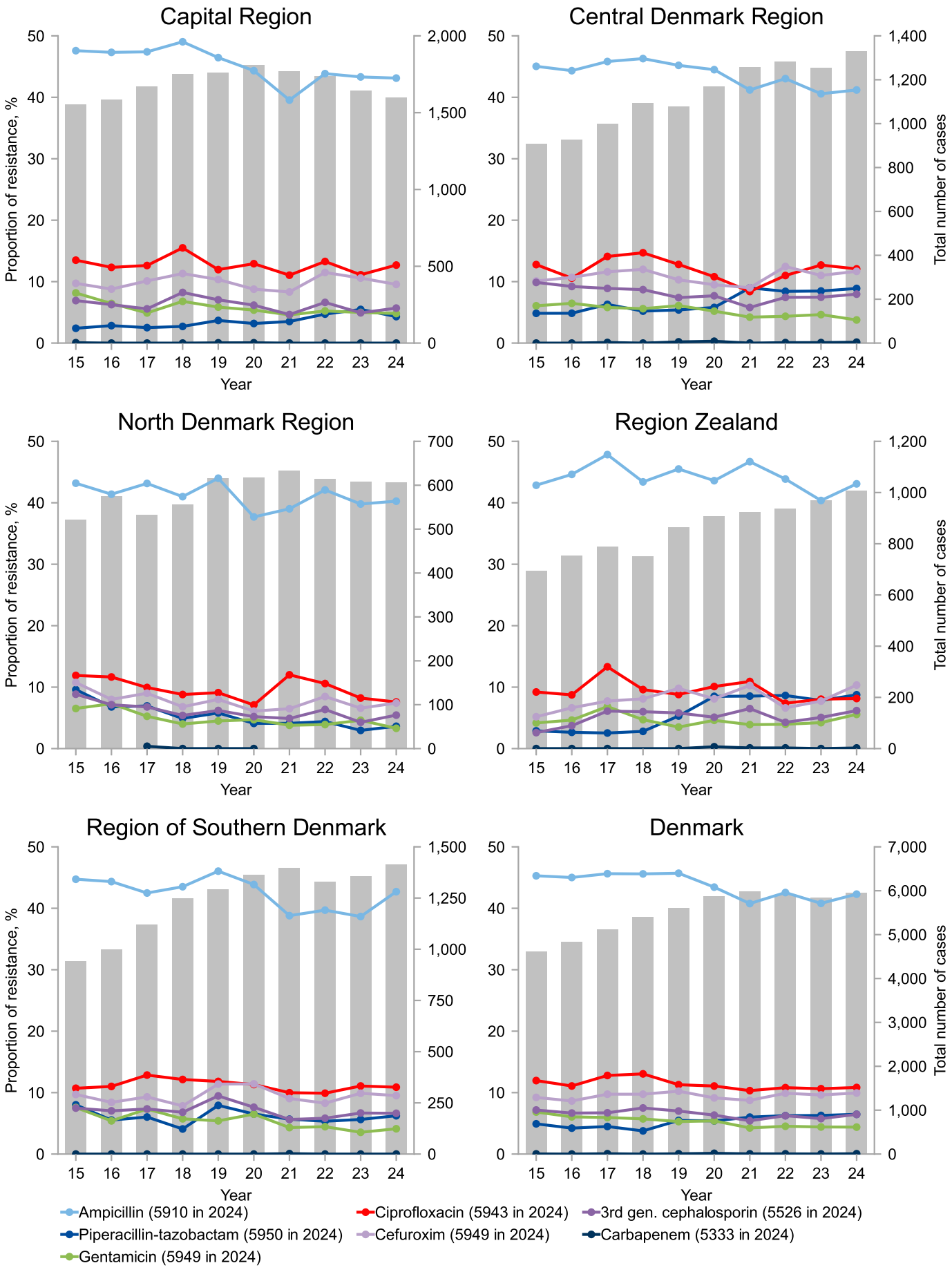


Table 8.3 Invasive *Escherichia coli*. Table of resistance percentages, Denmark, 2015-2024 DANMAP 2024

Substance	Percent resistant invasive *E. coli* isolates									
	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Ampicillin	45.3	45.0	45.6	45.5	45.7	43.4	40.7	42.6	40.8	42.3
Piperacillin-tazobactam	4.9	4.2	4.5	3.8	5.5	5.4	6.0	6.3	6.3	6.5
Gentamicin	6.8	6.1	6.0	5.7	5.3	5.4	4.3	4.5	4.4	4.4
Ciprofloxacin	12.0	11.1	12.8	13.0	11.3	11.1	10.3	10.8	10.6	10.8
Cefuroxime	9.2	8.6	9.7	9.8	10.2	9.2	8.7	9.9	9.6	9.9
3rd gen.cephalosporins	7.2	6.7	6.7	7.3	6.9	6.2	5.4	6.2	5.8	6.5
Carbapenem	0.0	0.0	0.1	0.0	0.1	0.1	0.0	0.0	0.0	0.1
Total number of isolates	4,618	4,841	5,114	5,398	5,613	5,870	5,981	5,905	5,835	5,957

Table 8.4 Invasive *Escherichia coli*. Combined resistance to 1) ampicillin and gentamicin and 2) 3rd generation cephalosporins, ciprofloxacin, and gentamicin (multiresistance) in invasive isolates from humans, Denmark, 2015-2024 DANMAP 2024

Combination		2015 % (N)	2016 % (N)	2017 % (N)	2018 % (N)	2019 % (N)	2020 % (N)	2021 % (N)	2022 % (N)	2023 % (N)	2024 % (N)
AMP/GEN	Resistance	6.3 (254)	5.8 (278)	5.8 (289)	5.5 (284)	5.2 (275)	5.1 (287)	4.0 (229)	4.1 (233)	4.1 (231)	4.0 (235)
	Percentage (no.) of isolates tested	87 (4,009)	99 (4,816)	98 (5,015)	96 (5,170)	95 (5,308)	95 (5,583)	96 (5,745)	96 (5,679)	96 (5,602)	99 (5,903)
3GC/CIP/ GEN	Resistance	2.3 (93)	1.8 (87)	1.8 (88)	2.0 (100)	1.8 (93)	1.5 (82)	1.1 (60)	1.3 (70)	1.2 (63)	1.0 (54)
	Percentage (no.) of isolates tested	88 (4,071)	98 (4,763)	95 (4,883)	93 (4,997)	94 (5,259)	93 (5,470)	93 (5,564)	93 (5,474)	93 (5,417)	93 (5,515)
	Total number of invasive isolates	4,614	4,841	5,114	5,398	5,613	5,870	5,981	5905	5,835	5,957

Table 8.5 *Escherichia coli* from hospital urines. Table of resistance percentages, Denmark, 2015-2024 DANMAP 2024

Substance	Resistance in *E. coli* urine isolates from hospitals									
	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Ampicillin	42.1	41	41.9	42.1	43.7	40.6	39.2	40.0	39.4	39,6
Mecillinam	7.7	7.4	7.5	7.4	8.1	7.3	6.9	6.8	6.5	6,7
Piperacillin-tazobactam	3.9	3.3	3.7	3.5	4.4	4.3	4.5	5.4	5.4	5,6
Sulfonamide	32	34.9	31.1	31*	31.4*	29.4*	28.5*	28.2*	30.9*	30.0*
Gentamicin	5.1	5.3	4.9	4.7	4.6	4.6	4.2	4.3	4.5	4,9
Ciprofloxacin	11	10.9	10.4	11	10.6	9.6	8.7	9.3	9.9	10,2
Cefuroxime	7	6.8	7.1	7.2	7.8	7.2	6.7	7.5	7.7	8,1
3rd gen. cephalosporins	5.9	5.9	6.2	6.4	6.9	6.3	5.8	6.2	6.5	6,9
Carbapenem	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0
Total number of isolates	46,723	46,865	46,884	47,914	47,235	48,962	49,986	48,559	44,389	40,624

* Indicates less than 6 DCMs reporting routine susceptibility testing

Table 8.6 *Escherichia coli* from urines from primary health care. Table of resistance percentages, Denmark, 2015-2024 DANMAP 2024

Substance	Resistance in *E. coli* urine isolates from primary health care									
	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Ampicillin	38.5	38.3	37.9	37.4	38.1	36.5	34.3	34.6	34.2	34.3
Mecillinam	5.4	5.6	5.5	5.1	5.3	4.9	4.6	4.3	4.0	3.9
Sulfonamide	30.9	29.5	29.1	28.3	27.9	26.7	25.2	25.0	25.5	23.7
Ciprofloxacin	8.6	10.1	8.4	8.1	8.0	7.5	6.9	6.9	7.5	7.7
3rd gen. cephalosporins	4.3	4.3	4.5	4.9	5.2	5.0	4.4	4.8	5.3	5.6
Total number of isolates	61,083	67,798	73,497	80,851	86,508	88,462	99,077	104,376	106,236	93,436

Figure 8.4 Antimicrobial resistance in *Escherichia coli* isolates from urine in humans (hospitals) by region, Denmark, 2015-2024

DANMAP 2024

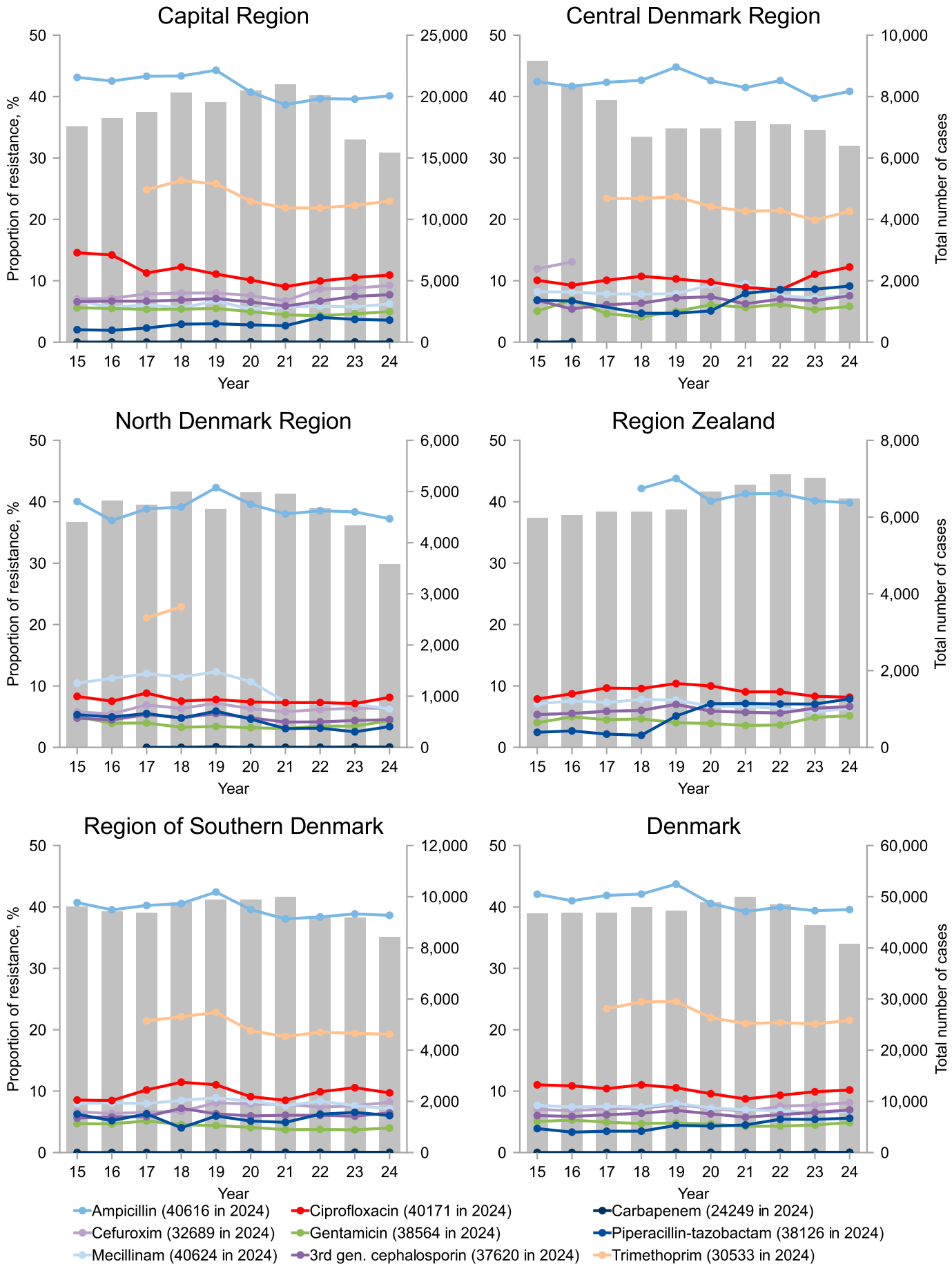
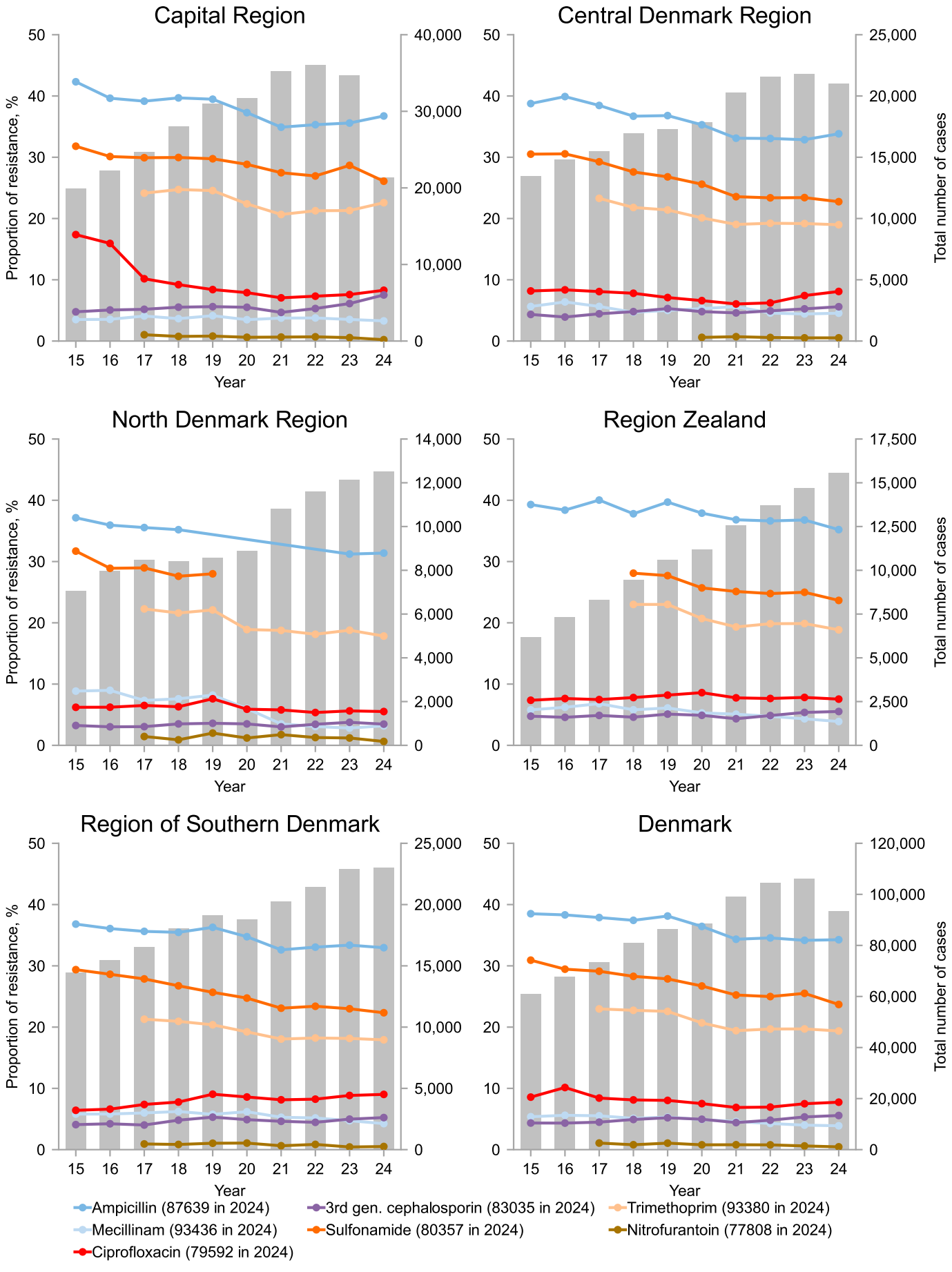


Figure 8.5 Antimicrobial resistance in *Escherichia coli* isolates from urine in humans (primary health care) by region, Denmark, 2015-2024

DANMAP 2024



8.2.2 *Klebsiella pneumonia*

Klebsiella pneumoniae is part of the human intestinal tract. The bacteria cause urinary tract infections, intra-abdominal infections, bacteraemia and ventilator-associated pneumonia (VAP). *K. pneumoniae* may cause nosocomial outbreaks. *K. pneumoniae* frequently displays plasmid-mediated resistance mechanisms, which are transferrable to other bacterial species.

The percentage of resistance in *K. pneumoniae* isolates for key antimicrobials in isolates from invasive infections, urines from hospitals and urines from general praxis, respectively, is presented in Table 8.7.

Invasive cases from hospitals

In 2024, a total of 1,457 individual patients were registered in MiBa with invasive *K. pneumoniae* isolates. From 2015 to 2021, particularly for cephalosporins decreasing trends in resistance were observed. From 2022 to 2024, resistance levels reverted and showed increases for most of the monitored antibiotics. Of particular interest is the almost continuous increase in resistance levels to piperacillin-tazobactam, which increased from 5.9% in 2015 to 10.9% in 2024 in total, an increase that was observed for all regions. The resistance level to carbapenems remained low (<1%), as did combined resistance to ciprofloxacin, cephalosporins and gentamicin (1.4% in 2024).

Figure 8.6 shows total annual numbers and numbers and percentages of resistance in invasive isolates by region and in total, for 2015 to 2024. The proportions of isolates resistant to key antimicrobials for the decade are presented in Table 8.8. The percentages of multidrug resistant invasive isolates are presented in Table 8.9.

Table 8.7 *Klebsiella pneumoniae*. Resistance (%) in isolates from humans, Denmark, 2024 DANMAP 2024

Substance	Invasive isolates, hospitals %	Urine isolates, hospitals %	Urine isolates, primary health care %
Mecillinam	7.1	10.0	7.9
Piperacillin/tazobactam	10.9	10.9	6.3 (2)
Amoxicillin/clavulanic acid	15.3 (5)	7.8	4.9 (5)
Sulfonamide		22.8 (4)	14.2
Trimethoprim		15.1	12.5
Nitrofuratoin		35	30
Gentamicin	2.7	3.4	1.4 (1)
Ciprofloxacin	8.3	8.6	5.4 (5)
Cefuroxime	10.0	9.5	6.1 (3)
3rd generation cephalosporins	5.7	6.2	4.5
Carbapenem	0.2	0.4	0.0 (1)
Max. number of isolates tested for resistance to the presented antibiotics	1,457	7,362	12,336

Included are results from all DCMs where >75% of the isolates in each antibiotic/sample group were susceptibility tested
Numbers in parantheses indicate the number of DCMs included if less than six

Figure 8.6 Invasive *Klebsiella pneumoniae* isolates from humans: proportion of resistant isolates and annual number of isolates from individual cases, Denmark, 2015-2024

DANMAP 2024

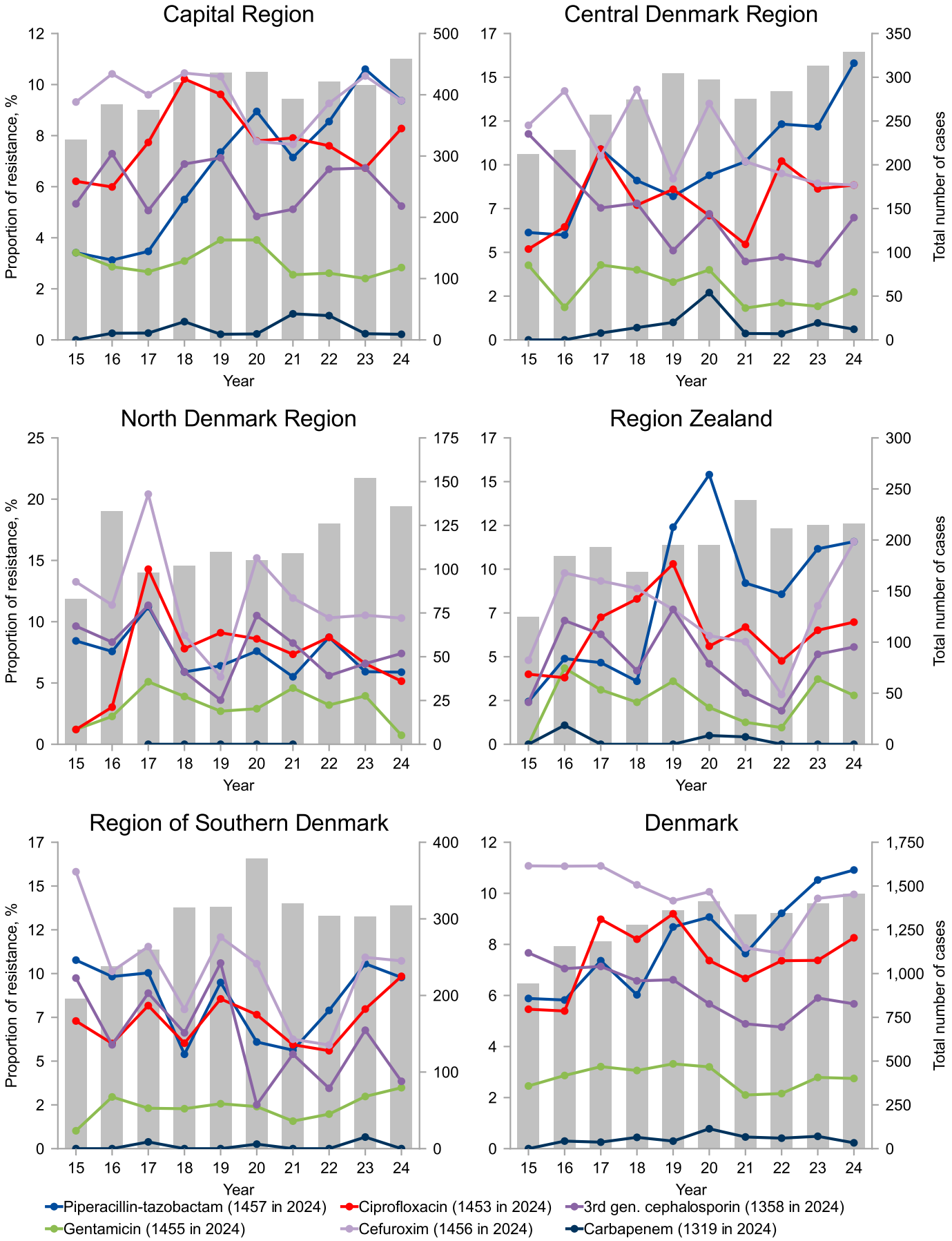


Table 8.8 Invasive *Klebsiella pneumoniae*. Table of resistance percentages, Denmark, 2015-2024 DANMAP 2024

Substance	Percent resistant invasive *K. pneumoniae* isolates									
	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Piperacillin/tazobactam	5.9	5.8	7.4	6.1	8.7	9.1	7.5	9.2	10.5	10.9
Gentamicin	2.5	2.9	3.2	3.1	3.3	3.2	2.1	2.2	2.8	2.7
Ciprofloxacin	5.5	5.4	9.0	8.1	9.2	7.4	6.7	7.4	7.4	8.3
Cefuroxime	11.1	11.1	11.1	10.3	9.7	10.1	7.9	7.7	9.8	10.0
3rd gen. cephalosporins	7.7	7.3	7.1	6.1	6.6	5.3	4.9	4.8	5.9	5.7
Carbapenem	0.0	0.3	0.3	0.5	0.3	0.8	0.5	0.4	0.5	0.2
Total number of isolates	939	1,156	1,183	1,280	1,361	1,413	1,336	1,346	1,399	1,457

Table 8.9 Invasive *Klebsiella pneumoniae*. Combined resistance to 3rd generation cephalosporins, ciprofloxacin, and gentamicin (multidrug-resistance) in invasive isolates from humans, Denmark, 2015-2024 DANMAP 2024

	2015 % (N)	2016 % (N)	2017 % (N)	2018 % (N)	2019 % (N)	2020 % (N)	2021 % (N)	2022 % (N)	2023 % (N)	2024 % (N)
Resistance	1.1 (9)	1.6 (18)	2.4 (27)	1.7 (20)	2.4 (30)	1.5 (19)	1.0 (13)	1.0 (13)	1.9 (24)	1.4 (19)
Percentage (no.) of isolates tested for combined resistance (multiresistance)	89 (840)	98 (1,131)	95 (1,122)	93 (1,188)	94 (1,275)	93 (1,308)	93 (1,248)	94 (1,259)	92 (1,287)	93 (1,356)
Total number of invasive isolates	943	1,156	1,183	1,280	1,361	1,413	1,336	1,346	1,399	1,457

Table 8.10 *Klebsiella pneumoniae* from hospital urines. Table of resistance percentages, Denmark, 2015-2024 DANMAP 2024

Substance	Resistance in *K. pneumoniae* urine isolates from hospitals									
	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Mecillinam	10	8.9	15.7	16.9	13.2	11.7	10.6	9.4	10.0	10.0
Piperacillin/tazobactam	6.3	5.6	6.7	8.7	8.5	8.0	8.7	9.9	10.5	10.9
Gentamicin	3.7	3.2	3.6	3.2	3.0	2.9	2.4	2.3	2.3	3.4
Ciprofloxacin	6.2	6.1	7.6	8.9	7.4	7.2	7.2	7.2	7.5	8.6
Cefuroxime	9.5	9.1	9.4	9.5	8.6	8.5	8.4	8.1	9.4	9.5
3rd gen. cephalosporins	6.8	6.8	7.1	6.8	6.0	5.5	5.4	4.7	5.7	6.2
Total number of isolates	7,175	7,467	8,106	8,047	7,926	7,814	7,701	7,911	7,492	7,362

Table 8.11 *Klebsiella pneumoniae* from urines from primary health care. Table of resistance percentages, Denmark, 2015-2024 DANMAP 2024

Substance	Resistance in *K. pneumoniae* urine isolates from primary health care									
	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Mecillinam	9.4	9.0	16.6	15.9	11.5	9.4	8.6	7.9	7.2	7.9
Sulfonamide	18.7	19.3	25.5	24.6	18.9	15.5	13.8	11.9	13.4	14.2
Ciprofloxacin	5.2	5.6	5.4	6.4	5.5	5.2	4.9	5.1	5.2	5.4
3rd gen. cephalosporins	4.8	5.4	4.9	5.3	4.5	4.4	3.7	3.4	4.6	4.5
Total number of isolates	6,372	7,615	8,948	9,227	9,696	9,387	10,196	11,039	11,502	12,336

Figure 8.7 *Klebsiella pneumoniae* isolates from urines in humans (hospitals): proportion of resistant isolates and annual number of isolates from individual cases, Denmark, 2015-2024

DANMAP 2024

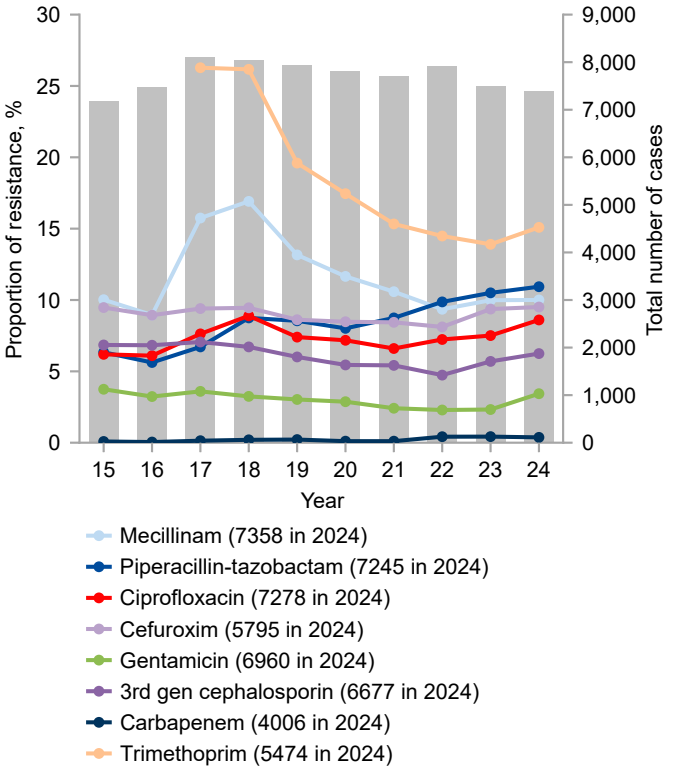
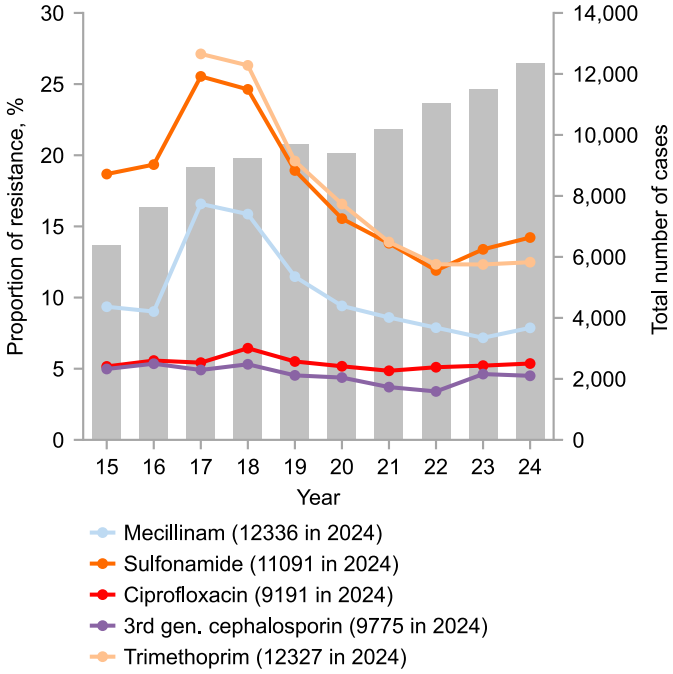


Figure 8.8 *Klebsiella pneumoniae* isolates from urines in humans (primary health care): proportion of resistant isolates and annual number of isolates from individual cases, Denmark, 2015-2024

DANMAP 2024



Urinary cases from hospitals

In 2024, *K. pneumoniae* from urine samples were isolated from 7,362 individual hospital patients in Denmark.

Summarized antibiotic-specific susceptibility results for *K. pneumoniae* isolates (invasive and urine specimen) for 2024 are shown in Table 8.7. In Figure 8.7 and Table 8.10, resistance for *K. pneumoniae* urine isolates from hospitals is shown for 2015-2024.

Urinary cases from primary health care

In 2024, *K. pneumoniae* was isolated from urine samples of 12,336 individual patients in primary health care. As for the results from invasive isolates and isolates from hospital urine samples susceptibility results for all tested antimicrobials are shown in Table 8.7. In Figure 8.8 and Table 8.11, resistance for *K. pneumoniae* urine isolates from primary health care is shown for the past decade.

Conclusion

The number of invasive cases of *K. pneumoniae* have increased by 55% since 2015. As for *E. coli*, a concerning trend is seen with regards to piperacillin-tazobactam for which resistance levels have now surpassed 10% for both invasive infections and hospital urines.

8.2.3 *Pseudomonas aeruginosa*

Pseudomonas aeruginosa is an opportunistic pathogen that can colonise the lung, urinary tract, burn wounds, superficial wounds and cause invasive infections. The pathogen is capable of biofilm formation and has the ability to colonise medical devices (e.g. indwelling catheters and implants) which in many cases causes complicated infections requiring prolonged and combination treatment with two broad spectrum antimicrobials. *P. aeruginosa* infections are more prevalent in certain at-risk groups such as immunocompromised, diabetes and cystic fibrosis patients. *P. aeruginosa* exhibits intrinsic resistance to various antimicrobial agents through chromosomal gene mutations and has the ability to acquire β-lactamases (extended-spectrum β-lactamases (ESBLs) and carbapenemases (especially class B carbapenemases or metallo-β-lactamases [MBLs]) by horizontal transmission.

Invasive cases from hospital patients

In 2024, a total of 488 individual patients with invasive *P. aeruginosa* isolates were registered in Denmark. Figure 8.9 shows the total annual number of invasive isolates and proportion of resistant isolates between 2015 and 2024.

Conclusion

The occurrence of invasive *P. aeruginosa* in Denmark is stable regarding the number of cases reported and resistance levels are low.

8.2.4 *Acinetobacter* species

The genus *Acinetobacter* includes several species and is found widespread in nature (soil and water) as well as in animals and humans. In humans, *Acinetobacter* species (spp.) can colonise the skin and wounds but may also cause hospital-acquired infections such as central line-associated bloodstream infections, nosocomial pneumonia, UTIs and wound infections, most often in severely ill patients. Many of the different subspecies are phenotypically alike, and thus identification at species level can be difficult. Species belonging to the *A. baumannii* group are considered as the most clinically important. *Acinetobacter* spp. is intrinsically resistant to a broad range of antimicrobials mediated by a low membrane permeability and constitutive expression of various efflux systems.

Invasive cases from hospitals

In 2024, a total of 92 individual patients with invasive *Acinetobacter* species were reported. Data are presented in Table 8.12 and in Figure 8.10.

Conclusion

The number of invasive *Acinetobacter* spp. appears to have stabilized at a new level compared to the marked increase from 2020 to 2021; however, the proportion of invasive isolates resistant to key antimicrobials remained low in Denmark.

Figure 8.9 Invasive *Pseudomonas aeruginosa* isolates from humans: proportion of resistant isolates and annual number of isolates from individual cases, Denmark, 2015-2024 DANMAP 2024

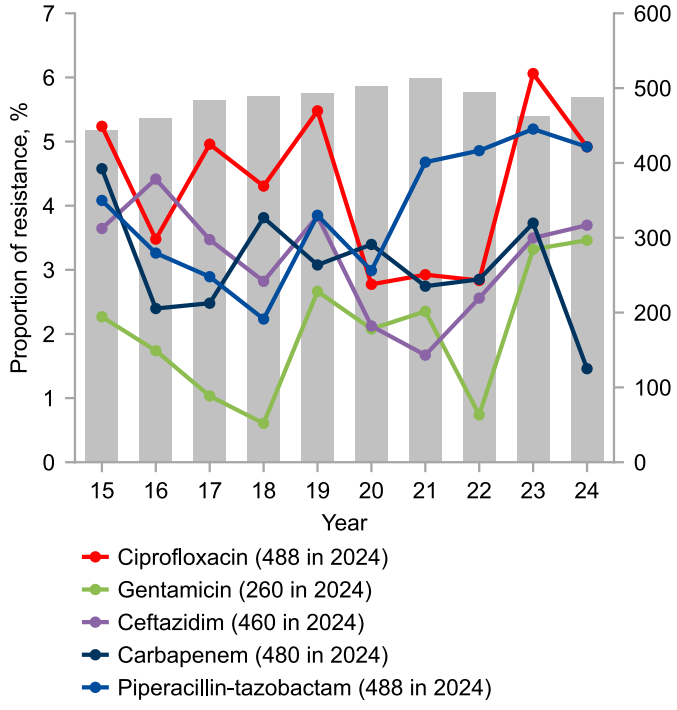


Figure 8.10 Invasive *Acinetobacter* spp. isolates from humans: a) annual number of isolates from individual cases and b) proportion of resistant isolates, Denmark, 2015-2024 DANMAP 2024

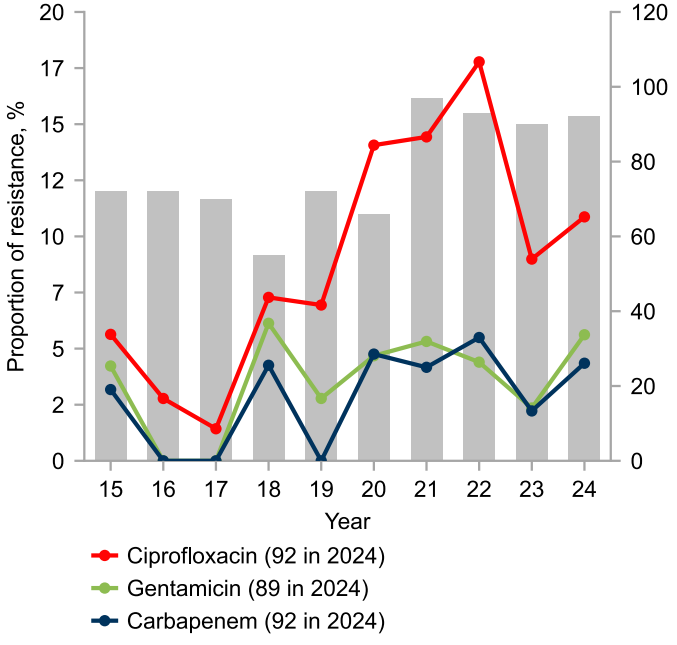


Table 8.12 *Acinetobacter* spp. tested and resistant invasive isolates, Denmark, 2015-2024 DANMAP 2024

	2015		2016		2017		2018		2019		2020		2021		2022		2023		2024	
	res.	n	res.	n	res.	n	res.	n	res.	n	res.	n	res.	n	res.	n	res.	n	res.	n
Ciprofloxacin	4	71	2	72	1	70	4	55	5	72	9	64	14	97	16	92	8	89	10	92
Gentamicin	3	71	0	70	0	70	3	49	2	72	3	64	5	94	4	92	2	85	5	89
Carbapenem	3	68	0	69	0	67	2	47	0	72	3	63	4	96	5	93	2	90	4	92
Total number of invasive isolates	71		72		70		55		72		66		97		93		90		92	

res. = number of resistant isolates. n = number of tested isolates

8.2.5 Enterococci

Enterococci are part of the normal intestinal microbiota in humans and animals. More than 54 species belonging to the genus *Enterococcus* have been described. The majority of human infections are caused by *E. faecalis* and *E. faecium* and in rare cases by *E. casseliflavus, E. gallinarum* and *E. raffinosus*. Most common clinical infections include urinary tract infections, intra-abdominal infections, bacteraemia and infective endocarditis. Enterococci are intrinsically resistant to many groups of antimicrobials which gives them a selective advantage in e.g. hospitalised patients under antibiotic treatment, leading to colonization or infection. The source of hospital infection is often associated with invasive medical devices and abdominal catastrophes.

Invasive cases from hospitals

In 2024, *E. faecalis* isolated from 594 individual patients and *E. faecium* isolated from 584 individual patients were reported in MiBa. Table 8.13 shows resistance percentages towards the most important antibiotics for both species for 2024 and Figure 8.11 shows the annual numbers of invasive isolates and resistance to vancomycin.

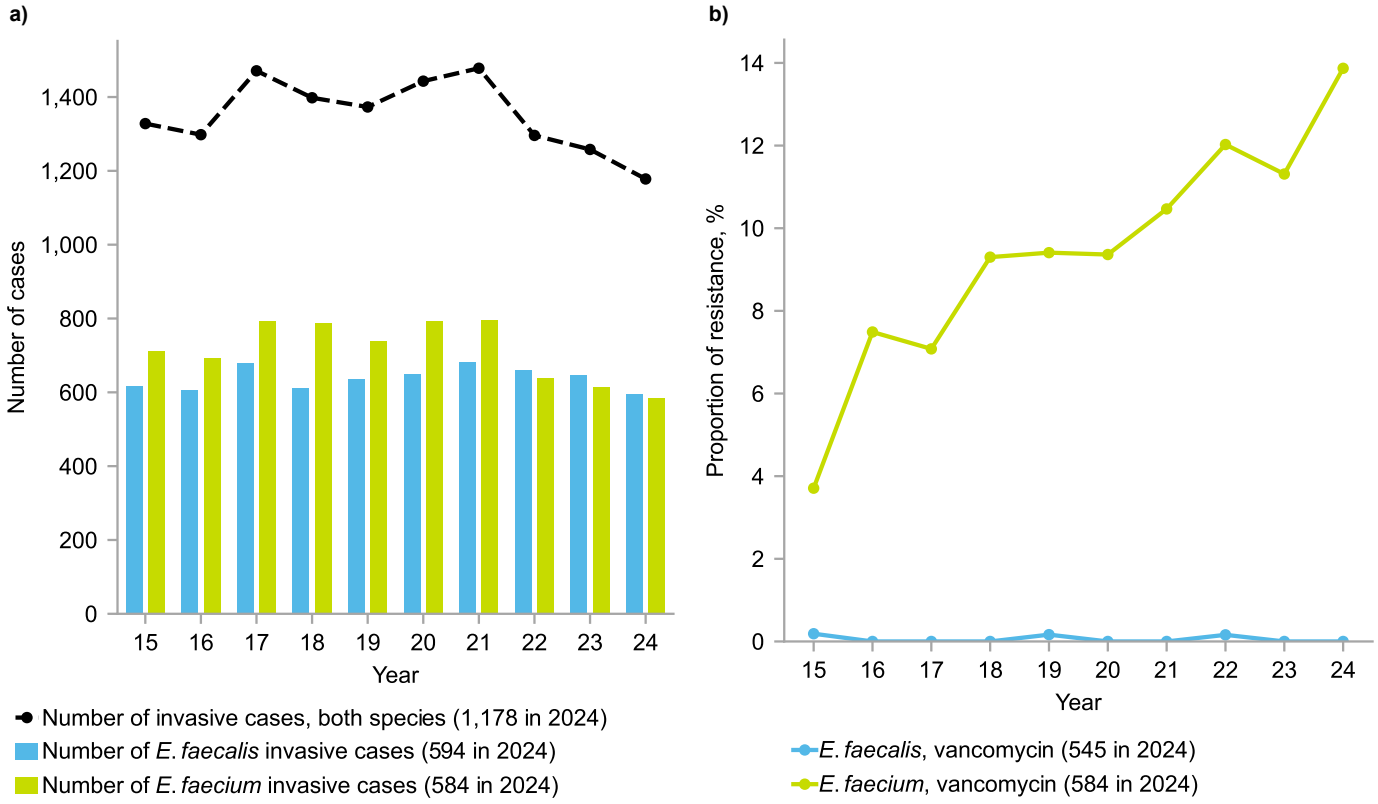
Table 8.13 Enterococci. Resistance (%) in invasive isolates from humans, Denmark, 2024 DANMAP 2024

	E. faecalis	*E. faecium*	Number of included isolates (number of DCM)	
	%	%	*E. faecalis*	*E. faecium*
Ampicillin	0.0	91	591 (10)	566 (9)
Vancomycin	0.0	13.9	545 (9)	584 (10)
Linezolid	1.5	0.2	465 (7)	460 (7)
Teicoplanin	1.0	1.8	209 (2)	171 (2)
Tigecycline	0.0	3.7	95 (1)	81 (1)

All proportions of resistance are presented for each antibiotic as a mean of the resistance rates reported by the DCMs. Included are all DCMs that reports routine testing (>75% of the isolates). The number in parentheses tells the number of included DCMs

Figure 8.11 Invasive *Enterococci faecalis/faecium* isolates from humans:
a) annual number of isolates from individual cases and b) proportion of vancomycin resistant isolates, Denmark, 2015-2024

DANMAP 2024



Conclusion

The number of invasive cases for both *E. faecium* and *E. faecalis* has been decreasing since 2021, for *E. faecalis* following peaks during 2017 to 2021. Resistance to vancomycin has only rarely been observed in *E. faecalis* and no invasive cases with vancomycin resistance were detected in 2024, however for *E. faecium* it has been increasing for the last decade and has surpassed 10% for the past four years.

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8.3 Results from the reference laboratories

8.3.1 Characterization of ESBL- and pAmpC-producing *Escherichia coli* from bloodstream infections

Background

Resistance to third-generation cephalosporins in *Escherichia coli* often occurs through production of extended-spectrum beta-lactamases (ESBLs), carbapenemases, plasmid-mediated AmpC (pAmpC) or through mutations within the promoter/attenuator region of chromosomal AmpC (cAmpC) leading to overexpression/hyperproduction.

Since 2014, the Danish Departments of Clinical Microbiology (DCMs) have, on a voluntary basis, submitted third-generation cephalosporin-resistant *E. coli* (3GC-R *Ec*) from bloodstream infections for further characterization at the National Reference Laboratory for Antimicrobial Resistance at Statens Serum Institut (SSI) by adhering to the EUCAST criteria for reduced susceptibility towards cefpodoxime, ceftriaxone, cefotaxime or ceftazidime.

At SSI, the 3GC-R *Ec*'s collected in Denmark through 2024, were phenotypically tested for ESBL-production. ESBL- and/ or pAmpC-positive isolates from January, March, May, July, September, and November were subjected to whole-genome sequencing and characterized according to Multilocus Sequence Types (MLST) and the encoding ESBL-, pAmpC- and carbapenemase genes.

Results

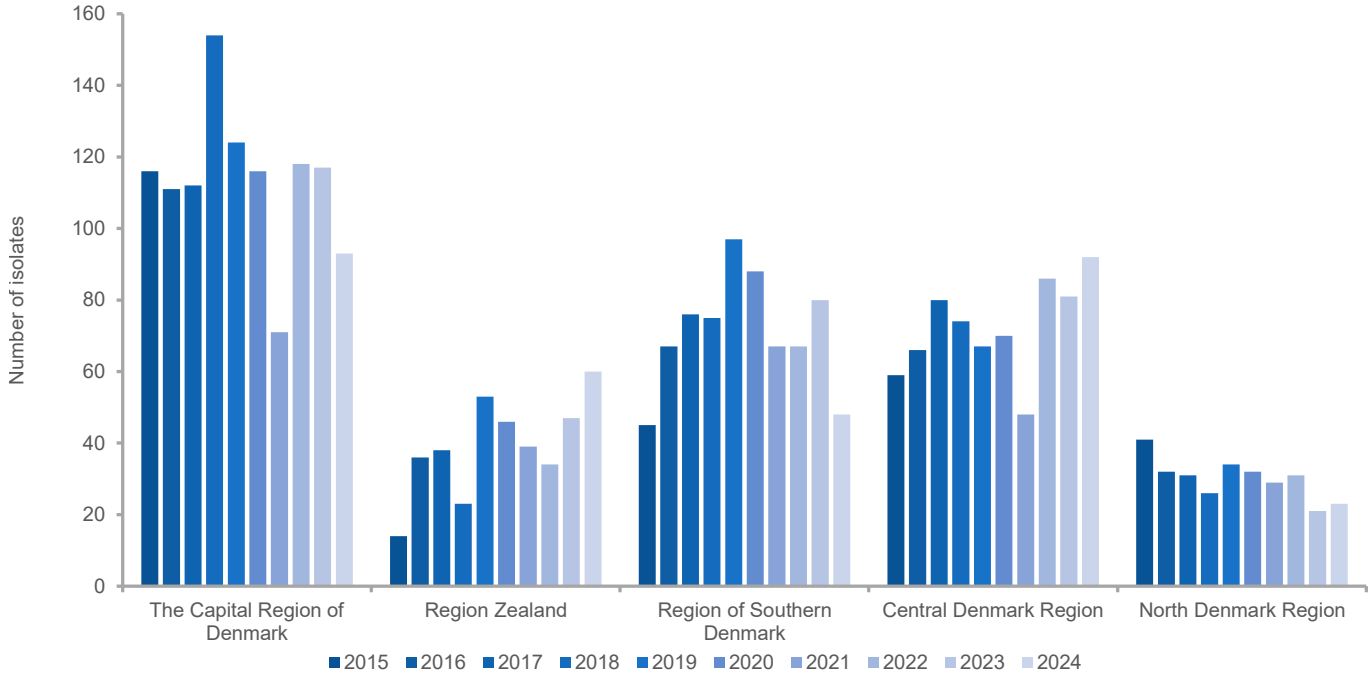
In 2024, a total of 316 *E. coli* blood isolates from individual patients, were identified with phenotypic test, as ESBL- and/ or AmpC- and/or carbapenemase positive isolates. Compared to 2023 (comprising 346 isolates), this represents a slight decrease in numbers of isolates forwarded to SSI. Demographic data was available for all 316 *E. coli* isolates; the median age at diagnosis was 70 years, ranging from ten years to 99 years. In 2024, the proportion of 3GC-R *Ec* from male patients remained at 47% (148/316), thus repeating the observation made in 2023 where 3GC-R *Ec* from female patients outnumbered those from male patients for the first time since the origin of the surveillance in 2014.

The regional distribution of the 316 isolates with ESBL-, AmpC- or carbapenemase phenotype was compared to data from previous years (Figure 8.12 and Table 8.14). Forwarded isolates from the Region of Southern Denmark decreased significantly from 80 isolates in 2023 to 48 isolates in 2024 (40%). The numbers of isolates from the remaining four regions did not change as markedly.

Whole genome sequencing data were obtained from 168 *E. coli* isolates (as only isolates from every second month and carbapenemase producing *E. coli* were sequenced). Genes encoding ESBL, pAmpC and/or carbapenemase were detected in 149 isolates, and 19 isolates were AmpC hyperproducers caused by cAmpC mutations. The AmpC hyperproducers were not included in the further analysis.

In 2024, 16 different genes associated with ESBL-, and pAmpC enzymes were detected among the 149 sequenced isolates encoding ESBL and/or pAmpC genes, (Table 8.15). As in previous years, CTX-M-15 was the most prevalent enzyme, albeit significantly decreasing in occurrence from 58% in 2023 to 40% in 2024. Similarly, the proportion of CTX-M-14 observed, decreased significantly from 9% in 2023 to 2% in 2024. This is

Figure 8.12. ESBL/pAmpC producing *E. coli* from bloodstream infections by region, Denmark, 2015-2024 DANMAP 2024



the lowest observed proportion of these two enzymes since the origin of the surveillance in 2014. In addition, eight carbapenemase producing isolates (five OXA-244 producers, two OXA-48 producers and one NDM-5 producer) was observed among the 149 whole genome sequenced blood infection isolates.

In 2024, the 149 analyzed whole genome sequenced *E. coli* isolates belonged to 29 different known STs; a less diverse distribution of STs compared to the 46 observed in 2023. ST131 was still the most common ST in 2024 (47%), followed by ST69 (13%). No significant changes in the distribution of STs were observed compared to the distribution in 2023 (Table 8.16).

Table 8.14 Distribution of ESBL, pAmpC and Carbapenemase producing *E. coli* from bloodstream infections, Denmark, 2015-2024

DANMAP 2024

	DANMAP 2015	DANMAP 2016	DANMAP 2017	DANMAP 2018	DANMAP 2019	DANMAP 2020	DANMAP 2021	DANMAP 2022	DANMAP 2023	DANMAP 2024
Region	Numbers	Numbers	Numbers	Numbers	Numbers	Numbers	Numbers	Numbers	Numbers	Numbers
The Capital Region of Denmark	116	111	112	154	124	116	71	118	117	93
Region Zealand	14	36	38	23	53	46	39	34	47	60
Region of Southern Denmark	45	67	76	75	97	88	67	67	80	48
Central Denmark Region	59	66	80	74	67	70	48	86	81	92
North Denmark Region	41	32	31	26	34	32	29	31	21	23
Total Numbers	275	312	337	352	375	352	254	336	346	316

Table 8.15 Most common ESBL enzymes and carbapenemases detected in *E. coli* from bloodstream infections, Denmark, 2016-2024

DANMAP 2024

	DANMAP 2016		DANMAP 2017		DANMAP 2018		DANMAP 2019		DANMAP 2020		DANMAP 2021		DANMAP 2022		DANMAP 2023		DANMAP 2024	
Enzyme	Number	%	Number	%	Number	%	Number*	%	Number*	%	Number*	%	Number*	%	Number*	%	Number*	%
CTX-M-1	8	3	17	5	25	7	8	4	7	4	6	4	1	<1	3	2	0	0
CTX-M-14	40	13	48	14	31	9	33	17	15	8	12	9	17	9	17	9	3	2
CTX-M-14b	9	3	3	1	10	3	3	2	4	2	0	0	3	2	2	1	10	7
CTX-M-15	157	50	164	49	200	57	82	43	100	52	63	46	94	52	103	57	60	40
CTX-M-27	44	14	52	15	53	15	37	19	36	19	29	21	34	19	32	18	40	27
CTX-M-3	7	2	8	2	5	1	4	2	1	1	3	2	1	<1	0	0	3	2
CTX-M-55	6	2	13	4	4	1	8	4	4	2	5	4	3	2	1	<1	4	3
CMY-2	10	3	7	2	6	2	5	3	5	3	2	1	2	1	3	2	1	1
DHA-1	5	2	6	2	10	3	4	2	7	4	3	2	11	6	9	5	14	9
SHV-12	5	2	3	1	4	1	2	1	5	3	3	2	3	2	3	2	3	2
Other CMY variants	3	1	3	1	3	1	5	3	0	0	1	1	1	<1	1	<1	5	3
Other ESBL enzymes	17	5	10	3	10	3	3	2	8	4	6	4	7	4	2	1	3	2
Carbapenemase enzymes	1	<1	1	<1	5	1	0	0	7	4	4	3	5	3	1	<1	8	5

In some isolates more than one enzyme was detected

* Numbers based on sequenced data from odd months

Table 8.16 Distribution of MLSTs in *E. coli* from bloodstream infections, Denmark, 2016-2024

DANMAP 2024

	DANMAP 2016		DANMAP 2017		DANMAP 2018		DANMAP 2019		DANMAP 2020		DANMAP 2021		DANMAP 2022		DANMAP 2023		DANMAP 2024	
MLST	Number	%	Number	%	Number	%	Number*	%	Number*	%	Number*	%	Number*	%	Number*	%	Number*	%
ST131	177	57	175	52	189	54	93	47	89	46	64	49	89	50	68	38	66	47
ST69	16	5	20	6	27	8	14	7	20	10	7	5	9	5	27	15	19	13
ST38	21	7	23	7	22	6	13	7	8	4	1	1	11	6	7	4	13	9
ST1193	10	3	7	2	8	2	6	3	9	5	9	7	5	3	7	4	6	4
ST95	5	2	4	1	4	1	3	2	4	2	3	2	2	1	5	3	6	4
ST73	4	1	2	1	6	2	4	2	8	4	1	1	5	3	5	3	4	3
Other STs[1]	65	21	100	30	89	25	59	30	50	26	39	30	51	29	47	26	25	18

[1] Found in less than 3% in 2024

* Numbers based on sequenced data from odd months

Among the 68 *E. coli* isolates belonging to ST131, CTX-M-15 (50%) was the most common enzyme, followed by CTX-M-27 (46%). Further, among the 19 *E. coli* isolates belonging to ST69, CTX-M-15 (43%) was also the most common enzyme, followed by DHA-1 (33%), CTX-M-27 and CMY-4 (both 11%).

Conclusion

In 2024, the number of ESBL- and/or AmpC positive isolates decreased slightly compared to 2023. The significant shift in the gender distribution noted from 2022 to 2023 was also observed in 2024. CTX-M-15 remained the most prevalent ESBL enzyme in Danish *E. coli* (3GC-R *Ec*) in 2024 (40%), albeit proportionally decreasing compared to 2023. The relative occurrence of isolates belonging to the two most common STs, ST131 and ST69, remained stable compared to 2023.

In 2024, eight carbapenemase producer were observed among the 149 sequenced ESBL- and/or pAmpC blood infection isolates. The relative distribution of sequence types for the whole genome sequenced isolates was stable compared to the previous year; the worldwide disseminated ST131 clone was still strongly represented in 2024 (47%).

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8.3.2 Carbapenemase-producing organisms (CPO)

Background

Carbapenems comprise one of the only classes of antimicrobial agents that can be used for treatment of infections caused by multidrug-resistant Gram-negative bacteria like *Klebsiella pneumoniae, Escherichia coli, Pseudomonas aeruginosa* and *Acinetobacter baumannii*. Treatment options for infections with carbapenem-resistant bacteria are often none or suboptimal. Resistance can be expressed by the presence of various carbapenemases of which the five most frequently occurring are *K. pneumoniae* carbapenemase (KPC), Oxacillinase (OXA), Verona integrin encoded metallo-β-lactamase (VIM), New Delhi metallo-β-lactamase (NDM) and Imipenemase (IMP).

Carbapenemase-producing organisms (CPO) comprise two main groups: 1) Intestinal bacteria: Carbapenemase-producing Enterobacterales (CPE), e.g., *E. coli* and *K. pneumoniae*, and 2) environmental bacteria: *P. aeruginosa* and *A. baumannii*. The term CPE is used to designate intestinal bacteria. Thus, CPE are a subset of CPO.

CPO have been notifiable in Denmark since the guideline from 5th September 2018 [https://www.retsinformation.dk/eli/lta/2018/1091]. Before this date, Danish departments of clinical microbiology (DCMs) have submitted carbapenem-resistant isolates for verification and genotyping at the National Reference Laboratory for Antimicrobial Resistance at Statens Serum Institut on a voluntary basis. This section describes findings for carbapenemase-producing Enterobacterales (CPE), *Pseudomonas* spp. and *Acinetobacter* spp.

During 2024, 677 CPOs were identified from 527 patients compared with 589 CPO isolates from 458 patients in 2023 (Figure 8.13, Table 8.17). More than one isolate from the same patient was included if the isolates belonged to different bacterial species and/or if the isolates harbored different carbapenemases.

Collection of travel information is part of the CPO surveillance in Denmark. Thus, information of travelling abroad in the period of 6 months prior to testing positive for CPO is requested and reported to SSI, together with the clinical sample information.

Carbapenemase-producing Enterobacterales

In 2024, 616 CPE isolates were reported from 497 patients compared with 552 CPE from 436 patients in 2023 (Figure 8.13). In 2024, 41 of the 616 CPE isolates produced both NDM and OXA-48 group enzymes, 425 produced OXA-48-like enzymes alone and 121 were only NDM-producing. Furthermore, 21 KPC-, two VIM-, one IMI-, one IMP-, one KPC-/NDM-/OXA-48-group as well as one KPC/OXA-48 group, one KPC/VIM and one KPC/NDM-producing CPE isolate(s) were identified (Figure 8.14).

Figure 8.13 Number of CPO/CPE isolates and cases in Denmark from 2015-2024 DANMAP 2024

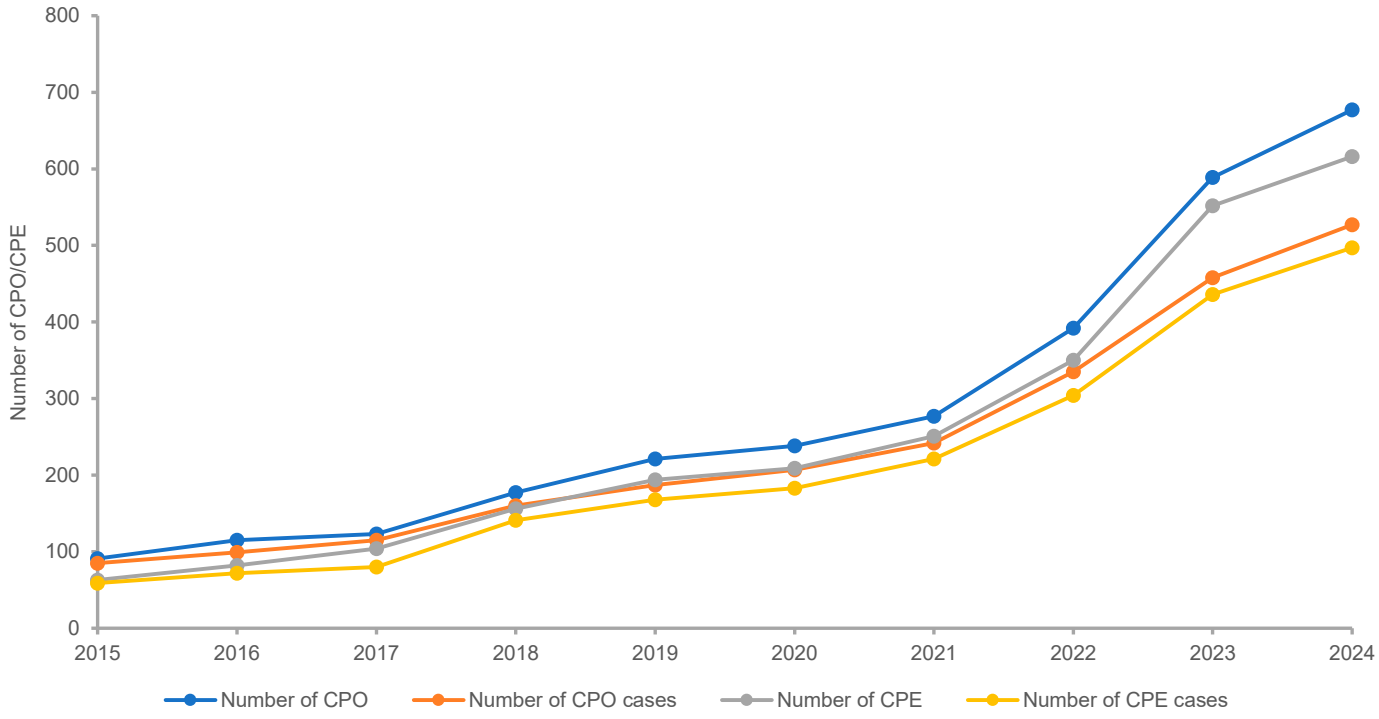


Figure 8.14 Numbers of carbapenemase-producing Enterobacterales (CPE), Denmark, 2008-2024 DANMAP 2024

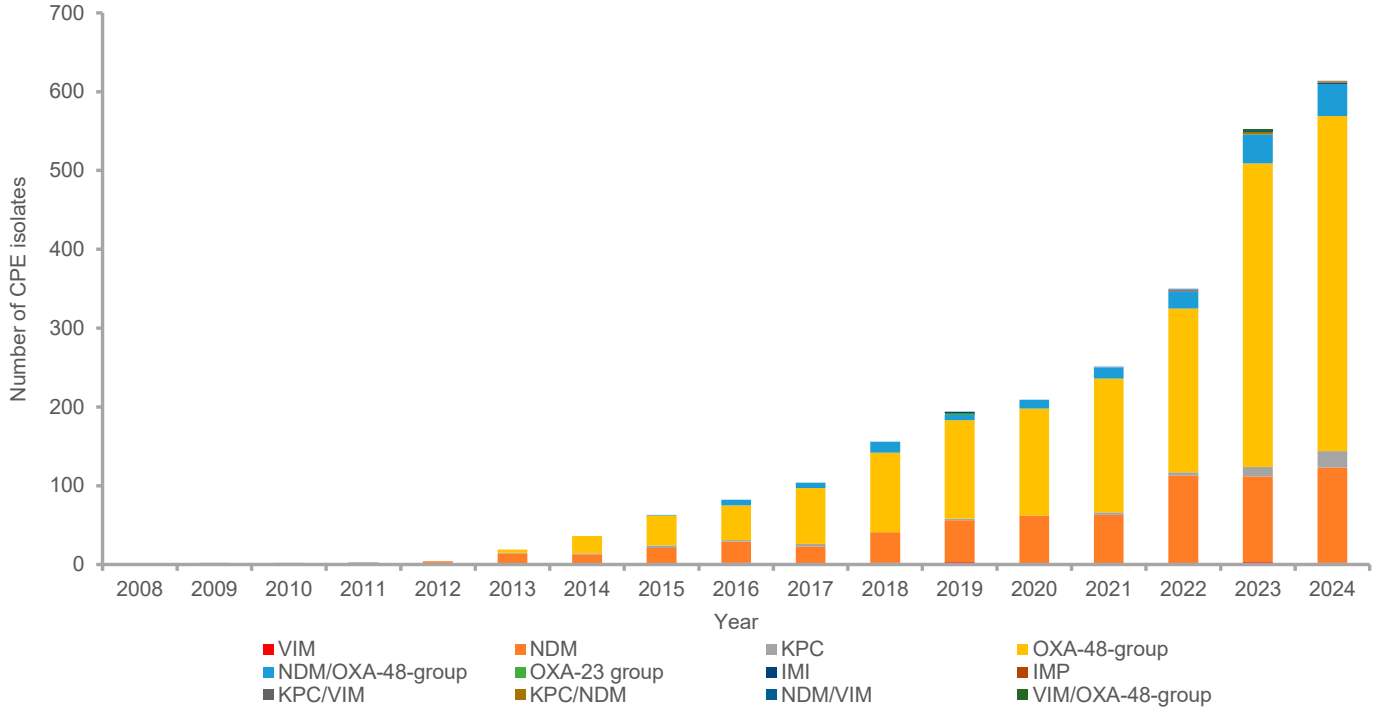


Table 8.17 Number of CPO/CPE isolates and cases in Denmark from 2015-2024 DANMAP 2024

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Number of CPO isolates	91	115	123	177	221	238	277	392	589	677
Number of CPO cases	85	99	115	160	187	207	242	335	458	527
Number of CPE isolates	63	82	104	156	194	209	251	350	552	616
Number of CPE cases	59	72	80	141	168	183	221	304	436	497

Carbapenemase-producing *Acinetobacter* spp.
In 2024, 40 carbapenemase-producing *Acinetobacter* spp. isolates were reported from 39 patients, compared with 21 isolates from 21 patients in 2023. Of these 39 patients, 9 patients were part of two outbreaks (Table 8.17) and 24 patients had been travelling abroad or had relation to Ukraine prior to identification of the carbapenemase-producing *Acinetobacter* spp. No information was reported for six of the patients.

A single patient had both an OXA-23 producing *Acinetobacter baumannii* and an OXA-24 producing *A. baumannii*. In 2024, 37 carbapenemase-producing *Acinetobacter baumannii* with the following enzymes were identified: OXA-23 (23), OXA-24 (1), OXA-23/OXA-58 (1), OXA-72 (2), OXA-72/NDM (1), OXA-23/OXA-72 (1) and NDM group/OXA-23 (8). Furthermore, two NDM-1 producing *Acinetobacter johnsonii* and, one OXA-72 *Acinetobacter bereziniae* were identified. (Figure 8.15).

Carbapenemase-producing *Pseudomonas* spp.
In 2024, 20 carbapenemase-producing *Pseudomonas* spp. isolates from 20 patients were reported compared to 16 isolates in 2023. Of these 20 patients, nine patients had been travelling abroad, seven patients had relation to Ukraine and no information was given for four patients prior to identification of the carbapenemase-producing *Pseudomonas* spp. In 2024, 19 carbapenemase-producing *Pseudomonas aeruginosa* with the following enzymes were identified: NDM-1 (10), VIM (3), IMP (5) and NDM/IMP (1). Furthermore, an NDM-producing *Pseudomonas putida* was detected.

In general, the number of carbapenemase-producing *Pseudomonas* spp. seems to be relatively stable over the years until the onset of Covid-19, which led to a large decrease in the number of isolates. This might be explained by less travel abroad. An increased in Carbapenemase-producing *Pseudomonas* spp. has been seen after the onset of the war in Ukraine (Figure 8.16).

Figure 8.15 Carbapenemase-producing *Acinetobacter* spp. and enzymes identified, Denmark, 2008-2024 DANMAP 2024

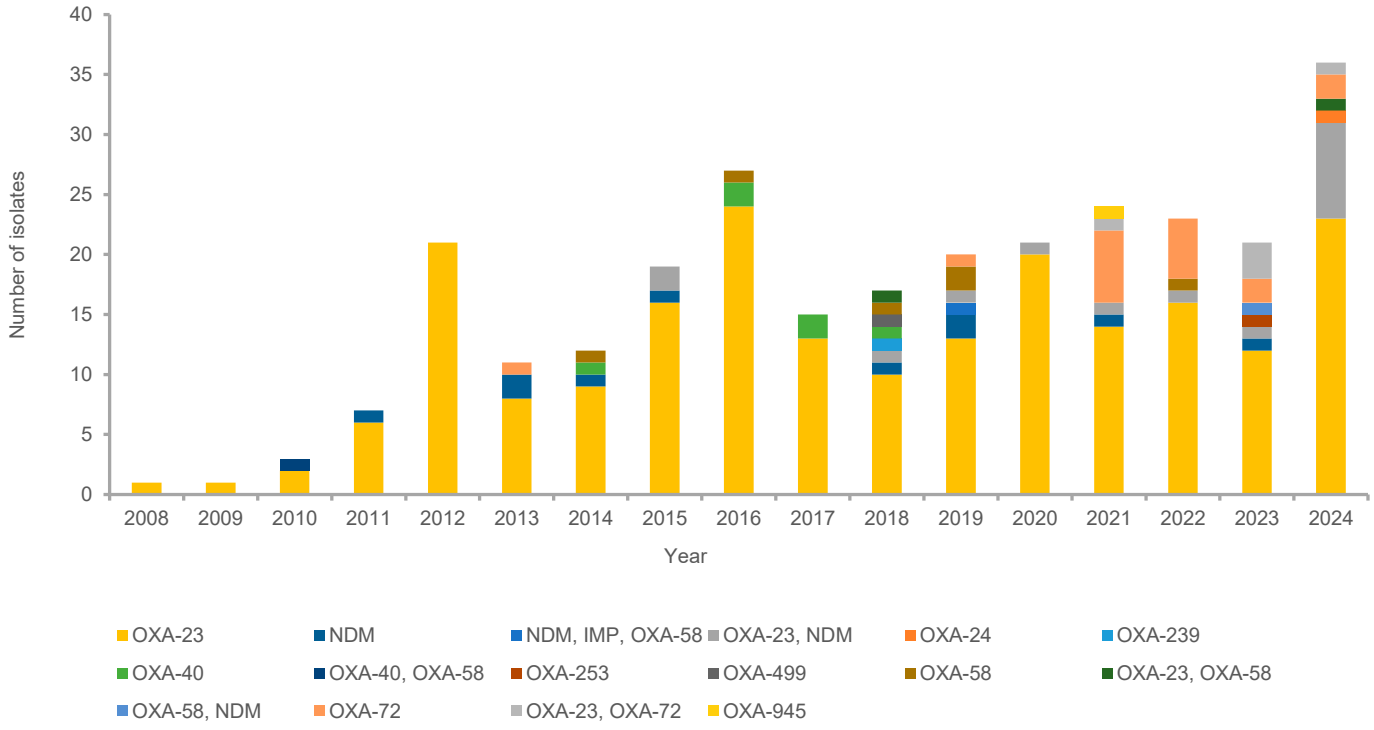
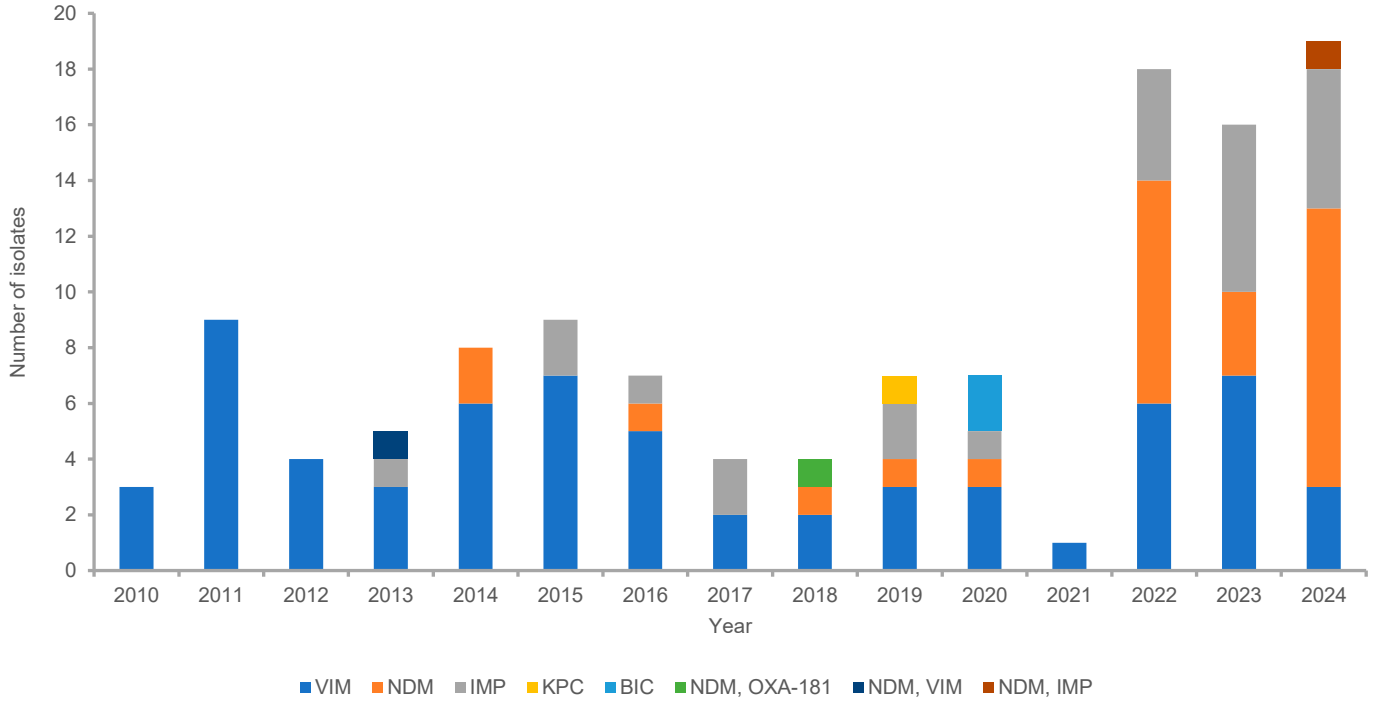


Figure 8.16 Carbapenemase-producing *Pseudomonas* spp. and enzymes identified, Denmark, 2010-2024 DANMAP 2024



CPO - Place of origin 2019-2024

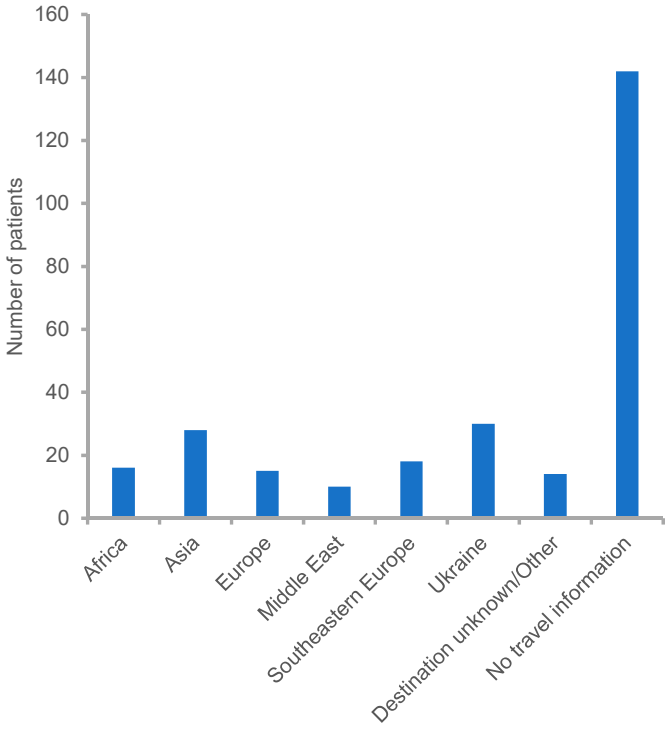
The Clinical Departments or a clinical physician can report travel in the period of six months before a colonization with CPO is detected, and the CPO-patient will be classified as a travel-associated CPO-patient. In order to qualify the information regarding the origin of a colonization with CPO in a Danish patient, the reported CPO-data from 2019 to 2024 has been evaluated and categorized into four categories: 1) Denmark, 2) Danish outbreak, 3) travel outside the Nordic countries, and 4) unknown (Figure 8.17).

The Clinical Departments or a clinical physician can also report a CPO-patient to be colonized in Denmark implicating that the patient has not been travelling prior to colonization. A CPO-patient can be affected by a Danish nosocomial outbreak and will be classified as an outbreak-patient. For some patients, no information is reported and the classification for place of origin will be unknown. The presumed index patient (the first patient identified) in an outbreak will be registered according to possible travel information.

In 2024, the reported travel data show that 101 of 527 CPO-positive patients reported travelling outside the Nordic countries. These cases were not part of nosocomial outbreaks. The number of cases where no travel information was provided is high (27%). In total, there was no travel information for 142 cases, suggesting that the actual travel rate is higher. Denmark was reported as the origin of the CPO-infection or colonization in 64 of the cases.

The most frequent reported travel destinations in 2024 were Asia (28), Southeastern Europe (18), Europe (15) and Middle East (10). The most single reported travel destinations were Turkey (20), Egypt (13), India (7), Thailand (6) and Pakistan (5).

Figure 8.17 Place of origin of CPO, 2019-2024 DANMAP 2024



Due to the still ongoing war in Ukraine, a number of patients from Ukraine are still receiving care in the Danish health care system. According to the Danish Health Authority, Denmark received a total of 41 patients from Ukraine as part of medical evacuations in 2024. These patients are screened for CPO according to the guideline. In 2024, a total of 57 CPO isolates were collected from 30 patients from Ukraine. More than one isolate was included from individual patients, if the isolates belonged to different bacterial species and/or had different carbapenemases. Among the 57 CPO, 46 were CPE isolates, seven were *Pseudomonas* ssp. and four were *Acinetobacter* ssp. The findings show that the patients originating from Ukraine were colonized and/or infected by several CPO per patient [Skjold Stolberg et al. 2023, Genotypic characterization of carbapenemase-producing organisms obtained in Denmark from patients associated with the war in Ukraine - ScienceDirect, https://www.sciencedirect.com/science/article/pii/S2213716523000917].

Outbreaks with CPO during 2024

In Denmark, outbreaks caused by CPO in healthcare settings are registered at SSI in the national database (KURS). The database also includes CPO-outbreaks identified in community settings, e.g. nursing homes and travel related outbreaks. At SSI, CPO isolates are routinely characterized by whole genome sequencing (WGS). Cluster analysis is conducted on all isolates using cgMLST to detect possible clustering between the CPO isolates. A genomic cluster is defined as at least two isolates (from different patients) belonging to the same cgMLST cluster (or having less than 15 alleles difference between the isolates). Due to the risk of long-term colonization of the patients, cluster analysis is carried out regardless of the time of isolation. When epidemiological investigations can establish a link between at least two patients in a genomic cluster (e.g. the patients had been at the same hospital ward at the same time), the patients are classified as belonging to a "verified outbreak". When no epidemiological link can be established, the patients related to the genomic cluster are classified as part of a possible outbreak (Materials and methods, section 9.12).

In 2024, a total of 33 CPO-outbreaks were registered compared to 26 CPO-outbreaks in 2023 (Table 8.17). In 15 of the outbreaks, an epidemiological link could be established between the majority of the patients, thereby indicating that the outbreaks were connected to healthcare settings. In health care settings the verified outbreaks were found to be caused by patients sharing the same ward or staying at the same hospital at the same time. In all, 19 of the 31 outbreaks have been ongoing for more than two years and two outbreaks for more than ten years, meaning that new patients have been identified as belonging to the same cgMLST cluster as found in the previous years.

In total, 166 new patients were associated with CPO-outbreaks in Denmark in 2024. Of these, seven patients were part of more than one outbreak. This is an increase compared to 2023 where 138 new patients were affected. Of the 33 outbreaks registered in 2024, nine new small clusters were identified involving 2 - 3 patients each. It is suspected that a part of the detected outbreaks may be attributable to the potential transfer of plasmids between different species, suggesting some smaller outbreaks actually belong to the same outbreak. The role of plasmid transfer in CPO-outbreaks will be further investigated.

Outbreaks with CPO of special interest

The ST18 NDM-1-producing *Citrobacter freundii* outbreak (ID41), which started in 2012 in the North Denmark Region, continued in 2024 [Hammerum et al. 2016, J. Antimicrob. Agents, 71:3117-3124]. Since 2012, the outbreak has spread to all five Danish regions. The main reason for the spread is the movement of infected patients between the regions. By the end of 2024, a total of 113 cases were involved in this outbreak. The number of new detected cases has been decreasing over the last two years. In 2024, a total of five new cases were identified, representing a decrease from the 15 cases registered in 2023 and the 20 cases in 2022. None of the cases had a history of travel.

Since 2015, another large outbreak (ID21) has been ongoing, primarily in two regions, Region Zealand and the Capital Region. The outbreak is associated with the spread of ST410 NDM-5/OXA-181 *E. coli*. [Roer et al. 2018, mSphere;3(4).]. Fifteen new cases were detected as part of this outbreak. By the end of 2024, a total of 111 cases had been identified as part of this outbreak. With the exception of the initial cases reported in 2015, who had been traveling to Egypt [Overballe-Petersen et al. 2018, Genome Announc.6(5): e01542-17], none of the other cases had a history of travel.

Since 2021, twelve isolates have been detected positive for ST131 OXA-244 *E. coli* in the Danish surveillance of CPO (ID1091). The cases were distributed across the country and no epidemiological link to the Danish health care system has been identified. In March 2024, the national contact point for EURGen-Nets at Staten Serum Institut (SSI) contacted the European Centre for Disease Prevention and Control (ECDC) regarding the increasing detection of OXA-244-producing *E. coli* ST131 in Denmark. ECDC initiated a European investigation involving 17 countries. The investigation showed a considerable heterogeneity in the geographical distribution and speed of spread of specific carbapenemase genes. This heterogeneity was particularly evident in the recent rapid emergence of ST131 isolates carrying chromosomally localised bla OXA-244 associated with large multi-country clusters [Kohlenberg, et al., Euro Surveill. 2024;29(47)]).

As part of the national surveillance of CPO-outbreak in Danish hospital, a cluster of *K. pneumoniae* ST39 CT7737 KPC-2 NDM-1 with eight cases was identified. This specific genotype has not previous been identified in Denmark. The cases were reported from different parts of the country involving all five Danish regions. Investigation revealed that the cases originated from Ukraine and presumably had been colonized with the CPO genotype in Ukraine (data not shown in Table 8.17).

In Denmark, CPO-outbreaks due to *Acinetobacter baumannii* are rare. In 2024, eight cases of ST2063 OXA-23 *A. baumannii* were detected in the national surveillance as part of an outbreak. The initial four outbreak cases with the same *A. baumannii* were reported in 2022 - 2023. The cases are spread all over the country. The investigation identified that the outbreak was primarily attributable to the medical evacuations from Ukraine. In total, twelve cases have been involved in this outbreak (ID1141).

Table 8.18 Outbreaks of carbapenemase-producing organisms (CPO) during 2024, Denmark, n=33 DANMAP 2024

Outbreak ID	Year	Patients total	Patients 2024	Carbapene-mase	Type of outbreak	Species (clonal spread)	Regions	Status
41	2012-2024	113	5	NDM-1	Clonal/plasmid	ST18 *C. freundii*	1 / 2 / 3 / 4 / 5	Verified
48	2013-2024	44	6	OXA-436	Clonal/plasmid	ST90 *E. hormaechei*/ST22 *C. freundii*	1 / 4 / 5	Verified
21	2015-2014	111	15	NDM-5/OXA-181	Clonal	ST410 *E. coli*	1 / 2 / 5	Verified
42	2015-2024	18	2	OXA-48	Clonal	ST65 *C. freundii*	1 / 3 / 5	Verified
1066	2017-2024	62	38	OXA-48	Clonal	ST91 *C. freundii*	1 / 5	Verified
1070	2017-2024	15	6	OXA-48	Clonal	*C. farmeri*	5	Possible
1145	2017-2024	11	7	OXA-48	Clonal/plasmid	ST65 *C. freundii*	3	Possible
1052	2018-2024	8	3	NDM-1	Clonal	ST18 *C. freundii*	2 / 4	Possible
43	2019-2024	33	11	OXA-48	Clonal/plasmid	ST323 *C. freundii*	1 / 5	Possible
1061	2020-2024	18	4	OXA-181	Clonal	ST22 *C. freundii*	2	Possible
1062	2020-2024	40	1	NDM-5	Clonal/plasmid	ST79 *E. hormaechei*	National	Verified
1091	2021-2024	12	5	OXA-244	Clonal	ST131 *E. coli*	1 / 2 / 3 / 4 / 5	Verified
1107	2022-2024	10	5	OXA-181	Clonal	ST636 *C. freundii*	5	Possible
1108	2022-2024	5	1	OXA-181	Clonal	ST410 *E. coli*	2	Possible
1113	2022-2024	11	5	OXA-48	Clonal	ST22 *C. freundii*	5	Verified
1115	2022-2024	9	5	NDM-1	Clonal	ST2 *K. oxytoca*	3	Verified
1141	2022-2024	12	8	OXA-23	Clonal	ST2063 *A. baumannii*	1 / 2 / 3 / 4	Verified
1148	2022-2024	4	2	OXA-48	Clonal	ST214 *C. freundii*	5	Possible
1154	2022-2024	5	4	KPC-3	Clonal/plasmid	ST22 *C. freundii*	4	Possible
1135	2023-2024	4	1	OXA-181	Clonal	ST36 *K. oxytoca*	5	Possible
1139	2023-2024	7	3	OXA-181	Clonal	ST65 *C. freundii*	5	Possible
1146	2023-2024	12	8	OXA-244	Clonal	ST13730 *E. coli*	1 / 2 / 3 / 5	Possible
1172	2023-2024	2	1	OXA-48	Clonal	ST116 *C. freundii*	2	Verified
1150	2024	2	2	OXA-48	Clonal	ST135 *K. aerogenes*	5	Possible
1162	2024	2	2	OXA-48	Clonal	*A. subterranea*	1	Verified
1170	2024	2	2	KPC-3	Clonal	ST307 *K. pneumoniae*	5	Possible
1176	2024	2	2	OXA-48	Clonal	ST4081 *K. pneumoniae*	5	Verified
1179	2024	2	2	OXA-232	Clonal	ST18 *C. freundii*	2	Verified
1180	2024	2	2	OXA-48	Clonal	ST114 *C. freundii*	5	Possible
1181	2024	2	2	OXA-48	Clonal	ST111 *C. freundii*	5	Possible
1183	2024	2	2	OXA-181	Clonal	ST98 *C. freundii*	5	Possible
1184	2024	2	2	OXA-48	Clonal	ST405 *E. coli*	5	Verified
1186	2024	2	2	OXA-244	Clonal	ST46 *E. coli*	3	Possible

1 Regions will be listed as: 1) Capital Region, 2) Central Denmark Region, 3) North Denmark Region, 4) Southern Denmark Region and 5) Zealand Region

Conclusion

The occurrence of carbapenemase-producing bacteria in Denmark continued to increase throughout 2024. The patients received from Ukraine are contributing to this increase, but the main contributing factor is a general increase in positive findings of CPO in humans and the increase in CPO nosocomial outbreaks. Furthermore, intensified screening also contributed to the increase in CPO cases in 2024.

The number of new nosocomial detected outbreaks in 2024 has increased since 2023, mainly due to the detection of small new outbreak clusters. Some of these outbreaks may be attributable to the potential transfer of plasmids between different species. The role of plasmid transfer in CPO-outbreaks will be further investigated. Intensified screening regime for CPO also identified more outbreaks than previous years. The screening strategy recommended in the CPO guideline is an important tool, together with the infection control measures (IPC) to control and stop outbreak due to antimicrobial resistance.

Travel outside the Nordic countries is a contributing factor to the number of CPO isolates detected in Denmark. The most frequently reported travel destinations in 2024 were Asia and Southeastern Europe. The number of cases where no travel information is provided is high, suggesting that the actual travel rate is higher than reported.

The spread of CPO among patients in Denmark is of concern, since Enterobacterales can be carried in the intestine for a long time (years) without any symptoms of infection, which makes outbreak control difficult and have consequences for medical treatment.

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8.3.3 Vancomycin-resistant/vancomycin-variable enterococci

Background

Enterococci are intrinsically resistant to a number of first-line antimicrobial agents, including cephalosporins, which increases the risk of enterococci being selected for in hospital environments and emerging in patients that receive cephalosporins for other conditions. Most hospital-acquired *Enterococcus faecium* are resistant to ampicillin, further limiting the treatment options. Vancomycin is an important drug for the treatment of severe *E. faecium* infections, however an increase in the occurrence of vancomycin resistant enterococci (VRE) has been observed within the last decade, both internationally and in Denmark. Newer antibiotics such as linezolid and daptomycin can be used for treatment of VRE, but both antimicrobial agents may lead to adverse events. In recent years, in various countries isolates of phenotypically vancomycin-susceptible *E. faecium* have been described to harbor a *vanA*-gene complex. These isolates are referred to as vancomycin-variable enterococci (VVE). In 2016, a new VVE clone belonging to ST1421-CT1134, displaying variable vancomycin susceptibility due to a deletion in the *vanX* gene, was detected [TA Hansen et al., J. Antimicrob. Agents, 2018, 73: 2936–2940]. The VVE clone has spread to all five Danish regions [Hammerum et al. Euro Surveill. 2024;29(23)]. Conclusively, VVE may be of clinical relevance and timely detection as well as continuous monitoring are critical to avoid treatment failure and further transmission.

Surveillance of VRE/VVE

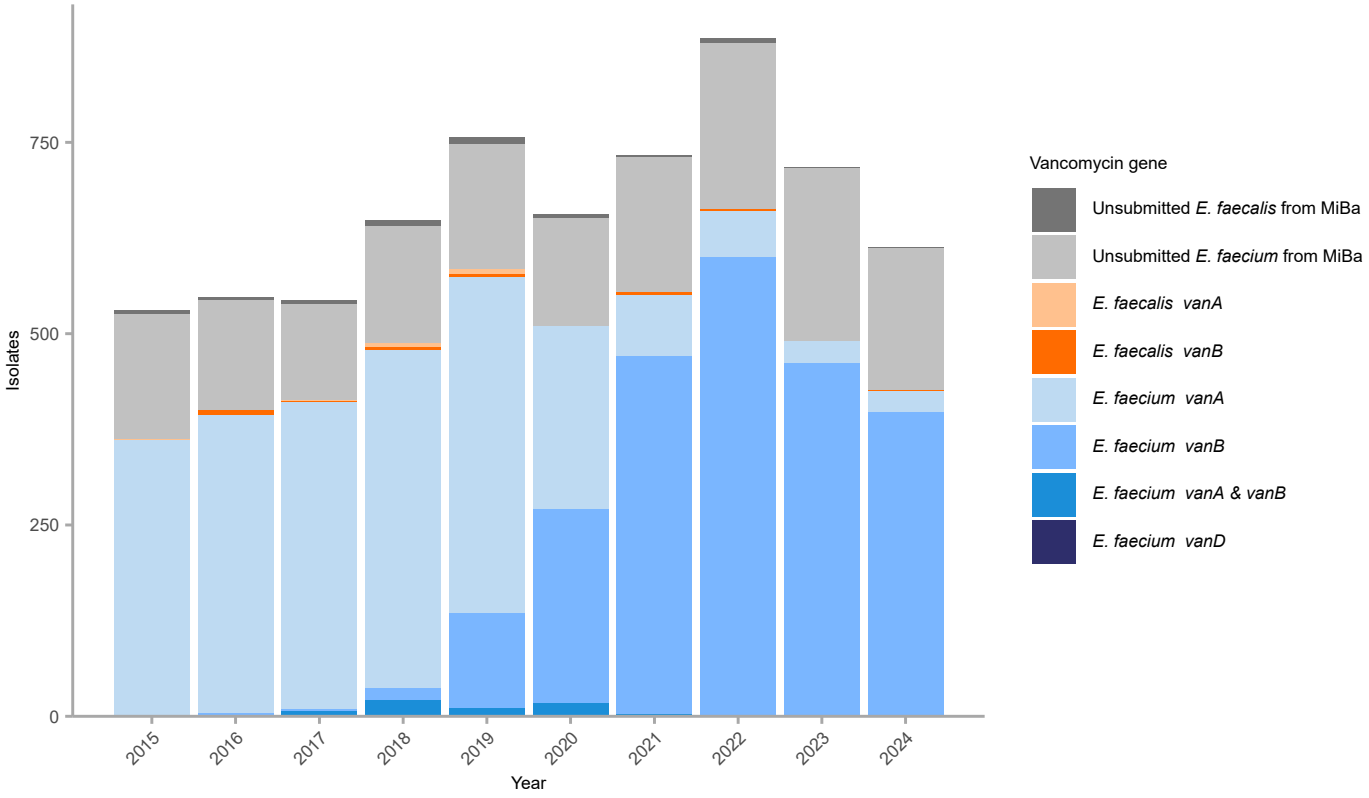
Since 2005, Danish departments of clinical microbiology (DCMs) have voluntarily submitted clinical VRE (one VRE/VVE isolate per patient, isolated within 12 months) for species identification, genotyping and surveillance purposes to the Reference Laboratory for Antimicrobial Resistance at Statens Serum Institut (SSI).

Since 2015, the received clinical VRE/VVE isolates have been analysed using whole-genome sequencing (WGS). The WGS data are used for *in silico* genotyping of isolate characteristics such as species identification, multilocus sequence typing (MLST), core genome sequence typing (cgMLST) and detection of van-genes and core locus MLST (cgMLST) combined for clonal detection (see Section 9.13.3).

To determine any underreporting in the submissions of VRE isolates, the number of VRE/VVE isolates submitted to SSI since 2015 were compared to data from clinical VRE in MiBa (the Danish Microbiology Database). This comparison showed that the number of submitted VRE/VVE isolates to SSI was not complete (Figure 8.18). The isolates only recorded in MiBa were distributed evenly throughout the study period and it did not seem to be a systematic loss. In 2024, 426 VRE/VVE isolates were submitted to SSI, and were genotyped by WGS. Furthermore, 187 VRE/VVE isolates were identified in MiBa, which had not been submitted to SSI and hence have not been genotyped. This was a decrease compared to 2023, were 494 VRE/VVE isolates were sent to SSI, while 228 VRE/VVE isolates were identified in MiBa yet not submitted to SSI (Figure 8.18).

Figure 8.18 Overview and distribution of vancomycin resistance genes in *E. faecium* and *E. faecalis*, Denmark, 2015-2024

DANMAP 2024



Of the 426 clinical VRE/VVE isolates sequenced in 2024, 28 were *vanA E. faecium*, 397 *vanB E. faecium*, and 1 *vanB E. faecalis* (Figure 8.18). Until 2020, *vanA E. faecium* were most common, but during the last years this has changed. In 2024, 93% of the *E. faecium* isolates had the *vanB* gene.

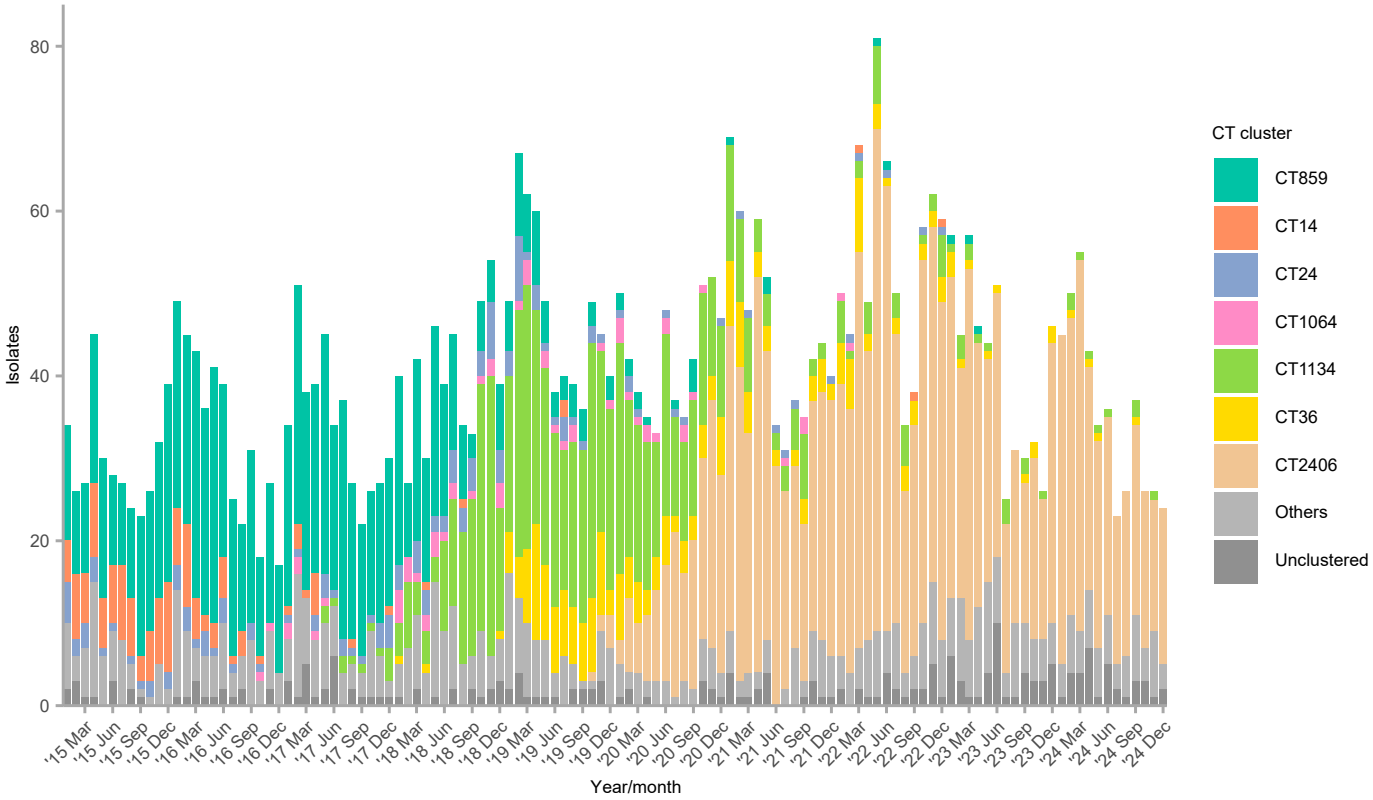
WGS-based cgMLST analysis was performed on the 425 *E. faecium* isolates using SeqSphere+ (Ridom). The 425 *E. faecium* isolates belonged to unique 113 CT clusters. When investigating the composition of sequence types (ST) and clonal types (CT) for *E. faecium*, we observed a clustering tendency between isolates, where ST's and CT's were diverging while the allelic differences were minimal within each cluster. Minimum Spanning Tree (MST) clusters were set up using the MST algorithm of SeqSphere+, setting the maximal allelic distances to 20. The top seven complex type clusters was devised, based on clustering of the isolates. Each complex type cluster were named according to the ST and CT of the earliest observed isolate within each cluster. One clonal group (covering several different CTs but presumably originating from the same clone) was predominant: The ST80-CT2406 *vanB E. faecium* group containing 312 isolates (73%) (Table 8.19).

Table 8.19 Description of the most common types of *vanA* and/or *vanB Enterococcus faecium* according to MLST and Complex type cluster, Denmark, 2016-2024

DANMAP 2024

Complex type Cluster	2016		2017		2018		2019		2020		2021		2022		2023		2024	
	n = 393		n = 410		n = 478		n = 574		n = 510		n = 551		n = 660		n = 490		n = 425	
ST203-CT859	250	63.6%	261	63.7%	153	32.0%	57	9.9%	12	2.4%	3	0.5%	2	0.3%	3	0.6%	0	0%
ST80-CT14	37	9.4%	12	2.9%	2	0.4%	2	0.3%	0	0%	0	0%	3	0.5%	0	0%	0	0%
ST117-CT24	18	4.6%	20	4.9%	39	8.2%	25	4.4%	8	1.6%	6	1.1%	5	0.8%	0	0%	0	0%
ST80-CT1064	2	0.5%	6	1.5%	23	4.8%	12	2.1%	14	2.7%	3	0.5%	2	0.3%	0	0%	0	0%
ST1421-CT1134	0	0%	13	3.2%	161	33.7%	285	49.7%	197	38.6%	63	11.4%	35	5.3%	14	2.9%	9	2.1%
ST117-CT36	0	0%	0	0%	3	0.6%	94	16.4%	54	10.6%	43	7.8%	41	6.2%	12	2.4%	4	0.9%
ST80-CT2406	0	0%	0	0%	0	0%	7	1.2%	178	34.9%	370	67.2%	476	72.1%	332	67.8%	312	73.4%
Other clusters	72	18.3%	74	18.0%	83	17.4%	73	12.7%	37	7.3%	45	8.2%	73	11.1%	87	17.8%	66	15.5%
Unclustered	14	3.6%	24	5.9%	14	2.9%	19	3.3%	10	2.0%	18	3.3%	23	3.5%	42	8.6%	34	8.0%

Figure 8.19 Timeline of the complex type clusters prevalence in all sequenced VRE isolates. Complex type clusters are named according to sequence type and complex type of the earliest observed member, Denmark, 2015-2024 DANMAP 2024



From 2015 to 2024, seven *E. faecium* clusters dominated: ST80-CT14 vanA, ST117-CT24 *vanA*, ST203 -CT859 *vanA*, ST1421-CT1134 *vanA*, ST80-CT1064 *vanA*/*vanB*, ST117-CT36 *vanB* and ST80-CT2406 *vanB* [Hammerum et al. Euro Surveill. 2024;29(23)]. Figure 8.19 shows the monthly count of these seven clusters alongside the remaining clusters during the period 2015 to 2024.

During 2015, We detected ST80-CT14 *vanA E. faecium* in all Danish Regions. On a national level, the numbers of ST80-CT14 *vanA E. faecium* decreased signifcantly from 2016 to 2019, disappearing completly from 2020. In 2022, a few isolates ST80-CT14 *vanA E. faecium* were detected. ST117-CT24 *vanA E. faecium* was first detected in the Capital Region in January 2015. Between 2015 and 2022 it was detected in all five regions. ST203-CT859 *vanA E. faecium* was first detected in Denmark in December 2014. It was one of the dominating clones from 2015 through July 2018 and was detected in all five regions. In 2022, only a few isolates belonging to ST203-CT859 *vanA E. faecium* were detected. ST80-CT1064 *vanA-vanB E. faecium* was first detected in Central Denmark Region in October 2016. It spread to the North Jutland Region during April 2018. During 2019, a single case of ST80-CT1064 *vanA-vanB E. faecium* was detected. This clone disappeared during January 2022. *E. faecium* isolates belonging to ST1421-CT1134 *vanA E. faecium* (VVE cluster) were first detected in clinical samples in 2016. In 2018, 34% of the *E. faecium* isolates belonged to ST1421-CT1134, and they were mostly detected in The Capital Region. During 2019, ST1421-CT1134 *vanA E. faecium* was the most prevalent type (44%) but decreased during 2021 and 2022. ST117-CT36 *vanB E. faecium* was detected in January 2019 in Capital Region of Denmark. During 2019, ST117-CT36 *vanB E. faecium* was detected in all five Danish Regions. In October 2019, the first clinical ST80-CT2406 *vanB E. faecium* sample was detected in a patient hospitalised in the Capital Region. It spread further to other patients in the Capital Region in 2019. During 2020, this cluster was detected in all Danish regions except the Northern Region of Denmark but during 2021, it was also detected there [Hammerum et al. Euro Surveill. 2020;25(32)]. Since 2022, the ST80-CT2406 has been and continues to be, the main dominant complex type cluster in all Danish regions [Hammerum et al. Euro Surveill. 2024;29(23)].

Infection prevention and control guidelines for VRE

Acting in compliance with the national guidelines for infection prevention and control (published by National Centre for Infection Control at SSI) is key in preventing the spread of multidrug-resistant microorganisms (MDRO), with correct hand hygiene and correct use of personal protective equipment (PPE) among the most important control measures [https://hygiejne.ssi.dk/NIRgenerelle]. The supplemental national guideline for infection prevention and control (IPC) includes specific guidance on VRE/VVE and should be followed when examining and treating patients, residents and citizens with these (and other) multidrug-resistant microorganisms [https://hygiejne.ssi.dk/

NIRsupplerende]. According to the national supplemental (IPC) guideline, screening of a patient is recommended on admission to hospital if the patient: 1) is transmitted from a hospital outside the Nordic countries, 2) has been hospitalised outside the Nordic countries within the last 6 months, 3) has been hospitalised in wards in Denmark or another Nordic country with outbreaks of VRE within the last 6 months or 4) previously has been diagnosed with a VRE-infection or carrier state. Isolation is recommended in the national supplemental IPC-guideline in case of verification of VRE in the patient. Precautions include the use of PPE such as a disposable gown and gloves and proper cleaning of the environment [https://hygiejne.ssi.dk/NIRdesinfektion]. Moreover, the guidelines emphasise the importance of prescribing antibiotics with caution.

Conclusion

The number of VRE/VVE cases have decreased from 2022 to 2024. While the decrease is a desired development, the level of VRE infections is still high. Therefore, more prevention strategies are required to prevent spread of VRE in the Danish health care system.

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8.3.4 *Staphylococcus aureus*

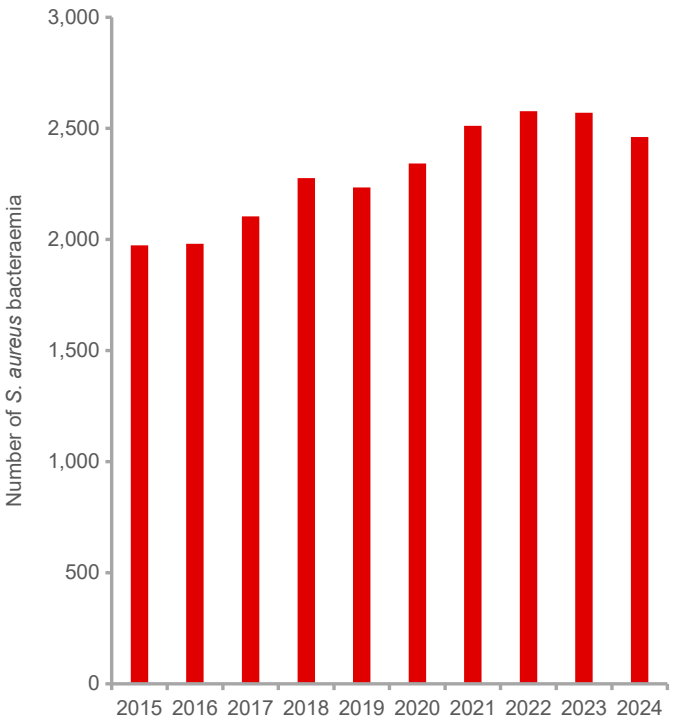
Staphylococcus aureus is part of the normal flora of the skin and mucosa. Approximately 50% of humans will be colonized with *S. aureus* in their nose or throat at any given time, some of these carrying the strain only intermittently, others for longer periods of time. *S. aureus* causes infections ranging from superficial skin infections e.g. impetigo and boils to deeper and invasive life-threatening infections such as bacteraemia, septic arthritis, osteomyelitis, endocarditis. The infections can be healthcare-associated such as postoperative wound infections and infections related to intravenous catheters and prosthetic devices or the bacteria can spread endogenously.

In Denmark, a voluntary surveillance program of all *S. aureus* bacteraemia cases was established in 1957. By comparison with the numbers of bacteraemia cases registered in the Danish Microbiology Database (MiBa) since 2010, the number of reported cases and bacterial isolates submitted to SSI demonstrates almost complete reporting and submission (94-97%). Laboratory and clinical notification of all cases of methicillin-resistant *S. aureus* (MRSA) has existed since November 2006.

Surveillance of *S. aureus* bacteraemia

The number of *S. aureus* bacteraemia cases were 2,461 in 2024 corresponding to 41 cases per 100,000 inhabitants. This is slightly less compared to 2023 (n=2,571), but the long-term trend is still an increasing number of cases (Figure 8.20). Within 30 days from the bacteraemia onset, 572 (23%) patients died (all-cause mortality). Forty-seven (1.9%) of the bacteraemia cases were caused by methicillin-resistant *S. aureus* (MRSA). During the last decade this proportion of MRSA bacteraemia cases has been between 1.5% and 2.2% and remains below most other European countries participating in the European Antimicrobial Resistance Surveillance Network (EARS-Net). Livestock-associated MRSA (LA-MRSA) CC398 caused seven of the 47 MRSA bacteraemia cases. The 30-day all-cause mortality for the MRSA bacteraemia cases was 13%.

Figure 8.20 Number of new *Staphylococcus aureus* bacteraemia cases in Denmark 2015-2024 DANMAP 2024



The antimicrobial susceptibility remained at the same level as in previous years for most agents (Table 8.20). The highest frequency of resistance to antimicrobials other than penicillin was observed for fusidic acid (13%), erythromycin (9%) and clindamycin (9%).

Typing revealed a high diversity with 709 different *spa* types distributed in 30 different clonal complexes (CCs). The ten most prevalent *spa* types, representing 31% of the total number, are presented in Table 8.21. The distribution of the most prevalent *spa* types has been very stable over the last decade with only minor changes in the relative order. The PVL toxin was present in 32 (1.3%) cases of which four were MRSA. The 38 isolates with the PVL gene were distributed among 22 different *spa* types.

Table 8.20 Resistance (%) in isolates from *Staphylococcus aureus* bacteraemia cases 2015-2024, Denmark DANMAP 2024

	2015	2016	2017	2018	2019	2020*	2021	2022	2023	2024
Antimicrobial agent	%	%	%	%	%	%	%	%	%	%
Methicillin	1.5	2.1	2.2	1.6	2.1	1.6	1.6	1.9	1.5	1.9
Penicillin	71	71	72	72	72	72	69	68	68	69
Erythromycin	7	7	6	5	9	7	7	9	9	9
Clindamycin	7	6	5	4	8	7	7	8	8	9
Tetracycline	4	3	3	3	2	3	2	3	2	3
Fusidic acid	16	12	14	17	14	14	13	13	12	13
Rifampicin	<1	<1	<1	<1	<1	<1	<1	<1	<1	1
Moxifloxacin#	6	4	4	4	5	6	4	4	4	3
Gentamicin	3	<1	1.1	1.0	<1	<1	<1	1.1	1.2	1
Linezolid	0	0	0	0	0	0	0	0	0	0
Mupirocin	<1	0	<1	0	<1	<1	<1	<1	<1	<1
Trimethoprim-sulfamethoxazole	<1	<1	<1	0	<1	<1	<1	<1	<1	<1

* From 2020 and onwards, resistance data was extracted from the Danish Microbiology database, MiBa. # Prior to 2021 testing for fluoroquinolone resistance was reported for norfloxacin

Table 8.21 The ten most prevalent *spa* types demonstrated in SAB cases 2024 DANMAP 2024

spa type	CC group	No. of cases
t127	CC1	135
t084	CC15	114
t091	CC7	107
t002	CC5	83
t1451	CC398	71
t008	CC8	53
t571	CC398	50
t230	CC45	50
t012	CC30	49
t021	CC30	47

Surveillance of methicillin-resistant *S. aureus*

In 2024, a total of 3,372 MRSA new cases were detected (57 per 100,000 inhabitants), an 8% decrease compared to 2023 (3,649; Figure 8.21a). A case was defined as the first time an individual tested positive for a specific MRSA strain regardless of clinical context (infection or colonisation). A case was defined as infection or colonisation based on the information in the notification form. Infections constituted 59% of the cases. The proportion of infections in the years 2015 to 2024 has varied between 38% to 59% (Figure 8.21b).

Figure 8.21a Number of new MRSA cases in Denmark 1994-2024 DANMAP 2024

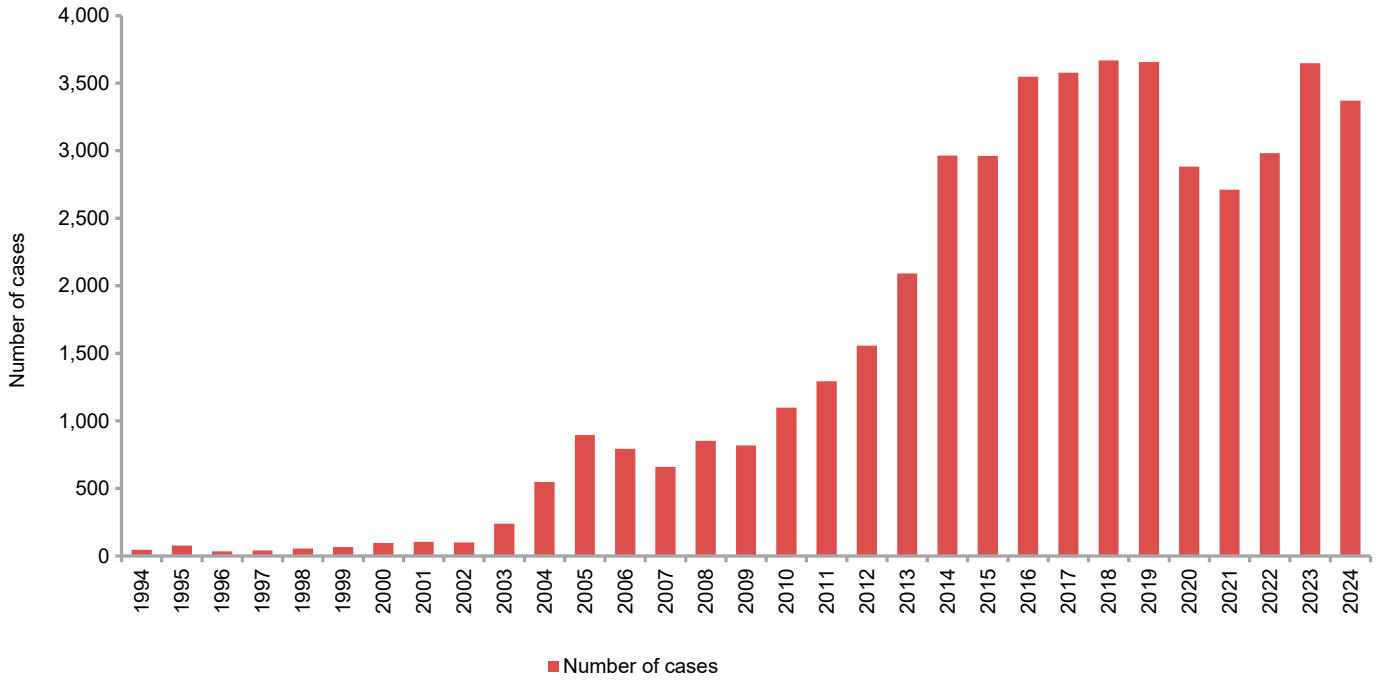
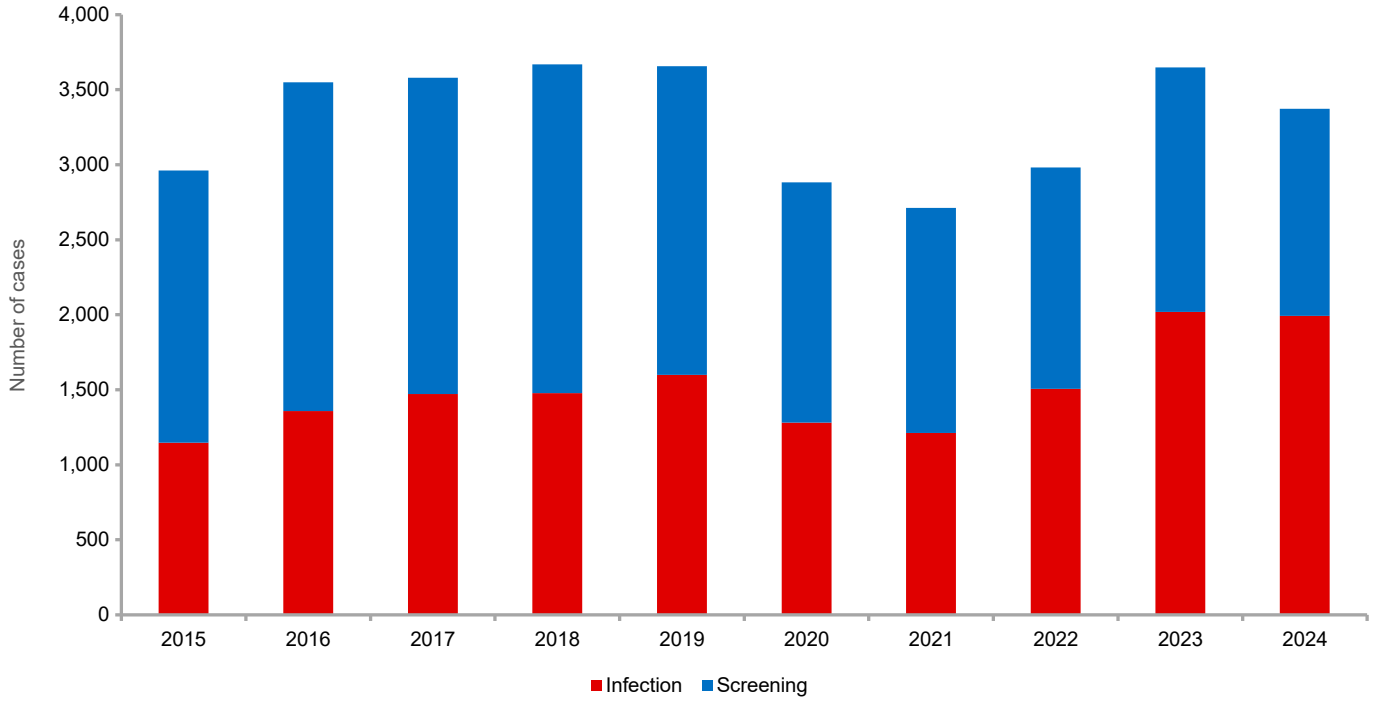


Figure 8.21b Number of new MRSA cases 2015-2024, Denmark, divided in infection and screening samples DANMAP 2024



CC398 cases constituted 22% (n=744) of new MRSA cases, of which 701 belonged to LA-MRSA CC398 and the remaining 43 to a human adapted variant harbouring the PVL encoding genes. A higher proportion of LA-MRSA CC398 isolates (65%) were identified in healthy carriers compared to other MRSA types (34%), likely reflecting the active screening of patients with livestock contact upon admission to healthcare facilities.

MRSA isolates carrying *mecC* were detected in 66 cases (2%). Fifty-one of the cases (77%) had infections at the time of diagnosis. None of the patients reported contact to hedgehogs, which recently has been shown to be a major environmental reservoir for *mecC* MRSA. Two patients had occupational exposure to pigs and one to horses, and two patients had other exposure to horses, while the remaining 61 patients did not report any contact to livestock or other animals.

spa typing revealed 404 different strain types. Among the infections, 349 *spa* types were identified. The 10 dominating non-LA-CC398 *spa* types isolated in 2024 are listed in Table 8.22. They constituted 48% of the total number of non-LA-CC398 MRSA isolates. Table 8.22 does not list *spa* types in CC398, which for many years has been the dominating CC. *spa* types t304 and t223 have been among the five most prevalent *spa* types since 2016, when their increase was linked to the refugee crisis following the civil war in Syria.

For the second year in a row *spa* type t127 was the second most numerous. This type has been involved in several outbreaks in neonatal units in recent years but is also a common type among community associated cases.

The PVL encoding gene was detected in 33% of the infections and in 12% of the asymptomatic carriers and most often in relation to isolates with *spa* types t008 (n = 66), t355 (n = 61), t005 (n = 46), t021 (n = 43) and t034 (n = 31).

Thirty-eight MRSA outbreaks were registered at hospitals, nursing homes and other institutions (Table 8.23). These outbreaks comprised a total of 191 cases of which 86 had an infection. Four of the outbreaks occurred in neonatal departments, comprising a total of 72 cases. Additionally, eight outbreaks were registered in other hospital department, comprising 24 patients and twelve outbreaks were observed in nursing homes (counting a total of 27 patients). The number of outbreaks in nursing homes has increased in the last 5 years. The average number of outbreaks in 2015-2019 was 4 and in 2020-2024 11.

The total number of cases and the number of cases presenting with infection according to epidemiological classification are shown in Table 8.24. Most of the cases (85%) were acquired in Denmark.

Table 8.22 The ten most prevalent spa types demonstrated in non-LA-CC398-MRSA in Denmark 2024 DANMAP 2024

spa type	CC group	No. of cases	No. causing infections (%)
t304	CC6	288	167 (58)
t127	CC1	210	101 (48)
t223	CC22	138	69 (50)
t008	CC8	135	98 (73)
t002	CC5	129	77 (60)
t4549	CC8	100	93 (93)
t688	CC5	89	61 (69)
t355	ST152/377	63	47 (75)
t005	CC22	63	51 (81)
t021	CC30	55	42 (76)

Table 8.23 Outbreaks of methicillin-resistant *Staphylococcus aureus* (MRSA) during 2024 in Denmark DANMAP 2024

Start of outbreak (year)	Patients in total	Patients in 2024	*spa* type	CC	Place of outbreak	Region
2016	35*	7	t2846	CC97	Nursing home	Capital Region of Denmark
2017	23	3	t3802	CC6	Hospital	Central Denmark Region
2019	136*	39	t127	CC1	Hospital (neonatal)	Capital Region of Denmark
2019	8	2	t5485	CC22	Nursing home	North Denmark Region
2019	16	1	t002	CC5	Nursing home	Capital Region of Denmark
2021	22	1	t034	CC398 pvl+	Educational facility	Central Denmark Region
2021	9	1	t136	CC30	Community acquisition	Region of Southern Denmark
2022	14	5	t553	CC45	Home care	Region Zealand
2022	7	1	t304	CC6	Hospital	Capital Region of Denmark
2022	7*	1	t511	CC45	Nursing home	Capital Region of Denmark
2023	61*	26	t272	CC121	Child care institution	Region of Southern Denmark
2023	7	4	t701	CC8	Hospital	Capital Region of Denmark
2023	10	2	t 11822 / t9867	CC80	Hospital (neonatal)	North Denmark Region
2023	24	23	t037	CC30	Hospital (neonatal)	Region of Southern Denmark
2024	7	7	t1802	CC22	Hospital	Capital Region of Denmark
2024	8	8	t1476	CC8	Hospital (neonatal)	Central Denmark Region
2024	6*	4	t359	CC97	Educational facility	Region Zealand
Multiple (21 smaller outbreaks)	68*	49	Multiple	Multiple	Various	Denmark

* Including patients until May 2025

Table 8.24 Epidemiological classification of new MRSA cases, Denmark 2024 DANMAP 2024

Epidemiologic classification	Exposure	No. of cases (% of total)	No. (%) of cases with infections (% of cases in same epi. class)
Imported (IMP)		**515 (15)**	373 (72)
Hospital-acquired (HA)		**83 (2)**	16 (19)
Health-care associated, community onset (HACO)		**304 (9)**	
	with known exposure	21	16 (76)
	without known	283	262 (93)
Health care worker		**36 (1)**	15 (42)
Community-acquired (CA)		**1,734 (51)**	
	with known exposure	684	102 (15)
	without known	1049	968 (92)
LA-MRSA CC398		**701 (21)**	
	with known exposure	563	127 (23)
	without known	138	114 (83)
Total		**3,372**	**1,993**

Numbers shown in bold are totals

Figure 8.22 Number of MRSA infections according to epidemiological classification, Denmark, 2015-2024 DANMAP 2024

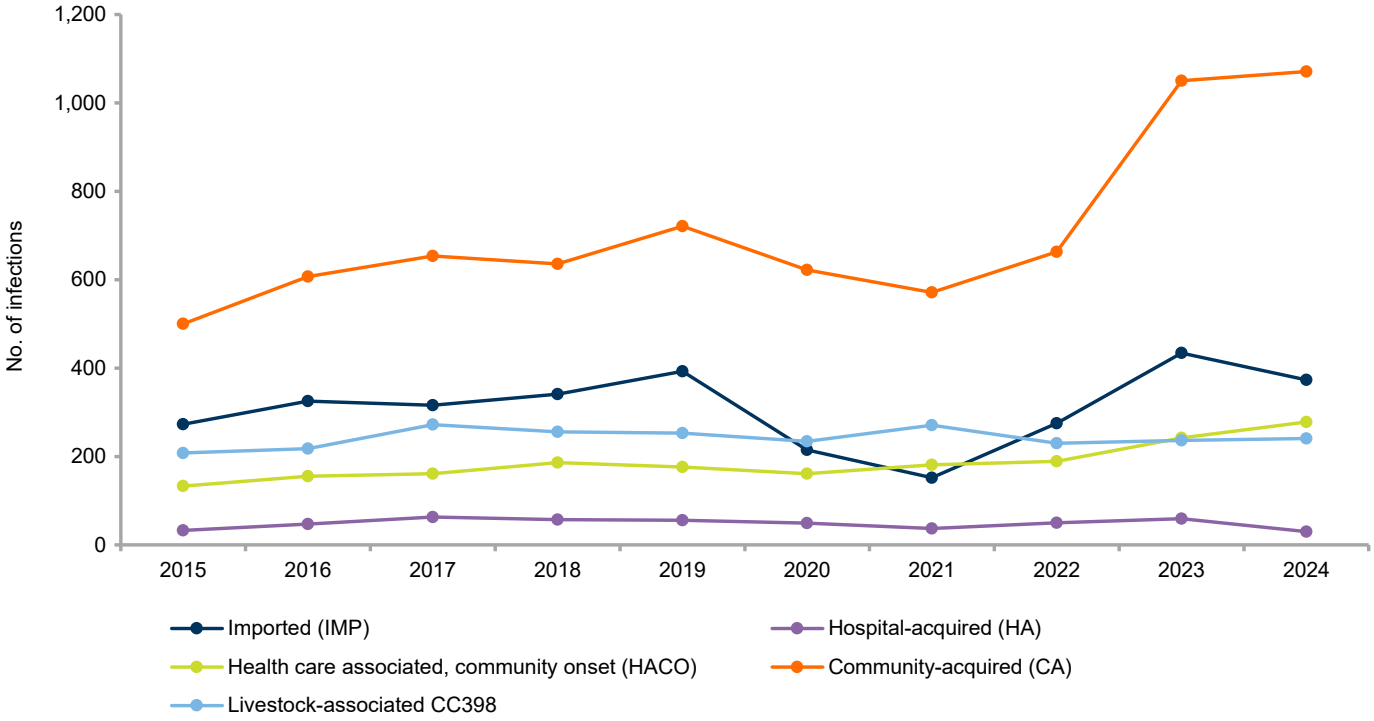


Table 8.25 Resistance (%) in non Livestock-associated CC398 MRSA isolates, Denmark, 2015-2024 DANMAP 2024

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Erythromycin	37	34	34	33	33	30	29	34	32	33
Clindamycin	29	25	27	28	23	22	19	21	21	22
Tetracycline	24	26	24	26	22	22	21	23	21	24
Fusidic acid	19	18	16	18	23	22	21	22	26	27
Rifampicin	<1	1	1	1	<1	<1	<1	<1	1	<1
Moxifloxacin#	21	19	20	21	21	17	19	23	24	26
Linezolid	0	<1	0	<1	0	<1	<1	<1	<1	<1
Mupirocin	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Trimethoprim-sulfamethoxazole	4	2	3	3	4	2	<1	1	1	2
Number of tested isolates	1,242	1,184	1,193	1,233	1,025	1,920*	1,520*	2,043*	2,696*	2,605*

* Not all isolates were tested for all listed antimicrobials
\# Prior to 2021 testing for fluoroquinolone resistance was reported for norfloxacin

The trend of MRSA infections for 2015-2024 based on their epidemiological classification is shown in Figure 8.22. The number of infections in imported cases and hospital-acquired cases decreased in 2024 when compared to 2023. Importantly, number of infections among hospital-acquired MRSA remained low in 2024 (30 cases).

Resistance among MRSA isolates

Resistance data for non-LA-CC398 isolates are presented in Table 8.25. Resistance prevalences were similar to previous years, with the highest resistance to erythromycin (33%), fusidic acid (27%), moxifloxacin (26%), tetracycline (24%) and clindamycin (22%), and low resistance (<1%-2%) to trimethoprim-sulfamethoxazole, linezolid, mupirocin and rifampicin.

Conclusion

The number of *S. aureus* bacteraemia cases was 2,461 in 2024, a slight decrease compared to 2023. Of these, 47 cases (1.9%) were caused by methicillin-resistant *S. aureus* (MRSA) with seven being livestock-associated-MRSA (LA-MRSA).

There were 3,372 cases of MRSA from both screening (41% of cases) and infections (59%), which was an 8% decrease compared to 2023. Thirty-eight MRSA outbreaks were registered at hospitals, nursing homes and other institutions for a total of 191 cases with 86 being infections.

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8.3.5 *Streptococcus pneumoniae*

Background

Streptococcus pneumoniae (*S. pneumoniae*) (pneumococcus) causes various infectious diseases that are classified as either non-invasive or invasive. Among these, invasive pneumococcal diseases (IPD) are the most severe, while non-invasive pneumococcal infections are less severe, but much more commonly observed. Pneumonia, which can be categorized as non-invasive or invasive, is estimated to be the most frequent pneumococcal disease worldwide, affecting both children and adults. This is followed by the severe cases of the invasive diseases bacteraemia and meningitis.

Pneumococcus often causes acute otitis media (AOM) in children, with more than half of Danish children estimated to experience this conditionduring their childhood. AOM is frequently treated with antibiotics, although their effectiveness is uncertain. In addition to these well-known pneumococcal diseases, pneumococci are also associated with other common non-invasive infections such as sinusitis and bronchitis, as well as invasive diseases like endocarditis, peritonitis, and septic arthritis.

Laboratory surveillance

The laboratory surveillance of IPD in Denmark is conducted through mandatory submission of isolates from invasive cases to Statens Serum Institut (SSI). At SSI, the isolates are serotyped and tested for antimicrobial susceptibility. Cases without a submitted isolate are identified through The Danish Microbiology Database (MiBa).

Results

In 2024, 634 cases of IPD were registered (Table 8.26). Pneumococci were mainly found in either blood (567) or cerebrospinal fluid (44). For 23 cases, pneumococci were found in other normally sterile sites. Before 2023, only cases with pneumococci found in blood or cerebrospinal fluid were included in the DANMAP report. For the years 2023 and 2024 all IPD cases are included in the report. Among the 634 IPD cases identified in MiBa for 2024, 594 isolates were received at the reference laboratory. Regarding the 40 remaining cases where isolates were not submitted, data were retrieved from MiBa. Serotypes for these cases are unknown. Failure of submitting an isolate for serotyping was mainly due to non-viable isolates (n = 25) or diagnosis achieved by PCR (n = 15). Data for serotype and penicillin susceptibility were thus available for 594 cases.

The predominant serotype in 2024 was serotype 3 (15.3%) (Table 8.26). All 91 serotype 3 isolates were susceptible to penicillin. The second and third most frequently isolated serotypes were serotype 22F (75; 12.6%) and serotype 8 (50; 8.4%), and these isolates were all susceptible to penicillin.

Figure 8.23 The incidence of invasive pneumococcal infection (IPD) and the percentage of penicillin non-susceptible IPD isolates in Denmark, 2000-2024
DANMAP 2024

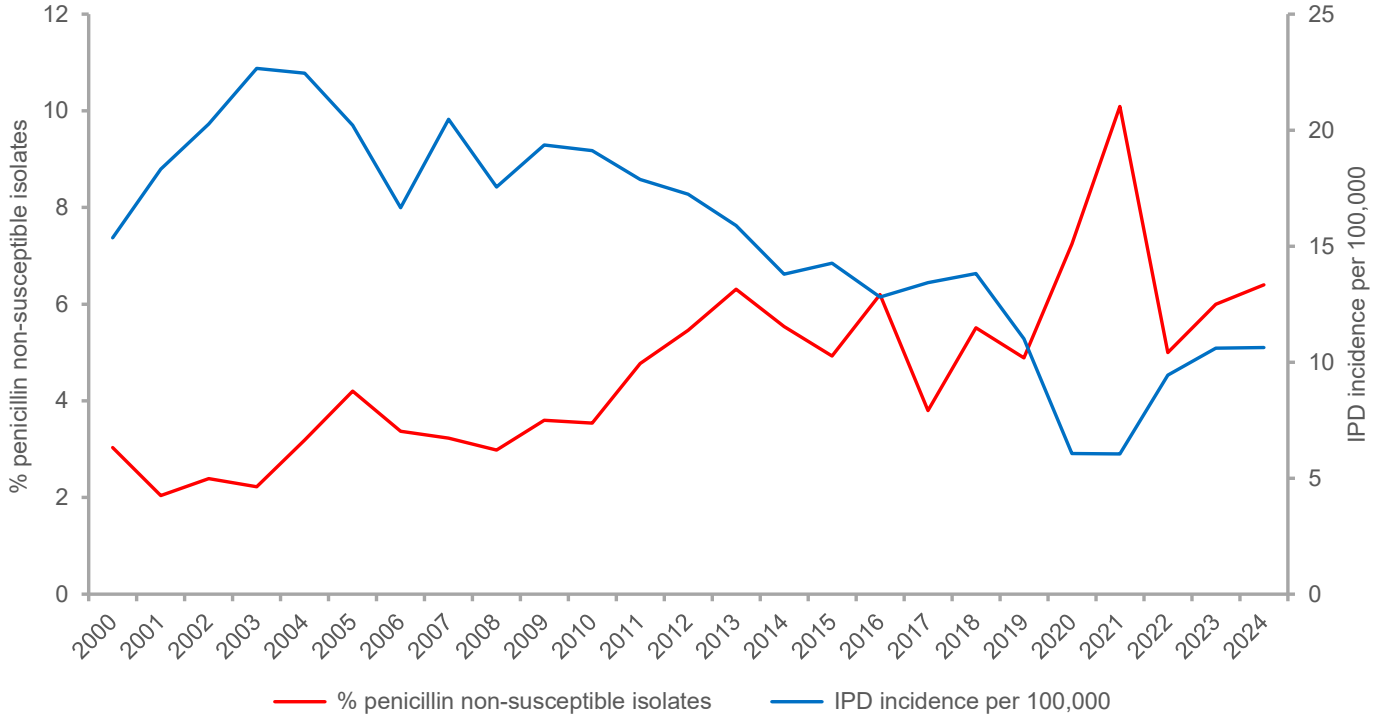

Table 8.26 Number of cases of invasive pneumococcal disease in Denmark 2024; serotype distribution and penicillin susceptibility

DANMAP 2024

Serotype	Included in pneumococcus vaccines					Total number	Penicillin susceptible, numbers			% Pen-S
	PCV13	PCV15	PCV20	PCV21	PPV23		Pen-S	Pen-non-S	Unknown	
3	+	+	+	+	+	91	91	0		100%
22F		+	+	+	+	75	75	0		100%
8			+	+	+	50	50	0		100%
9N				+		49	48	1		98%
33F		+	+	+	+	29	29	0		100%
24F				+		24	24	0		100%
19A	+	+	+	+	+	23	20	3		87%
15A				+		22	15	7		68%
10A			+	+	+	17	17	0		100%
23A		+	+	+	+	15	13	2		87%
11A			+	+	+	14	14	0		100%
19F	+	+	+		+	12	10	2		83%
31				+		12	12	0		100%
15C				+		10	9	1		90%
35B				+		10	6	4		60%
23B				+		8	1	7		13%
12F			+	+	+	7	5	2		71%
15B			+		+	7	7	0		100%
16F				+		7	7	0		100%
17F				+		6	3	3		50%
4	+	+	+		+	4	4	0		100%
7F	+	+	+	+	+	3	3	0		100%
20				+		2	2	0		100%
6A	+	+	+	+		1	1	0		100%
23F	+	+	+		+	1	0	1		0%
6B	+	+	+		+	1	1	0		100%
38						28	28	0		100%
7C						19	19	0		100%
6C						15	13	2		87%
35F						9	9	0		100%
10B						3	3	0		100%
17A						3	3	0		100%
35A						3	2	1		67%
24A						2	2	0		100%
28F						2	2	0		100%
35D						2	1	1		50%
7B						2	1	1		50%
13						1	1	0		100%
27						1	1	0		100%
29						1	1	0		100%
34						1	1	0		100%
9A						1	1	0		100%
9L						1	1	0		100%
Unknown						40	25	0	15 (*)	
Total						634	581	38	15 (*)	

Pen-S = penicillin susceptible; Pen-non-S = penicillin non-susceptible; % Pen-S = percentage of isolates susceptible to penicillin; (*) = no penicillin susceptibility resultats available if pneumococci were diagnosed by PCR only

Conclusion
The incidence of IPD per 100,000 population was unchanged in 2024 compared to 2023. The level of penicillin non-susceptible IPD isolates in 2024 (6.4%) was slightly higher than that in 2023. Both the great fluctuation in the prevalence of penicillin non-susceptible IPD isolates and the general IPD incidence in the years 2020 and 2021 is assumed to be an effect of the COVID-19 restrictions on the general prevalence of infectious diseases associated with respiratory droplet transmission. Such fluctuations have been seen in other countries as well [Shaw et al., Lancet Digit Health. 2023 Sep;5(9)]

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8.3.6 Beta-haemolyic streptococci

Beta-haemolytic streptococci (BHS) are classified into serological groups according to antigenic properties of the polysaccharide capsule. In human infections, groups A, B, C and G are the most frequent species. Approximately 10% of humans are asymptomatic throat carriers of BHS of any group.

Streptococcus pyogenes (group A streptococci; GAS) cause pharyngitis, tonsillitis, otitis media, wound infections, and superficial skin infections, but also more severe infections, e.g., bacteraemia, necrotizing soft tissue infections, and rarely meningitis. In Denmark, the rate of asymptomatic throat carriage of GAS is approximately 2%.

Streptococcus agalactiae (group B streptococci; GBS) may be present in the vaginal flora of 20-25% of women in the childbearing age. If these bacteria are transferred to the child during labour, meningitis and septicaemia may develop in the newborn. Such infections also occur in elderly or immunocompromised patients.

Streptococcus dysgalactiae subsp. *equisimilis*, which comprise group C streptococci (GCS) and group G streptococci (GGS) predominantly cause soft-tissue infections and sometimes bacteraemia.

This report presents data on antimicrobial resistance in non-duplicate invasive isolates (i.e. from blood, cerebrospinal fluid or other normally sterile anatomical sites) submitted from the departments of clinical microbiology (DCMs) in 2024 to the Neisseria and Streptococcus Reference laboratory (NSR). This report includes only non-duplicate isolates, i.e. isolates obtained with an interval of more than 30 days. Isolates are received from all DCMs in Denmark. It is voluntary to submit isolates of BHS.

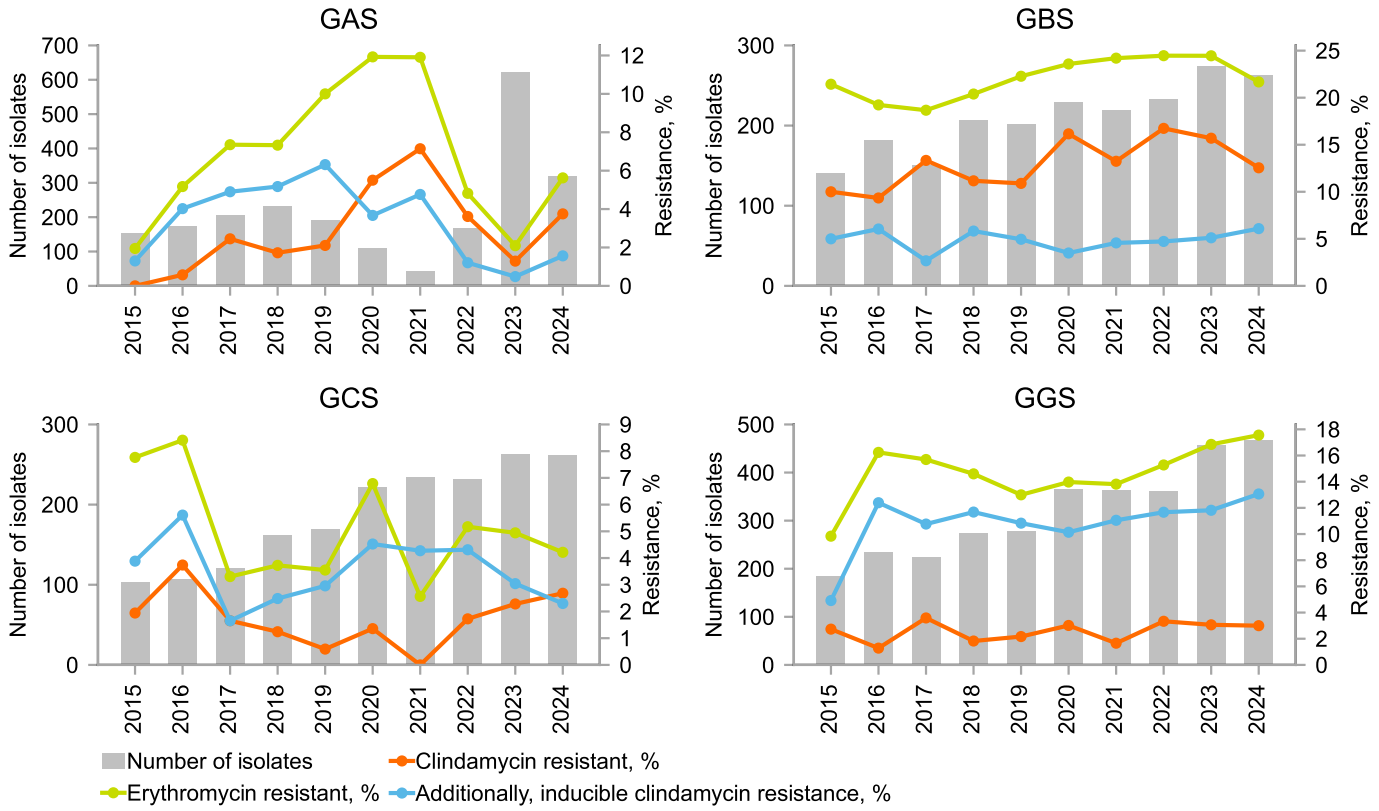
Infections with BHS are usually treated with penicillins or macrolides. All submitted isolates of BHS were therefore tested for susceptibility to penicillin, erythromycin and clindamycin as well as inducible clindamycin resistance. Susceptibility testing was performed with disk diffusion methods. If resistance was observed, MIC was determined with Etest. All results were interpreted according to MIC breakpoints issued by EUCAST (http://www.eucast.org/) (version 14.0).

In 2024, a total of 1,343 isolates from invasive cases were received. The number of isolates from individual invasive cases was 1,311, a decrease of 19% compared to 2023 (1,615).

The number of GAS isolates changed by a factor 0.52 compared to 2023, while the number in 2023 had increased by a factor 3.7 compared to 2022. For GBS these ratios were 0.96 and 1.2, respectively. For GCS they were 0.99 and 1.1, respectively, and for GGS they were 1.0 and 1.3.

Figure 8.24 shows the resistance findings for the years 2015 through 2024. All isolates were fully susceptible to penicillin. Comparing GAS in 2024 to 2023, the rates of erythromycin resistance, clindamycin resistance, and inducible clindamycin resistance had all increased, but not to higher levels than they were in 2022. For GBS, GCS and GGS these rates all remained nearly unchanged. The percentage of fully susceptible isolates compared to 2023 was decreased for GAS (94% versus 98%), increased for GBS (78% versus 74%), and remained virtually unchanged for the two other serogroups.

Figure 8.24 Invasive beta-haemolytic streptococci, Denmark, 2015-2024: Antimicrobial resistance testing results DANMAP 2024



Comments and conclusions

The substantial increase from 2021 to 2022 and further in 2023 for GAS was part of the national as well as international surge of invasive and non-invasive GAS infections, including a high proportion of cases with a serious course (Johannesen, et al., Euro Surveill. 2023 Jun;28(26):2300291). This increase was probably a consequence of discontinued COVID-19 related restrictions on upper respiratory tract colonization and airborne transmission of this species. In 2024, this effect waned in the second half of 2023, and the number of submitted GAS isolates in 2024 was only 0.52 of the number in 2023.

The increase cannot be explained by changes in the prevalence of antimicrobial resistance. All isolates were fully susceptible to penicillin.

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8.3.7 *Neiserria gonorrhoeae*

Neisseria gonorrhoeae is the causative agent of the sexually transmitted infection gonorrhoea, which is usually located in the urethra in males and cervix in females. *N. gonorrhoeae* (gonococci) may also sometimes be demonstrated in specimens from the pharynx or rectum in either gender. In females, the finding of gonococci in ano-rectal specimens is usually due to contamination with vaginal secretion, while in men who have sex with men (MSM) it is due to unprotected anal sex leading to infection. In both genders, the condition is generally asymptomatic. Pharyngeal gonorrhoea is virtually always asymptomatic.

Complications of gonorrhoea include e.g. salpingitis, epididymitis, orchitis, and prostatitis. Furthermore, conjunctivitis may occur in new-borns after transmission from an infected mother during labour and rarely in adults following direct or indirect inoculation.

Laboratory surveillance

Since 1962, the departments of clinical microbiology in Denmark have voluntarily submitted isolates of gonococci to the Neisseria and Streptococcus Reference (NSR) laboratory at Statens Serum Institut for national surveillance of antimicrobial resistance.

Both resistant and intermediary susceptible isolates were categorized as resistant in this report. However, isolates with intermediary susceptibility are non-existing according to EUCAST breakpoints for ceftriaxone and azithromycin and they are exceedingly rare regarding ciprofloxacin.

As part of NSR's participation in ECDC's surveillance (Euro-GASP) of sexually transmitted infections since 2009, approximately 100-200 gonococcus isolates are collected consecutively each year in September-October and investigated for susceptibility to an expanded panel of antimicrobial agents. This panel includes cefixime and in selected years also tetracycline, spectinomycin, and sometimes gentamicin.

Results and discussion

The annual number of received isolates increased considerably from 2011 through 2017 (Figure 8.25). This was most likely due to the widespread use of combined nucleic acid amplifications tests (NAATs) for *Chlamydia trachomatis* and *N. gonorrhoeae* which have identified unexpected cases of gonorrhoea (sometimes followed by culture), and also to an increasing incidence of gonorrhoea, especially among young heterosexual persons, among whom an increasing proportion until 2016 were women. The proportion of female cases has decreased slightly since 2017, but it is still substantially higher than in the beginning of the observation period (2003-2016). A decrease in the annual number of isolates from individual cases was seen in 2018 followed by an increase in 2019-2021 and in particular from 2021 to 2023 (Pedersen et al., Euro Surveill 2024 Feb;29(7)). It should be recalled, however, that many cases diagnosed by NAATs are not followed-up by culture.

Repetitive detections of gonococci in a patient are considered to represent individual cases of gonorrhoea if separated by more than 21 days. The same distinction is applied when enumerating individual episodes of testing. In 2024, there were 365,263 episodes of testing for gonococci, for the most part consisting of dual testing for gonococci and *Chlamydia trachomatis*. Among these episodes of testing, 5,108 were positive for gonococci, including 1,852 individual episodes of positive cultures. The NSR laboratory received isolates from 1,803 individual cases of gonorrhoea (1,218 males, 585 females). Only one isolate from each individual case is counted in this report.

If more than one isolate is received from an individual episode of gonorrhoea, the following hierarchy of the isolates are used, in accordance with the ECDC guidelines for Euro-GASP:

Males: 1. Pharyngeal 2. Rectal 3. Urethral 4. Other
Females: 1. Pharyngeal 2. Cervical 3. Other anogenital (high vaginal swab/rectal/urethral) 4. Other

Among the isolates included in this report, 1,353 were from urogenital sites, 152 from anorectal areas, 119 from pharynx, one from blood, one from conjunctiva, and 177 from uninformed or other anatomical sites, such as joint fluid, Bartholin's abscess, etc. The high number of uninformed sites is mainly caused by sparse details given in electronic information accompanying the isolates.

The ciprofloxacin resistance rate was 61% in 2024 (63% in 2023 and 40% in 2022), (Figure 8.25). Only 2.5% of the isolates were classified as ciprofloxacin intermediate (MIC 0.047-0.064 mg/L).

The percentage of strains producing penicillinase was 16% (14% in 2023 and in 2022). Previously, it has fluctuated between 22% in 2005 and 7% in 2016. Azithromycin resistance (MIC above the present ECOFF 1 mg/L) was found in 3.5% of the tested isolates (6.0% in 2023 and 2.9% in 2022).

Figure 8.25 Number of submitted gonococcus isolates from individual cases of gonorrhoea in males and females, and the percentage of isolates with ciprofloxacin resistance, azithromycin resistance, and penicillinase production, Denmark, 2003-2024 DANMAP 2024

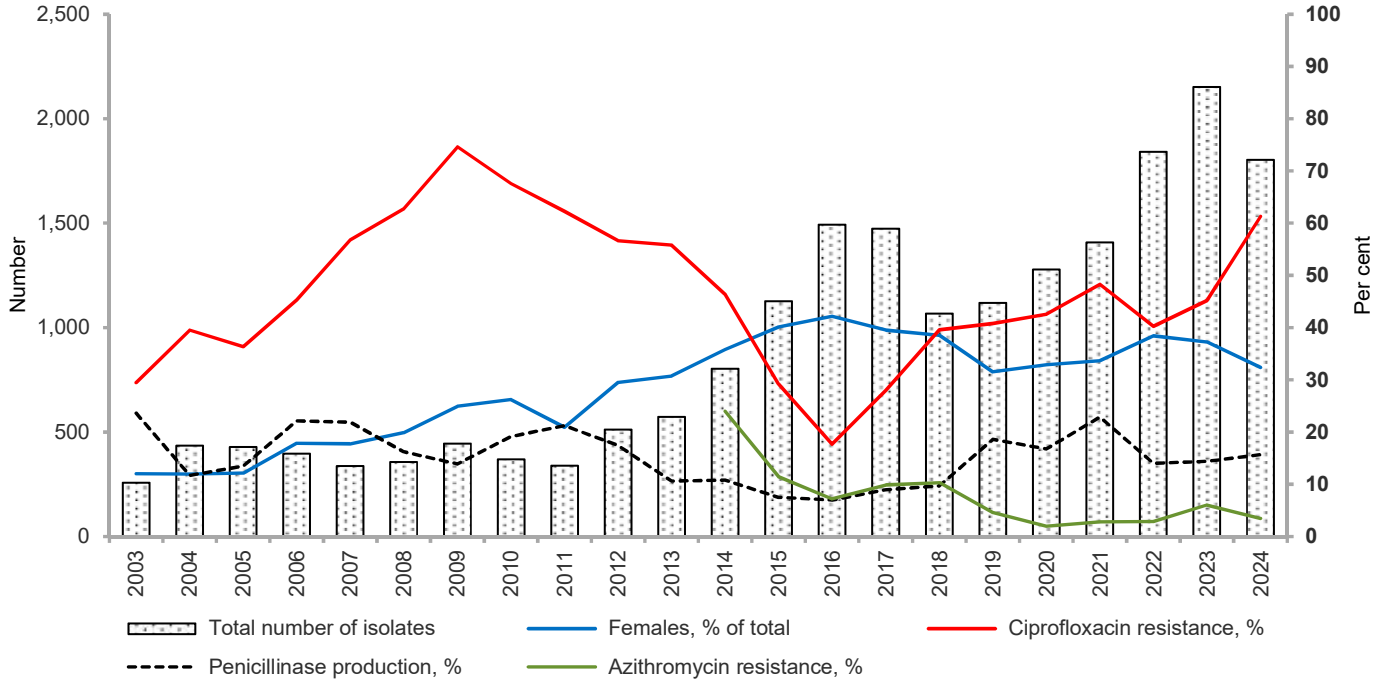


Figure 8.26 Distribution of ceftriaxone MIC (mg/L) values in gonococci, Denmark, 2003–2024 DANMAP 2024

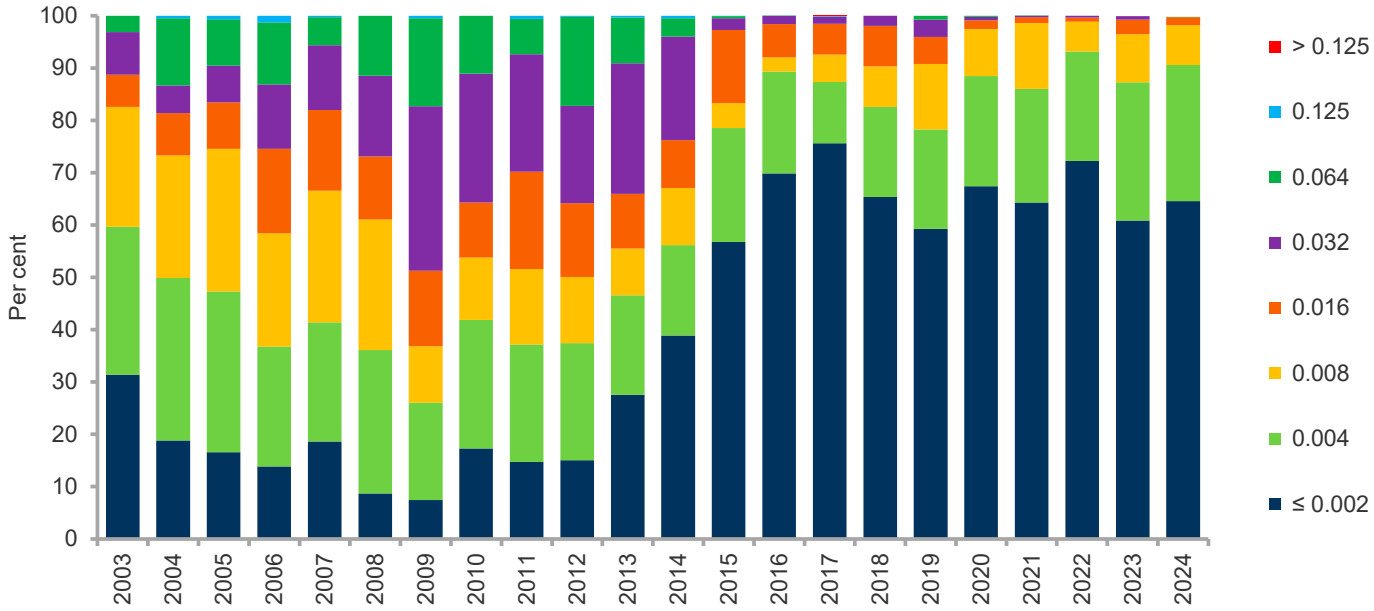


Figure 8.27 Distribution of cefixime MIC (mg/L) values in gonococci, Denmark, 2003–2024 DANMAP 2024

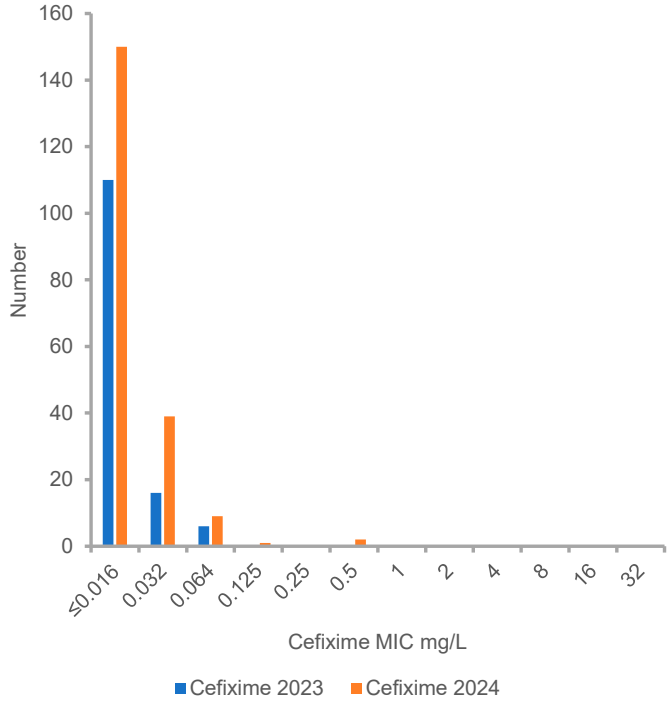
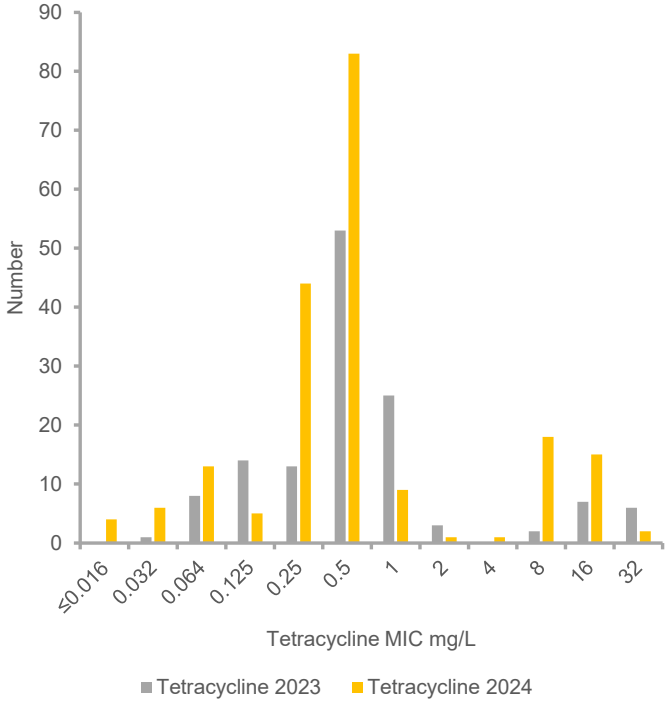


Figure 8.28 Distribution of tetracycline MIC (mg/L) values in gonococci, Denmark, 2003–2024 DANMAP 2024



Ceftriaxone resistant gonococci (MIC >0.125 mg/L) as well as ceftriaxone treatment failure in patients with gonorrhoea have occurred in several countries during recent years. As shown in Figure 8.26, the ceftriaxone MIC distribution changed from 2003 through 2009 with the highly susceptible isolates becoming gradually less frequent. However, since then, this change has completely reversed. In 2017, there was a single case among the submitted isolates with ceftriaxone MIC of 0.25 mg/L (i.e. resistant) and azithromycin MIC of 0.25 mg/L.

Secondary cases were not reported and no strains with ceftriaxone resistance have been encountered among the submitted isolates since 2017.

The Danish National Board of Health issued guidelines in 2015 for the diagnosis and treatment of sexually transmitted infections. A combination of ceftriaxone (500 mg i.m.) and azithromycin (2 g p.o.) was recommended for the empiric treatment of gonorrhoea. This therapeutic regimen has gradually been abandoned during 2019 and onwards by most clinicians.

Ciprofloxacin (500 mg p.o. as a single dose) may still be used for treatment if the strain is fully susceptible and if appropriate investigation has excluded pharyngeal gonorrhoea.

Participation in Euro-GASP

In a subset of 201 isolates tested as part of the Danish participation in Euro-GASP, resistance against cefixime (MIC >0.125 mg/L) was 0% in 2023 as in 2022, and 1% in 2024, Figure 8.27. Cefixime is an oral cephalosporin that has never been used in Denmark. Resistance against tetracycline (MIC >0.5 mg/L) was 33% in 2023 and 23% in 2024, Figure 8.28. Susceptibility testing against spectinomycin and gentamicin are only performed in selected years and was not carried out in 2024.

Resistance findings by gender and anatomical origin of the isolates

In males, the ciprofloxacin resistance rate was higher in anorectal isolates than in urogenital and pharyngeal isolates, while no major difference was observed among isolates from females (Table 8.27).

In males as well as in females, the azithromycin resistance rate was higher in pharyngeal isolates than in anorectal and urogenital isolates (Table 8.28).

In males, penicillinase production was demonstrated at a similar rate (approximately 16%), irrespective of the site of infection. In females, it was highest in pharyngeal isolates (Table 8.29).

Table 8.27 Ciprofloxacin resistance rates by gender and anatomical origin of the isolates, 2024 DANMAP 2024

	Males		Females		Total	
	No. resistant / total no.	% resistant	No. resistant / total no.	% resistant	No. resistant / total no.	% resistant
Urogenital	546 / 878	62	249 / 475	52	795 / 1,353	59
Anorectal	104 / 143	73	5 / 9	56	109 / 152	72
Pharynx	45 / 73	52	27 / 46	59	72 / 119	61
Blood	1 / 1	100	0 / 0	-	1 / 1	100
Eye	1 / 1	100	0 / 0	-	1 / 1	100
Other or unknown	89 / 122	73	40 / 55	73	129 / 177	73
Total	786 / 1,218	65	321 / 585	55	1,107 / 1,803	61

Table 8.28 Azithromycin resistance rates by gender and anatomical origin of the isolates, 2024 DANMAP 2024

	Males		Females		Total	
	No. resistant / total no.	% resistant	No. resistant / total no.	% resistant	No. resistant / total no.	% resistant
Urogenital	31 / 878	3,5	17 / 475	3,6	48 / 1,353	3,5
Anorectal	1 / 143	0,7	0 / 9	0	1 / 152	6,6
Pharynx	3 / 73	4,1	3 / 46	6,5	6 / 119	5
Blood	0 / 1	0	0 / 0	-	0 / 1	0
Eye	0 / 1	0	0 / 0	-	0 / 1	0
Other or unknown	7 / 122	5,7	2 / 55	3,6	9 / 177	5,1
Total	42 / 1,218	3,4	22 / 585	6,6	64 / 1,803	3,5

Table 8.29 Penicillinase production by gender and anatomical origin of the isolate, 2024 DANMAP 2024

	Males		Females		Total	
	No. resistant / total no.	% resistant	No. resistant / total no.	% resistant	No. resistant / total no.	% resistant
Urogenital	149 / 878	17	63 / 475	13	212 / 1,353	16
Anorectal	24 / 143	17	1 / 9	11	25 / 152	27
Pharynx	11 / 73	15	9 / 46	20	20 / 119	16
Blood	1 / 1	100	0 / 0	-	1 / 1	100
Eye	0 / 1	0	0 / 0	-	0 / 1	0
Unknown	17 / 122	14	8 / 55	-	25 / 177	14
Total	202 / 1,218	17	81 / 585	15	283 / 1,803	16

Conclusions

The ciprofloxacin resistance rate was at the same high level (61%) as in in 2023 (63%) and thus substantially higher than in 2022 (40%). However, the ceftriaxone MIC distribution was unchanged and showed no signs of a drift towards resistance. Although resistance problems among gonococci are still not present in Denmark, the frequent emergence globally of gonococcal resistance to antibiotics underlines the importance of maintaining the centralised national surveillance of antimicrobial resistance in gonococci.

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8.3.8 *Haemophilus influenzae*

Background

Haemophilus influenzae is part of the normal upper respiratory tract flora, with colonization varying by age. *H. influenzae* frequently causes upper and lower respiratory infections, while invasive infections are relatively rare and primarily occur in young children and elderly individuals, particularly those with underlying conditions like chronic obstructive pulmonary disease or cancer. Bacteraemia/sepsis is the predominant form (80-90%), while meningitis is observed in approximately 10% of cases. *H. influenzae* is categorized into six capsular serotypes (a, b, c, d, e, and f), also known as Hia, Hib, Hic, Hid, Hie, and Hif, and there are noncapsular (non-typeable, NTHi) strains as well. The introduction of the polysaccharide type b vaccine in 1993 significantly reduced the incidence of systemic infection caused by *H. influenzae* type b (Hib), as the vaccine specifically protects against Hib. Antimicrobial resistance in *H. influenzae* is an increasing problem globally, especially within beta-lactam antibiotics. The molecular antibiotic resistance in *H. influenzae* is complex, where both beta-lactamase production and alterations in penicillin binding proteins (PBPs), contribute to resistance to beta-lactam antibiotics.

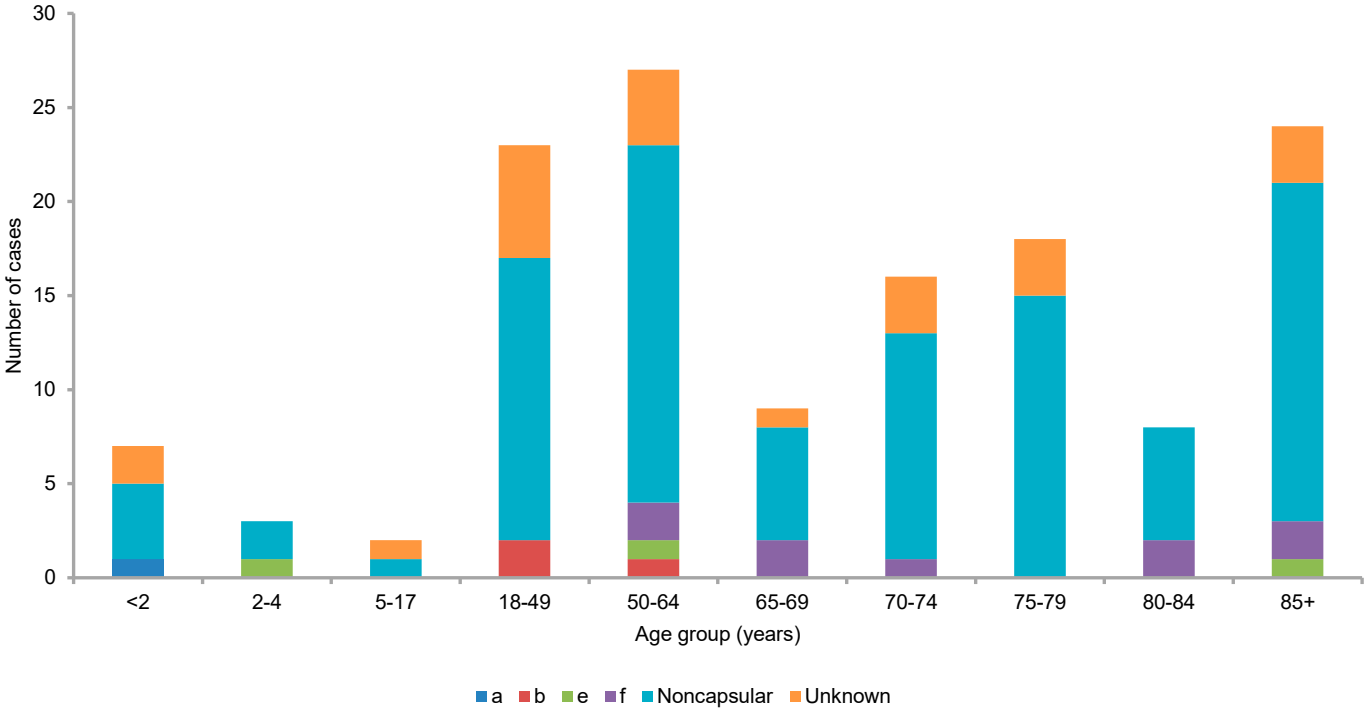
Surveillance of *Haemophilus influenzae*

The surveillance of *H. influenzae* causing invasive disease in Denmark involves submitting clinical isolates to Statens Serum Institut (SSI). Cases without a submitted isolate are identified through MiBa. At SSI, the isolates are only subjected to whole-genome sequencing to extract the serotype, sequence type, and beta-lactam resistance genes (beta-lactamase genes and mutations in the *ftsI* gene encoding penicillin-binding protein 3). Phenotypic beta-lactam susceptibility is retrieved through MiBa, if available.

Results

In 2024, a total of 137 cases of invasive *H. influenzae* were registered. The majority of cases were in blood (117), cerebrospinal fluid (10), or both (4). In three cases, *H. influenzae* was found in pleural fluid and in one case of each of the following: Blood and pleural fluid, joint fluid, and peritoneal-dialysis fluid. 114 isolates were submitted to SSI as part of the Danish surveillance program. The patient age and serotype distribution of the submitted isolates can be seen in Figure 8.29.

Figure 8.29 Distribution of invasive *H. influenzae* cases by age group and serotype (a, b, e, and f), Denmark, 2024 DANMAP 2024



Noncapsular *H. influenzae* is still the most commonly tested type (98/114; 86%), with Hif being the most common serotype (7.9%), followed by Hib (2.6%), Hie (2.6%), and Hia (0.9%).

Data on both molecular and phenotypic antimicrobial susceptibility were available for 89 *H. influenzae* isolates. Of these, 29% were penicillin/ampicillin-resistant (Table 8.30). Fourteen isolates were tested positive for TEM beta-lactamase genes (all were TEM-1). BLNAR-defining mutations in the *ftsI* gene were found in 12 isolates (11 had the N526K mutation and one had the R517H mutation). The most common *ftsI* type were IIa and IIb (four each), and one each of IIc, IId, III+ and III-like+.

Table 8.30 Phenotypic resistance against penicillin/ampicillin in *Haemophilus influenzae* DANMAP 2024

Sensitivity	Number (%)
Resistant	26 (29)
Susceptible	63 (71)
Total	89

A comparison between phenotypic beta-lactam susceptibility and beta-lactam resistance mechanisms (BLNAS = beta-lactamase-negative ampicillin-susceptible; BLPAR = beta-lactamase positive ampicillin-resistant; BLNAR = beta-lactamase negative ampicillin-resistant; BLPACR = beta-lactamase-positive amoxicillin-clavulanic acid-resistant) can be found in Table 8.31. A 98% concordance was observed between phenotypic susceptibility testing and molecular resistance gene detection: one isolate with no beta-lactam resistance markers was tested penicillin/ampicillin resistant, and one isolate with a BLNAR resistance mechanism was tested penicillin/ampicillin susceptible.

Table 8.31 Phenotypic resistance against penicillin/ampicillin vs. beta-lactam resistance mechanism in *Haemophilus influenzae* DANMAP 2024

Beta-lactam resistance mechanism	Pen/ampi resistant	Pen/ampi susceptible	Total (%)
BLNAS	1	62	63 (71)
BLPAR	13	0	13 (15)
BLNAR	11	1	12 (13)
BLPACR	1	0	1 (1)
Total	26	63	89

BLNAS = beta-lactamase-negative ampicillin-susceptible; BLPAR = beta-lactamase positive ampicillin-resistant; BLNAR = beta-lactamase negative ampicillin-resistant; BLPACR = beta-lactamase-positive amoxicillin-clavulanic acid-resistant

No *H. influenzae* isolates had other resistance genes.

Conclusions

The number of invasive *H. influenzae* cases in 2024 were 137, somewhat higher than the 123 cases in 2023 and 118 cases in 2022. The majority of isolates are still of the noncapsular type (86%) while Hif was the most common serotype (7.9%). Resistance towards penicillin and ampicillin was 26% with 13% BLNAR and 15% BLPAR, and one isolate with a BLPACR resistance mechanism.

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8.3.9 Meningococci

Neisseria meningitidis (meningococci) are capable of causing invasive meningococcal disease (IMD), usually meningitis or septicaemia or both, which may be life threatening and may cause permanent neurological sequelae. Asymptomatic throat carriage is frequent and only rarely leads to invasive disease. Non-invasive meningococcal diseases include, e.g. conjunctivitis and urethritis. IMD is usually treated with intravenous penicillin or ceftriaxone. Single-dose ciprofloxacin or rarely rifampicin may be used for prophylaxis to close contacts to patients with IMD.

Meningococci are classified into serological groups (A, B, C, W, X, Y, Z, and 29E) according to antigenic properties of the polysaccharide capsule. In Denmark, serogroups B and C are the most frequent ones in most years, although serogroup W was quite frequent in 2016 through 2019 and serogroup Y has been increasingly prevalent during 2022-2024. Vaccination against meningococci has never been part of the Danish childhood immunization programme but is used for prophylaxis to close contacts to patients with IMD. Specific vaccines exist for group B and combined vaccines for groups A, C, W, and Y.

This report presents data on antimicrobial resistance in non-duplicate invasive isolates (i.e. usually from blood, cerebrospinal fluid) submitted from the departments of clinical microbiology (DCMs) during 2012-2024 to the Neisseria and Streptococcus Reference laboratory (NSR). Isolates are received from all DCMs in Denmark. As of November 1, 2023, it became mandatory to submit isolates of meningococci, but the coverage rate until then was estimated to be 100% when compared to the mandatory clinical notification system. The two surveillance systems continuously supplement each other.

Figure 8.30 Number and serogroup of meningococcal isolates received during 2012-2024 DANMAP 2024

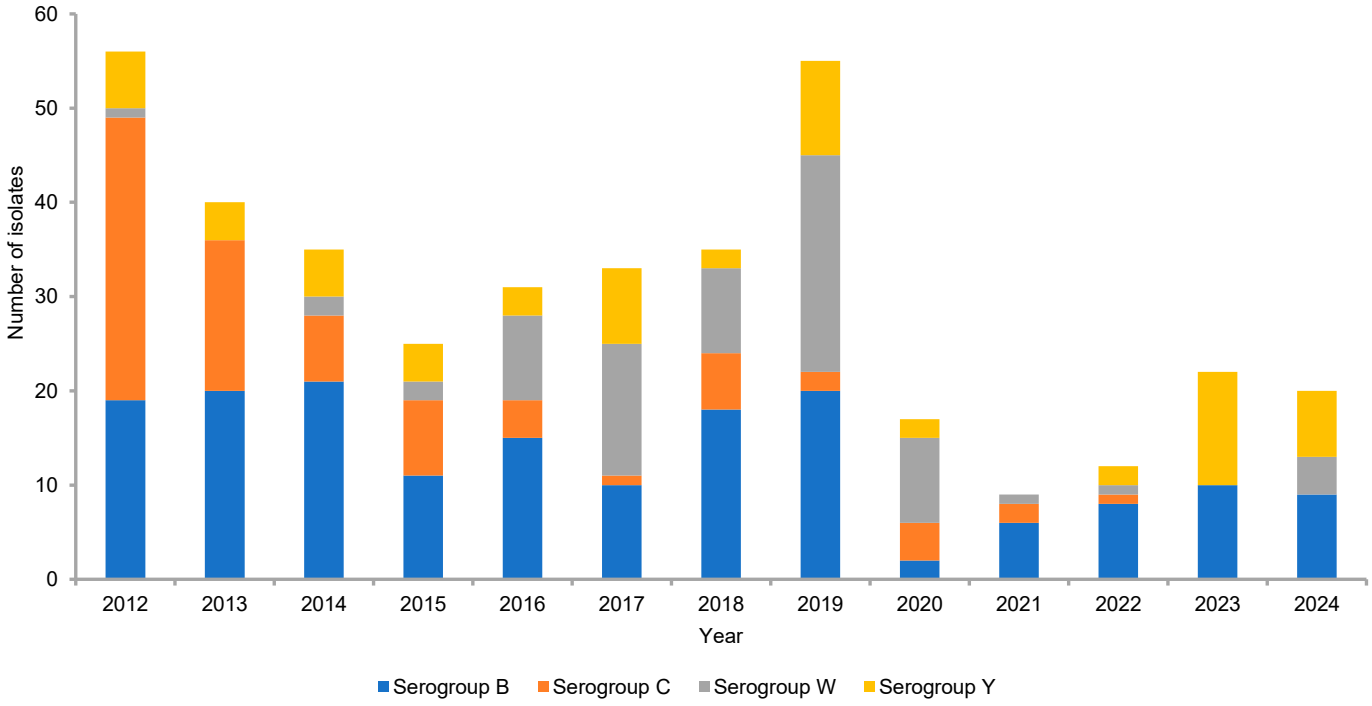


Figure 8.31 Distribution of ceftriaxone MIC values (mg/L) by serogroup of meningococcal isolates, 2012-2024 DANMAP 2024

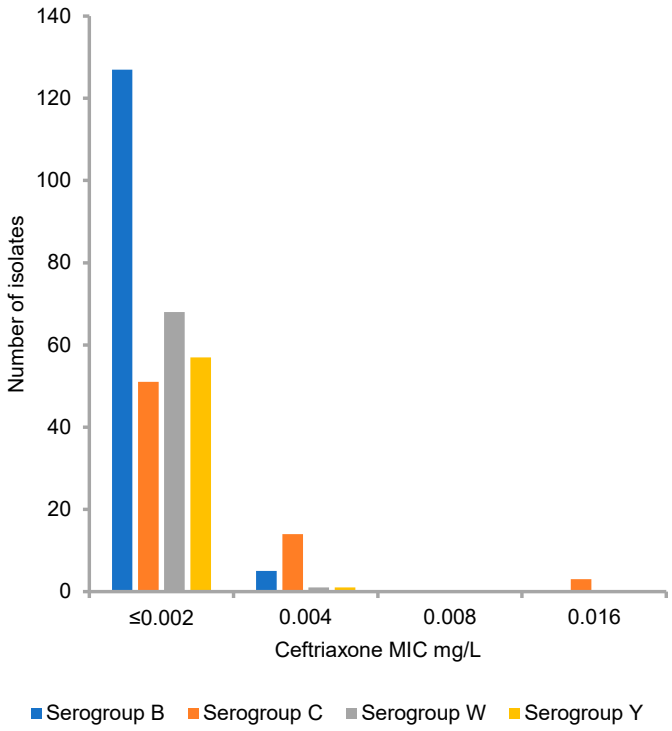
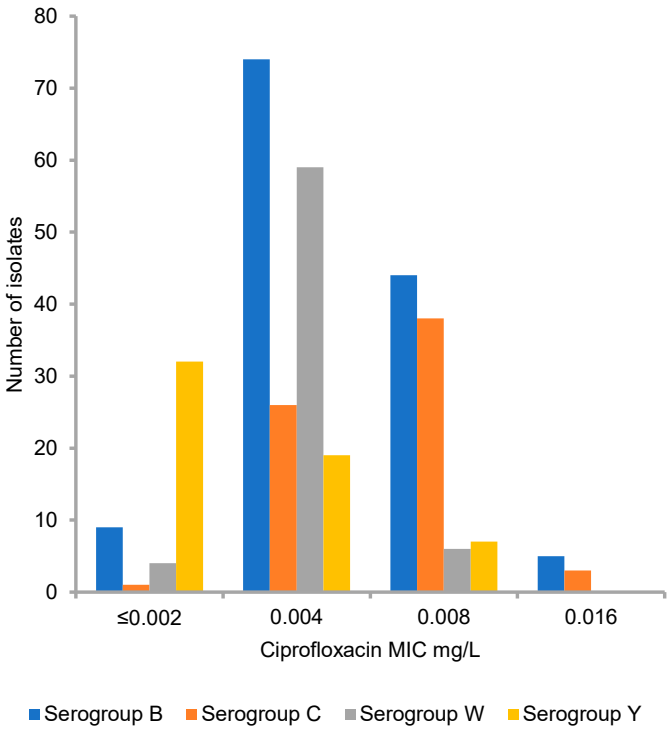


Figure 8.32 Distribution of ciprofloxacin MIC values (mg/L) by serogroup of meningococcal isolates, 2012-2024 DANMAP 2024



During the years 2012 through 2019, 18 to 52 isolates were received annually. In 2020, where restrictions to counteract the spread of COVID-19 were implemented, the number was 14, decreasing to 8 and 11, respectively, in 2021 and 2022. Figure 8.30 shows the number of isolates of groups B, C, W, and Y received during 2012-2024. Because of low numbers the following have been omitted: One isolate of group 29E (2017), three isolates of group X (2016, 2019 and 2023), and two isolates which were non-groupable (2019 and 2023). The susceptibility pattern of these six isolates did not show any specific deviations from the remaining findings and are therefore not further included in the present report.

All isolates were susceptible to ceftriaxone (MIC ≤0.125 mg/L), Figure 8.31.

All isolates were susceptible to ciprofloxacin (MIC ≤0.016 mg/L), Figure 8.32. Isolates of serogroup W (none in 2023 and 4 in 2024) and serogroup Y (11 in 2023 and 7 in 2024) tended to have slightly lower levels of ciprofloxacin MIC values than isolates of serogroup B and C.

Regarding rifampicin, only one (0.3%) of the isolates received during the study period was resistant (MIC ≤0.25 mg/L), Figure 8.34.

In total, 95% of the isolates during the study period were susceptible to penicillin (MIC ≤0.25 mg/L), Figure 8.33.

Figure 8.33 Distribution of penicillin MIC values (mg/L) by serogroup, 2012-2024 DANMAP 2024

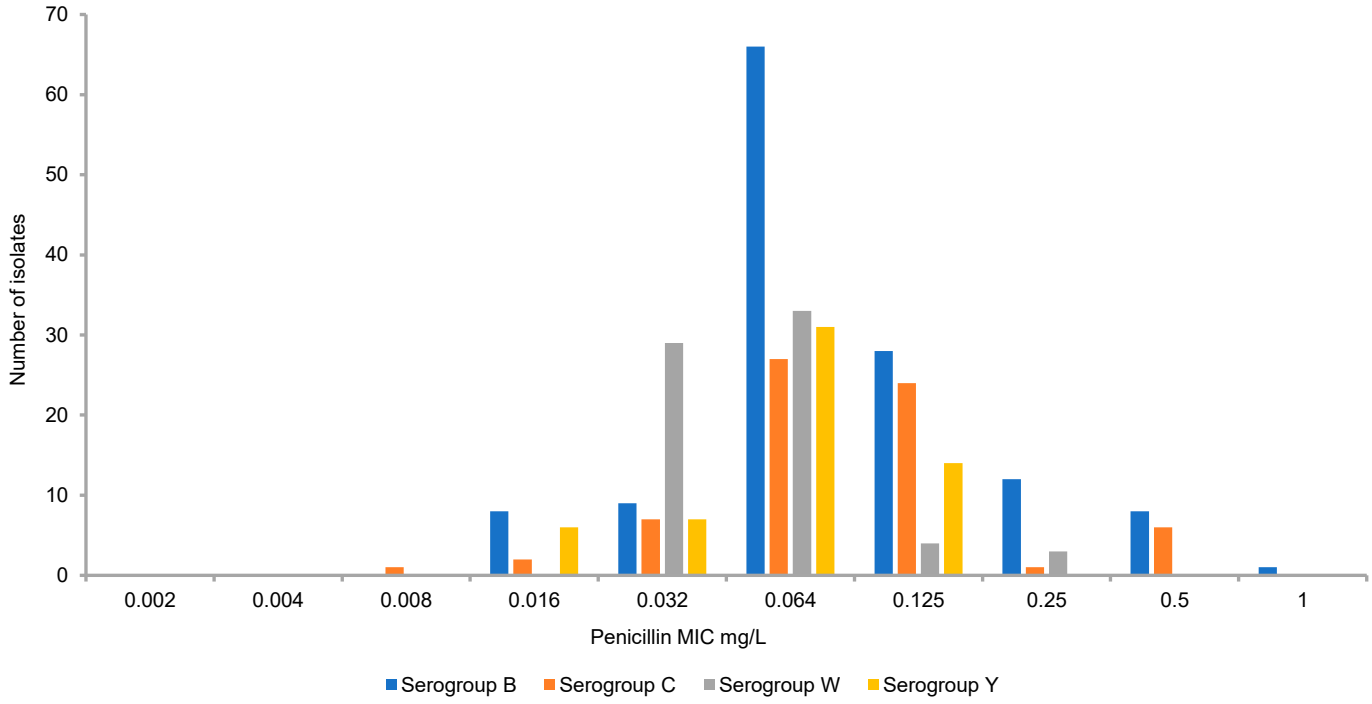


Figure 8.34 Distribution of rifampicin MIC values (mg/L) by serogroup, 2012-2024 DANMAP 2024

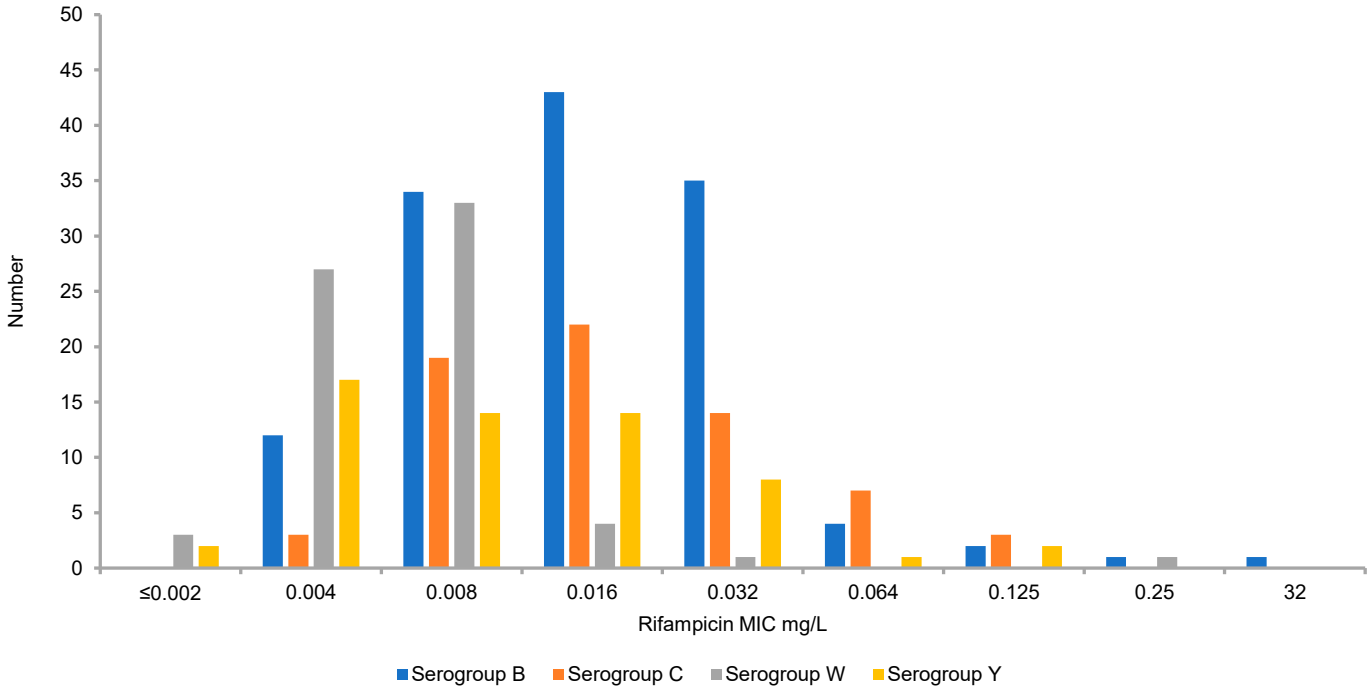


Table 8.31 Number of penicillin-resistant meningococcal isolates (MIC≥ 0.5 mg/L), serogroups B and C, 2013-2024 DANMAP 2024

	2013	2014	2016	2017	2018	2020	2022	2023	2024
Serogroup B	1	2	1	2			1	1	1
Serogroup C		1			2	3			

Only one isolate had an MIC value at 1 mg/L (serogroup B in 2024)

Nine isolates of serogroup B including one from each of the years 2022, 2023, and 2024, and six isolates of serogroup C were penicillin-resistant (MIC ≥0,5 mg/L), Table 8.33. Only one isolate had an MIC value at 1 mg/L (serogroup B in 2024).

Comments and conclusions

The substantial decrease of received meningococcal isolates during and following 2020 is most likely due to the social restrictions implemented in April 2020 because of COVID-19. Likewise, the modest increase during 2023 and also in 2024 probably represent the influence of the lifting of the restrictions which have enabled more respiratory transmission than during the preceding 2-3 years.

The antibiotic susceptibility patterns of meningococci do not reveal any imposing threats of resistance.

During the first six months of 2025 a total of 21 cases of IMD have been diagnosed in Denmark (not described in this report).

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Textbox 8.1

20 years of fungemia surveillance in Denmark (2004-2023)

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Fungaemia (blood stream infection with fungi) is most commonly caused by species currently or previously classified as *Candida*. Some of these have now formally been reclassified as other genera or species (e.g. *Candida glabrata* as *Nakaseomyces glabratus*, *Candida krusei* as *Pichia kudriavzevii* etc) meaning that only about 50% of "candidaemia" cases are due to *Candida* species if the novel taxonomy is adopted. For easy recognition we maintain the previously used *Candida* names and species groupings. *Candida* are part the human microflora. Most invasive infections are encountered in severely ill hospitalised patients and fungemia is associated with a significant overall mortality of ~40 percent in Denmark, necessitating prompt and correct treatment[1].

Denmark has had an active prospective voluntary surveillance since 2004, which in 2009 became nationwide with retrospective data retrieved from 2004-2009[2,3]. This has enabled a detailed surveillance of incidence rates, species distribution and acquired resistance patterns over 20-years[3]. Here we present new data from 2023 and patterns over the full period.

During 2023, a total of 573 isolates from 551 episodes and 509 individual patients were included. The incidence rate was 9.3 episodes/100,000 inhabitants and stable over the recent four years but consistently higher than other published European national surveys. The highest incidence rate groups are males aged >60 years and the peak incidence age has increased over time to ≥80 years (Figure 1). The reason for this is unclear but may reflect the longer lifetime and that more intensive treatment is offered to higher age groups.

The species distribution followed the pattern from previous years with a marked decrease in the percentage of the intrinsically susceptible species *C. albicans* (36% in 2023) concomitantly with an increase in the less susceptible species *C. glabrata* (33% in 2023) (Figure 2). This has been linked to the increase in azole use until 2014, with a high fluconazole use in the GP sector (figure 3). Furthermore, *C. auris* fungemia has been detected for the second time since 2021.

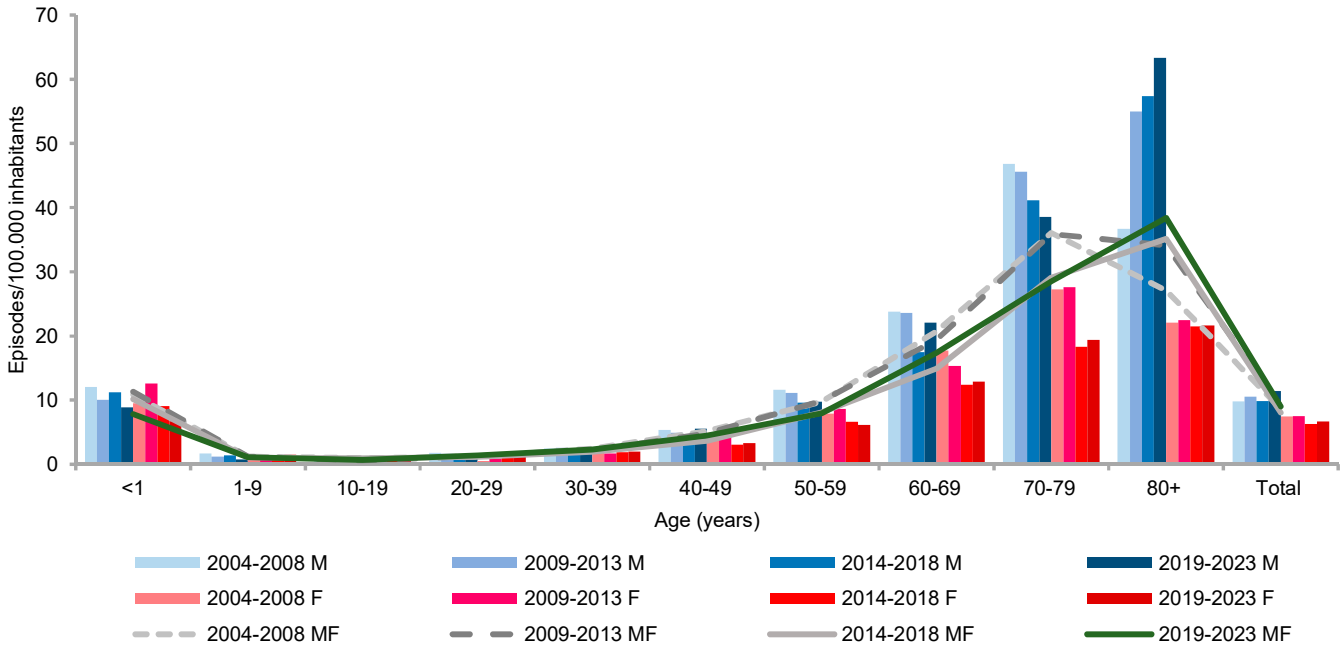
Mainly due to the increase in *C. glabrata*, the fluconazole susceptibility has decreased from 71% (2004-2009) to 57% (2023)[2]. During the past 3 years (2021-2023), acquired fluconazole resistance has been detected in 0%/2.3%/9%/5.7% in *C. albicans*, *C. dublinensis*, *C. glabrata*, *C. tropicalis*. For *C. parapsilosis* no fluconazole resistance (MIC >4 mg/L) was detected in 2021-2022 but high-level resistance was found in 2 out of 36 (5.6%) susceptibility tested isolates of *C. parapsilosis* in 2023, both harbouring ERG11 alterations associated with clonal hospital outbreaks in e.g. Southern and Middle Europe, Asia, North and South America. [4-6]. The amphotericin B coverage remains high at (1666/1688) 98.7%. Acquired echinocandin resistance remained low among intrinsically susceptible species (C. *albicans/dublinensis/glabrata/krusei/tropicalis*) during the years 2021-2023 (≤1% yearly for all species combined) whereas no acquired resistance was found in *C. parapsilosis*.

Conclusion

The nationwide surveillance has revealed a notable change in the species distribution towards the less susceptible species *C. glabrata*, which today is almost as common as *C. albicans* as cause of fungaemia. This may be linked to azole usage[7]. Despite an increase in echinocandin usage little resistance has emerged, securing our first line treatment for candidemia. It will be interesting to follow the echinocandin resistance rates during the forthcoming years when the once weekly dosed echinocandin rezafungin will allow outpatient use. The new species *C. auris* and azole resistant *C. parapsilosis* have both been detected in Denmark, emphasising the need for continued vigilance and screening of potentially colonized patients from countries with outbreaks or high endemicity to avoid hospital outbreaks.

continued ... Textbox 8.1

Figure 1 Incidence by patient age and gender across four 5-year periods DANMAP 2024



F: Females. M: Males. MF: All

Figure 2 Number of yearly isolates and species distribution in percentage over the years DANMAP 2024

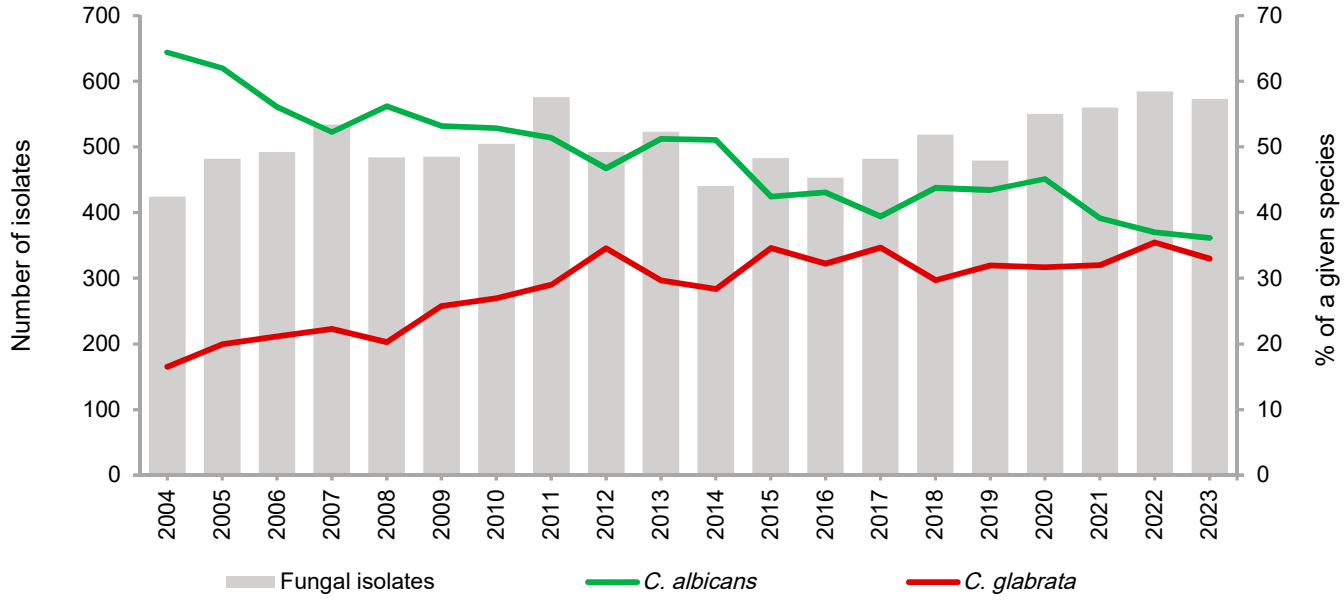
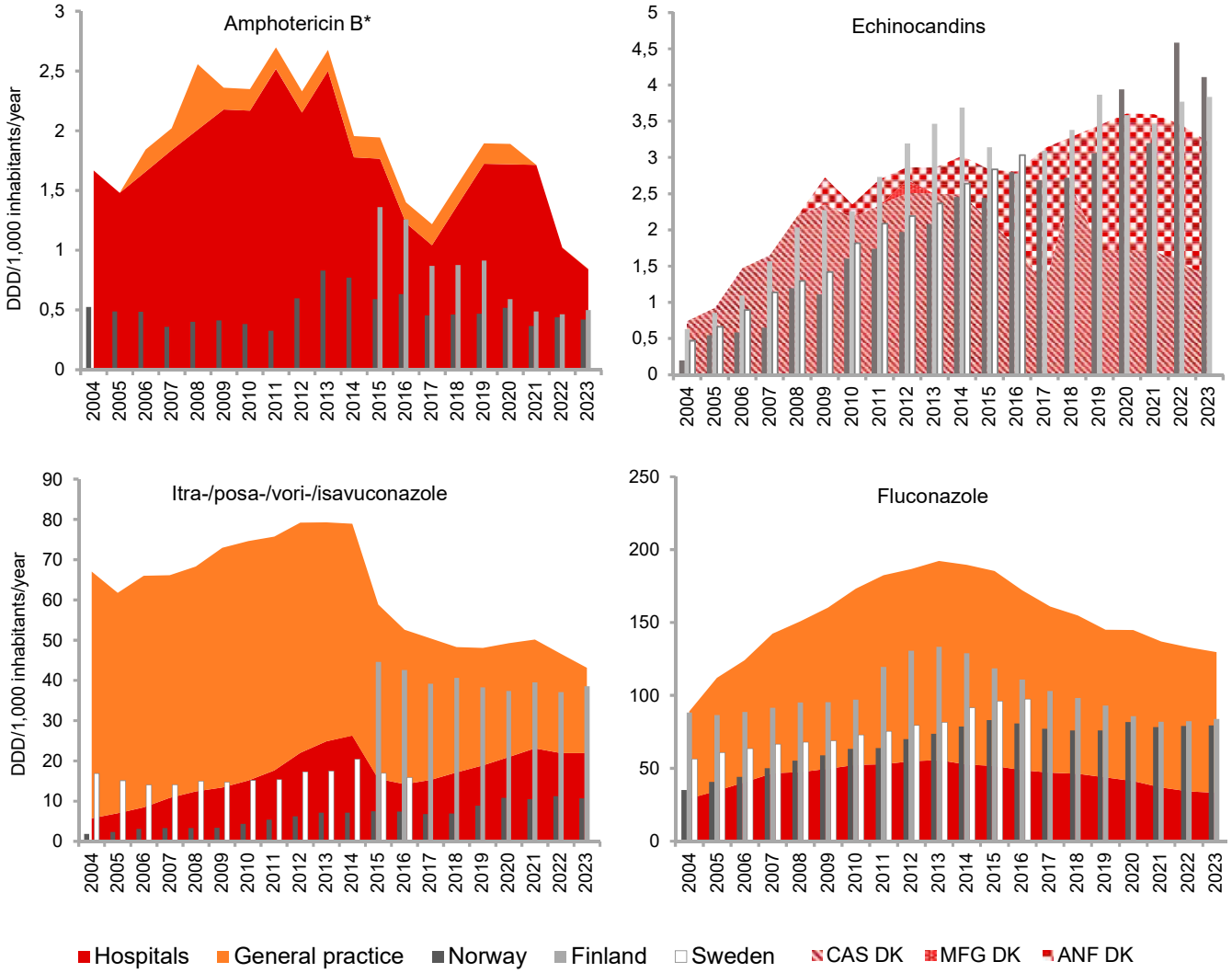


Figure 3 Systemic antifungal usage in the Nordic countries. Data for Denmark is shown for both primary sector (GP) and hospital use

DANMAP 2024



ANF: Anidulafungin. MFG: Micafungin. CAS: Caspofungin. *) Lipid formulations of amphotericin B have recently been assigned a separate, higher DDD from the conventional formulations due to a considerably higher dosage; updated DDDs used here. The figures above are based on own calculations based on data from Sundhedsdatastyrelsen (www.medstat.dk) and www.dst.dk, data from www.hfi.no (Norway) and www.fimea.fi (Finland) (provided via personal correspondence). Data from Sweden (www.socialstyrelse.se) not available after 2016. Updated amphotericin B DDDs not available from Sweden or Finland (prior to 2015). Part of the decline in hospital azole use after 2014 is caused by technical issues following a change in posaconazole DDDs and available formulations

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continued ... Textbox 8.1

[1] Lausch KR, Søgaard M, Rosenvinge FS, et al. High incidence of candidaemia in a nationwide cohort: Underlying diseases, risk factors and mortality. *Int J Infect Dis*. 2018;76:58-63. doi:10.1016/j.ijid.2018.08.010

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[3] Risum M, Astvad K, Johansen HK, et al. Update 2016–2018 of the Nationwide Danish Fungaemia Surveillance Study: Epidemiologic Changes in a 15-Year Perspective. *J Fungi*. 2021;7(6):491. doi:10.3390/jof7060491

[4] Daneshnia F, de Almeida Júnior JN, Ilkit M, et al. Worldwide emergence of fluconazole-resistant Candida parapsilosis: current framework and future research roadmap. *The Lancet Microbe*. 2023;4(6):e470-e480. doi:10.1016/S2666-5247(23)00067-8

[5] Brassington PJT, Klefisch FR, Graf B, et al. Genomic reconstruction of an azole-resistant Candida parapsilosis outbreak and the creation of a multi-locus sequence typing scheme: a retrospective observational and genomic epidemiology study. *The Lancet Microbe*. 2025;6(1):100949. doi:10.1016/j.lanmic.2024.07.012

[6] Misas E, Witt LS, Farley MM, et al. Molecular and Epidemiological Investigation of Fluconazole-resistant Candida parapsilosis - Georgia, United States, 2021. *Open Forum Infect Dis*. 2024;11(6):1-9. doi:10.1093/ofid/ofae264

[7] Astvad KMT, Johansen HK, Røder BL, et al. Update from a 12-Year Nationwide Fungemia Surveillance: Increasing Intrinsic and Acquired Resistance Causes Concern. Diekema DJ, ed. *J Clin Microbiol*. 2018;56(4):e01564-17. doi:10.1128/JCM.01564-17

Textbox 8.2

Azole resistance in clinical isolates of *A. fumigatus* - the first 5 years of surveillance

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Aspergillus can cause disease in vulnerable patients with decreased immune response or severely impacted lung function. The azoles are the most efficacious and the only orally available treatment options. Consequently, azole-resistance constitutes a clinical problem in the management of these patients[1]. Resistance can develop during long term patient treatment but has also been shown to emerge in the environment due to agri- and horticultural azole fungicide use. Such isolates have unique *cyp51A* target gene mutations, of which the most common ones involve TR_{34}/L98H and TR_{46}/Y121F/T289A ± other alterations in the Cyp51A protein [2]. As these isolates can cause infection in patients not previously treated and therefore not suspected of azole resistant infection, the mortality can be high unless promptly diagnosed and the patient treated with alternative drug classes[3]. Internationally it is recommended that alternative treatment should be used empirically, when the azole resistance rates exceeds 10%[4]. Denmark instituted a voluntary azole resistance surveillance in October 2018 with all clinical isolates of *A. fumigatus* being susceptibility tested using the EUCAST MIC or azole agar screening methods. Azole resistant isolates were *Cyp51A* sequenced [5]. Here we report new data from the fifth year (October 2022- September 2023) in a 5-year context.

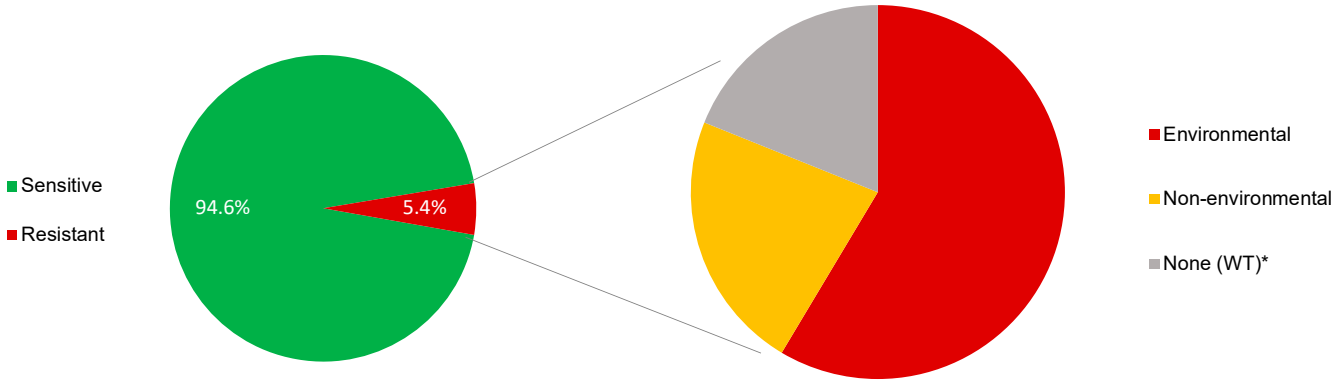
A total of 729 isolates from 588 patients were included during the 5th year, giving a total of 4184 isolates from 3131 patients over the 5 years. The majority of cultured isolates came from respiratory tract samples (85%; 3568/4184) or from ear samples (13%; 544/4184). The number of annual isolates decreased from 978 to 729 over the 5 years. The reason for this is unknown, but may involve changes in sampling during the COVID-19 period, local laboratory practises and advances in cystic fibrosis treatment resulting in decreased risk of airway infections. The amphotericin B coverage remained high (99.8%), whereas 5.9% (245/4184) of isolates displayed resistance to at least one azole, with resistance rates for the individual azoles ranging from 5.3%-5.5%. Based on sequencing of the *Cyp51A* target gene in isolates from patients with resistance (5.4%, 169/3131), more than half of the resistance (59%) was caused by environmental alternations, mainly TR_{34}/L98H, which is associated with pan-azole resistance (Figure 1). TR_{46}/Y121F/T289A was only detected in year 3 and 5. Almost half (43%) of patients with resistant isolates also had susceptible/*Cyp51A* wild-type isolates within the same year.

Conclusion

The overall resistance (5.9% of isolates) remained below the 10% mark. Environmental resistance, especially that caused by the TR_{34}/L98H mechanism associated with pan-azole resistance, is well established Denmark and is found in approximately 3.2% of culture-positive patients annually. A plethora of other alterations were detected in the remaining resistant isolates. No increase in resistance has been demonstrated over the last 5 years; however, much lower levels of resistance were found in a previous study from 2010-14[6]. TR_{46}/Y121F/T289A was detected only in the second half of the period, coinciding with the findings in the environment in 2021-2022 (but not 2020), together indicating that resistance may be slowly developing and continued resistance monitoring is important [7]. Finally, the diverse picture of patients harbouring both susceptible and resistant isolates underscores the need for susceptibility testing of all isolates as patients may be simultaneously or sequentially infected by multiple isolates, and a given treatment may not provide coverage for all.

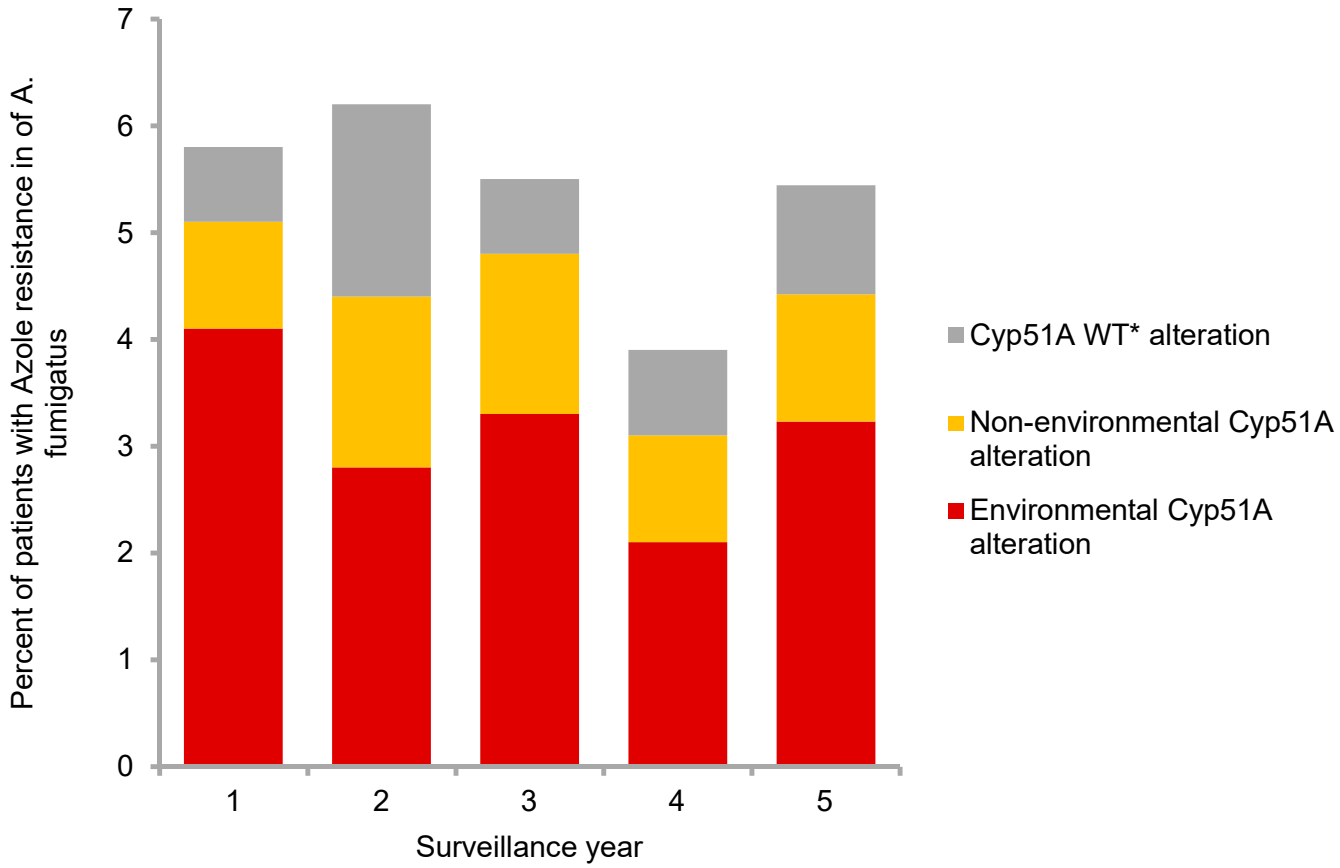
continued ... Textbox 8.2

Figure 1 The proportion of patients with susceptible or resistant isolates (left) and the associated Cyp51A alterations in the resistant isolates (right). Of note patients may harbour both resistant and susceptible isolates (not detailed here) DANMAP 2024



TR34/TR46 var.: Isolates with TR_{34}/L98H or TR_{46}/Y121F/T289A may also have additional alterations not detailed further here. R (WT)*: Resistant isolates that were Cyp51A wildtype or had Cyp51A alterations not uniformly associated with elevated azole MICs

Figure 2 The annual percentage of patients with resistant isolates and the proportion of environmental resistance mechanisms (TR_{34} or TR_{46}) compared to other resistance mechanisms DANMAP 2024



*) Cyp51A wildtype/with alterations not uniformly associated with elevated azole MICs

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Textbox 8.3

Mycoplasma genitalium

New *Mycoplasma genitalium* (MG) cases are defined similar to *Chlamydia trachomatis* (CT) cases by a timespan of at least 42 days since the last positive analysis result. The same case definition applies to negative results, with the exception that a positive case can start within the 42-day window of a negative case. The data presented here have been extracted from The Danish Microbiology Database (MiBa) in 2025.

In 2023, an increased number of positive cases were observed compared to 2022 (4,972 vs 4,343). This was a result of an increased number of tests performed, resulting in a lower positive rate (from 12.4% to 11.9%). In 2024 however, the number of positive cases was similar to 2022 (4,352 cases), and the positive rate continued to decrease compared to 2023 (11.6% vs 11.9%).

Treatment for MG in Denmark is based on the European guidelines described by the International Union against Sexually Transmitted Infections (IUSTI), backed by the WHO and ECDC. The guideline recommends that treatment for MG is guided by the detection of macrolide resistance mutations (MRM) due to high rates of macrolide resistance, globally and in Denmark. As seen in Figure 1, the macrolide resistance rate rose gradually from 50% in 2011 to 64.8% in 2024 in the Danish population.

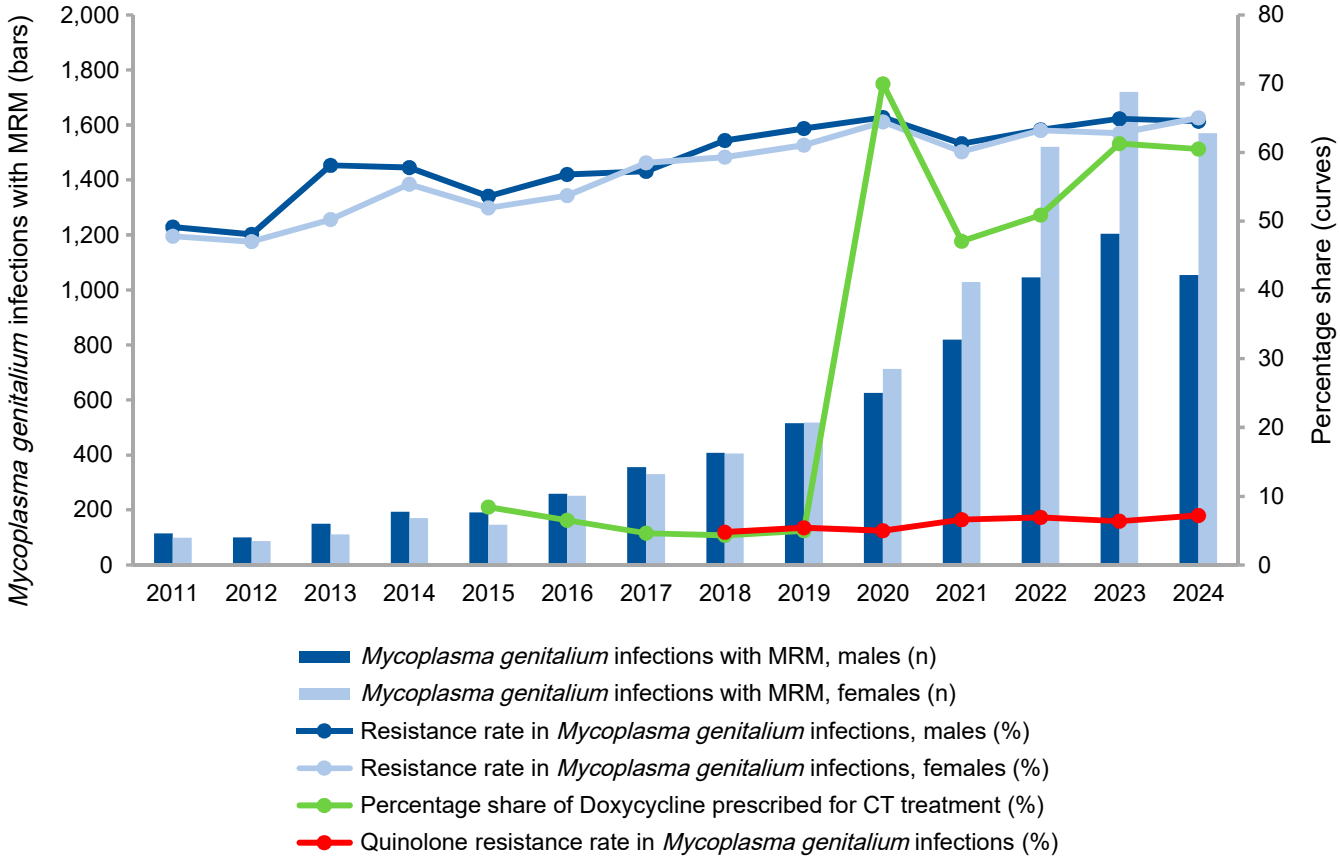
There is an increased awareness of the correlation between the treatment of CT with azithromycin and MRM in MG infections. Since 2019, SSI and international guidelines have recommended a change in first-line therapy for CT from azithromycin 1 g single dose to doxycycline 100 mg twice daily for 7 days. The purpose is to more effectively treat rectal CT infections, as well as decrease the selection of MRM in MG. This has led to a decline in azithromycin use and an increase in the use of doxycycline for the treatment of uncomplicated CT infections in Denmark (Figure 1). Data extracted from the Register of Pharmaceutical Sales indicate that the total number of azithromycin prescriptions issued for CT/MG infections dropped from 4.8 prescriptions per 1000 inhabitants in 2019 to 1.8 in 2024. Likewise, doxycycline for CT/ MG infections rose from 0.2 prescriptions per 1000 inhabitants in 2019 to 3 in 2024 (Figure 1). However, since the MRM rate continues to increase, a further reduction in the use of azithromycin for CT infections is desirable.

In a recent study by Drud, ST. *et al* (2025), resistance data from MG cases between 2014 and 2024 were extracted from MiBa and matched to a previous CT infection. Each MG case was categorized by the time since the latest CT infection: group 1: 15 - 365 days since latest CT infection, group 2: 366-1,095 days, control group: >1,095 days or no CT. Here, individuals in group 1 had the highest MRM rate of 76%, compared to 66% in group 2, and 56% in the control group. This pattern was observed across all years of the study period and confirms the association between MG MRM and CT treatment with azithromycin.

The recommended second-line treatment for MG is 400 mg moxifloxacin once daily (fluoroquinolone) for seven days. In cases where moxifloxacin treatment fails, detection of quinolone resistance-associated mutations (QRAM) is recommended to discriminate between reinfection and resistance. At Statens Serum Insitut, quinolone resistance rates are monitored by testing up to 500 randomly selected MG positive samples per year for QRAM. QRAM were detected in 4.8% (3 of 63) of samples in 2018 and in 7.2% (35 of 486) of samples in 2024, indicating a gradual increase in the resistance rate for quinolones in Denmark. Similarly, dual-class (macrolide and quinolone) resistance rates increased from 1.6% in 2019 to 7.7% in 2024.

In the absence of suitable and efficient third-line treatments for MG it is recommended to strengthen diagnostic stewardship aiming at limiting testing for MG in symptomatic individuals, and to reduce the use of azithromycin to treat CT.

Figure 1 Number of *Mycoplasma genitalium* infections (n) with macrolide resistance mutations (bars), percentage of macrolide resistance mutations, percentage of quinolone resistance-associated mutations and percentage share of Doxycycline prescriptions prescribed for *Chlamydia trachomatis* Infections, Denmark, 2011-2024 DANMAP 2024



MRM = Macrolide resistance mutations
CT = *Chlamydia trachomatis*

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9

RESISTANCE IN ANIMAL PATHOGENS

9. Resistance in animal pathogens

Highlights

Surveillance of antimicrobial resistance in 2024 focused on pathogenic bacteria from acute mastitis in dairy cows and from various organs in pigs and included results obtained through antimicrobial susceptibility testing.

Most pathogenic bacteria from **acute mastitis in dairy cows** displayed low frequencies of phenotypic resistance. A relatively high proportion of *Streptococcus uberis* isolates displayed resistance to penicillin, which is noteworthy because beta-lactamase sensitive penicillins are the most commonly used drugs for treatment of adult cattle in Denmark. However, there is currently no clinical breakpoint available for penicillin in *S. uberis* and most of the isolates had a MIC value of 0.25mg/L, which is just above the tentative ECOFF of 0.12 mg/L. Thus, it remains unclear whether penicillin is active against these borderline resistant *S. uberis* isolates.

Most **pathogenic bacteria isolated from pigs** in 2024 displayed similar frequencies of phenotypic resistance as in 2023 (1-year period) and 2019 (5-year period). However, six pathogen-drug combinations were associated with significantly increased resistance, whereas three were associated with significantly decreased resistance. The increased frequency of neomycin resistance in haemolytic *Escherichia coli* is worrisome because it is one of only a few drugs recommended in Denmark as first choice for treating *E. coli*-associated post-weaning diarrhoea. The increased frequency of gentamicin resistance in haemolytic *E. coli* is also worrisome because it is considered critically important for human medicine by the World Health Organization. It should also be noted that haemolytic *E. coli* displayed increased resistance to 3rd generation cephalosporins (cefpodoxime), from 4.7% in 2023 to 8.2% in 2024, although this change was nonsignificant.

9.1 Introduction

Surveillance of antimicrobial resistance in 2024 focused on pathogenic bacteria from mastitis in dairy cows and from various organs in pigs and included results obtained through antimicrobial susceptibility testing (AST).

9.2 Acute mastitis in dairy cows

9.2.1 Background

Milk samples for routine diagnosis of clinical mastitis in dairy cows are normally collected by and tested at the local veterinary clinics throughout Denmark. As part of the testing, veterinarians identify common pathogens using simple culture techniques and bacterial identification methods and sometimes perform AST to decide on therapeutic options. Normally, the samples and isolates are discarded after analysis. To establish a future-proof surveillance program for mastitis pathogens, we set up a diagnostic laboratory at Statens Serum Institut and asked veterinarians specialised in cattle to collect milk samples from dairy cows with acute mastitis. In total, 487 milk samples were collected by 15 veterinary clinics across Denmark during 2024. Isolates were identified to the genus or species level using MALDI-TOF. AST data were based on epidemiological cut-offs (ECOFFs) and clinical breakpoints when ECOFFs were unavailable (https://www.vetssi.dk/).

9.2.2 Results

Among the 487 milk samples tested, 82.5% were positive for one or more pathogenic bacteria, while the remaining milk samples were interpreted as negative, either because of lack of growth or unspecific growth. In total, 462 isolates were recovered, of which 85.9% belonged to well-known mastitis pathogens: *Streptococcus uberis* (27.5%), *Escherichia coli* (20.1%), *Staphylococcus aureus* (13.4%), *Streptococcus dysgalactiae* (10.8%), coagulase-negative staphylococci (CoNS) (5.4%), *Trueperella pyogenes* (3.2%), *Streptococcus agalactiae* (2.8%) and *Klebsiella pneumoniae* (2.6%). In addition, we identified a number of bacterial species and yeasts found in less than 2% of the milk samples. Table 9.1 provides an overview of the identified pathogenic bacteria.

AST was performed on 376 bacterial isolates representing well-known mastitis pathogens (Table 9.1). *T. pyogenes* isolates were not tested due to their relatively slow growth and specific methodological requirements for AST. Table 9.2 shows the frequencies of resistant isolates in 2024.

Among streptococci, we observed that 19.7% of the *S. uberis* isolates and 9.1% of the *S. agalactiae* isolates displayed resistance to penicillin. It should be noted, however, that most of these isolates had a MIC value of 0.25mg/L, which is just above the tentative ECOFF for *S. uberis* isolates and the ECOFF for *S. agalactiae* (both 0.12 mg/L). Tetracycline resistance was observed in 19.7% of the *S. uberis* and 14.0% of the *S. dysgalactiae* isolates. Tetracycline resistance was also found in 81.8% of the *S. agalactiae* isolates, which is consistent with a high prevalence of tetracycline resistance genes in this bacterial species (Da Cuna et al. Nat Commun. 2014 Aug 4;5:4544. doi: 10.1038/ncomms5544). Moreover, 18.2% of the *S. agalactiae* isolates were resistant to erythromycin, while 9.1% were resistant to chloramphenicol and clindamycin.

The relatively high frequency of borderline resistance to penicillin in *S. uberis* is particularly noteworthy because beta-lactamase sensitive penicillins are the most commonly used drugs for treatment of adult cattle in Denmark (Table 4.1).

Among staphylococci, we found that 12.0% of the CoNS and 4.8% of the *S. aureus* isolates were resistant to penicillin.

We observed that 10.1-13.5% of the *E. coli* isolates were resistant to ampicillin, sulfamethoxazole, tetracycline and trimethoprim. A single *E. coli* isolate displayed an extended-spectrum β-lactamase (ESBL) phenotype and was resistant to multiple drugs, including ampicillin, cefotaxime, ceftazidime, chloramphenicol, ciprofloxacin, nalidixic acid, sulphamethoxazole, tetracycline and trimethoprim. Due to the ESBL phenotype (resistance to cefotaxime and ceftazidime), this isolate was further analysed with extra disk diffusion tests and subjected to whole genome sequencing, which confirmed the ESBL phenotype and showed that it belongs to multilocus sequence type 46 and carries $bla_{\text{CTX-M-15}}$.

Finally, 16.7% and 8.3% of the *K. pneumoniae* isolates were resistant to tetracycline and trimethoprim, respectively. In addition, 91.7% of the *K. pneumoniae* isolates were resistant to ampicillin, reflecting that this bacterial species is intrinsically resistant to penicillins.

The remaining pathogenic bacteria from acute mastitis in dairy cows displayed low frequencies of phenotypic resistance (0.0-4.7%).

Table 9.1 Pathogenic bacteria from acute mastitis in dairy cows, Denmark, 2024 DANMAP 2024

Taxon	Culture		AST
	n	%	n
Streptococcus uberis	127	27.5%	127
Escherichia coli	93	20.1%	89
Staphylococcus aureus	62	13.4%	62
Streptococcus dysgalactiae	50	10.8%	50
Coagulase-negative staphylococci	25	5.4%	25
Trueperella pyogenes	15	3.2%	ND
Streptococcus agalactiae	13	2.8%	11
Klebsiella pneumoniae	12	2.6%	12
Coagulase-negative staphylococci in mixed cultures	8	1.7%	ND
Lactococcus garviae	7	1.5%	ND
Enterococcus faecium	4	0.9%	ND
Lactococcus lactis	4	0.9%	ND
Pseudomonas spp.	4	0.9%	ND
Serratia liquefaciens	4	0.9%	ND
Streptococcus spp.	4	0.9%	ND
Enterococcus faecalis	3	0.6%	ND
Helcococcus ovis	3	0.6%	ND
Pantoea agglomerans	3	0.6%	ND
Corynebacterium bovis	2	0.4%	ND
Enterococcus cecorum	2	0.4%	ND
Streptococcus parauberis	2	0.4%	ND
Aerococcus viridans	1	0.2%	ND
Bacillus licheniformis	1	0.2%	ND
Enterococcus spp.	1	0.2%	ND
Helcococcus kunzii	1	0.2%	ND
Lysinibacillus sphaericus	1	0.2%	ND
Mannheimia spp.	1	0.2%	ND
Mycobacterium smegmatis	1	0.2%	ND
Pseudomonas aeruginosa	1	0.2%	ND
Raoultella planticola	1	0.2%	ND
Serratia plymuthica	1	0.2%	ND
Serratia rubidea	1	0.2%	ND
Serratia spp.	1	0.2%	ND
Streptococcus canis	1	0.2%	ND
Streptococcus equinus	1	0.2%	ND
Streptococcus gallolyticus	1	0.2%	ND

Isolates were identified to the genus or species level using MALDI-TOF
Abbreviations: AST, antimicrobial susceptibility testing

Table 9.2 Phenotypic antimicrobial resistance among pathogenic bacteria from acute mastitis in dairy cows, Denmark, 2024

DANMAP 2024

Antimicrobial agent	Ec (n=89)	Kp (n=12)	Sau (n=62)	CoNS (n=25)	Sag (n=11)	Sd (n=50)	Su (n=127)
	R (%)	R (%)	R (%)	R (%)	R (%)	R (%)	R (%)
Amikacin	0.0%	0.0%*	ND	ND	ND	ND	ND
Ampicillin	13.5%	91.7%*	ND	ND	ND	ND	ND
Azithromycin	1.1%	ND	ND	ND	ND	ND	ND
Cefotaxime	1.1%	0.0%*	ND	ND	ND	ND	ND
Cefoxitin	ND	ND	0.0%	ND	ND	ND	ND
Ceftazidime	1.1%	0.0%*	ND	ND	ND	ND	ND
Chloramphenicol	1.1%	0.0%*	0.0%	4.0%	9.1%*	0.0%	0.0%
Clindamycin	ND	ND	0.0%	ND	9.1%*	0.0%	3.1%
Ciprofloxacin	1.1%	0.0%*	0.0%	ND	0.0%*	ND	ND
Colistin	0.0%	0.0%*	ND	ND	ND	ND	ND
Erythromycin	ND	ND	0.0%	4.0%	18.2%*	4.0%	4.7%
Fusidate	ND	ND	0.0%	ND	ND	ND	ND
Gentamicin	0.0%	0.0%*	0.0%	0.0%	0.0%*	ND	ND
Kanamycin	ND	ND	0.0%	ND	ND	ND	ND
Linezolid	ND	ND	0.0%	0.0%	0.0%*	ND	ND
Meropenem	0.0%	0.0%*	ND	ND	ND	ND	ND
Mupirocin	ND	ND	0.0%	ND	ND	ND	ND
Nalidixic acid	2.2%	ND	ND	ND	ND	ND	ND
Penicillin	ND	ND	4.8%	12.0%	9.1%*	ND	19.7%
Quinopristin/dalfopristin	ND	ND	0.0%	ND	ND	ND	ND
Rifampin	ND	ND	0.0%	0.0%	ND	ND	ND
Streptomycin	ND	ND	0.0%	ND	ND	ND	ND
Sufamethoxazole	12.4%	ND	ND	ND	ND	ND	ND
Tetracycline	10.1%	16.7%*	0.0%	0.0%	81.8%*	14.0%	19.7%
Tiamulin	ND	ND	0.0%	ND	ND	ND	ND
Tigecycline	0.0%	0.0%*	ND	ND	ND	ND	ND
Trimethoprim	11.2%	8.3%*	0.0%	ND	ND	ND	ND
Vancomycin	ND	ND	0.0%	0.0%	0.0%*	0.0%	0.0%

Data were based on epidemiological cut-offs (ECOFFs) or clinical breakpoints when ECOFFs were unavailable (https://www.vetssi.dk/)
Percentages based on small sample sizes (n<20) are indicated by asterices and should be interpreted with caution
Abbreviations: Ec, *Escherichia coli*; Kp, *Klebsiella pneumoniae*; Sau, *Staphylococcus aureus*; CoNS, coagulase-negative staphylococci; Sag, *Streptococcus agalactiae*; Sd, *Streptococcus dysgalactiae*; Su, *Streptococcus uberis*; R, resistant; ND, not determined

9.3 Pathogenic bacteria from pigs

9.3.1 Background

The Veterinary Laboratory, The Danish Agriculture and Food Council, performed AST of isolates belonging to *Actinobacillus pleuropneumoniae*, *Bordetella bronchiseptica*, haemolytic and non-haemolytic *Escherichia coli*, *Klebsiella pneumoniae*, *Salmonella enterica*, *Staphylococcus hyicus* and *Streptococcus suis*. Table 9.3 shows the frequencies of resistant isolates in 2024, while all results from 2016-2024 can be found on DK-VET's homepage (https://www.vetssi.dk/). AST data were based on epidemiological cut-offs (ECOFFs) and clinical breakpoints when ECOFFs are unavailable (https://www.vetssi.dk/).

9.3.2 Results

Most pathogenic bacteria isolated from pigs in 2024 displayed similar frequencies of phenotypic resistance as in 2023 (1-year period) and 2019 (5-year period). However, six pathogen-drug combinations were associated with significantly increased resistance, whereas three were associated with significantly decreased resistance. Table 9.4 and Figure 9.1 show all significant changes in phenotypic resistance over a 1-year period (2024 vs. 2023) and a 5-year period (2024 vs. 2019).

Haemolytic *E. coli* from pigs displayed significantly increased resistance to amoxicillin-clavulanic acid (2024 vs. 2023 and 2024 vs. 2019), florfenicol (2024 vs. 2019), gentamicin (2024 vs. 2023 and 2024 vs. 2019), neomycin (2024 vs. 2019) and spectinomycin (2024 vs. 2019).

Table 9.3 Phenotypic antimicrobial resistance among pathogenic bacteria from pigs, Denmark, 2024 DANMAP 2024

Antimicrobial agent	Ap (n=78)	Bb (n=35)	H-Ec (n=246)	NH-Ec (n=177)	Kp (n=18)	Se (n=32)	Sh (n=7)	Ss (n=106)
	R (%)	R (%)	R (%)	R (%)	R (%)	R (%)	R (%)	R (%)
Amoxicillin	0.0%	ND	74.4%	78.0%	ND	84.4%	85.7%*	ND
Amoxicillin-clavulanic acid	ND	ND	22.4%	23.9%	11.1%*	6.3%	ND	ND
Cefpodoxime	ND	ND	8.2%	3.4%	ND	ND	ND	ND
Cefquinome	ND	ND	ND	ND	0.0%*	ND	ND	ND
Ceftiofur	0.0%	ND	ND	ND	ND	ND	ND	ND
Colistin	ND	ND	0.0%	0.0%	0.0%*	ND	ND	ND
Doxycyclin	0.0%	ND	74.0%	63.8%	33.3%*	81.3%	ND	34.9%
Enrofloxacin	1.3%	ND	13.8%	6.8%	ND	ND	0.0%*	0.0%
Florfenicol	0.0%	0.0%	23.6%	22.0%	16.7%*	12.5%	14.3%*	0.0%
Gentamicin	ND	ND	46.5%	14.8%	11.1%*	18.8%	ND	ND
Lincomycin	ND	ND	ND	ND	ND	ND	85.7%*	ND
Neomycin	ND	ND	60.0%	19.3%	16.7%*	ND	ND	ND
Penicillin	0.0%	ND	ND	ND	ND	ND	100.0%*	0.9%
Spectinomycin	ND	ND	66.9%	44.9%	ND	59.4%	ND	ND
Streptomycin	ND	ND	82.1%	79.1%	ND	90.6%	ND	ND
Tetracycline	ND	ND	75.5%	63.6%	33.3%*	81.3%	ND	ND
Tiamulin	0.0%	ND	ND	ND	ND	ND	28.6%*	ND
Tildipirosin	0.0%	0.0%	ND	ND	ND	ND	ND	ND
Tilmicosin	0.0%	ND	ND	ND	ND	ND	85.7%*	ND
Trimethoprim-sulfamethoxazole	0.0%	ND	62.6%	65.0%	50.0%*	43.8%	42.9%*	13.2%
Tulathromycin	3.8%	2.9%	ND	ND	ND	ND	ND	ND
Tylosin	ND	ND	ND	ND	ND	ND	85.7%*	ND

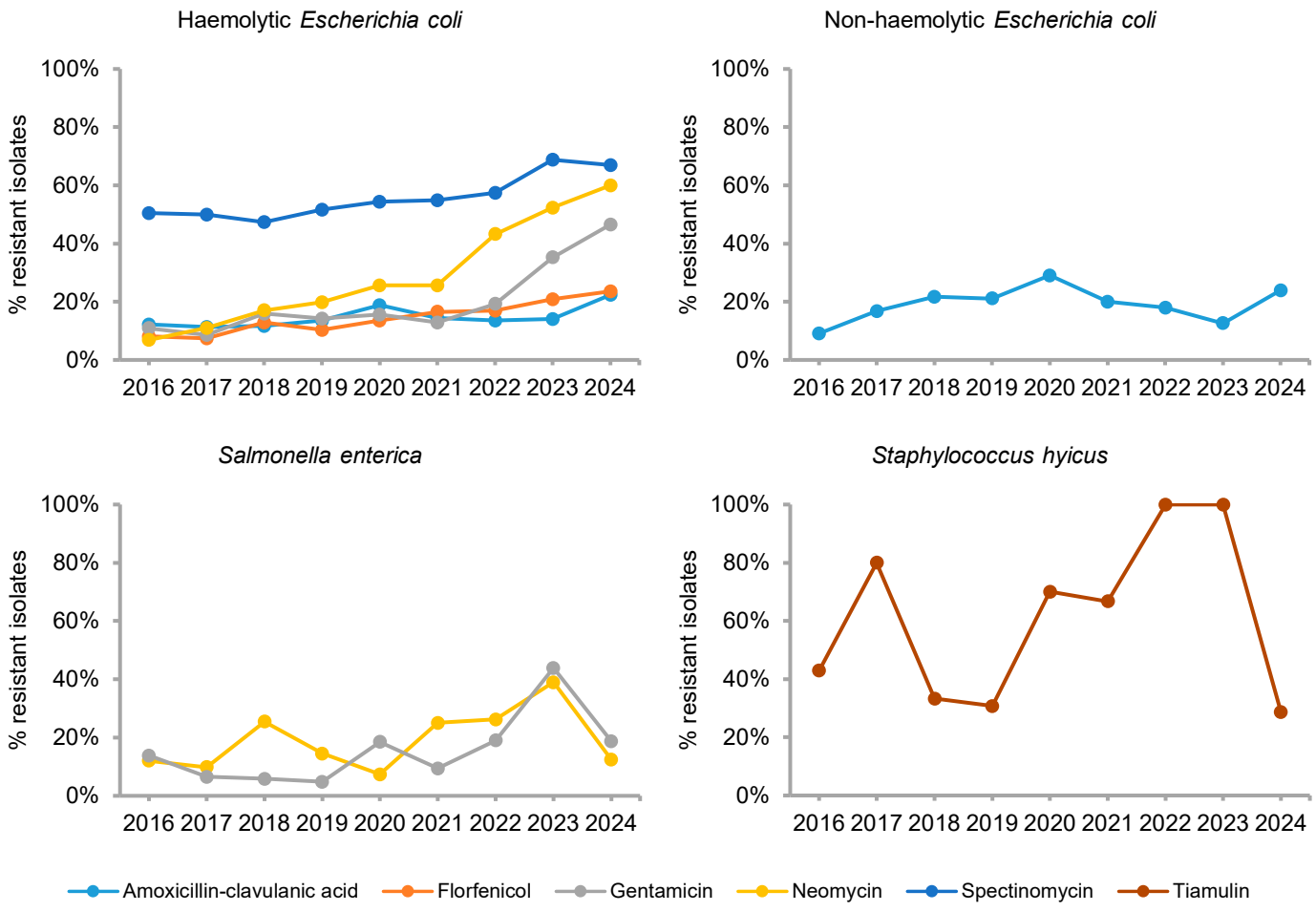
Data were based on epidemiological cut-offs (ECOFFs) or clinical breakpoints when ECOFFs were unavailable (https://www.vetssi.dk/)
Percentages based on small sample sizes (n<20) are indicated by asterices and should be interpreted with caution
Abbreviations: Ap, *Actinobacillus pleuropneumoniae*; Bb, *Bordetella bronchiseptica*; H-Ec, haemolytic *Escherichia coli*; NH-Ec, non-haemolytic *Escherichia coli*; Kp, *Klebsiella pneumoniae*; Se, *Salmonella enterica*; Sh, *Staphylococcus hyicus*; Ss, *Streptococcus suis*; R, resistant; ND, not determined

Table 9.4 Statistically significant temporal changes in antimicrobial resistance phenotypes among pathogenic bacteria from pigs, Denmark, 2024 vs. 2023 and 2024 vs. 2019 DANMAP 2024

Patho-gen	Antimicrobial agent	2016 R (%)	2017 R (%)	2018 R (%)	2019 R (%)	2020 R (%)	2021 R (%)	2022 R (%)	2023 R (%)	2024 R (%)	2024 vs. 2023 Trend (p value)	2024 vs. 2019 Trend (p value)
H-Ec	Amoxicillin-clavulanic acid	12.1%	11.3%	11.7%	13.5%	18.8%	14.5%	13.5%	14.1%	22.4%	↗ (0.0134)	↗ (0.0103)
H-Ec	Florfenicol	8.1%	7.4%	12.9%	10.3%	13.6%	16.5%	16.9%	20.8%	23.6%	→ (0.4678)	↗ (0.0001)
H-Ec	Gentamicin	10.9%	8.6%	15.9%	14.3%	15.6%	12.8%	19.3%	35.2%	46.5%	↗ (0.0084)	↗ (0.0000)
H-Ec	Neomycin	6.9%	10.9%	17.0%	19.8%	25.6%	25.6%	43.2%	52.3%	60.0%	→ (0.0826)	↗ (0.0000)
H-Ec	Spectinomycin	50.5%	50.0%	47.3%	51.6%	54.4%	55.0%	57.4%	68.8%	66.9%	→ (0.6455)	↗ (0.0005)
NH-Ec	Amoxicillin-clavulanic acid	9.1%	16.8%	21.7%	21.1%	29.1%	20.0%	18.0%	12.6%	23.9%	↗ (0.0063)	→ (0.5357)
Se	Florfenicol	12.1%	9.8%	25.5%	14.5%	7.4%	25.0%	26.2%	39.0%	12.5%	↘ (0.0167)	→ (1.0000)
Se	Gentamicin	13.8%	6.6%	5.9%	4.8%	18.5%	9.4%	19.0%	43.9%	18.8%	↘ (0.0267)	→ (0.0579)
Sh	Tiamulin	42.9%*	80.0%*	33.3%*	30.8%*	70.0%*	66.7%*	100.0%*	100.0%*	28.6%*	↘ (0.0070)	→ (1.0000)

Antimicrobial resistance phenotypes that remained at the same level during 2023-2024 and 2019-2024 were excluded (https://www.vetssi.dk/)
Percentages based on small sample sizes (n<20) are indicated by asterices and should be interpreted with caution
Abbreviations: H-Ec, haemolytic *Escherichia coli*; NH-Ec, non-haemolytic *Escherichia coli*; Se, *Salmonella enterica*; Sh, *Staphylococcus hyicus*; R, resistant

Figure 9.1 Statistically significant temporal changes in antimicrobial resistance phenotypes among pathogenic bacteria from pigs, Denmark, 2016-2024 DANMAP 2024



The percentages of tiamulin-resistant *Staphylococcus hyicus* isolates are based on small sample sizes (n<20) and should therefore be interpreted with caution

The increased frequency of neomycin resistance in haemolytic *E. coli* (60.0%) is worrisome because it is one of only a few drugs recommended in Denmark as first choice for treating *E. coli*-associated post-weaning diarrhoea. Furthermore, haemolytic *E. coli* also displayed medium to high frequencies of resistance to the other first-choice drugs, including amoxicillin-clavulanic acid (22.4%), spectinomycin (66.9%), trimethoprim-sulfamethoxazole (62.6%) and streptomycin (82.1%). *E. coli* isolates from 2023 and 2024 were not tested for susceptibility to the remaining first-choice drug ampicillin, but it should be noted that we observed a high frequency of ampicillin resistance in haemolytic *E. coli* from 2022 (60.9%) (DANMAP 2022). The rapid increase in neomycin resistance coincided with increased use of neomycin in weaners (DANMAP 2023) following two recent decisions to restrict the use of alternative drugs in pigs: 1) the Danish Yellow Card initiative to reduce the use of colistin in 2016 and 2) the European Union-wide ban of medicinal zinc in 2022.

The increasing frequency of gentamicin resistance in haemolytic *E. coli* (46.5%) is also worrisome because it is considered critically important for human medicine by the World Health Organization. We have previously shown that most of the gentamicin resistance genes found in haemolytic *E. coli* also confer resistance to apramycin, which is increasingly used in weaners (DANMAP 2023). In contrast, the use of gentamicin in pigs is negligible and cannot explain the rapidly increasing resistance to this drug (DANMAP 2023). Together, these observations suggest a causal relationship between increased use of apramycin and increased resistance to gentamicin in haemolytic *E. coli*.

It should also be noted that haemolytic *E. coli* displayed increased resistance to 3rd generation cephalosporins (cefpodoxime), from 4.7% in 2023 to 8.2% in 2024, although this change was nonsignificant.

Non-haemolytic *E. coli* displayed significantly increased resistance to amoxicillin-clavulanic acid (2024 vs. 2023). In addition, *S. enterica* displayed significantly decreased resistance to florfenicol (2024 vs. 2023) and gentamicin (2024 vs. 2023), while *S. hyicus* displayed significantly decreased resistance to tiamulin (2024 vs. 2023). However, the results for *S. hyicus* are based on <20 isolates and should be interpreted with caution.

9.4 Conclusions and perspectives

Pathogenic bacteria from acute mastitis in dairy cows generally displayed low frequencies of phenotypic resistance.

The increasing frequency of neomycin, gentamicin and cefpodoxime resistance in haemolytic *E. coli* from pigs is worrisome and should be monitored closely in the coming years.

Interpretation of resistance to antimicrobial agents of veterinary importance are often based on tentative ECOFFs and ECOFFs as animal-specific clinical breakpoints for many drugs are currently lacking (e.g., penicillin resistance in *S. uberis* and neomycin resistance in *E. coli*). ECOFFs are based on microbiological studies and do not necessarily indicate whether a drug will be clinically active. Future studies should therefore seek to establish clinical breakpoints in animals by considering what happens to the drug within a specific animal and body site (pharmacokinetics).

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Textbox 9.1

Antimicrobial resistance in clinical isolates from dogs and cats

In Denmark, reports on antimicrobial resistance in canine and feline pathogens have been published sporadically over the years, last time in DANMAP 2022. Susceptibility results have been reported for *Escherichia coli* and *Staphylococcus pseudintermedius*, which are the most frequently isolated bacterial pathogens of companion animals and the primary causes of urinary tract and skin infections, respectively. These species can have important resistant and multidrug-resistant phenotypes. Of particular concern are methicillin-resistant *S. pseudintermedius* (MRSP) and extended-spectrum cephalosporinase- (ESC) producing *E. coli*, which have emerged worldwide in the last two decades and constitute a threat to animal health, as they are well-known nosocomial pathogens that are resistant to all veterinary-licensed beta-lactams and commonly, other antibiotic classes too [1]. *E. coli* and to a lesser extent *S. pseudintermedius* are also pathogens of public health relevance due to the risk of zoonotic transmission.

Materials and Methods

MIC data were retrieved for 470 *S. pseudintermedius* and 401 *E. coli* isolates obtained in 2023-2024 from various infections in dogs and cats (Table 1). Diagnostic specimens had been shipped from primary care and referral veterinary hospitals from across Denmark to the diagnostic laboratory Sund Vet Diagnostik at the University of Copenhagen. For duplicates retrieved from a single patient at one point in time (e.g. two *S. pseudintermedius* from right and left ear, respectively), MIC data for only one randomly selected isolate was kept. Susceptibility testing was done using broth microdilution with the commercial Sensititre plates COMPGP1F for gram-positives and COMPGPN1F for gram-negatives (ThermoFisher Scientific). Interpretation of MIC data was according to clinical breakpoints published by the Clinical and Laboratory Standards Institute (CLSI) [2,3].

Table 1 Origin of *E. coli* and *S. pseudintermedius* isolates obtained from clinical specimens in Sund Vet Diagnostik, 2023-2024

DANMAP 2024

	Staphylococcus pseudintermedius		*Escherichia coli*	
	Dogs	Cats	Dogs	Cats
Urinary tract	45	0	216	48
Other	421	4	121	16
Total	466	4	337	64

Results and Discussion

Results are displayed in Table 2 along with comparable data from the periods 2018-2019 and 2020-2022. Overall, resistance levels are very similar over the three time periods with very limited fluctuations. In *E. coli*, cefpodoxime is the best indicator of ESC-production among the antibiotics tested. In 2023-2024, 5% of *E. coli* isolates were resistant to this antibiotic, indicating fairly stable, low levels of ESCs in Danish dogs and cats. It is worth noting that over the years there is a slight tendency of declining resistance to ampicillin and sulfamethoxazole/trimethoprim, which represent antimicrobials recommended in Denmark as first-choice for urinary tract infections in dogs and cats [4]. In *S. pseudintermedius*, oxacillin is used as indicator for detection of MRSP. In all three time periods, 6% of *S. pseudintermedius* were oxacillin-resistant, indicating a stable low level of MRSP. Another antibiotic worth mentioning for this species is clindamycin, as this is the recommended first systemic choice for skin infections in dogs. The level of 27% clindamycin resistance is not low but in line with previous years. Importantly, resistance to this drug was shown to be much lower (around 14%) in Danish isolates from first-time canine pyoderma [5]. This indicates bias, most likely due to submission of samples from patients having been treated with antibiotics before.

As stated in chapter 4 (Table 4.1), all veterinary fluoroquinolone usage in Denmark is for treatment of companion animals. Levels of resistance to this critically-important drug class have been stable in recent years, except for a minor increase in *S. pseudintermedius* (Table 2). Importantly, the clinical breakpoints for this class, chloramphenicol and doxycycline were recently updated by CLSI [3], and for the most recent data (2023-2024) we have indicated resistance proportions according to both the old and the new breakpoints (Table 2). All the new breakpoints are remarkably lower than the old ones, which means that a much higher proportion of isolates are now classified as clinically resistant. For fluoroquinolones, this means a 2-3 times higher proportion of isolates classified as resistant to enro- and marbofloxacin (Table 2). The recent tendency of lowering

continued ... Textbox 9.1

breakpoints for several antibiotics is due to new knowledge on drug pharmacokinetics and/or pharmacodynamics. It has the implication that small animal practitioners will encounter more resistance and thereby more limited treatment options despite the overall average MICs being stable over the years.

Table 2 Percentages of antimicrobial-resistant clinical *E. coli* and *S. pseudintermedius* isolates from dogs and cats in Denmark. MIC data from 2018-2022 were interpreted using [2], whereas data from 2023-2024 were interpreted using both [2] and [3]

DANMAP 2024

Antimicrobial agent	*Escherichia coli*			*Staphylococcus pseudintermedius*		
	2018-2019 (N=441)	2020-2022 (n=559)	2023-2024 (n=401)[2]	2018-2019 (N=602)	2020-2022 (n=726)	2023-2024 (n=470)[2]
	%	%	%	%	%	%
Amikacin	2	1	2	1	1	-
Ampicillin[1]	25	22	19	70	65	74
Amoxicillin/clavulanic acid[1]	5	6	4	7	6	6
Cefazolin	-	-	-	7	6	6
Cefpodoxime	5	3	5	-	-	-
Chloramphenicol	4	2	3 / 61	21	20	21 / -[3]
Clindamycin	-	-	-	27	26	27
Doxycycline	8	4	4 / 99	29	28	22
Enrofloxacin	4	4	3 / 7	2	4	5 / 12
Erythromycin	-	-	-	28	26	26
Gentamicin	4	3	2	2	5	8
Imipenem	0	0	0	-	-	-
Marbofloxacin	3	4	3 / 9	3	4	6 / -[3]
Oxacillin	-	-	-	6	6	6
Sulfamethoxazole/trimethoprim	9	8	6	6	8	9

[1] Susceptibility data for ampicillin and amoxicillin/clavulanic acid in *E. coli* have been determined only for isolates from urinary tract infections, as isolates from other infections are unequivocally classified as resistant to these drugs according to CLSI breakpoints.
[2] In these columns, the numbers to the left of the forward slashes were interpreted like the 2018-2019 and 2020-2022 data using CLSI breakpoints from 2020 [2], whereas the numbers to the right of the slashes were interpreted using CLSI breakpoints from 2024 [3]. When only one number is present in a cell, it means that the old and new breakpoints are identical.
[3] The dash here indicates that MIC data could not be interpreted using the new breakpoints due to insufficient concentration ranges in the plates used for MIC testing

Conclusion

Levels of antibiotic resistance in *S. pseudintermedius* and *E. coli* from dogs and cats have been stable over the last seven years. Most importantly, the proportions of ESC-producing *E. coli* and MRSP did not change from around 5% in the entire period. Comparison of AMR levels across countries is currently difficult, but this is about to change with the EARS-Vet initiative [https://eu-jamrai.eu/surveillance/ears-vet/], which aims to monitor AMR in animal clinical isolates from across Europe. With a recent opening of AMR data submission, it is expected that a report with comparison of AMR data from different animal species (including dogs and cats) in European countries will become available in 2026.

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10

MATERIALS AND METHODS

10. Materials and methods

10.1 General information

For the DANMAP 2024 report, population sizes and geographical data were obtained from Statistics Denmark [www.dst.dk] and data on the number of general practitioners from the Danish Medical Association [www.laeger.dk].

The epidemiological unit for pigs and cattle was defined at the individual farm level, meaning that only one isolate per bacterial species per farm was included in the report. The individual flock of broilers was defined as the epidemiological unit, and for food, the epidemiological unit was defined as the individual meat sample.

For humans, the epidemiological unit was defined as the individual patient and the first isolate per species per patient per year was included for analyses of AMR trends. An overview of all antimicrobial agents registered for humans and animals in Denmark is presented in Table 2.4.

10.2 Data on antimicrobial consumption in animals

10.2.1 Data

In Denmark, all antimicrobial agents used for treatment are available on prescription only. Until 2007, antimicrobial agents were exclusively sold by pharmacies or as medicated feed from the feed mills. This monopoly was suspended in April 2007, and since then private companies have been able to obtain license to sell prescribed veterinary medicinal products for animals, if they adhere to the same guidelines that apply to pharmacies. A pharmacy or licensed company either sells the medicine to veterinarians for use in their practice or for resale to farmers or sells the medicine directly to the animal owner upon presentation of a prescription.

Data on all sales of veterinary prescription medicine from pharmacies, private companies, feed mills and veterinarians are sent electronically to a central database, VetStat, which is hosted by the Danish Veterinary and Food Administration. Veterinarians are required by law to report all use of antibiotics and prescriptions for production animals to VetStat monthly.

For most veterinarians, the registration of data is linked to their invoice system. Electronic registration of the sales at pharmacies is linked to the billing process and stock accounts at the pharmacy. This ensure a very detailed data of high quality. Data are transferred daily from pharmacies to The Register of Medicinal Product Statistics at The Danish Health Authority and to VetStat.

In addition, data on coccidiostatics as feed additives (non-prescription) and antimicrobial growth promoters (not used since 2000) are also collected by VetStat, providing an almost complete register of all antimicrobial agents used for animals in Denmark since 2000. In very rare instances, medicine is prescribed on special license, i.e. medicines not approved for marketing in Denmark. These are not included in VetStat data.

VetStat contains detailed information about source (veterinarian/pharmacy/feed mill) and consumption for each prescription item: date of sale, identity of prescribing veterinarian, source ID (identity of the pharmacy, feed mill, or veterinarian practice reporting), package identity code and amount, animal species, age group, disease category and code for farm-identity (CHR Danish Central Husbandry Register). The package code is a unique identifier, relating to all information on the medicinal product, such as active ingredient, content as number of unit doses (e.g. number of tablets), package size, and code of the antimicrobial agent in the Veterinary Anatomical Therapeutic Chemical (ATCvet) classification system.

Knowledge of the target animal species enables the presentation of consumption data in "defined animal daily doses" (DADD) a national veterinary equivalent to the international defined daily doses (DDDs) system applied in the human sector [www.whocc.no]. The data presented in DANMAP 2024 were extracted from VetStat on 20 May 2025.

10.2.2 Methods

In DANMAP, we report use of antimicrobials in different animal populations. As a first step, the amount of antimicrobial agents used in animals is measured in kg active compound. This enables an overall crude comparison of consumption among different animal species and between the veterinary and human sectors.

Furthermore, a more detailed comparison of antimicrobial use is performed, taking into account potency, formulation, route of administration and the age of the animals (where relevant), by generating defined animal daily doses (DADDs). For these calculations, we select data with relevant animal and age group codes and relevant codes for dispensation. For example, when calculating the antimicrobial use for systemic treatment in pigs, we select consumption data where the age groups are defined as finishers, weaners, and sows (including piglets and boars) and exclude antimicrobials dispensed as tablets, products for topical use, intramammaries and gynaecologicals.

Numerator - DADD

Defined animal daily dose (DADD) is the average maintenance dose per day for a drug used for its main indication in the appropriate animal species. The DADD is not defined at product level but as mg active compound per kg live animal for each antimicrobial agent, administration route and animal species.

DADD has been specifically defined for use in DANMAP and does not always completely match the "prescribed daily dose" or the recommended dosage in the Summaries of Product Characteristics (SPC).

The following principles are applied when setting the DADDs:

1. Minor inconsistencies are corrected (e.g. due to rounding of numbers);
2. Approved dosage for the most widely used antimicrobial products is given priority above dosage for products that are rarely used;
3. Approved dosage for older products within the group is maintained as the common DADD even if a new product is approved with a higher dosage;
4. If the dosage for a group shows large variation in approved dosages of the products, the dosages provided by "The Veterinary Formulary" [British Veterinary Association 2005, 6th edition] are applied;
5. Dosages may vary within active compound and administration route, if different dosages have been approved for different age groups, indications or formulations.

When principles 3 and 4 are conflicting, principle 5 is applied.

Denominator - live biomass

The number of animals in a population (in epidemiological terms: the population at risk) is represented by their live biomass. The biomass of a species is calculated, taking into account average live bodyweight and the average lifespan in each age group. The estimation of live biomass and thus the number of standard animals at risk per day depends on the available data sources for each species. For DANMAP 2024, only the live biomass for pigs and cattle were updated. Pig production: The estimation was based on the number of pigs produced, including exports at different ages, productivity data for each year [Statistics Denmark; Danish Agriculture and Food Council] and census data for breeding animals [Statistics Denmark]. The average weight and life span for the growing animals (piglets, weaners and finishers) was estimated from the annual productivity numbers [Danish Agriculture and Food Council]. The size of the breeding animals (sows and boars) has probably increased over the last decade, but this was not accounted for.

Cattle production: The live biomass of the cattle population is estimated from census data [Statistics Denmark] and the average live weight of the different age groups. The Danish cattle population is mainly dairy, particularly Holstein Friesian, but also other breeds such as Jersey and a small population of beef cattle. Most of the cattle slaughtered are dairy cows and bull calves of dairy origin. The average live weight was estimated for 10 different age-gender categories.

Treatment proportion - DAPD

The treatment proportion is a statistical measure for AMU in animal populations, calculated as the annual number of DADDs administered in the population, divided by the estimated total population live biomass. For a single animal, the mg active compound (e.g. the number of DADDs) given in a daily treatment depends on the body weight. The treatment proportions, therefore, also represents the proportion of animals treated daily with an average maintenance- dose of a particular antimicrobial agent. These are reported as Defined animal daily dose per 1,000 animals per day (DAPD).

For example, 10 DAPDs indicate that an estimated 1% of the population, on average, receives a certain treatment on a given day. In principle, the metric DAPD is parallel to the metric DID, defined daily dose per 1,000 inhabitants per day (DID), used in pharmaco-epidemiology for the human sector, see Section 10.8.2.

In 2024, DAPD calculations were carried out for pigs and cattle.

For example, the antimicrobial use per pig produced is calculated as:

$$DAPD = \frac{DADD_{sows} + DADD_{weaners} + DADD_{finishers}}{\Sigma biomassdays}$$

Where DADDs, DADDw, and DADDf are amounts of antimicrobial agents used in finishers, weaners, and sows (including piglets and boars).

10.3 Collection of bacterial isolates from animals and meat

In DANMAP, samples originate both from the EU harmonised monitoring of antimicrobial resistance in zoonotic and commensal bacteria, and the national *Salmonella* surveillance programs. Since 2014, most isolates available for DANMAP have been collected in accordance with the EU harmonised monitoring, according to Decision 2013/652/EU. This Decision was repealed by Decision 2020/1729/EU, applied from 1 January 2021. With the aim to ensure continuity in assessing future trends in antimicrobial resistance, the new Implementing Decision includes adaptations of food categories to be sampled, sampling design to be followed, bacterial species to be tested and the analytical methods to be used.

EU harmonized monitoring from 2021 to 2027 shall cover *Salmonella* spp., *Campylobacter coli*, *Campylobacter jejuni*, indicator commensal *Escherichia coli*, ESBL-, AmpC- or carbapenemase- producing *Salmonella* spp. and *E. coli*, and may cover *Enterococcus faecalis* and *Enterococcus faecium*. Previously, monitoring of *Campylobacter coli* was voluntary. For the monitoring of *Salmonella* in poultry, it is now possible to report only samples collected within the national control programme in poultry farms, while the monitoring of *Salmonella* in fattening pigs at slaughter is still required for most countries, including Denmark, due to the inexistence of an implemented national surveillance programme which has been approved at EU level.

Additionally to monitoring of fresh meat at retail, the present EU legislation requires monitoring of indicator *E. coli* and ESBL-, AmpC- and CP-producing *E. coli* on fresh imported meat sampled at border control posts, and the fresh meat categories to be monitored include turkey, both at retail and at the border.

Decision 2020/1729/EU further allows the use of whole genome sequencing as an alternative method for the specific monitoring of ESBL-, AmpC- or CP-producing *E. coli* or for further testing of indicator *E. coli* and *Salmonella* showing resistance to cefotaxime, ceftazidime or meropenem.

The legislation continues to require mandatory sampling of broilers and fattening turkeys and meat thereof in even years (2022, 2024, 2026), and sampling of fattening pigs and cattle <1 year, and meat thereof in odd years (2021, 2023, 2025, 2027). In Denmark, fattening turkeys are not sampled at slaughter as part of the EU harmonised monitoring, because the national production of turkey meat is below 10.000 tonnes per year.

10.3.1 Animals

In 2024, most of the sampling for DANMAP was allocated to the mandatory sampling of caeca from at slaughter, and additional sampling of caeca from broilers fattening pigs and cattle <1 year was also carried out.

Caecal samples from healthy broilers, cattle (<1 year) and pigs were collected by meat inspection staff at the slaughterhouses. Samples were collected throughout the year, in major Danish slaughterhouses slaughtering conventionally produced broilers, pigs and cattle.

Sampling was stratified per slaughterhouse by allocating the number of samples from domestically produced animals per slaughterhouse, proportionally to the annual throughput of the slaughterhouse. For broiler flocks, ten intact caeca were pooled into one sample. For pigs and cattle, samples contained 30-100 g caecal material from a single animal.

All samples were processed by the Danish Veterinary and Food Administration's (DVFA) laboratory in Ringsted or by a DVFA-approved private laboratory. Samples from all three animal species were examined for indicator *E. coli*, and samples from broilers and cattle were examined for *Campylobacter jejuni* and *C. coli.*

Furthermore, broiler samples were also examined for ESBL/AmpC/carbapenemase-producing *E. coli*, and for *Enterococcus faecalis and Enterococcus faecium* (Table 10.1).

Pathogenic bacteria from pigs reported in 2024 comprised *Actinobacillus pleuropneumoniae*, *Bordetella bronchiseptica*, haemolytic and non-haemolytic *Escherichia coli*, *Klebsiella pneumoniae*, *Salmonella enterica*, *Staphylococcus hyicus*, and *Streptococcus suis* isolates identified in clinical samples submitted by veterinarians to the Veterinary Laboratory, The Danish Agriculture and Food Council. Pathogenic bacteria from acute mastitis in dairy cows reported in 2024 were isolated from milk samples submitted to Statens Serum Institut by veterinarians.

10.3.2 Meat

In 2024, ESBL/AmpC/carbapenemase-producing *E. coli* were isolated from packages of fresh, chilled broiler and turkey meat collected in Danish wholesale and retail outlets. These samples were collected throughout the year by DVFA officers (Table 10.1). Products with added saltwater or other types of marinade as well as minced meat were not included. Packages of meat were selected without pre-selecting by country of origin, as requested for the harmonised EU monitoring.

The number of establishments and samples selected by each regional DVFA control unit was proportional to the number of establishments in the region in relation to the total number of establishments in the country. One unit of meat (minimum of 200 g) was collected and all samples were processed at the DVFA laboratory.

Salmonella isolates from domestically produced pork originated from the national control programme at the slaughterhouses (Table 10.1). Carcasses were swabbed in four designated areas (covering 4 x 100 cm^2) after min. 12 hours of chilling. All samples were processed at DVFA-approved Industry laboratories and isolates were sent to the DVFA laboratory.

Table 10.1 Legislative and voluntary sampling plans under national control programmes and EU harmonised monitoring that contributed with isolates to DANMAP 2024 DANMAP 2024

Bacteria	Origin of isolates	Legislative reporting frequency (2020/1729/EU)	Number of tested and positive samples in 2024
Campylobacter spp.	Caecal samples from broilers[a] Caecal samples from cattle <1 yr[a]	Even years Odd years	714 flocks (284 positive) 156 animals (105 positive)
Enterococcus spp.	Caecal samples from broilers[b]	Even years	303 flocks (296 positive)
Indicator *E. coli*	Caecal samples from broilers Caecal samples from fattening pigs Caecal samples from cattle <1 yr	Even years Odd years Odd years	178 flocks (173 positive) 205 animals (184 positive) 166 animals (154 positive)
Specific monitoring of ESBL/AmpC and carbapenemase-producing *E. coli*	Caecal samples from broilers Fresh broiler meat at retail (Danish) Fresh broiler meat at retail (Imported) Fresh turkey meat at retail (Imported) WGS data for collected ESBL/AmpC isolates	Even years Even years Even years Even years Even years	652 flocks (19 positive)[c] 260 units (5 positive)[c] 41 units (14 positive)[c] 137 units (48 positive)[c] 86 isolates[d]
Salmonella spp.	Carcase swabs from fattening pigs[e]	Odd years	15,623 units (96 positive)[f]

a) Broilers: *C. jejuni* (n=202), *C. coli* (n=54), *C. lari* (n=1), unspecified (n=15) ; Cattle <1 yr: *C. jejuni* (n=94), *C. coli* (n=4), unspecified (n=7);
b) Broilers: *E. faecalis* (n=17), *E. faecium* (n=278)
c) Positive for ESBL/AmpC-producing *E. coli* and negative for carbapenemase-producing *E. coli*
d) 86 isolates from the positive samples were sequenced (19 from broilers, 5 from Danish broiler meat, 14 from imported broiler meat and 48 from imported turkey meat)
e) Carcass swab samples are part of the national *Salmonella* surveillance program and are classified in DANMAP as meat of domestic origin. Samples collected at slaughterhouses slaughtering more than 30,000 pigs are analysed in pools of 5 individual samples. The total number of animals tested and the total number of positives refer to individual pooled samples
f) Pork meat (carcass): *S*. 4,[5],12:i:- (n=40), *S*. Derby (n=28), *S*. Typhimurium (n=15), other serotypes or unspecified (n=13)

10.4 Microbiological methods – isolates from animals and meat

10.4.1 *Salmonella*

Salmonella from pork not originating from the national *Salmonella* surveillance program were isolated at DVFA in accordance with the methods issued by the NMKL [NMKL No. 187, 2007] and in accordance with Annex D, ISO 6579-1 [ISO6579-1:2017]. Serotyping of those isolates was performed at DVFA by whole genome sequencing using the Illumina MiSeq platform, paired-end sequencing 2x250 cycles. For bioinformatics, a CGE service (Centre for Genomic Epidemiology, DTU) for *Salmonella* serotyping was applied based on the genetic background for antigenic formulas given by the White-Kauffmann-Le Minor scheme.

Salmonella from carcasses originating from the national *Salmonella* surveillance program were isolated and serotyped according to the White-Kauffmann-Le Minor scheme at DVFA-approved Industry laboratories.

10.4.2 *Campylobacter*

Campylobacter from broiler and cattle caeca was isolated and identified according to the methods issued by the NMKL [NMKL No. 119, 2007] with modifications, with pre-enrichment in Bolton broth, and followed by species-determination by BAX® rtPCR assay (Hygiena, BAX® System PCR Assays for Campylobacter). Only one *Campylobacter* isolate per broiler flock or cattle herd was selected for antimicrobial susceptibility testing.

10.4.3 *Escherichia coli*

Indicator *E. coli* from broilers, pigs and cattle was isolated by direct spread onto violet red bile agar incubated for 24h at 44 °C. Presumptive *E. coli* was identified on TBX agar incubated at 44 °C o/n. Only one indicator *E. coli* isolate per flock or herd was selected. The specific isolation of ESBL/AmpC or carbapenemase-producing *E. coli* from broiler and turkey meat and caecal samples from broilers occurred within 96 h after sample collection, applying the current EURL-AR laboratory protocol [https://www.eurl-ar.eu/protocols.aspx]. Carbapenemase-producing *E. coli* screening was done with ChromID CARBA and ChromID OXA-48 plates. ESBL/AmpC-producing *E. coli* screening was done with MCA cefotaxime plates. All presumptive ESBL/AmpC or carbapenemase producing *E. coli* isolates were sequenced by WGS using the Illumina MiSeq platform (paired-end sequencing 2x250). Only one ESBL/AmpC-producing *E. coli* isolate per herd and meat sample was selected for antimicrobial susceptibility testing.

10.4.4 Enterococci

Indicator enterococci were isolated from broiler caeca by adding 2 ml buffered peptone water to the content of a cotton swab, after which 100 µl were inoculated onto Slanetz agar and incubated for 48 h at 41,5 °C. Presumptive *E. faecium/E. faecalis* were identified by real-time PCR assay. When present, only one *E. faecalis or E. faecium* isolate per herd was selected for antimicrobial susceptibility testing.

10.5 Susceptibility testing – isolates from animals and meat

Antimicrobial susceptibility testing of *Salmonella, Campylobacter* and *E. coli* was carried out by Minimum Inhibitory Concentration (MIC) determination, using broth microdilution by Sensititre (Trek Diagnostic Systems Ltd.). Inoculation and incubation procedures were performed in accordance with the CLSI guidelines [Clinical and Laboratory Standards Institute, USA] and the European standard [ISO 20776-1:2020]. The isolates were tested for antimicrobial susceptibility in accordance with the Decision 2020/1729/EU about the EU harmonised monitoring of antimicrobial resistance.

The quality control strains used were: *E. coli* ATCC 25922, *E. faecalis* ATCC 29212, *C. jejuni* ATCC 33560 and *P. aeruginosa* ATCC 27853. Isolates from animals and meat were tested for antimicrobial susceptibility at the DVFA laboratory in Ringsted, which is accredited by DANAK (the national body for accreditation).

Antimicrobial susceptibility testing of pathogenic bacteria from pigs was performed at the Veterinary Laboratory, The Danish Agriculture and Food Council. In brief, MICs were determined by broth microdilution using customised Sensititre panels according to CLSI standards. The analysis is accredited by DANAK.

Table 10.2 Interpretation criteriae for MIC-testing by EUCAST- and EFSA-provided epidemiological cut-off values (ECOFFs)

DANMAP 2024

Antimicrobial agent	*Salmonella*	*E. coli*	*E. faecalis*	*C. jejuni*	*C. coli*
	ECOFF µg/ml	ECOFF µg/ml	ECOFF µg/ml	ECOFF µg/ml	ECOFF µg/ml
Amikacin	>4	>8	Not tested	Not tested	Not tested
Ampicillin	>8	>8	>4	Not tested	Not tested
Azithromycin	>16	>16 [a]	Not tested	Not tested	Not tested
Cefepime	>0.125 [a]	>0.125 [a]	Not tested	Not tested	Not tested
Cefotaxime	>0.5	>0.25	Not tested	Not tested	Not tested
Cefotaxime-clavulanic acid	>0.5 [a]	>0.25	Not tested	Not tested	Not tested
Cefoxitin	>8	>8	Not tested	Not tested	Not tested
Ceftazidime	>2	>0.5	Not tested	Not tested	Not tested
Ceftazidime-clavulanic acid	>2 [a]	>0.5	Not tested	Not tested	Not tested
Chloramphenicol	>16	>16	>32	>16 [d]	>16 [d]
Ciprofloxacin	>0.064	>0.064	>4	>0.5	>0.5
Colistin	>2 [a] [b]	>2	Not tested	Not tested	Not tested
Daptomycin	Not tested	Not tested	>4	Not tested	Not tested
Ertapenem	>0.064 [a]	>0.064 [a]	Not tested	>0.5 [a] [d]	>0.5 [a] [d]
Erythromycin	Not tested	Not tested	>4	>4	>8
Gentamicin	>2	>2	>64	>2 [a]	>2 [a]
Imipenem	>1	>0.5	Not tested	Not tested	Not tested
Linezolid	Not tested	Not tested	>4	Not tested	Not tested
Meropenem	>0.125 [a]	>0.125	Not tested	Not tested	Not tested
Nalidixic acid	>8	>8	Not tested	Not tested	Not tested
Quinopristin-dalfopristin	Not tested	Not tested	>1 [a] [c]	Not tested	Not tested
Sulfamethoxazole	>256 [a]	>64 [a]	Not tested	Not tested	Not tested
Teicoplanin	Not tested	Not tested	>2	Not tested	Not tested
Temocillin	>16 [a]	>16	Not tested	Not tested	Not tested
Tetracycline	>8	>8	>4	>1	>2
Tigecycline	>0.5 [a]	>0.5	>0.25	Not tested	Not tested
Trimethoprim	>2	>2	Not tested	Not tested	Not tested
Vancomycin	Not tested	Not tested	>4	Not tested	Not tested

EUCAST epidemiological cut-off values (ECOFFs) and ECOFFs provided by EFSA for EU harmonized reporting

a) ECOFF as provided by EFSA [EFSA Supporting publication 2023:EN-7826]

b) For colistin, a tentative ECOFF of 16 µg/ml for *Salmonella* Dublin is established by EUCAST. The same ECOFF is used in DANMAP to interpret results of *Salmonella* Enteritidis. Both serotypes belong to the O-group (O:1, 9,12), which has been associated with increased MIC for colistin [https://www.doi.org/10.1089/fpd.2011.1015]

c) For quinopristin-dalfopristin, ECOFF only applies for *E. faecium*. ECOFF >1 for *E. faecalis* (intrinsically resistant to quinopristin-dalfopristin) is used only for the purpose of EU harmonized reporting

d) In 2021, chloramphenicol and ertapenem were introduced in the test panel for *Campylobacter* spp.

Milk samples from dairy cows with acute mastitis were collected by veterinarians at clinics across Denmark and submitted to Statens Serum Institut. Pathogens were isolated using standard culture techniques and identified to genus or species level by MALDI-TOF. Antimicrobial susceptibility testing was performed by broth microdilution using organism-specific Sensititre panels according to CLSI standards.

10.6 Whole genome sequencing - isolates from animals and meat

Whole genome sequencing (WGS) and in silico bioinformatics tools were used to detect the genetic background of the ESBL/AmpC and carbapenemase-producing *E. coli*. At the DVFA laboratory in Ringsted, strains were sequenced using the Illumina MiSeq platform and the bioinformatics analysis was conducted at DTU National Food Institute using the ResFinder application v. 4.4.2 and the ResFinder database v. 2.2.1.

Whole genome sequences of all sequenced *S.* Typhimurium and monophasic *S.* Typhimurium isolates from Danish pork were analysed for AMR determinants using the AMRFinderPlus tool (v. 4.0.19) with the AMRFinderPlus database (v. 2025-03-25.1). Detection parameters were set a minimum length coverage of 0.5 and the sequence identity threshold of 0.9. From the identified AMR proteins, only core resistance proteins were included in the analysis.

10.7 Data handling - isolates from animals and meat

For the samples processed at the DVFA laboratory, sampling details and laboratory results were stored in the DVFA Laboratory system. Following validation by DVFA, data were sent to DTU National Food Institute (Excel sheets). At the DTU National Food Institute, data were harmonised and one isolate per epidemiological unit was selected for reporting.

For the samples processed at the Veterinary Laboratory, The Danish Agriculture and Food Council, sampling details and laboratory results were stored in the information management system used at the Veterinary Laboratory. Following internal validation and anonymisation, data were sent to DK-VET (Excel sheets). At DK-VET, data were harmonised and one isolate per epidemiological unit was selected for reporting.

10.7.1 Interpretation of MIC values

MIC values were retained as continuous variables, from which binary variables (resistant/sensitive) were created using the relevant cut-off. Since 2007, MIC results have been interpreted using EUCAST epidemiological cut-off (ECOFF) values, with a few exceptions, as described in Table 10.2. An isolate is considered multidrug-resistant if resistant to three or more of the antimicrobial classes defined in Table 10.3 and fully sensitive if susceptible to all antimicrobial agents included in the test panel.

Table 10.3 Definitions of antimicrobial classes for calculation of multidrug-resistance in *Salmonella* and indicator *E. coli*
DANMAP 2024

Antimicrobial classes	*Salmonella* and *E. coli*
Beta-lactam penicillins	Ampicillin
Macrolides	Azithromycin
Cephalosporins	Cefotaxime and/or ceftazidime
Phenicols	Chloramphenicol
Quinolones	Ciprofloxacin and/or nalidixic acid
Polymyxins	Colistin
Aminoglycosides	Gentamicin and/or amikacin
Carbapenems	Meropenem
Sulfonamides	Sulfamethoxazole
Tetracyclines	Tetracycline
Glycylcyclines	Tigecycline
Trimethoprim	Trimethoprim

An isolate is considered multidrug-resistant if resistant to three or more of the defined antimicrobial classes and fully sensitive if susceptible to all antimicrobial agents included in the test panel; The aminoglycoside antimicrobial amikacin has been introduced in the test panel in 2021

For pathogenic bacteria from pigs, MIC values were interpreted with ECOFFs (1st choice) or tentative ECOFFs (2nd choice) established by EUCAST. When ECOFFs were unavailable, interpretation was based on CLSI-approved animal-specific or human clinical breakpoints (3rd and 4th choice, respectively) (available at https://www.vetssi.dk/). 10.7.2 ESBL/AmpC phenotypes.

Classification of CP-, ESBL- or AmpC-producing phenotypes was done according to the scheme provided by EFSA. [EFSA 2023. EFSA Journal 21(3):7867].

1. ESBL phenotype if cefotaxime and/or ceftazidime MIC >1 µg/ml and meropenem MIC <=0.12 µg/ml and cefoxitin MIC <=8 µg/ml and synergy (clavulanic acid and cefotaxime/ceftazidime);
2. AmpC phenotype if cefotaxime and/or ceftazidime MIC >1 µg/ml and meropenem MIC <=0.12 µg/ml and cefoxitin MIC >8 µg/ ml and no synergy (clavulanic acid and cefotaxime/ceftazidime);
3. ESBL-AmpC phenotype if cefotaxime and/or ceftazidime MIC >1 µg/ml and meropenem MIC <=0.12 µg/ml and cefoxitin MIC >8 µg/ml and synergy (clavulanic acid and cefotaxime/ ceftazidime);
4. CP phenotype if meropenem MIC >0.12 µg/ml;
5. Other phenotype if not in 1-4.

Synergy is defined as ≥3 twofold concentration decrease in MIC for clavulanic acid combined with cefotaxime/ceftazidime vs the MIC of cefotaxime/ceftazidime alone.

10.7.3 Statistical tests

Significance tests of differences between proportions of resistant isolates were calculated using Chi-square, or Fisher's Exact Tests as appropriate depending on sample size. Significance tests for trends in rates of resistance were performed by applying the Cochran-Armitage test, using the DescTools R package version 0.99.45. One-sided tests were chosen because of preliminary expected trend directions. A significance level of 0.05 was considered in all significance tests.

Analyses were done using R statistical software version 4.4.1 [R Core Team (2019). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org].

10.8 Data on antimicrobial consumption in humans

10.8.1 Data registration

Annual data on antimicrobial consumption in Denmark has been provided to DANMAP by the Register of Medicinal Product Statistics at the Danish Health Data Authority every year since 1997. Since 2020, DANMAP also reports monthly antimicrobial consumption data to allow analysis of the impact of the Covid-19 pandemic on antimicrobial consumption in humans since 2020.

Until 2012, data from hospitals on certain infusion substances such as cephalosporins, carbapenems and trimethoprim were obtained by DANMAP directly from hospital pharmacies. Since 2013, all data from hospitals are reported to and provided to DANMAP by The Register of Medicinal Product Statistics at the Danish Health Data Authority.

Reports of human antimicrobial consumption in Denmark existed already before 1997. These were prepared by the Association of Medicine Importers (Medicinimportørforeningen, MEDIF) and the Association of Danish Medicinal Factories (Foreningen af danske Medicinfabrikker, MEFA) based on whole sales data to pharmacies. These reports became less reliable over time since there was an increasing amount of parallel imported drugs from the late 1980s, which were not covered by MEDIF/MEFA.

In the primary sector, all antibacterial agents for human use are prescription-only medicines. Sales are reported by pharmacies using a code relating to the defined package. The code includes information on the active drug, the brand name of the product, formulation, size and number of packages. The report also includes age, gender and regional residence of the patient. Since 2004, the sales registration has included a code for indication of the prescription as well. However, clinical indications provided for the treatment of infectious diseases were often quite unspecific ("against infection"). Since 2016, the use of more specific indication codes has increased following the implementation of electronic prescribing via the "common medicine card" (fælles medicinkortet, FMK), a digital pharmacy platform which is mandatory to be used by all medical doctors. In 2023, indication codes were available for 94% of prescriptions, but specific indication codes still only accounted for 75%.

For hospitals, reporting is based on deliveries from the hospital pharmacies to the different clinical departments and includes all generic products that are supplied through general trade agreements between different medical suppliers and Amgros, a private company under agreement with the five Danish Regions. Amgros is responsible for harmonisation of prices and for ensuring deliveries to all hospitals and works closely together with the Regions' Joint Procurement. Detailed information is given on the different drugs delivered on ATC5 level. For surveillance purposes, it has to be assumed that the amount of delivered antimicrobials is similar to the consumption at the different departments. In reality, antimicrobials may be exchanged between different specialties and departments belonging to the same hospital making precise calculations of the consumption on specialty level difficult. In DANMAP, reporting of data on hospital consumption is therefore kept at national and regional level. In case of production failures and shortages in delivery of specific products, the hospitals have to apply for special delivery through the Danish Medicines Agency (Figure A5.2 in web annex). These special deliveries are reported separately to DANMAP through the hospital pharmacies. An example is the shortages in delivery of piperacillin with tazobactam and pivmecillinam as well as mecillinam in 2017. The shortage in piperacillin with tazobactam had significant impact on the amount used, while the shortage in (piv)mecillinam could not be clearly tracked in changes in consumption. In 2023, 126.490 DDD (3%) of the total antimicrobial consumption were special deliveries. Data on consumption at patient level are available at some hospitals and have so far been used in local quality assurance only but have not been available to DANMAP.

10.8.2 Method

Primarily somatic hospitals were included in the DANMAP reporting. Data from private hospitals and clinics, psychiatric hospitals, specialised non-acute care clinics, rehabilitation centres and hospices were excluded from DANMAP in most calculations since their activity and functions are not comparable to public, somatic hospitals and therefor may skew the data. Their consumption accounts for approximately 3% of the antimicrobial consumption at hospitals in Denmark.

The present report includes data on the consumption of "antibacterials for systemic use", or group J01, of the 2023 update of the Anatomical Therapeutic Chemical (ATC) classification, in primary healthcare and in hospitals as well as consumption of oral and rectal preparations of metronidazole (P01AB01) and for hospitals oral preparations of vancomycin (A07AA09). As recommended by the World Health Organization (WHO), consumption of antibacterial agents in primary healthcare is expressed as DIDs, i.e. the number of DDDs per 1,000 inhabitants per day.

The consumption in hospital healthcare is expressed as the number of DDDs per 100 occupied beds per day (DDD/100 occupied bed-days or DBD). Since reporting in DBD does not necessarily reflect changes in hospital activity and production, consumption at hospitals is also presented as DAD (the number of DDDs per 100 admissions) and crude DDD. Finally, the consumption of antibacterial agents at hospitals has also been calculated in DIDs, primarily for comparison with primary healthcare.

10.8.3 DDD

Defined daily dose is the assumed average maintenance dose per day for a drug used for it's main indication in adults. DDDs provide a fixed unit of measurement independent of price and formulation, enabling the assessment of trends in drug consumption and to perform comparisons between population groups. The DDDs are defined and revised yearly by the WHO Collaborating Centre for Drug Statistics and Methodology [https://www.whocc.no/atc_ddd_index/].

Per January 2019 the WHO updated the DDDs for seven main antimicrobial agents, based on recommendations from an expert working group in collaboration with the European Center for Disease Control (ECDC) (Table 10.5). From DANMAP 2018, the new DDD values were applied and all tables and figures were updated ten years back.

10.8.4 DBD

DDD/100 occupied bed-days. The number of occupied bed-days are calculated as the exact duration of a hospital stay in hours divided by 24 hours. Number of bed-days was extracted from the National Patient Registry at the Danish Health Data Authority [www.sundhedsdatastyrelsen.dk].

The National Patient Registry was upgraded in 2019 and data are still being validated and may be adjusted in the future. This has to be kept in mind when data are interpreted.

10.8.5 DAD

DDD/100 admissions. One admission is registered whenever a patient is admitted to a specific hospital for ≥12 hours. If a patient is transferred between wards within 4 hours, it will not count as a new admission. The admissions were extracted from the National Patient Registry at the Danish Health Data Authority [www.sundhedsdatastyrelsen.dk].

The National Patient Registry was upgraded in 2019 and data are still being validated and may be adjusted in the future. This has to be kept in mind when data are interpreted.10.8.6 Antimicrobial consumption for elderly living in long care facilities.

Data from the Care Home Register were combined with data from the Danish Civil Registration System (CPR) and with data from the Register of Medicinal Product Statistics in order to determine the antimicrobial consumption for elderly people living in care homes and for elderly people living in their own homes.

10.9 *Salmonella* and *Campylobacter* isolates from humans

10.9.1 Data source

Antimicrobial susceptibility was performed on human clinical isolates submitted to Statens Serum Institut (SSI). *Salmonella* isolates were submitted from all clinical microbiology laboratories in Denmark and *Campylobacter* isolates were submitted from clinical microbiology laboratories representing the island of Zealand excluding the Capital Region, Funen, and Northern Jutland. As in previous years, SSI collected information on travel history from the patients. Cases were categorised as "domestically acquired" if the patients had not travelled abroad within the week prior to the onset of disease. Data on *Salmonella* and *Campylobacter* infections are stored in the Danish Registry of Enteric Pathogens (SQL database) that is maintained by SSI. This register includes only one isolate per patient within a window of six months and includes the recorded data on susceptibility testing of *Salmonella* and *Campylobacter*.

Table 10.5 New DDDs assigned by WHO Collaborating Centre per January 2019 DANMAP 2024

ATC5 code	ATC level name	Previous DDD			New DDD		
		Weight	Unit	Route of administration	Weight	Unit	Route of administration
J01CA01	Ampicillin	2.0	g	Parenteral	6.0	g	Parenteral
J01CA04	Amoxicillin	1.0	g	Oral	1.5	g	Oral
J01CA04	Amoxicillin	1.0	g	Parenteral	3.0	g	Parenteral
J01CA17	Temocillin	2.0	g	Parenteral	4.0	g	Parenteral
J01CR02	Amoxicillin and beta-lactamase inhibitor	1.0	g	Oral	1.5	g	Oral
J01DE01	Cefepime	2.0	g	Parenteral	4.0	g	Parenteral
J01DH02	Meropenem	2.0	g	Parenteral	3.0	g	Parenteral
J01MA02	Ciprofloxacin	0.5	g	Parenteral	0.8	g	Parenteral
J01XB01	Colistin	3.0	MU	Parenteral	9.0	MU	Parenteral

10.9.2 Serotype and species identification

Salmonella isolates were analysed by whole genome sequencing and the serotypes were derived from the DNA sequences. In a few cases, the DNA information was supplemented with slide agglutination according to the Kauffman-White Scheme. *Campylobacter* species identification was performed by the use of MALDI-TOF.

10.9.3 Susceptibility testing

Antimicrobial susceptibility testing of *Salmonella* and *Campylobacter* was performed as Minimum Inhibitory Concentration (MIC) determination using the Sensititre broth microdilution system (ThermoFisher Scientific). Inoculation and incubation procedures were in accordance with the EU protocol for harmonised monitoring of antimicrobial resistance in human *Salmonella* and *Campylobacter* isolates – June 2016, see "http://www.ecdc.europa.eu/en". The interpretation criteria for MIC testing were done using ECOFFs, see Table 10.2.

10.9.4 Identification of AMR determinants in *Salmonella* isolates

Whole genome sequences of all sequenced *S.* Typhimurium and monophasic *S.* Typhimurium were analysed for AMR determinant using the AMRFinderPlus tool (v. 4.0.19) with the AMRFinderPlus database (v. 2025-03-25.1). Detection parameters were set a minimum length coverage of 0.5 and the sequence identity threshold of 0.9. From the identified AMR proteins, only core resistance proteins were included in the analysis.

10.10 *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacter* species, *Enterococcus faecium* and *Enterococcus faecalis* isolates from humans

10.10.1 Data source

The surveillance of invasive isolates of *E. coli, K. pneumoniae, E. faecalis* and *faecium, P. aeruginosa* and A. spp. and urine isolates of *E. coli* and *K. pneumoniae* are all based on data from routine diagnostics at the ten Departments of Clinical Microbiology (DCMs) in Denmark. All data were extracted directly from the Danish Microbiology Database (MiBa) [https://miba.ssi.dk]. Before 2018, data were reported by the individual DCM to SSI. A description of MiBa and the usage and validation of MiBa-data is given in Textbox 8.1 in DANMAP 2018 [www.danmap.org].

10.10.2 Microbiological methods

All microbiological analyses including species identification, susceptibility testing and interpretation of test results, were performed by the DCM. Since November 2015, all Danish DCMs used the EUCAST terminology with the EUCAST clinical breakpoints and the EUCAST methods for roughly all species. Few exceptions exist at some DCMs where local rules were applied to the susceptibility interpretations in specific cases - e.g. susceptibility to mecillinam in invasive cases. In 2019 EUCAST introduced the Area of Technical Uncertainty (ATU) for some combinations of species and agents reflecting problematic areas regarding variations and uncertainty of susceptibility categorisation. Piperacillin-tazobactam, ciprofloxacin and amoxicillin-clavulanic acid (in systemic breakpoints) and Enterobacterales are examples where ATUs were applied. ATUs can be handled differently by individual DCMs and may influence interpretation results. This was commented on when necessary in the affected sections.

To be included in resistance surveillance more than 75% of respective isolates need to be antimicrobial susceptibility tested for a given antibiotic, if not stated otherwise. Data of antimicrobial susceptibility testing was mainly performed by disc diffusion. The presented data consist of the registered interpretation results, performed by the respective DCM, based on the S-I-R system. In addition, zone diameters have also been registered since 2015 and will be commented upon in specific cases.

Urine specimen taken in primary health care are also being tested at DCMs except for some samples taken by GPs in the Capital Region of Denmark that are being tested at a private laboratory.

All enterococci isolates reported as VRE in MiBa (based on PCR results for *vanA/B* genes) were reported as vancomycin-resistant independent of the actual zone/MIC result. It was not distinguished between VRE and VVE (vancomycin-variable enterococci). High-level resistance to gentamicin was defined using EUCAST break points (MIC >128 mg/L and/or zone diameters <8 mm) for MIC and/or zone diameters reported in MiBa. Gentamicin MIC and/or zone diameters were routinely reported by three DCMs in 2020.

10.10.3 Data handling

Cases and susceptibility results were extracted from MiBa and analysed in Python 3.8.10.

The case definition has been harmonised with the definition used by the European Antimicrobial Resistance Surveillance Network (EARS-Net): The first sample, by date of sample collection, of each given bacterial species per unique patient per year of observation. Duplicates from the same patient, within the year of observation, were removed. Thereby only resistance data on the first isolate per patient per specimen per year were included. Resistance data from DCMs were excluded if not tested or registered in MiBa routinely (minimum 75% of the specific species/antimicrobial agent combination). Samples were either invasive (including blood cultures or cerebrospinal fluid) or urinary samples from patients at hospitals or primary healthcare settings.

10.11 ESBL-producing bacterial isolates from humans

10.11.1 Data source

Since 2014, the Danish DCMs have on a voluntary basis submitted 3rd generation cephalosporin-resistant *Escherichia coli* isolates from bloodstream infections for verification and genotyping at the Antimicrobial Resistance Reference Laboratory, Statens Serum Institut.

10.11.2 Microbiological methods of isolates from patients

Since 2014, whole genome sequencing (WGS) and in silico bioinformatics analysis have been applied for isolates predicted to carry ESBL and/or AmpC genes based on initial phenotypic tests, to characterize the genetic background of the ESBL and/or AmpC phenotypes. Only one isolate from each patient was included if less than 12 months were between isolation of the two isolates.

10.11.3 Data handling

The quality of the raw sequencing and assembly data was ensured using the analytical tool BIFROST [https://github.com/ssi-dk/bifrost/]. An in-house bacterial analysis pipeline, building on a weekly update of the ResFinder database [https://bitbucket.org/genomicepidemiology/resfinder/src/master/] was used for the in silico detection of acquired ESBL genes, pAmpCs, carbapenemase genes and MLST from assembled WGS data. For isolates with no ESBL-, pAmpC-, or carbapenemase-encoding genes detected, the sequences were investigated for promotor mutations presumed to up-regulate chromosomal AmpC by the use of myDb-Finder version 1.2 [https://cge.food.dtu.dk/]. Possible clonal clusters were detected using the SeqSphere+ (Ridom) software to call cgMLST types (*E. coli* scheme).

10.12 CPO isolates from humans

10.12.1 Data source

Historically, Danish DCMs have submitted carbapenem-resistant isolates for verification and genotyping on a voluntary basis to the Antimicrobial Resistance Reference Laboratory at the Statens Serum Institut. Since 5 September 2018, notification of CPO has been mandatory in Denmark. For outbreak investi-gation Data from The National Patient Register (LPR), informa-tion gathered at the hospitals and information of residence from the Danish Civil Registration System (CPR) has been included in the analysis for this report.

10.12.2 Microbiological methods

All submitted isolates (originating both from screening and clinical samples) predicted to carry a carbapenemase based on initial phenotypic tests were analysed using WGS. More than one isolate from the same patient was only included in the dataset if the isolates belonged to different bacterial species and/or if isolates within the same species harboured different carbapenemases.

10.12.3 Data handling

The quality of the raw sequencing and assembly data was ensured using the analytical tool BIFROST [https://github.com/ssi-dk/bifrost/]. An in-house bacterial analysis pipeline, building on a weekly update of the ResFinder database [https://bitbucket.org/genomicepidemiology/resfinder], was used for the in silico detection of acquired CPO genes and MLST from assembled WGS data. Possible clonal clusters were detected using the SeqSphere+ (Ridom) software to call cgMLST types where such schemes are available (*E. coli*, *Klebsiella pneumoniae* and *Acinetobacter baumannii*). For outbreak investigations, identified clonal clusters were linked with patient data like time and place of hospitalization and place of residence. Identification of isolates from two or more persons (cases) sharing the same unique genotype was defined as an outbreak. An outbreak was defined as a verified outbreak if an epidemiological link could be established between two or more cases in the cluster, e.g. the patients had been at the same hospital ward at the same time or lived at the same geographical location such as a nursing home. When no epidemiological link could be establish between cases with the same unique genotype, the outbreak was classified as a possible outbreak. A possible outbreak can be reclassified as a verified outbreak if new cases or information providing an epidemiological link between two or more of the cases becomes available. Both, possible and verified outbreaks, are registered in the CPO-outbreak database KURS (coordinated outbreak registration).

Outbreak investigations of a cluster of cases are closed when no new cases have been reported within 6 months after the last reported case, but can be reopened, if new cases are being detected.

10.13 VRE isolates from humans

10.13.1 Data source

Danish DCMs are submitting VRE for species identification, genotyping and surveillance on a voluntary basis to the Antimicrobial Resistance Reference Laboratory at Statens Serum Institut.

10.13.2 Microbiological methods

All clinical VRE isolates have been whole-genome sequenced. Only one isolate from each patient was included if less than 12 months were between isolation of the two isolates.

10.13.3 Data handling

The quality of the raw sequencing and assembly data was ensured using the analytical tool BIFROST [https://github.com/ssi-dk/bifrost/]. An in-house bacterial analysis pipeline, building on a weekly update of the ResFinder database [https://bitbucket.org/genomicepidemiology/resfinder], was used for the in silico detection of genes related to vancomycin resistance in enterococci and MLST from assembled WGS data. Possible clonal clusters were detected using the SeqSphere+ (Ridom) software to call cgMLST types.

10.14 Invasive *Streptococcus pneumoniae* isolates from humans

10.14.1 Data source

Invasive pneumococcal disease is a notifiable disease in Denmark and it is mandatory to submit all invasive isolates of *S. pneumoniae* for serotyping and susceptibility testing to the Neisseria and Streptococci Reference Laboratory at Statens Serum Institut. For cases of invasive pneumococcal disease, where isolates from blood/spinal fluid could not be submitted, identification and registration of cases is conducted by extracting the required information from the Danish Microbiology Database (MiBa).

10.14.2 Microbiological methods

Identification or confirmation of the species *S. pneumoniae* was based on: visual evaluation of colonies, positive optochin test and test with either latex omni test (ImmuLex™ *S. pneumoniae* Omni, SSI Diagnostica, Denmark) or Neufeld based Omni serum (SSI Diagnostica, Denmark). If challenging results occurred, MALDI-TOF, bile solubility test, or whole genome sequencing were performed to further confirm the correct species identification. For non-viable isolates, species identification was based on the detection of the lytA and Ply gene by the use of PCR.

Serotype identification of invasive *S. pneumoniae* was performed by the use of latex agglutination (ImmuLex™ Pneumotest Kit, SSI Diagnostica, Denmark) and serotype specific antisera by the Neufeld test (SSI Diagnostica, Denmark). For non-viable isolates, serotyping was often possible by the use of PCR.

10.14.3 Susceptibility testing

Screening for penicillin- and erythromycin-resistant *S. pneumoniae* was performed with 1 µg oxacillin discs and 15 µg erythromycin discs (Oxoid, Roskilde, Denmark), respectively, on Mueller-Hinton agar (Mueller-Hinton plate, 5% blood, SSI Diagnostica, Denmark). Breakpoints were according to EUCAST Clinical Breakpoint Tables v. 11.0. Isolates, that were found non-susceptible by screening were further analysed for penicillin and erythromycin MICs by broth microdilution using the STP6F plate, Sensititre (Trek Diagnostic Systems, Thermo Scientific) as recommended by the manufacturer. All breakpoints used were as defined by EUCAST (Eucast Clinical Breakpoint Tables v.11.0). For cases, where an isolate was not received at the reference laboratory, susceptibility data could often be found in MiBa.

10.14.4 Data handling

Only cases with isolates from blood or spinal fluid were included in the DANMAP report. Repeated samples within a 30 days window were classified as duplicates and were omitted from the analysis.

10.15 Isolates of beta-haemolytic streptococci of groups A, B, C, and G from invasive infections in humans

10.15.1 Data source

All invasive isolates of beta-haemolytic streptococci (BHS) (e.g., blood, cerebrospinal fluid, synovial fluid, pleural fluid, ascites, and tissue obtained during surgery) were submitted to SSI from the departments of clinical microbiology on a voluntary basis.10.15.2 Microbiological methods

Identification of streptococcal group was performed by latex agglutination (Streptococcal Grouping Reagent, Oxoid, Denmark). Genomic DNA was extracted using an enzymatic pre-lysis step before automated purification on MagNA Pure 96 DNA Small Volume Kit (Roche Diagnostics). Fragment libraries were constructed using the Nextera XT DNA Library Preparation Kit (Illumina, San Diego, CA), followed by 150-bp paired-end sequencing on a NextSeq (Il- lumina) according to manufacturer's instructions. The sequencing reads were assembled using SKESA [https://github.com/ncbi/SKESA]. The isolates were species typed using Kraken [https://ccb.jhu.edu], and MLST typed using https://github.com/tseemann/mlst.

For Group A Streptococcus (GAS), isolates were *emm* typed by performing a BLAST search to all published *emm* types by CDC [https://www.cdc.gov/streplab/protocol-emm-type.html]. For Group B Streptococcus (GBS), all isolates were serotyped by latex agglutination test and, if needed, confirmed using Lancefield tests. In addition, blasting of capsular sequencing was used for identification of genotypes. No additional identification tests were performed for isolates from Group C or G.

10.15.3 Susceptibility testing

Screening for penicillin, erythromycin and clindamycin resistance was performed with 1 unit penicillin G discs, 15 µg erythromycin discs and 2 µg clindamycin discs (Oxoid, Denmark) on Mueller-Hinton agar (Mueller-Hinton plate, 5% blood, SSI Diagnostica, Denmark). Isolates were also tested for inducible clindamycin resistance. For non-susceptible streptococci the MIC was determined with ETEST (Biomérieux), with erythromycin or clindamycin on Mueller-Hinton agar. The breakpoints used were as defined by the EUCAST (EUCAST v. 14.0 Breakpoint Tables).

Isolates that were either resistant or susceptible to increased exposure were categorised together as resistant.

10.15.4 Data handling

A case of invasive BHS disease was defined as the isolation of BHS from a normally sterile site (e.g., blood, cerebrospinal fluid, synovial fluid, pleural fluid, ascites, and tissue obtained during surgery). A new case was defined as an invasive isolate with a different Lancefield group within 30 days from the first one or an invasive isolate of any Lancefield group more than 30 days after the first episode, or the isolation of a new type (*emm*-type or GBS serotype) if the group was identical on both occasions.

Only one isolate from each unique case of BHS infection was included in the DANMAP report.

10.16 Invasive *Haemophilus influenzae* isolates from humans

10.16.1 Data source

Invasive infections with *Haemophilus influenzae* type b (Hib) is a notifiable disease in Denmark and all invasive isolates nationwide are sent to the reference laboratory at SSI. By tradition, invasive isolates of other serotypes have also been submitted on a voluntary basis, and thus a broader picture of invasive *H. influenzae* in Denmark can be obtained. All cases were identified through MiBa and registered in the surveil-lance database at SSI. Cases, where isolates were not submit-ted to the reference laboratory were registered as "unknown serotype".

10.16.2 Microbiological methods

At SSI, the received isolates were analysed by whole-genome sequencing, from which serotype and biotype were extracted.

10.16.3 Susceptibility testing

Susceptibility data for the 2024 isolates were retrieved from MiBa. In cases where a series of isolates from the same episode developed non-susceptibility over time, the most non-susceptible profile was used for the analysis in DANMAP. In addition, for isolates received at SSI, whole-genome sequencing data was analysed for the presence of beta-lactamase encoding plasmids TEM-1 and ROB-1 as well as for the presence of mutations in the *ftsI* gene that encodes for penicillin-binding protein 3 (PBP3).

10.16.4 Data handling

A case was defined as isolation of *H. influenzae* from normally sterile sites (e.g. blood, spinal fluid, pleura, joint). Repeated samples within a 30 days window were classified as duplicates and were omitted from the analysis.

10.17 *Staphylococcus aureus* including MRSA isolates from humans

10.17.1 Data source

Blood isolates were referred on a voluntary basis by all DCMs to the National reference laboratory for antimicrobial resistance at SSI. Detection of methicillin-resistant *Staphylococcus aureus* (MRSA) is a notifiable condition in Denmark and therefore all MRSA isolates from all sample types were sent to the reference laboratory.

10.17.2 Microbiological methods

At SSI, all isolates were initially tested using a multiplex PCR detecting the *spa, mecA, hsd, scn* and *pvl* (LukF-PV) genes [Larsen *et al.* 2008. Clin Microbiol Infect. 14: 611-614; Stegger *et al.* 2012. Clin Microbiol Infect. 18: 395-400]. *spa* was used as *S. aureus* specific marker and for subsequent typing by Sanger sequencing [Harmsen *et al.* 2003. J Clin Microbiol. 41: 5442-5448], mecA to determine MRSA status, and scn and *hsd* as markers for human adaptation and relation to CC398, respectively. All bacteremia cases and *mecA* negative presumed MRSA were tested for presence of the *mecC* gene. *spa*-negative isolates were confirmed as *S. aureus* by MALDI-TOF. Based on the *spa* type and known association with MLST typing, each isolate was assigned to a clonal complex (CC).

10.17.3 Susceptibility testing

Data on antimicrobial susceptibility was extracted from MiBa.

10.17.4 Data handling

For blood isolates, a case was defined as a patient with a positive blood culture. Subsequent isolates from the same patient was only included if the positive blood cultures were obtained at least one month apart (new episode).

For MRSA, data on the characteristics of the isolates and the clinical/epidemiological information were obtained from the Danish MRSA register at SSI (mandatory reportable). Patients were registered, regardless of colonisation or clinical infection, the first time they were diagnosed with MRSA or when a new subtype was demonstrated. Based on the reported information, MRSA cases were classified as colonisation/active screening (i.e. surveillance samples to detect nasal, throat, gut or skin colonisation), imported infection (i.e. acquired outside Denmark), infection acquired in a Danish hospital, defined as diagnosed >48 hours after hospitalisation with no sign of infection at admittance (HA-MRSA) or infection diagnosed outside hospitals (community onset). MRSA cases with community onset were further classified according to risk factors during the previous 6 months as either health-care associated with community onset (HACO) or community-acquired (CA). Health-care associated risk factors included prior hospitalisations, stay in long-term care facilities and being a health-care worker. Community risk factors included known MRSA-positive household members or other close contacts. Due to the increasing numbers of cases belonging to CC398, this type was treated separately as both epidemiology and relevant exposure are different from other CA cases.

10.18 Gonococcal isolates

10.18.1 Data source

Isolates of gonococci (*Neisseria gonorrhoeae*) were submitted from the departments of clinical microbiology to SSI on a voluntary basis. The isolates were obtained by culture of specimens from a variety of anatomical locations, most often urethra, cervix, rectum, throat, and rarely from other sites, e.g. eyes, joint fluid, and blood.

10.18.2 Microbiological methods

The bacteriological identification of the received isolates was performed by MALDI-TOF.

10.18.3 Susceptibility testing

For all isolates the MICs of azithromycin, ceftriaxon and ciprofloxacin were determined with ETEST (Biomérieux) on chocolate agar incubated at 35 °C in 5% CO_2. The breakpoints used were those defined by EUCAST (EUCAST v. 14.0 Breakpoint Tables). A cefinase disc technique was used to examine the isolates for beta-lactamase production.

The breakpoints for azithromycin were changed as of January 1, 2019 (EUCAST version 9.0) (S: MIC ≤1 mg/L; R: MIC >1 mg/L) and it was advised that azithromycin should only be used in conjunction with another efficient agent. Until January 1, 2019, S was defined by MIC ≤0.25 mg/L and R by MIC >0.5 mg/L.

In addition to the above, the MIC of cefixime was determined for 117 consecutive isolates as part of an ECDC project on gonococcal antimicrobial resistance (Euro-GASP). The breakpoints used were those defined by EUCAST (EUCAST v. 14.0 Breakpoint Tables).

10.18.4 Data handling

Only one isolate from each unique case of gonorrhoea were included in the DANMAP report. Laboratory demonstration of gonococci in repetitive specimens was considered to represent a new case of gonorrhoea if the specimens were obtained with an interval of more than 21 days.

11

TERMINOLOGY

List of abbreviations

AGP	Antimicrobial growth promoter
AMU	Antimicrobial use
AMR	Antimicrobial resistance
ATC	Anatomical Therapeutic Chemical Classification System
ATCvet	Anatomical Therapeutic Chemical Classification System for veterinary medicines
CA	Community-acquired
CC	Clonal complex
CHR	Central Husbandry Register
CPE	Carbapenemase producing Enterobacterales/Enterobacteriaceae
CPO	Carbapenemase producing organisms
CPR	Danish Civil Registry, register for social security numbers
DAD	Defined Daily Doses per 100 admissions
DADD	Defined Animal Daily Dose
DAPD	Defined Animal Daily Dose per 1,000 animals per day
DBD	Defined Daily Doses per 100 occupied bed-days
DCM	Department of clinical microbiology
DDD	Defined Daily Dose
DID	Defined Daily Doses per 1,000 inhabitants per day (DDD/1,000 inhabitants/day)
DTU	Technical University of Denmark
DVFA	Danish Veterinary and Food Administration
EARS-Net	The European Antimicrobial Resistance Surveillance Network
ECDC	European Centre for Disease Prevention and Control
EFSA	European Food Safety Authority
ESC	Extended Spectrum cephalosporinase
EUCAST	European Committee on Antimicrobial Susceptibility Testing
GP	General Practitioner
HACO	Health care associated community onset
MiBa	The Danish Microbiology Database
MIC	Minimum inhibitory concentration
MDR	Multidrug-resistant
MRSA	Methicillin-resistant *Staphylococcus aureus*
PCR	Polymerase chain reaction
SPC	Summaries of Product Characteristics
SSI	Statens Serum Institut
ST	Serotype/Sequence type
VASC	Veterinary advisory service contracts
VMPs	Veterinary medicinal products
VetStat	Danish Register of Veterinary Medicines
VRE	Vancomycin-resistant enterococci
VVE	Vancomycin-variable enterococci
WGS	Whole-genome sequencing
WHO	World Health Organization

Glossary

Anatomical Therapeutic Chemical (ATC) classification: An international classification system for drug consumption studies. The ATC code identifies the therapeutic ingredient(s) of each drug for human use according to the organ or system on which it acts and its chemical, pharmacological and therapeutic properties. Antibacterials for systemic use are known as ATC group J01. The ATC classification is maintained by the WHO Collaborating Centre for Drug Statistics and Methodology (Oslo, Norway) [www.whocc.no/atcddd/indexdatabase/]. The ATC classification for veterinary medicinal products, ATCvet, is based on the same main principles as the ATC classification system for medicines for human use and is also maintained by the WHO Collaborating Centre for Drug Statistics and Methodology [www.whocc.no/atcvet/database/].

Antibacterial agents: Synthetic (chemotherapeutics) or natural (antibiotics) substances that destroy bacteria or suppress bacterial growth or reproduction [Source: Dorland's Illustrated Medical Dictionary]. In the section on human consumption, 'antibacterial agents' are referred to as 'antimicrobial agents' (see below).

Antimicrobial agents: The term 'antimicrobial agents' covers antibacterial, antiviral, coccidiostatic and antimycotic agents. In the section on veterinary consumption, the broad term 'antimicrobial agents' is generally used because coccidiostats are included. Antiviral substances are not used in veterinary medicine, and antimycotics are only registered for topical veterinary use and used mainly in companion animals. Antimycobacterial agents are not included. The term 'antibacterial agents' is only used in the veterinary section for precision, to distinguish from use of coccidiostats as feed additives (poultry only). In the chapter on human consumption, the term 'antimicrobial agents' refers to all antibacterial agents for systemic use (J01 in the ATC system) including metronidazole and vancomycin, which are used for systemic treatment but registered under the ATC code P01AB01 and A07AA09, respectively.

Broiler: A type of chicken raised specifically for meat production. In Denmark, the average weight after slaughter is 1.51 kg.

Central Husbandry Register (CHR): This is a register of all Danish farms defined as geographical sites housing production animals. It contains information concerning ownership, farm size, animal species, age groups, number of animals and production type. Each farm has a unique farm identity number (CHR-number).

Defined Daily Dose (DDD): This is the assumed average maintenance dose per day for a drug used for its main indication in adults. It should be emphasised that the Defined Daily Dose is a unit of measurement and does not necessarily reflect the recommended or prescribed daily dose. DDDs provide a fixed unit of measurement independent of price and formulation, enabling the assessment of trends in drug consumption and to perform comparisons between population groups. The DDDs are defined and revised yearly by the WHO Collaborating Centre for Drug Statistics and Methodology [https://www.whocc.no/atc_ddd_index/].

Defined Daily Dose per 100 admissions (DAD): DAD measures the amount of daily doses consumed per 100 admitted patients at hospitals during a given timeframe (one year). It is used for benchmarking consumption related to the hospital activity and will typically be compared to the consumption measured in DBD (see below). DAD and DBD will generally be applied to comparing individual hospitals and consumption of individual drug classes over time. In DANMAP DAD covers all patients attended at somatic hospitals only. Admission-days are extracted from the National Patient Registry (Landspatientregistret, LPR).

Defined animal daily dose (DADD): DADD is the average maintenance dose per day for a drug used for its main indication in the appropriate animal species. DADD has been specifically defined for use in DANMAP and does not always completely match the "prescribed daily dose" or the recommended dosage in the Summaries of Product Characteristics (SPC). The DADD is defined as mg active compound per kg live biomass for each antimicrobial agent, administration route and animal species. In DANMAP 2012, the DADD replaced the ADD (as defined in VetStat and assigned at product level). For more details, see section 9.2, Materials and Methods and the applied DADD's are listed in the web annex.

DADD per 1,000 animals per day (DAPD): Trends in veterinary consumption, both within and across species, are presented in DAPD, which allows for comparison between sectors and adjustment for changes in live biomass. The estimated live biomass is expressed as the number of standard animals with an estimated average weight and lifetime. This may also be referred to as the 'standard-animals-at-risk' and takes into account species differences in body-mass and lifespan. The DAPD is a statistical measure, providing an estimate of the proportion of animals (in thousands) treated daily with a particular antimicrobial agent. For example, 10 DAPDs indicate that an estimated 1% of the population, on average, receives a certain treatment on a given day (see section 9.2, Materials and Methods).

Defined Daily Doses per 100 occupied bed-days (DBD): DBD is the consumption calculated in defined daily doses at hospitals, divided through the number of bed-days. This allows comparison of hospitals related to the length of patient stays. The number of bed-days is extracted from The National Patient Registry (Landspatientregistret, LPR). Time of reporting

differs between hospitals and closing time for reporting is later than extraction time for the DANMAP report. Every patient admitted to a hospital accounts for the exact length of the hospital stay. This corresponds to the actual hours at hospital divided by 24 hours.

DDD per 1,000 inhabitants per day (DID): Consumption in both primary health care, hospital care and the overall total consumption is presented in DID, allowing for comparison between sectors and for illustration of the consumption in hospital care without taking hospital activity (discharges and length of stays) into account. Data presented in DID provide a rough estimate of the proportion of the population within a defined area treated daily with certain drugs. For example, 10 DIDs indicate that 1% of the population on average gets a certain treatment daily. In figures presented as DDD/1,000 inhabitants/day.

Finishers: Pigs from 30-100 kg live weight from after the weaner stage to time of slaughter.

Fully susceptible: An isolate will be referred to as fully susceptible if sensitive to all antimicrobial agents included in the test panel for the specific bacteria.

Human clinical samples/isolates: In the DANMAP report, human clinical samples and/or isolates refers to the sample being taken in a clinical situation, meaning in the course of diagnosing and treating a possible infection in a patient.

Human screening samples/isolates: In the DANMAP report, human screening samples and/or isolates refers to sampling being performed for monitoring purposes in a defined group of asymptomatic individuals. Examples are rectal swaps to determine carriage of multidrug-resistant bacteria in the intestine or swaps from the throat, nostrils or perineum to determine carriage of methicillin-resistant *Staphylococcus areus* (MRSA).

Intramammaries: Antimicrobial agents for local application in the mammary gland (udder) to treat mastitis.

Layer: A hen raised to produce eggs for consumption.

Minimum inhibitory concentration (MIC): This is the lowest concentration of antimicrobial agent in a given culture medium, e.g. broth or agar, below which growth of the bacteria is not inhibited.

Multidrug-resistant: A *Salmonella*, *Campylobacter*, *Enterococcus* or *E. coli* isolate is assumed multidrug-resistant if it is resistant to three or more of the main antimicrobial classes. The number of antimicrobial classes and antimicrobial agents included in this definition depends on the test panel for each bacterium.

Pets or pet animals: Dogs, cats, birds, mice, Guinea pigs and more exotic species kept at home for pleasure, rather than kept for work or food. Horses are not included as pet animals. The live biomasses of Danish pets used for estimating veterinary consumption only include dogs and cat.

Piglet: The new-born pig is called a piglet from birth till they are permanently separated from the sow at 3-4 weeks of age. The weight of the piglet at weaning is approximately 7 kg.

Poultry: The major production species are fowl *Gallus gallus* (broilers, layers, including breeding and rearing) and turkey. Regarding antimicrobial consumption, 'poultry' also includes domesticated ducks, geese, game birds and pigeons.

Sow: Any breeding female pig on the farm.

Weaner: Any pig of 7–30 kg live weight after it has been weaned (dry diet and water only).

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