Textbox 3.1

Environmental AMR surveillance: From detection to decisions

The purpose of environmental AMR surveillance

Taking action against AMR without surveillance data to base mitigation decisions on has been likened to "flying blind" [1]. Along the same lines, one could argue that AMR surveillance without a clear objective is similar to getting into the cockpit without knowing the directions to the destination. It would take an awful lot of time and resources figuring out where to go with the plane in the air, which is why commercial air flights are – of course – planned meticulously. The same should be true for AMR surveillance: we need to know *why* we want to do surveillance and *what* we want to achieve before we start. This is particularly true for environmental surveillance, which easily becomes a task of figuring out what everything AMR-related looks like everywhere, all the time.

In clinical and veterinary AMR surveillance, surveillance data could influence the prescription and use of antimicrobials and can often be specific to particular pathogens and antimicrobial treatment regimes. The value then comes in the form of damage control, but also an opportunity to get ahead of the curve and detect emerging AMR threats before they become common in clinics or among production animals [2].

Such direct application links are harder to establish for environmental AMR surveillance. One could organize the environmental surveillance efforts into three different overarching 'use cases':

- Track AMR circulating in populations (e.g. a city or a farm) through wastewater.
- Evaluate environmental releases, dissemination and potential exposure to resistant microbes.
- Identify emerging resistance mechanisms before they become established clinical or veterinary problems.

None of these use cases does by itself provide a clear actionable outcome for the surveillance. Say that an increase in a gene providing resistance to a last-resort antibiotic is detected in Copenhagen wastewater; what action would that warrant? Covid-style lockdowns? Screening of incoming patients to hospitals? Protective measures towards the elderly? All these options are disproportional to the evidence, making it clear that we need prior definitions of:

1) What risks are we aiming to reduce through AMR surveillance?
2) What meaningful actions could we take based on surveillance to reduce these risks? Who would be responsible for taking these actions?
3) What would be the different 'trigger levels' measured in surveillance to initiate such actions?
4) How can we assess the efficiency of the measures taken?

The risks and actions landscape

The risks associated with AMR can be divided into two major groups: transmission risks and emergence risks, and both can be further subdivided. The transmission risks constitute the spread of resistant pathogens or mobile genetic elements carrying antibiotic resistance genes in various settings (hospital, agriculture, wastewater and so on). Actions to reduce those transmission risks involve hygiene, isolation of carriers, separation of animals, reducing releases of AMR into the environment and measures to avoid exposure of animals and humans to environmentally transmitted AMR [2]. Those measures are well understood, but generally not easy or popular to implement.

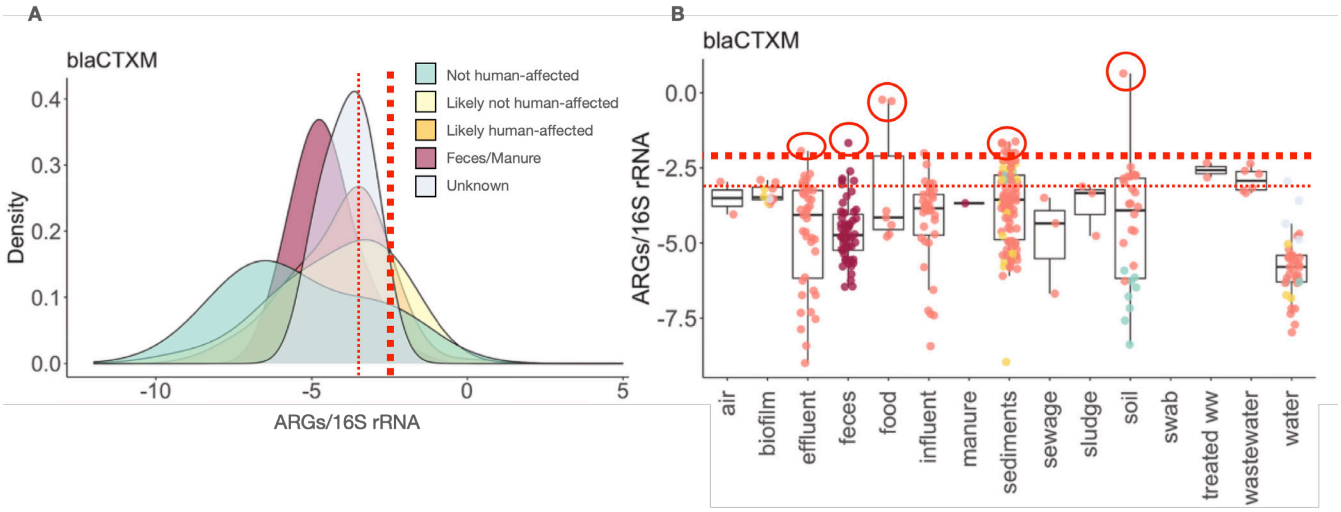
The emergence risks, on the other hand, are connected to new forms of resistance appearing in pathogens, through selection, mutations, or transfer of new resistance genes into pathogens. Here, any mitigation efforts would need to target the flow of AMR into human or animal populations, or trying to contain transmission early. For this type of risks, only two courses of action are available: preventive measures to avoid AMR flow into humans and animals, or early-warning monitoring coupled to isolation of patients or sick animals [3].

continued ... Textbox 3.1

What is a meaningful change?

The other major issue is to couple actions to measurements. What detections would warrant a certain set of responses? Here, it is crucial to define what are the normal, expected variations of a given AMR target in a specific setting. This requires repeated sampling to establish baselines and understand, for example, seasonal variation [4]. It may also be important to consider what the host organism and genetic context is for a particular resistance gene, and if it is associated with mobile genetic elements. Once such background data is obtained, it is possible to make priorities and set levels that would trigger specific actions (Figure 1).

Figure 1 Example of a 'trigger level' method for AMR surveillance DANMAP 2025



Example of the 'trigger level' method suggested in Abramova et al. (2023) [4], using 10 times the third quartile (3Q) abundance values for a given ARG to determine the upper limit for what should be viewed as a deviation from normal background levels in the environment. In the example, the overall levels of blaCTX-M is shown with the 3Q indicated in thin dots and the 10x trigger level indicated by the thick dotted line (A). in (B), the same approach is taken but on an environment basis, showing the samples that would have triggered potential actions in red circles at the top.

Beyond established surveillance targets

For the emergence risks, AMR surveillance is dependent on being able to identify new forms of high-priority resistance before it has appeared (or become widely spread) among pathogens. In order to do that, we need to know what forms of resistance we are looking for. That, in turn, means that there is a need for characterizing and prioritizing new forms of AMR that have a high potential to transfer to pathogens. Recent work has shown that there is a substantial reservoir of resistance genes that conventional analyses overlook [5]. Most of these genes exist in harmless environmental or commensal bacteria and never make it into pathogens; the important task is to identify the ones that are able to early. This would involve investigating candidates for evidence of resistance function, mobility and occurrence in species that are close relatives to pathogens. For such purposes, it is also important to keep track of non-clinical resistance genes across strains of bacteria, environments and studies. This is one of the purposes of the recently launched CLEVER database (https://microbiology.se/clever/), that keeps track of both clinically established and latent resistance genes, giving them names and organizing them by verification status and mobility. This type of information can help prioritizing resistance genes that are likely to become clinical problems, rather than blindly looking for all forms of AMR.

Conclusions

In the end, AMR surveillance shouldn't start with detection and work towards decisions. It should start with the decisions and work its way backwards to the appropriate settings, methods and frequencies for detection. All AMR surveillance efforts, but particularly those in the environment, should be evaluated by whether they identify important changes, inform appropriate responses and have measurable intervention effects. With the EU now strongly pushing for wastewater surveillance of AMR, the issue of purpose has become urgently pertinent [6]. The question we should all ask before we venture into surveillance should be: "What decision will this measurement enable?"

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Textbox 4.1

VetStat: 25 Years of Monitoring Veterinary Antimicrobial Use

The overall purpose of the Danish database VetStat is to support the monitoring and prudent use of veterinary medicinal products through the collection of data on prescription medicine use, thereby contributing to the fight against antimicrobial resistance and promoting a One Health approach. VetStat has been in operation for 25 years. Over time, it has evolved from a research database into a cornerstone of Danish surveillance of veterinary antimicrobial use and an essential data source for DANMAP and international reporting.

Establishment of VetStat

A national register to collect data on veterinary use of prescription medicine was conceived in the late 1990s following the phase-out of antimicrobial growth promoters in the Danish animal production, partly to monitor trends in antimicrobial use. VetStat was subsequently developed in 1999 by the Danish Technical University (DTU) and launched in 2000. Initially, the database and its data were maintained by DTU and the main use of data was for research purposes, including the relationship between antimicrobial use and antimicrobial resistance, and as the foundation for DANMAP's chapters on antimicrobial use.

From Research Tool to Regulatory Instrument

After a rise in the veterinary use of antibiotics up throughout the 2000s it was decided, that the data in VetStat should be used more actively in policy making and initiatives. As a result, the responsibility for maintaining VetStat and its data was transferred from DTU to the Danish Veterinary and Food Administration (DVFA) in 2011. One of the most prominent examples of the regulatory use of VetStat data was the Yellow Card Initiative, targeting the highest users of antibiotics in the Danish pig production. VetStat also became an important tool for monitoring progress in national efforts to reduce antimicrobial use in animal production. Even though the responsibility was transferred from academia to the public sector, the data in VetStat continued and continues to play a key role in DANMAP and academic research into national antimicrobial use and resistance.

Modernization and Improved Data Quality

In 2017 it was decided that VetStat required modernization, both in terms of the user interface, improving data quality, balancing data access, and complying with increasing IT security demands. Additionally, it was decided to merge VetStat with the DVFA's register of authorized veterinarians, VetReg, to support data validation and user access management. The modernization of VetStat took place from 2018 to 2021 and the new platform was launched on 1 June 2021. Among other things, the modernized platform introduced improved data granularity regarding where medicine is being used, data quality validation, and improved data on intended animal species - especially for poultry and aquaculture. Even after its launch, New VetStat has continuously been improved and refined to enhance data quality, provide greater insights on medicine use, and support evolving regulatory needs.

Future Developments and Reporting Requirements

Apart from data in VetStat being used nationally in DANMAP, it also provides the foundation for Denmark's international reporting to the World Organization of Animal Health (WOAH) and to the European Union's European Sales and Use of Antimicrobials for Veterinary Medicine (ESUAvet) initiative. Especially the latter will expand VetStat's coverage of antimicrobial use in horses and companion animals, further strengthening national and international surveillance. ESUAvet will start collecting data on antimicrobial use in horses from 2027 and in companion animals from 2030, meaning that data must be collected in 2026 and 2029, respectively.

VetStat already collects sales data from pharmacies anytime prescription medicine is being sold for use in horses and companion animals; however, the total use data is incomplete, as veterinarians are currently not obligated to report their use of antimicrobials for these animal species. To meet these reporting requirements, equine veterinarians will be required to report their use of antimicrobials from 2027, followed by mandatory reporting for companion animal veterinarians from 2029. Additionally, sales for use in companion animals are currently reported collectively, but as ESUAvet requires antimicrobial use to be specified for dogs and cats, the reporting requirements for companion animals will have to follow suit.

As reporting requirements continue to expand, VetStat will remain a central tool for surveillance, research, and policy development related to veterinary antimicrobial use in Denmark.

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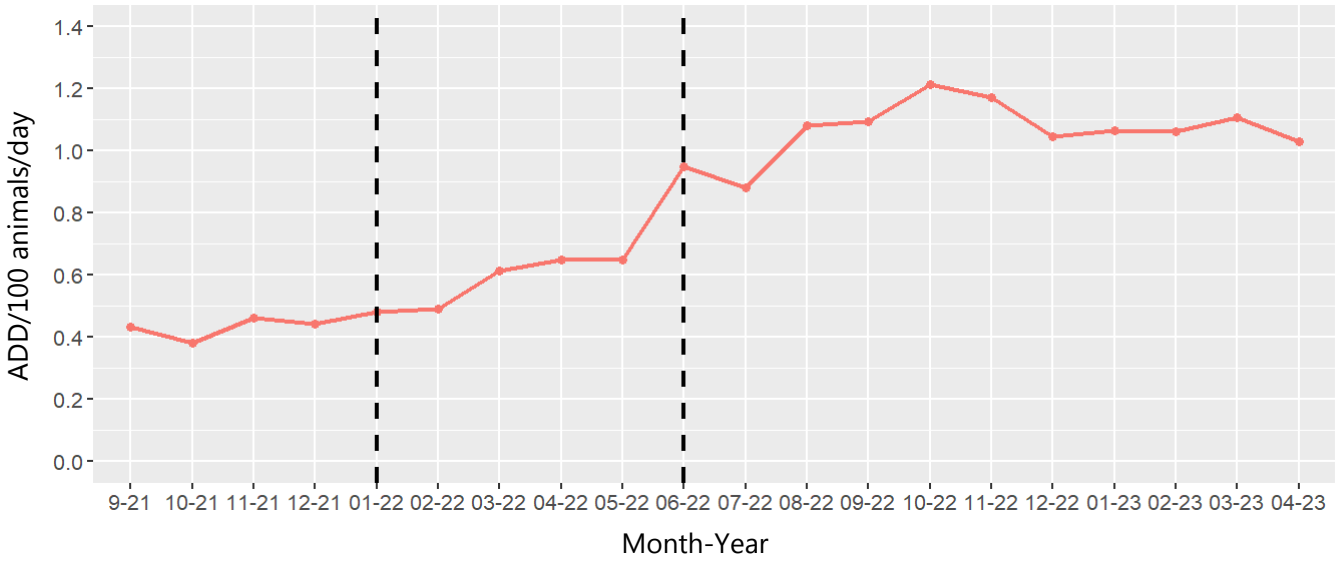
Textbox 4.2

Effect of the new Veterinary Medicinal Products Regulation on the antimicrobial use in Danish Weaners

The new Veterinary Medicinal Product Regulation came into force in January 2022. In June same year, medicinal zinc oxide was phased out and an increase in the national yearly antimicrobial use (AMU) was seen between 2021 and 2022. The increase in AMU was mainly driven by an increase in use of products prescribed for gastrointestinal indications in weaners. Medicinal zinc oxide was widely used in the Danish pig production to prevent post weaning diarrhoea. Thus, it seems reasonable to attribute the increase in AMU to the phasing out of medicinal zinc oxide. However, with the new regulation, the veterinarians were obliged to prescribe antimicrobials in accordance with the Summary of Product Characteristics (SPC). In Denmark, many antimicrobial products were prescribed with a shorter treatment duration than stated in the SPC. This was to keep the AMU as low as possible and below the yellow card limits. With the new regulation, this was not allowed, and the expectation was that the individual farmer would either increase AMU due to a longer treatment duration or change to products with a shorter treatment duration.

VetStat data were analysed to investigate the effect of the new Veterinary Medicinal Products Regulation on AMU for Danish Weaners on a monthly national. Data consisted of all antimicrobial products prescribed for oral administration and gastrointestinal indications in weaners from January 2020 – December 2023. The AMU was measured in ADD per 100 animals per day and the percentage changes in antimicrobial use between 2021 and 2022 were calculated for each product. The project focused on the products with an increase in use above 50% or a decrease in use below 50%. Veterinarians in Danish pig practice were consulted about the previous treatment regimens for the specific products, and this was compared with the requirements in the SPC.

Figure 1 Monthly prescriptions of *Neomay* for gastrointestinal indications in weaners DANMAP 2025



Monthly prescriptions of the antimicrobial product Neomay (active ingredient is Neomycin) in the period from September 2021 to April 2023. National prescriptions are summarised per month and measured in ADD per 100 animals per day. The first dotted line marks the New Veterinary Medicinal Product regulation coming into force (January 2022). The second dotted line marks the phasing out of medicinal zinc oxide (June 2022).

The use of *Doxycyclin "ScanVet" Vet.* increased with 500% from 2021-2022. The products *Apravet, Neomay* and *Lismay* increased with 171%, 121% and 88%, respectively. The use of *Octacillin Vet.* decreased with 79%. The use of *Doxx-Sol* decreased with 91% for gastrointestinal indications, but increased equally for respiratory indications, which is the officially approved indication for *Doxx-Sol*. These changes were observed already before the phasing out of medicinal zinc oxide, which could indicate an effect of the new regulation. The veterinarians who were consulted confirmed that the changes seen could be attributed to the difference between the previous treatment regimens and the SPC for these products. For example, for *Neomay*, the SPC requires a treatment duration of 3-4 days, which according to the veterinarians was previously used in a double dose but only as a one-day treatment. The change in monthly prescriptions for *Neomay* is illustrated in Figure 1.

A further increase was seen after the phasing out of medicinal zinc oxide, which again can be attributed to more farmers implementing longer treatment duration, but also to an increased need for treatment when weaning pigs without the use of medicinal zinc oxide.

This project was part of the veterinary contingency work carried out by the VetStat cluster at University of Copenhagen under the veterinary public service agreement. The results are presented in this report (In Danish): https://dkvet.dk/rapporter/Analyse af veterin rl gemiddelforordningens art. 106 stk 1s p virkning p udviklingen af antibiotikaforbrug til grise.pdf.

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Textbox 4.3

Challenges in quantifying and presenting cattle antimicrobial use: Insights from studies of Danish rosé veal calf farms

Monitoring antimicrobial use (AMU) is essential for antimicrobial stewardship. However, quantifying and presenting AMU can be challenging. Measures such as the weight of active compound and standardised doses are commonly used and related to the population at risk, as in DANMAP. Antimicrobial use is frequently stratified by species, age groups, or indication. Understanding how quantified AMU reflects the underlying on-farm use can provide valuable context for interpreting the reported results.

As part of the PhD project *Improving quantification and understanding of patterns in antimicrobial use in Danish cattle*, VetStat data on antimicrobial sales for cattle were combined with treatment records and observations collected in a field study of Danish rosé veal farms. Experiences from this project are summarised in three key points:

Transparency in quantification methods is crucial
Methods used to quantify AMU vary and, in some cases, differ even when using the same data. For example, data from VetStat form the basis of both DANMAP and VetStat reports, yet the definition and calculations of animal daily doses differ between the two. In VetStat, a daily dose per kilogram live weight of an animal is defined for each unique product, whereas DANMAP defines daily doses for active compounds. Furthermore, the standardised animal is based on an assigned fixed weight in VetStat and on average live weight in DANMAP.

Additional factors that may influence animal daily dose calculations include dosage intervals, age-specific dosing recommendations, and durations of effect that are shorter or longer than one day. The approach to standardising a dose is not always clearly communicated. Consequently, an animal daily dose is the result of a series of methodological decisions, and differences in approach may significantly affect the summarised statistics presented. Transparency regarding methodological choices is therefore essential.

The composition of groups should be considered when making comparisons
AMU can be presented in many ways. Stratification by species, age groups, or indications preserves information that might otherwise be lost in aggregated summaries. Applying meaningful subgroups and maintaining clear, concise, and relevant reporting is a continuous balancing exercise.

Stratification choices can influence comparisons and benchmarking across farms, sectors, and national borders. Age groups provide a relevant example. In VetStat, the group 'calves' includes all animals younger than one year of age and is assigned a standard weight of 200 kg. Calves undergo a substantial weight gain during the first year, which is likely to affect the AMU estimates, as doses for most systemic antibiotics are calculated based on body weight. Using a standard weight is not inherently problematic, as it is merely a standardisation method applied equally across farms. Challenges arise when comparing farms, sectors, production types, and populations with marked differences in age distribution and, consequently, body weight at treatment.

Different treatment patterns can also pose a challenge for comparisons. Different production types or stages of production are often associated with different disorders. In VetStat, treatments for omphalitis (navel infection) and interdigital phlegmon (a hoof infection) are registered in the same indication group but they typically appear at different stages of a calf's life. When comparing AMU, the composition of the population within each stratified group should always be carefully considered.

Standardisation helps identify patterns, but reality is often more complex

Quantifying and standardising allow summaries of complex data across farms, regions, and borders in a more approachable way. This provides valuable insights into overall trends and patterns.

Results from studies in this project showed that the individual farm was an important explanatory factor for both the level of AMU and the way antimicrobials were used. Differences between farms were both visually and statistically significant. Each farm had its own strengths and challenges regarding antimicrobial use. These findings highlight the importance of farmers and local conditions in the ongoing effort to understand and evaluate AMU. The project was part of the veterinary contingency work carried out by the VetStat cluster at University of Copenhagen under the veterinary public service agreement. The project was co-funded by the Danish Cattle Levy Fund.

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Textbox 5.1

The Danish Hospital Medication Register: new opportunities for examining antibiotic therapy in Danish hospitals

The Danish Hospital Medication Register provides patient-level data on medication administered in all public hospitals and affiliated hospital outpatient clinics in Denmark (1, 2). This register expands opportunities for pharmacoepidemiological research by enabling analyses of hospital medication use, including antibiotic treatment choices such as de-escalation strategies, and the transition from intravenous to oral therapy across different patient populations. Opposite the aggregated annual data reported in the DANMAP reports, the Danish Hospital Medication Register provides patient-level information on actual medication administrations. The Danish Hospital Medication can be linked with other Danish health registries, including the Danish National Prescription Registry, the Danish Microbiology Database, and the Danish National Patient Register, which provides a unique opportunity to examine complete antibiotic treatment courses spanning both hospital and community settings.

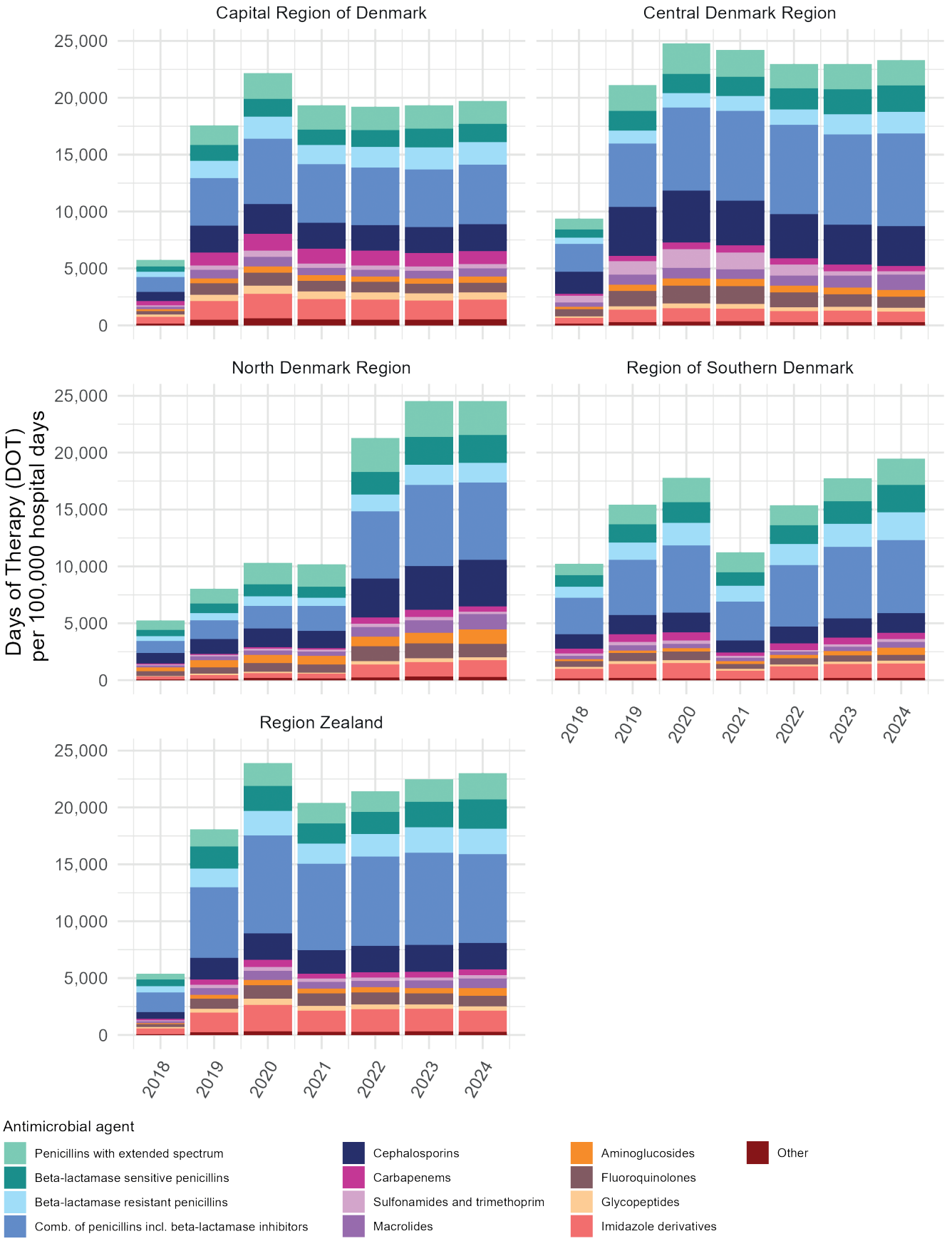
However, important differences in data recording should be considered. The Danish Hospital Medication Register records each medication administration, whereas the Danish National Prescription Registry records redeemed prescriptions, resulting in uncertainty regarding treatment duration and medication adherence. The patient-level data from the Danish Hospital Medication Register also enable calculation of measures relevant to antimicrobial stewardship such as the number of treated patients or Days of Therapy (DOT) (3). However, some variables, such as dose units, are incompletely recorded and/or coded using a wide range of different units, requiring substantial data management before analysis. No published studies have evaluated the validity of the Danish Hospital Medication Register.

This textbox aims to characterize the use of antimicrobial agents administered during hospitalization across hospital regions and age groups. The analyses include all antibiotics (ATC code group J01) recorded in the Danish Hospital Medication Register between 15 May 2018 and 11 November 2024. DOT were defined as the administration of at least one dose of a specific antimicrobial agent to an individual on a given calendar day (3). Each antimicrobial agent was counted separately (3). Therefore, a patient receiving several antimicrobial agents on the same day contributed one DOT per antimicrobial agent. Hospital days were defined as the total number of calendar days on which an individual had inpatient or outpatient hospital contact during the study period. A calendar day counts as one hospital day regardless of the number of hours spent at the hospital by the patient.

The number of DOT per 100,000 hospital days appeared lower in 2018 across all regions, likely reflecting incomplete reporting during the initial implementation of the register. In the North Denmark Region, DOT per 100,000 hospital days remained substantially lower until 2022, suggesting incomplete reporting during this period. Across all regions and years, combinations of penicillins including beta-lactamase inhibitors, accounted for the largest proportion of DOT. The distribution of antimicrobial agents was similar across hospital regions. The overall DOT per 100,000 hospital days was lower in the Region of Southern Denmark than in the other regions throughout the study period. In the Capital Region of Denmark, the Central Denmark Region, and Region Zealand, DOT per 100,000 hospital days was highest in 2020 (Figure 1).

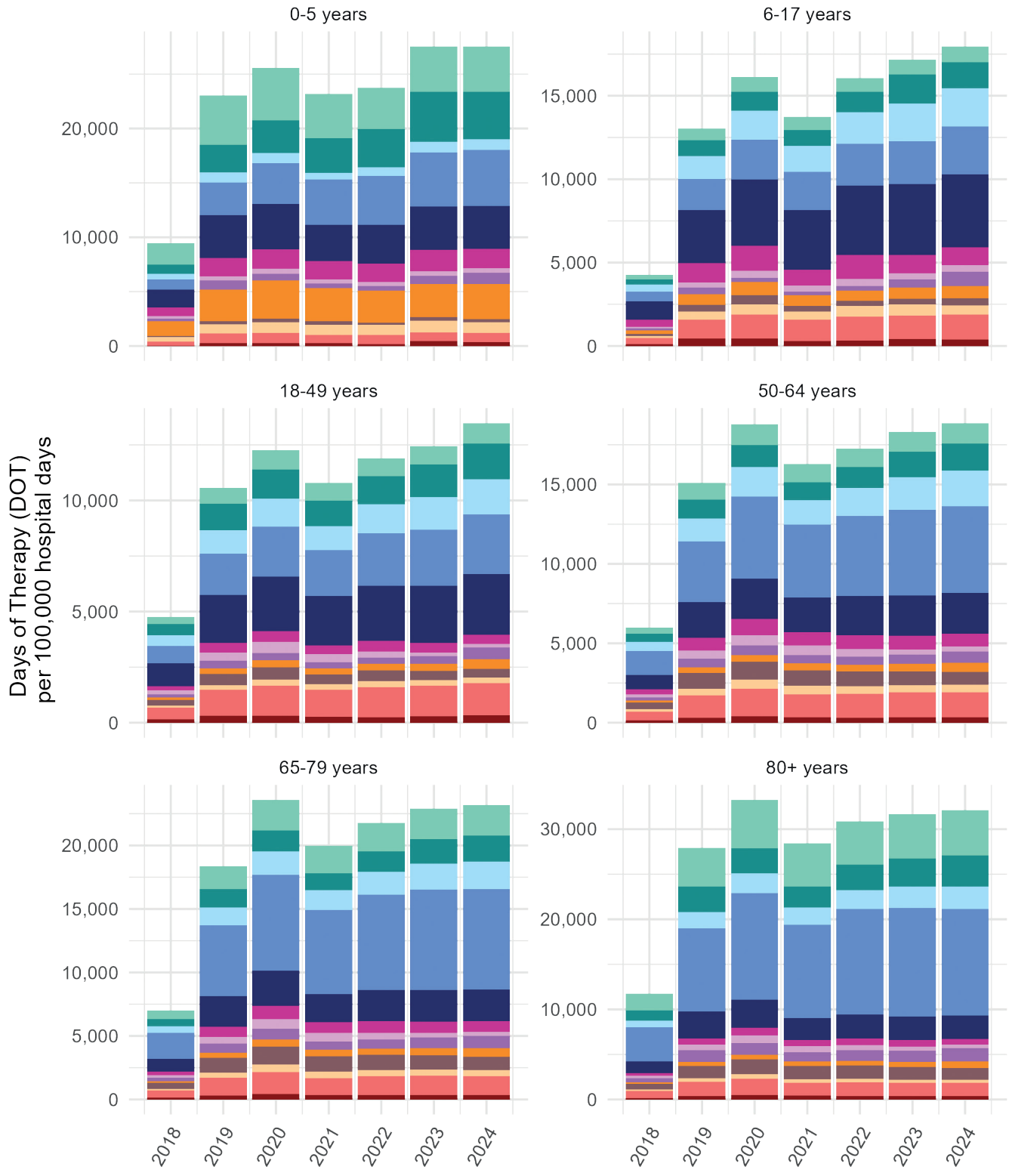
The overall DOT per 100,000 hospital days, summed across all antimicrobial agents, was highest among individuals aged 80 years and older, followed by children aged 0-5 years and individuals aged 65-79 years. Among individuals aged 0-5 years, 50-64 years, 65-79 years, and 80 years and older, combinations of penicillins including beta-lactamase inhibitors, accounted for the largest proportion of DOT. In contrast, cephalosporins accounted for the largest proportion of DOT among individuals aged 6-17 years and 18-49 years. Aminoglycosides contributed a higher proportion of DOT among children aged 0-5 years compared with the other age groups (Figure 2).

Figure 1. Days of Therapy (DOT) per 100,000 hospital days stratified by antimicrobial agent and hospital region DANMAP 2025



continued ... Textbox 5.1

Figure 2. Days of Therapy (DOT) per 100,000 hospital days stratified by antimicrobial agent and age group DANMAP 2025



In summary, the use of antimicrobial agents during hospitalization was similar across Danish regions, with combinations of penicillins including beta-lactamase inhibitors being the most commonly used antimicrobial agents. The overall DOT per 100,000 hospital days was highest among patients aged 80 years and older, while patterns of antimicrobial administration differed across age groups. Lower recorded use of antimicrobial agents in 2018 and in North Denmark until 2022 likely reflect incomplete reporting.

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Textbox 5.2

IMAGINE – improving antibiotic use in European nursing homes

Combining infection prevention and antimicrobial stewardship

Nursing home residents are particularly vulnerable to infections and are often treated with antibiotics. Suspected urinary tract infection (UTI) is the most common reason for antibiotic treatment[1], yet more than half of the treatments may be unnecessary[2]. This highlights the need for interventions that not only support appropriate diagnosis and antibiotic use but also strengthen infection prevention in nursing homes.

The aim of the European IMAGINE project – *Improving antibiotic use in long-term care facilities through infection prevention and control and antimicrobial stewardship* – was therefore to develop, in close collaboration with nursing home staff, a multifaceted intervention suitable for nursing homes across Europe. The intervention was designed to strengthen infection prevention and control (IPC) and antimicrobial stewardship (AMS), ultimately reducing unnecessary antibiotic use by targeting staff in nursing homes across eight European countries: Greece, Hungary, Lithuania, Poland, Slovakia, Slovenia, Spain, and Denmark.

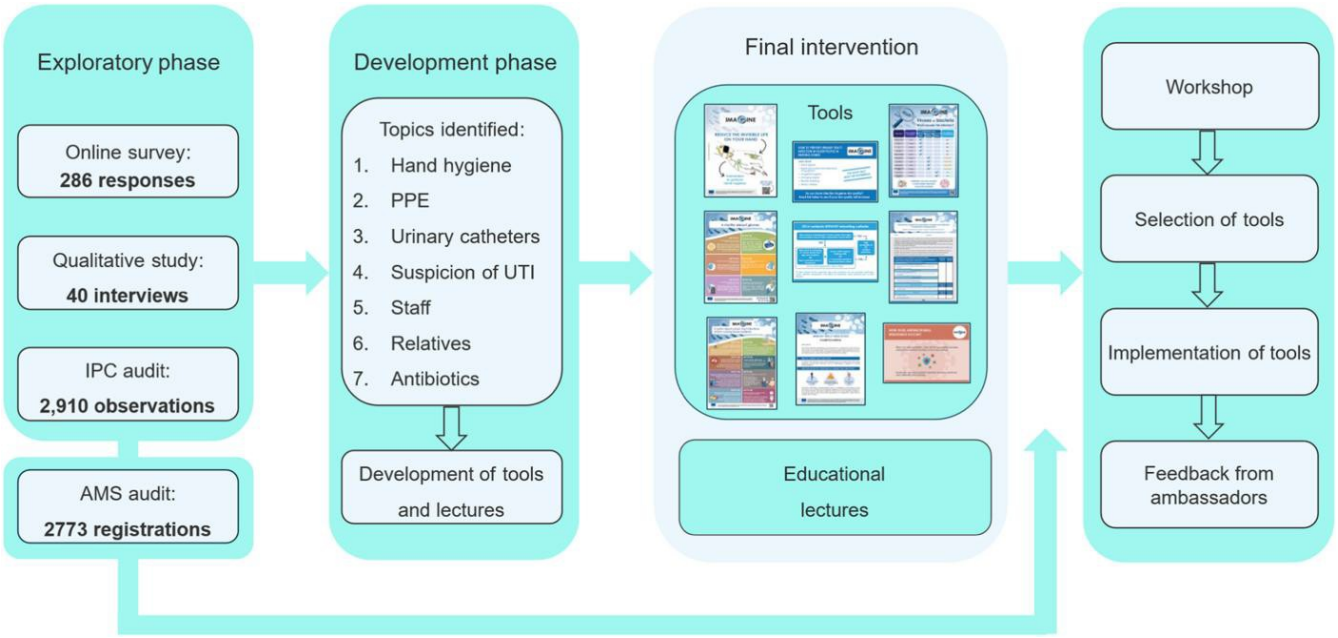
Not just an intervention *for* nursing home staff – but *with* them

A central feature of IMAGINE was the use of Participatory Action Research (PAR). Nursing home staff were recruited as IMAGINE ambassadors and participated as partners throughout the project. They collected audit data, contributed with their knowledge on everyday nursing home practice, participated in workshops and helped implement the intervention locally[3].

The intervention was designed around an exploratory phase. It included an online survey[4], a qualitative study[5], IPC audit, and AMS audit[6] (Figure 1). Data obtained were combined with input from nursing home staff to identify seven priority areas: hand hygiene, personal protective equipment, urinary catheters, suspicion of UTI, staff competences, relatives and antibiotics (Figure 1).

Based on these findings, ten practical tools were developed, ranging from posters and leaflets to an infection prevention quiz, educational material for newly employed staff and a pocket card with an decision algorithm for suspected UTI – (see Figure 1). The intervention also included educational sessions and workshops in each participating country.

Figure 1 Overview of the development and implementation of the IMAGINE intervention DANMAP 2025



Did it make a difference?

A total of 109 nursing homes across the participating countries signed on IMAGINE. 103 completed the project and participated in both the IPC and AMS audits conducted in spring 2024 and repeated one year later in spring 2025.

Overall, adherence improved significantly for 17 of the 29 assessed IPC practices. Improvements were particularly evident for the availability of IPC resources and practices related to the handling of indwelling urinary catheters, although considerable variation was observed between countries[7].

Antibiotic use for suspected UTI also changed. Among residents without an indwelling urinary catheter, the proportion of antibiotic treatments classified as potentially unnecessary decreased from 52.9% before the intervention to 46.1% after the intervention. The overall result, however, conceals considerable variation between countries.

Interestingly, the incidence of antibiotic-treated UTI, across the 103 nursing homes decreased from a mean of 12.2% to 8.9%, corresponding to a relative reduction of approximately 27%. Denmark showed a reduction from 17.0% to 9.7%, corresponding to a 43% reduction[7] (Table 1). In Denmark, this reduction was accompanied by a marked change in diagnostic practice, where the use of urinary dipsticks for suspected UTI decreased by 77%. Changes in antibiotic-treated UTI were smaller in most of the other participating countries, and Slovakia showed an increase.

Table 1 Incidence of antibiotic-treated UTIs during a three-month period among residents at 103 nurs-ing homes in eight European countries before and after the IMAGINE intervention, 2024-2025 DANMAP 2025

Country	Number of residents at participating nursing homes	First registration (2024)	Second registration (2025)	Paired t-test
		Mean UTI incidence (%)	Mean UTI incidence (%)	P-value
Denmark	1,066	17.0	9.7	0.026
Greece	440	17.8	16.0	0.405
Hungary	1,536	11.0	8.3	0.165
Lithuania	779	4.8	3.8	0.546
Poland	1,441	3.7	3.4	0.878
Slovakia	918	4.4	6.8	0.153
Slovenia	2,414	14.3	12.6	0.176
Spain	1,124	26.6	13.3	0.006
Total	9,718	12.2	8.9	0.000

What can we learn from IMAGINE?

The IMAGINE project was based on a before-and-after study without a control group, and the observed changes therefore cannot with certainty be attributed to the intervention. Nor can we determine which of the individual components – audit and feedback, education, practical tools, peer discussion or staff involvement – contributed most to the observed changes.

Nevertheless, the findings suggest an important direction for antimicrobial stewardship in nursing homes. Preventing infections and improving antibiotic use may be most effective when approached together.

One size can fit all

Despite differences in healthcare systems, organization and culture, IMAGINE identified common challenges across the 103 nursing homes, allowing the same core tools to be used in all eight countries – suggesting that sometimes "one size" may actually fit quite many.

continued ... Textbox 5.2

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Textbox 5.3

Free from UTI in the Region of Southern Denmark

An initiative to prevent urinary tract infections among nursing home residents

The aim of this initiative is to reduce the incidence of urinary tract infections (UTIs) among nursing home residents and to reduce antibiotic consumption within the nursing home sector.

Antibiotic consumption is high among Danish nursing home residents compared with other European countries [1]. The majority is prescribed against UTI, though more than half of these treatments may be unnecessary as diagnostic criteria for UTI are not met [2]. There is a great potential for reducing the number of antibiotic prescriptions for nursing home residents and thereby reducing unnecessary adverse effects.

The pilot project

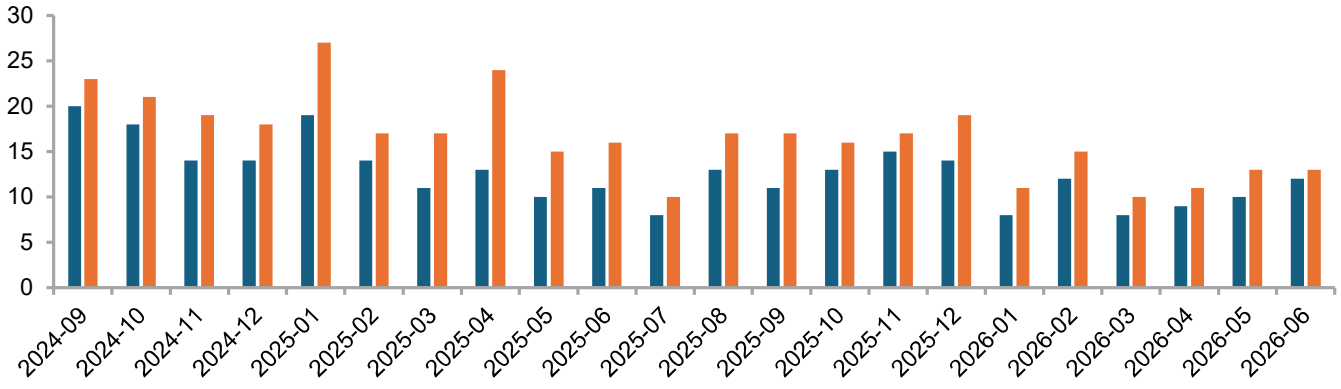
Free from UTI began as a pilot project in 2024 at two selected nursing homes in Nyborg and Odense [3]. Drawing inspiration from other initiatives in Denmark and abroad, the Department of Clinical Microbiology at Odense University Hospital developed a two-hour interactive training seminar in close collaboration with Nyborg and Odense municipalities. This seminar, including short instructional sessions, exercises, and case discussions, was attended by all staff at the two nursing homes. The seminar covered the basics of UTI and antibiotics as well as prevention of UTI and basic hygienic measures. Decision-support tools were developed to assist nursing home staff in assessing residents with suspected UTI. The use of urine dipsticks was discontinued as part of the project.

Both nursing homes succeeded in significantly reducing the incidence of UTIs and antibiotic consumption. One nursing home achieved a 66% reduction in the total number of UTI treatments (from 65 in 2023 to 22 in 2024). The other nursing home achieved a 46% reduction (from 67 in 2024 to 36 in 2025).

Continuation of the project

In 2025, *Free from UTI* was implemented at the remaining public nursing homes in Nyborg and Odense by a "train-the-trainers" method. Key staff members such as specialist nurses, managers, and nursing home doctors were trained to implement *Free from UTI* in their own settings. This effort has been well received in general and antibiotic consumption continues to decline (Figures 1 and 2). Successful implementation of *Free from UTI* principles depends on interdisciplinary collaboration and requires strong leadership commitment. Furthermore, it is essential to have permanent staff members acting as project ambassadors to maintain the effect. The aim is to expand the initiative to nursing homes throughout the Region of Southern Denmark.

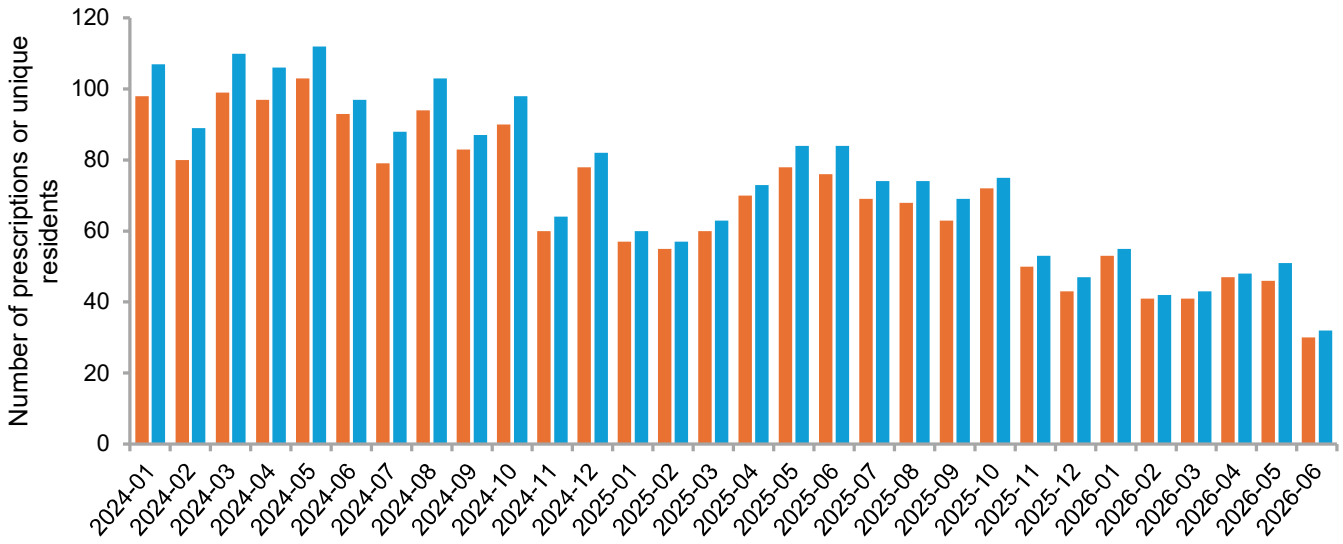
Figure 1 Use of antibiotics against UTI among nursing home residents in Nyborg from September 2024 to June 2026 DANMAP 2025



Number of prescriptions against UTI (orange) and number of unique residents treated against UTI (blue) per month in public nursing homes in Nyborg (approximately 186 residents in total).
The figure is based on cumulated medicine data from the municipality. Data is not adjusted for date of residency; some treatments may have been initiated before moving into the nursing home. Prescriptions of UTI specific antibiotics cover pivmecillinam, trimethoprim, sulfamethizol, or nitrofurantoin.

continued ... Textbox 5.3

Figure 2 Use of antibiotics against UTI among nursing home residents in Odense from January 2024 to June 2026 DANMAP 2025



Number of prescriptions against UTI (orange) and number of unique residents treated against UTI (blue) per month in public nursing homes in Odense (approximately 929 residents in total).
The figure is based on cumulated medicine data from the municipality. Data is not adjusted for date of residency; some treatments may have been initiated before moving into the nursing home. Prescriptions of UTI specific antibiotics cover pivmecillinam, trimethoprim, sulfamethizol, or nitrofurantoin.

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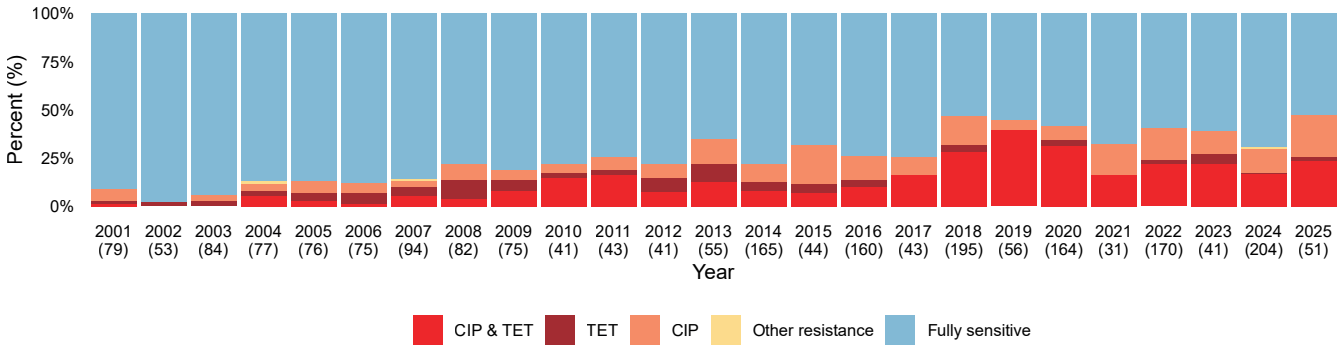
Textbox 6.1

30 years of *Campylobacter jejuni* surveillance in Denmark

Denmark has had a nationwide surveillance of antimicrobial resistance in *Campylobacter* recovered from healthy food-producing animals since 1995. A retrospective comparison of resistance patterns in *Campylobacter jejuni* over the past 25 years of the DANMAP programme[1] was performed. *C. jejuni* is a common cause of bacterial gastrointestinal infection in humans in Denmark, and broilers are an important zoonotic reservoir. It is hence of public health interest to continuously monitor the development of antimicrobial resistance in *C. jejuni* from broilers.

A total of 2,199 *C. jejuni* isolates from broilers were collected and reported in DANMAP between 2001 and 2025.

Figure 1 Relative distributions (%) of AMR profiles among *C. jejuni* from broilers by year, Denmark, 2001-2025 DANMAP 2025



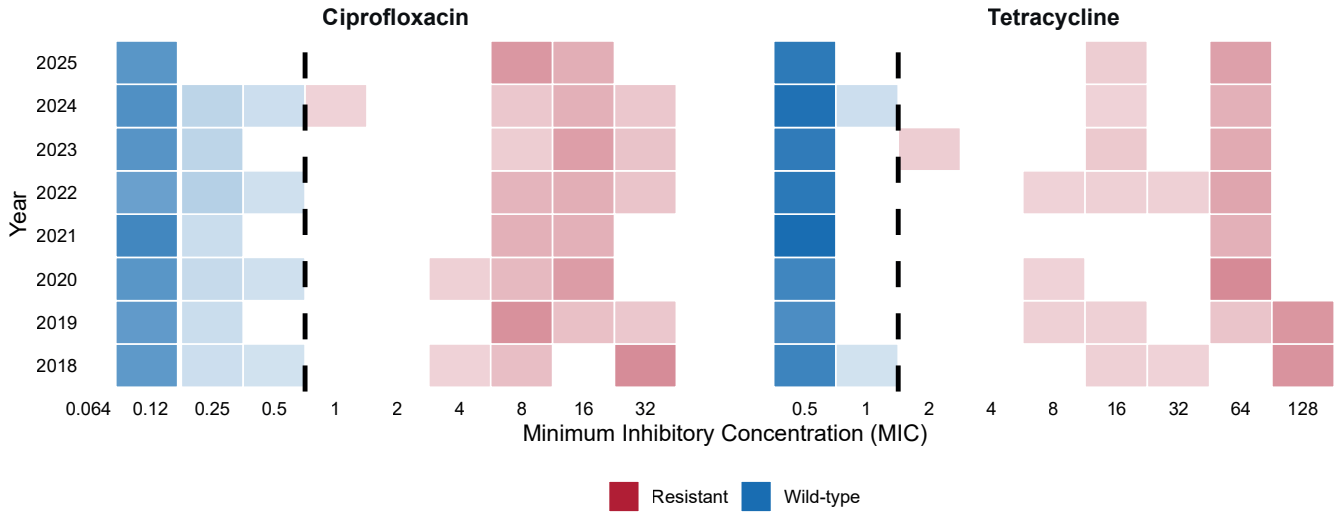
The bars show the percentage of isolates classified as having resistance to ciprofloxacin (CIP), tetracycline (TET), both CIP and TET, other resistance or being fully sensitive (sensitivity to all antimicrobial substances tested). The number of isolates included for each year is given in parentheses below each bar.

The relative occurrence of the different resistance profiles fluctuated over the 25-year period, with overall resistance (CIP, TET, CIP & TET and Other resistance) becoming more prominent from the late 2000s onwards and remaining common in the most recent years. In the early years, most isolates were fully sensitive. A first increase in the occurrence of resistance was observed in 2004, followed by a stable level until 2007, and a gradual increase from 2008 onwards for several years (see textbox 6.1. in DANMAP 2023). No statistically significant differences in the proportion of fully sensitive isolates were observed between years in 2018-2025, during which 31-47% of isolates had some form of resistance. Across the surveillance period, resistance was mainly associated with ciprofloxacin and tetracycline, either alone or in combination. Resistance to TET alone was more consistently observed, although at relatively low frequencies after 2016, while resistance to CIP alone became more frequent from 2013 onwards. Resistance to both CIP and TET became particularly prominent from 2018 onwards, while resistance classified as other resistance was rarely observed throughout the whole period.

MIC distributions for ciprofloxacin and tetracycline were examined for selected years to assess changes in the distribution of MIC values over time (Figure 2). Statistical comparisons were performed separately for wild-type and resistant isolates for each antimicrobial using the Kruskal-Wallis test followed by Dunn's post hoc test with Bonferroni correction, to assess whether the MIC distributions changed across the years considered.

[1] Although *C. jejuni* surveillance in DANMAP was established in 1995, MIC results are included from 2001 onwards as data from 1995-2000 was digitally unavailable at the time of writing.

Figure 2 Distribution of MIC values from *C. jejuni* from broilers by antimicrobial substance and year DANMAP 2025



Blue indicates wild-type isolates while red indicates resistant isolates. The intensity of the colour shading represents the percentage of isolates with the respective MIC value within each year, with darker shading indicating higher percentages. The dashed line represents the ECOFF value applied for interpretation.

For ciprofloxacin, significant differences in the MIC distribution of sensitive isolates were observed between 2018 and 2022 (with a slight shift towards the ECOFF) and between 2022 and 2025 (shift towards lower MIC values), whereas no significant differences were observed between the other years. The MIC distribution for resistant isolates differed significantly between 2018 and the subsequent years (except for 2023), with the distribution remaining stable from 2019 through 2025.

For tetracycline, no significant differences in the MIC distribution were observed among sensitive isolates in the selected years, although among resistant isolates there was a shift towards lower MIC values from 2020 onwards compared with 2018 and 2019.

Overall, combined resistance to ciprofloxacin and tetracycline, as well as resistance to ciprofloxacin alone in *C. jejuni* from broilers was more common in the later years of the programme. Some changes were also observed in the MIC distribution among both sensitive and resistant isolates, for ciprofloxacin and tetracycline, respectively, between the years 2018-2019 and the more recent years. An expanded analysis of the MIC distribution among ciprofloxacin-resistant isolates with and without combined CIP & TET resistance may provide further insights into the development of ciprofloxacin resistance in *C. jejuni* isolates from Danish broilers.

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Textbox 6.2

30 years of *Salmonella* surveillance in Denmark

Denmark has had a nationwide surveillance of antimicrobial resistance in *Salmonella* spp. recovered from healthy food-producing animals since 1995. A retrospective comparison of resistance patterns in *Salmonella* isolates over time was performed. *Salmonella* has been monitored in different sources including pigs, pork, cattle and broilers, although most consistently in pigs and pork, considered important sources of *Salmonella* infections in humans. This textbox focuses on *Salmonella* Derby, monophasic *Salmonella* Typhimurium and *Salmonella* Typhimurium, the most commonly detected serotypes in pigs and pork in Denmark, collected between 2000 and 2025[1].

A total of 9,841 *Salmonella* Derby, monophasic *Salmonella* Typhimurium and *Salmonella* Typhimurium isolates from pig and pork samples have been collected and reported in DANMAP between 2000 and 2025. The number of isolates varies by year, sample origin and serotype. For pigs, sampling has most recently only been done in alternating years, following the rules of the EU harmonized antimicrobial resistance monitoring [Commission Implementing Decision (EU) 2020/1729].

The relative distribution of antimicrobial resistance profiles varies by serotype, sample origin and year (Figure 1). The occurrence of resistance in *S.* Derby is generally lower than in *S.* Typhimurium and monophasic *S.* Typhimurium for both pigs and pork across the 26 years.

Among *S.* Derby from pigs, the proportion of fully sensitive isolates accounted for 45–50% in 2000-2005, followed by an increase in 2015 reaching a maximum of 73%. Since then, the level has fluctuated annually, reaching values of 70% or above in 2021, 2023 and 2025. In contrast, the proportion of fully sensitive *S.* Derby from pork has shown a gradual decrease since 2021, reaching a minimum of 42.1% in 2023.

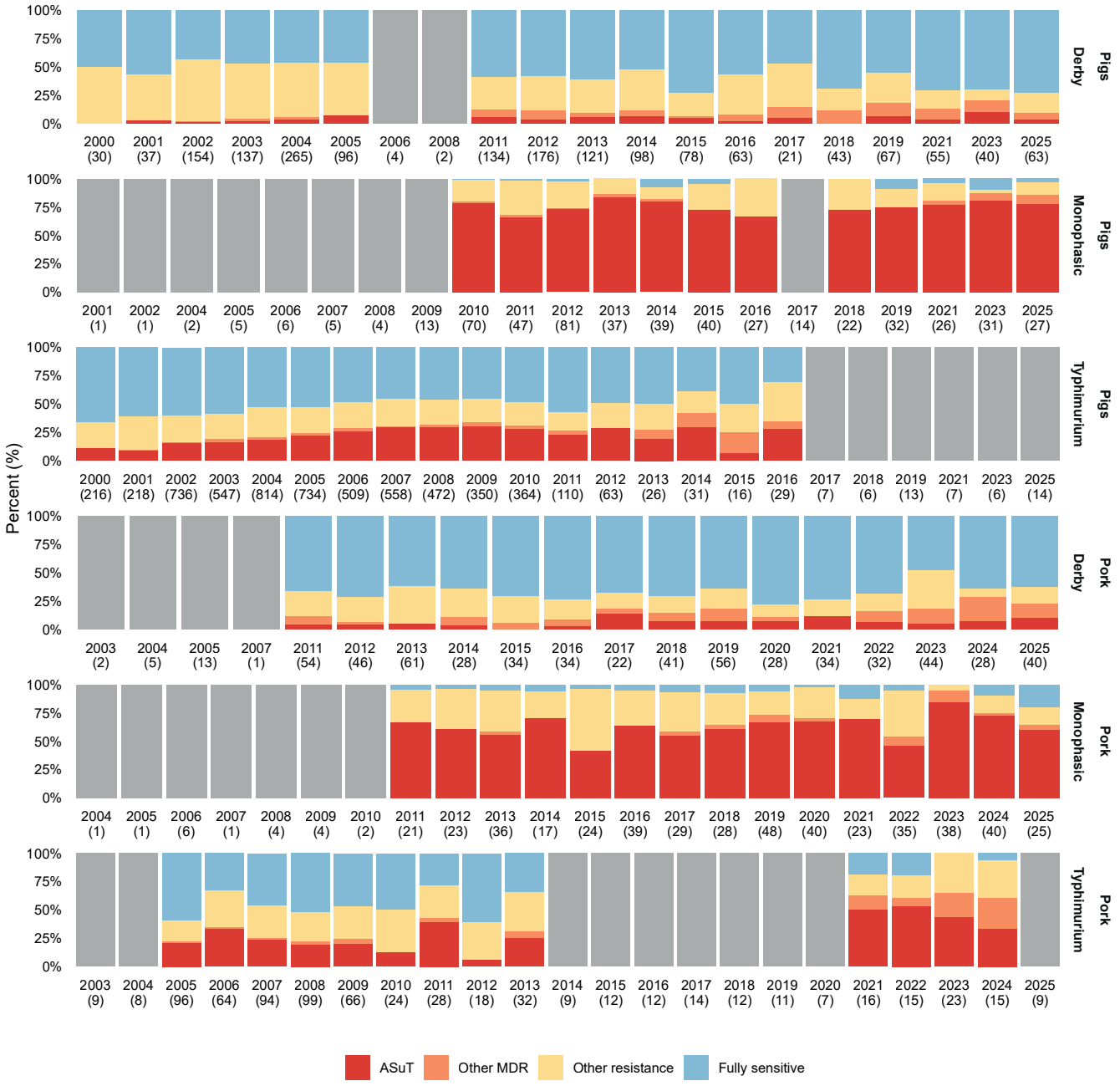
Among monophasic *S.* Typhimurium from pigs, ASuT remained the predominant resistance profile across all years, with proportions accounting for 66–84% of isolates, and the highest value observed in 2013. Among isolates from pork, ASuT accounted for 55–71% of isolates during 2011–2021, except in 2015, when the proportion was 41.7%. This was followed by a decrease in 2022 and an increase again in 2023 and 2024. Both in pigs and pork, the frequency of other MDR profiles in monophasic *S.* Typhimurium became more pronounced and consistent in the period 2022-2025, although this has not been a statistically significant change.

Among *S.* Typhimurium from pigs, the proportion of ASuT isolates increased from 10.6% in 2000 to 29.0% in 2008 and remained at a similar level through 2016 except for in 2015 (note that only 15 isolates were reported in this year). After 2016, very few *S.* Typhimurium isolates (<15) have been recovered from pigs under the scope of DANMAP sampling. Among *S.* Typhimurium from pork, the proportion of ASuT isolates varied between 19% and 33% during 2005–2009, followed by a more pronounced variation in 2010-2013. In the most recent years, ASuT accounted for 33-53%. In comparison to the earlier years, in the latest years the occurrence of complete sensitivity was markedly lower, and the occurrence of other MDR profiles markedly higher.

Overall, resistance profiles differed between serotypes, with lower resistance occurrence observed among *S.* Derby, followed by *S.* Typhimurium and higher occurrence observed among monophasic *S.* Typhimurium, where ASuT remained the predominant resistance profile across the monitoring period.

[1] Although Salmonella surveillance in DANMAP was established in 1995, MIC results are included from 2000 onwards as data from 1995-1999 was digitally unavailable at the time of writing.

Figure 1 Relative distributions (%) of AMR profiles among *Salmonella* Derby, monophasic *Salmonella* Typhimurium and *Salmonella* Typhimurium from pigs and pork by serotype and year, Denmark, 2000-2025 DANMAP 2025

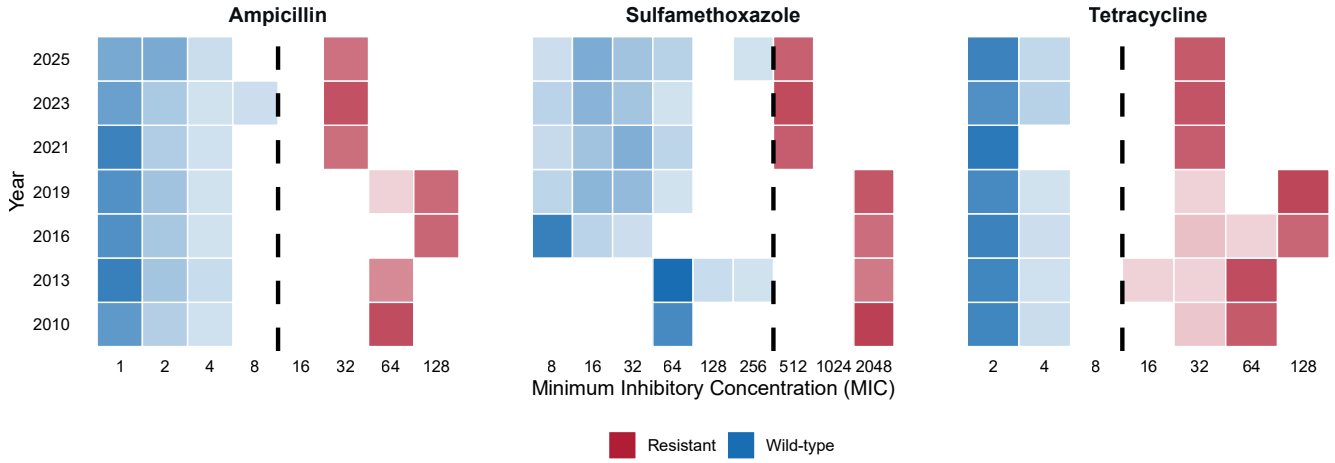


The bars show the percentage of isolates classified as ASuT (resistant to at least ampicillin, sulfamethoxazole and tetracycline), other MDR (other multidrug resistance profiles than ASuT), other resistance (resistance to one or two antimicrobial classes), or fully sensitive (sensitivity to all antimicrobial substances tested). Isolates included are shown separately for S. Derby, S. Typhimurium and monophasic S. Typhimurium with antigenic formula S 4,[5],12:i:-, and separately for pigs and pork. The number of isolates included for each year is given in parentheses below each bar. Bars with fewer than 15 isolates per year and serotype are coloured grey.

continued ... Textbox 6.2

Figure 2 Distribution of MIC values from *Salmonella Derby*, monophasic *Salmonella* Typhimurium and *Salmonella* Typhimurium isolates from pigs by antimicrobial substance and year

DANMAP 2025



Blue indicates wild-type isolates while red indicates resistant isolates. The intensity of the colour shading represents the percentage of isolates with the respective MIC value within each year, with darker shading indicating higher percentages. The dashed line represents the ECOFF value applied for interpretation.

MIC distributions for ampicillin, sulfamethoxazole and tetracycline were examined for selected years to assess changes in the distribution of MIC values over time (Figure 2). Statistical comparisons were performed separately for wild-type and resistant isolates for each antimicrobial using the Kruskal-Wallis test followed by Dunn's post hoc test with Bonferroni correction, to assess whether the MIC distributions changed across the years considered.

Among ampicillin-sensitive isolates, the MIC distribution below the ECOFF remained relatively stable from 2010 to 2023, followed by a significant shift towards the ECOFF in 2025. However, the 2025 distribution did not differ significantly from those observed in the individual years of 2019 and 2023. For sulfamethoxazole, the MIC distribution of sensitive isolates differed significantly between the period 2010-2013 and the year 2016, and between 2016 and the period 2019-2025, with observed MIC values being lower in 2016 than in 2010-2013 and higher in 2019-2025 compared to 2016. For tetracycline-sensitive isolates, the MIC distribution below the ECOFF remained stable from 2010 through 2021. A significant shift was observed in 2023 towards higher MIC values, while the 2025 distribution was not significantly different from either the preceding years or 2023.

Among isolates resistant to each of the three ASuT substances, there has been a clear shift towards lower MIC values in the years 2021, 2023 and 2025, which could in time also lead to a decrease in the occurrence of ASuT resistance among *Salmonella* isolates recovered from pigs. An apparent ongoing reduction in ASuT occurrence has already been observed among *S.* Typhimurium and monophasic *S.* Typhimurium from pork in the period 2023-2025 (Figure 1). However, due to the relatively low number of isolates recovered particularly from pork every year, caution should be taken in the interpretation of resistance trends in this source.

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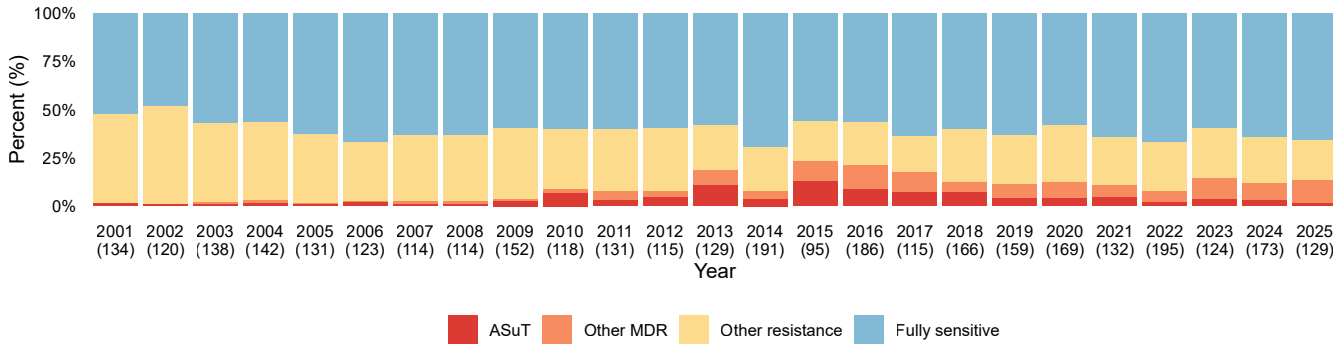
Textbox 7.1

30 years of *Escherichia coli* surveillance in Danish broilers

Denmark has had a nationwide surveillance of antimicrobial resistance in indicator *Escherichia coli* recovered from healthy food-producing animals since 1995. A retrospective comparison of resistance patterns in *E. coli* over the past 25 years of the DANMAP programme[1] was performed.

A total of 3,495 *E. coli* isolates from broilers were collected and reported in DANMAP between 2001 and 2025. The sampling strategy has changed over time, with a more standardized approach being implemented after 2014, following the introduction of the harmonized antimicrobial resistance monitoring in the European Union [Commission Implementing Decision (EU) 2020/1729].

Figure 1 Relative distributions (%) of AMR profiles among *E. coli* from broilers by year, Denmark, 2001-2025 DANMAP 2025



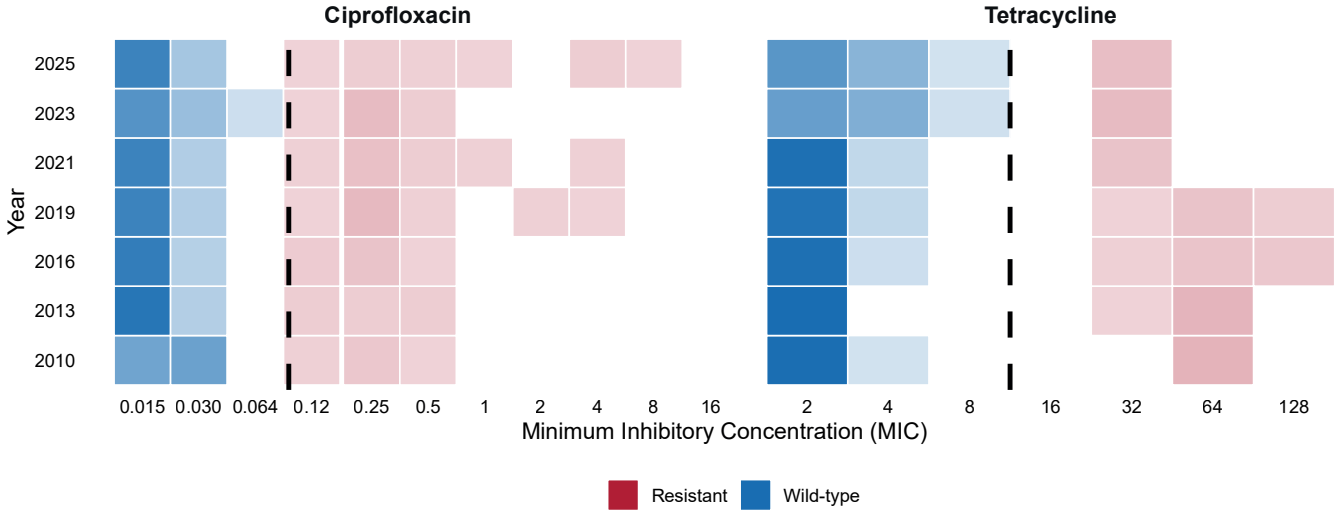
The bars show the percentage of isolates classified as ASuT (resistant to at least ampicillin, sulfamethoxazole and tetracycline), other MDR (other multidrug resistance profiles than ASuT), other resistance (resistance to one or two antimicrobial classes), or fully sensitive (sensitivity to all antimicrobial substances tested). The number of isolates included for each year is given in parentheses below each bar.

The relative distribution of antimicrobial resistance profiles varied between years (Figure 1). Fully sensitive *E. coli* isolates were dominant across all years, ranging from 52% to 70%, except in 2002, when 48% of the isolates were fully sensitive and 51% had other resistance. The proportion of ASuT and other MDR was generally low and increased from 2009, reaching a maximum of 23% in 2015 before decreasing and plateauing from 2019 onwards.

MIC distributions for ciprofloxacin and tetracycline were examined for selected years to assess changes in the distribution of MIC values over time (Figure 2). Statistical comparisons were performed separately for wild-type and resistant isolates for each antimicrobial using the Kruskal-Wallis test followed by Dunn's post hoc test with Bonferroni correction, to assess whether the MIC distributions changed across the years considered.

[1] Although *E. coli* surveillance in DANMAP was established in 1995, MIC results are included from 2001 onwards as data from 1995-2000 was digitally unavailable at the time of writing.

Figure 2 Distribution of MIC values from *E. coli* from broilers by antimicrobial substance and year DANMAP 2025



Blue indicates wild-type isolates while red indicates resistant isolates. The intensity of the colour shading represents the percentage of isolates with the respective MIC value within each year, with darker shading indicating higher percentages. The dashed line represents the ECOFF value applied for interpretation.

Among wild-type isolates, the MIC distribution for ciprofloxacin shifted towards lower MIC values after 2010 and remained similar in 2013, 2016, 2019 and 2021. In 2023, the distribution shifted towards higher MIC values, closer to the ECOFF, and was significantly different from 2013 and 2016. In 2025, a significant shift towards lower MIC values was observed compared with 2023. For tetracycline, the distribution in 2023 and 2025 differed significantly from the previous years, shifting towards higher MIC values and closer to the ECOFF. Among resistant isolates, no significant differences were observed in the distribution of MIC values across years for ciprofloxacin except in 2025. In recent years, higher MIC values have been observed, although not at a level significantly different from previous years. For tetracycline, the MIC distribution among resistant isolates was significantly different in 2025, 2023 and 2021 compared to previous years.

Overall, changes in resistance profiles and MIC distributions were observed over time for *E. coli* in broilers, with a tendency towards higher MIC values in recent years while the overall distribution of resistance profiles remained similar.

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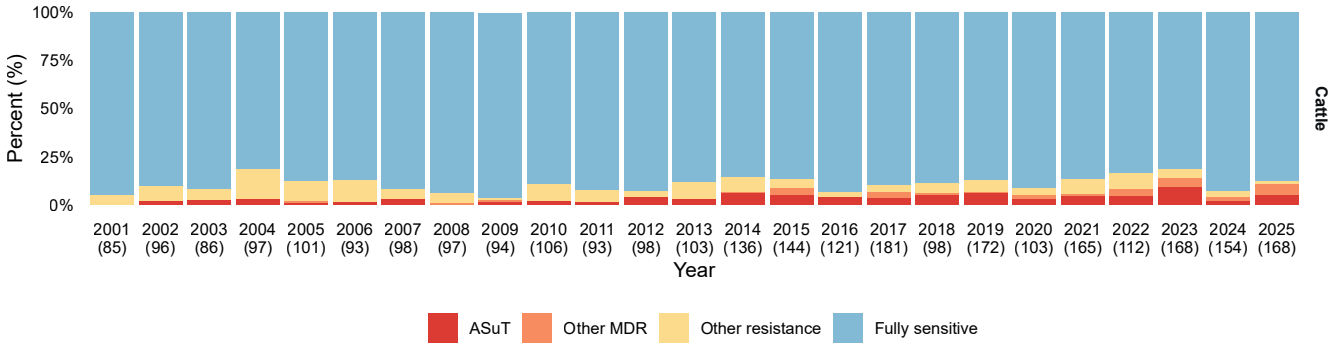
Textbox 7.2

30 years of *Escherichia coli* surveillance in Danish cattle

Denmark has had a nationwide surveillance of antimicrobial resistance in indicator *Escherichia coli* recovered from healthy food-producing animals since 1995. A retrospective comparison of resistance patterns in *E. coli* over the past 25 years of the DANMAP programme[1] was performed.

A total of 2,969 *E. coli* isolates from cattle were collected and reported in DANMAP between 2001 and 2025. The sampling strategy has changed over time, with a more standardized approach being implemented after 2014, following the introduction of the harmonized antimicrobial resistance monitoring in the European Union [Commission Implementing Decision (EU) 2020/1729].

Figure 1 Relative distributions (%) of AMR profiles among *E. coli* from cattle by year, Denmark, 2001-2025 DANMAP 2025



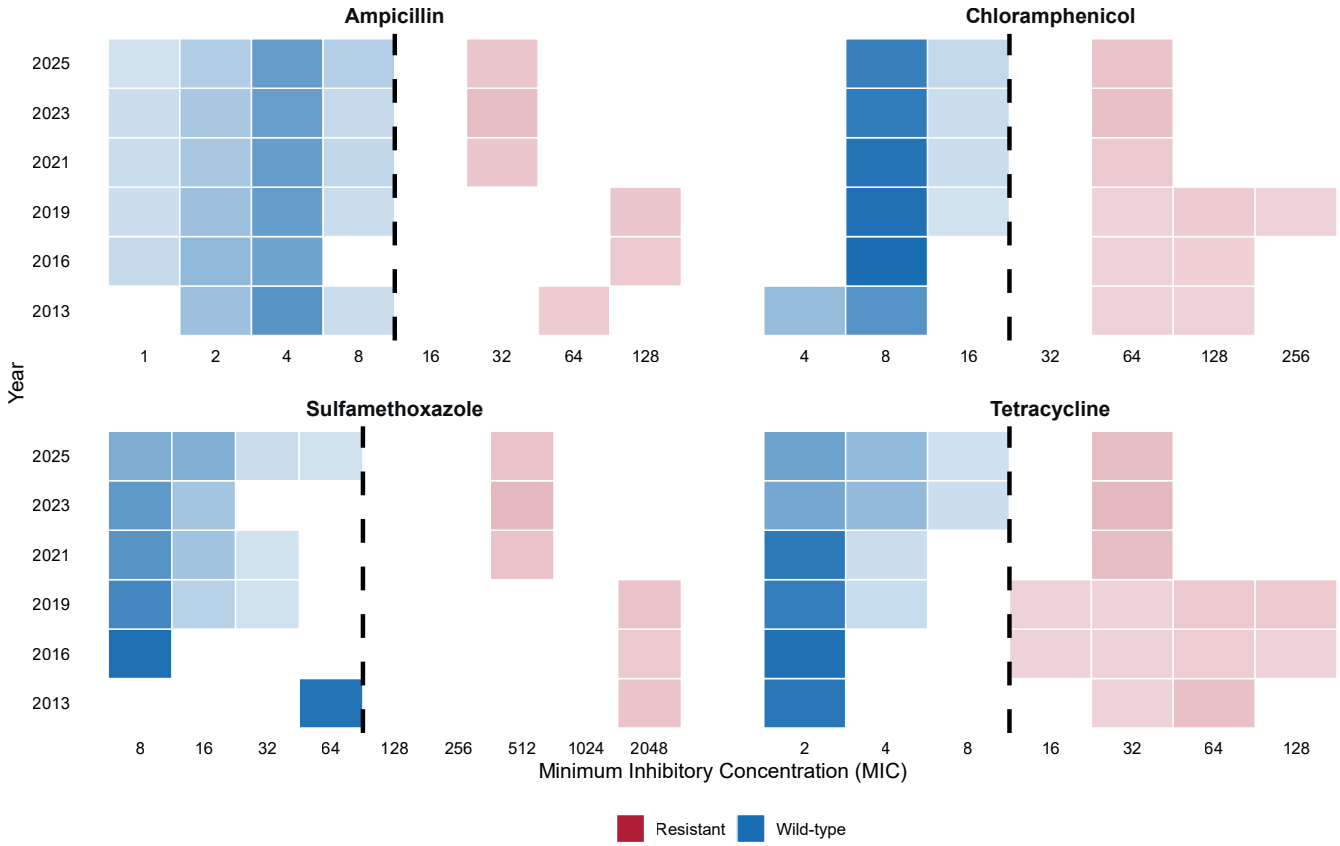
The bars show the percentage of isolates classified as ASuT (resistant to at least ampicillin, sulfamethoxazole and tetracycline), other MDR (other multidrug resistance profiles than ASuT), other resistance (resistance to one or two antimicrobial classes), or fully sensitive (sensitivity to all antimicrobial substances tested). The number of isolates included for each year is given in parentheses below each bar.

The relative distribution of antimicrobial resistance profiles varied between years (Figure 1). Fully sensitive *E. coli* isolates were dominant across all years, ranging from 81% to 97%. ASuT was the predominant resistance profile throughout the study period, although other MDR accounted for a larger proportion of isolates in 2025. Although the proportion of ASuT isolates was generally low from 2001 to 2013, it subsequently fluctuated without a significant trend, reaching a maximum of 9% in 2023.

MIC distributions for ampicillin, chloramphenicol, sulfamethoxazole and tetracycline were examined for selected years to assess changes in the distribution of MIC values over time (Figure 2). Statistical comparisons were performed separately for wild-type and resistant isolates for each antimicrobial using the Kruskal-Wallis test followed by Dunn's post hoc test with Bonferroni correction, to assess whether the MIC distributions changed across the years considered.

[1] Although *E. coli* surveillance in DANMAP was established in 1995, MIC results are included from 2001 onwards as data from 1995-2000 was digitally unavailable at the time of writing.

Figure 2 Distribution of MIC values from *E. coli* from cattle by antimicrobial substance and year DANMAP 2025



Blue indicates wild-type isolates while red indicates resistant isolates. The intensity of the colour shading represents the percentage of isolates with the respective MIC value within each year, with darker shading indicating higher percentages. The dashed line represents the ECOFF value applied for interpretation.

Among wild-type isolates, the MIC distribution for tetracycline remained similar in the earlier years, followed by a significant shift towards the ECOFF in 2023 and 2025. For chloramphenicol, a significant shift towards higher MIC values was observed after 2013. For sulfamethoxazole, the MIC distribution showed more pronounced differences between years. The distribution in 2013 differed significantly from those observed in all subsequent years, while the distributions in 2019, 2021 and 2023 were similar. In 2025, a significant shift towards higher MIC values and closer to the ECOFF was observed compared with all previous years. For ampicillin, the MIC distribution remained relatively stable across years, although significant differences were observed between 2016 and 2021, 2023 and 2025. The distribution in 2025 also differed significantly from 2019.

Among resistant isolates, a shift in the MIC distributions was observed from 2019 onwards. For sulfamethoxazole and ampicillin, this was characterised by a significant shift towards lower MIC values in the later years. For tetracycline and chloramphenicol, the MIC distributions observed in 2019 differed significantly from those observed in 2021, 2023 and 2025.

Overall, the MIC distributions appear to be moving towards the ECOFF, with wild-type isolates shifting towards higher MIC values, and resistant isolates shifting towards lower MIC values.

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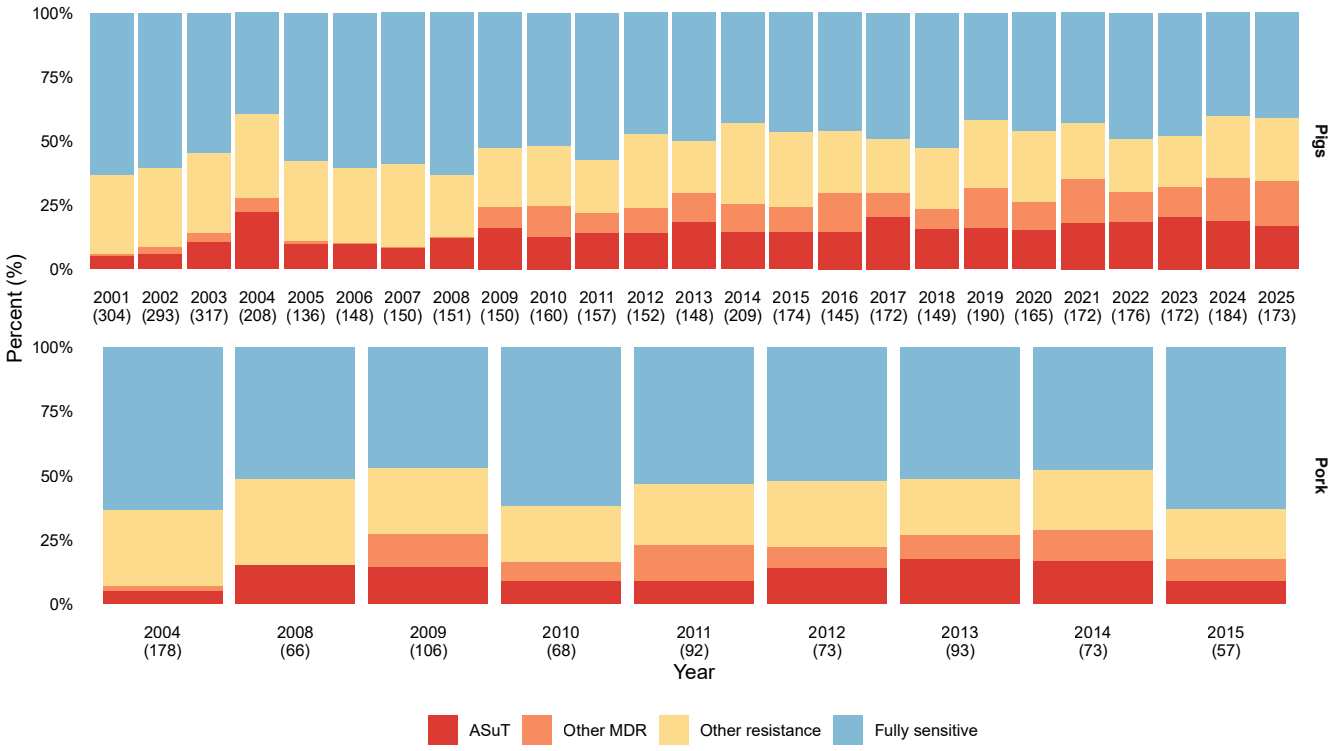
Textbox 7.3

30 years of *Escherichia coli* surveillance in Danish pigs and pork

Denmark has had a nationwide surveillance of antimicrobial resistance in indicator *Escherichia coli* recovered from healthy food-producing animals since 1995. A retrospective comparison of resistance patterns in *E. coli* over the past 25 years of the DANMAP programme[1] was performed.

A total of 4,546 *E. coli* isolates from pigs and 806 *E. coli* isolates from pork have been collected and reported in DANMAP from 2001 to 2025. Isolates from pigs were collected consistently throughout the 25-year period, whereas isolates from pork were only collected in 2004 and from 2008 to 2015. The sampling strategy has changed over time, with a more standardized approach being implemented after 2014, following the introduction of the harmonized antimicrobial resistance monitoring in the European Union [Commission Implementing Decision (EU) 2020/1729].

Figure 1 Relative distributions (%) of AMR profiles among *E. coli* from pigs and pork by year, Denmark, 2001-2025 DANMAP 2025

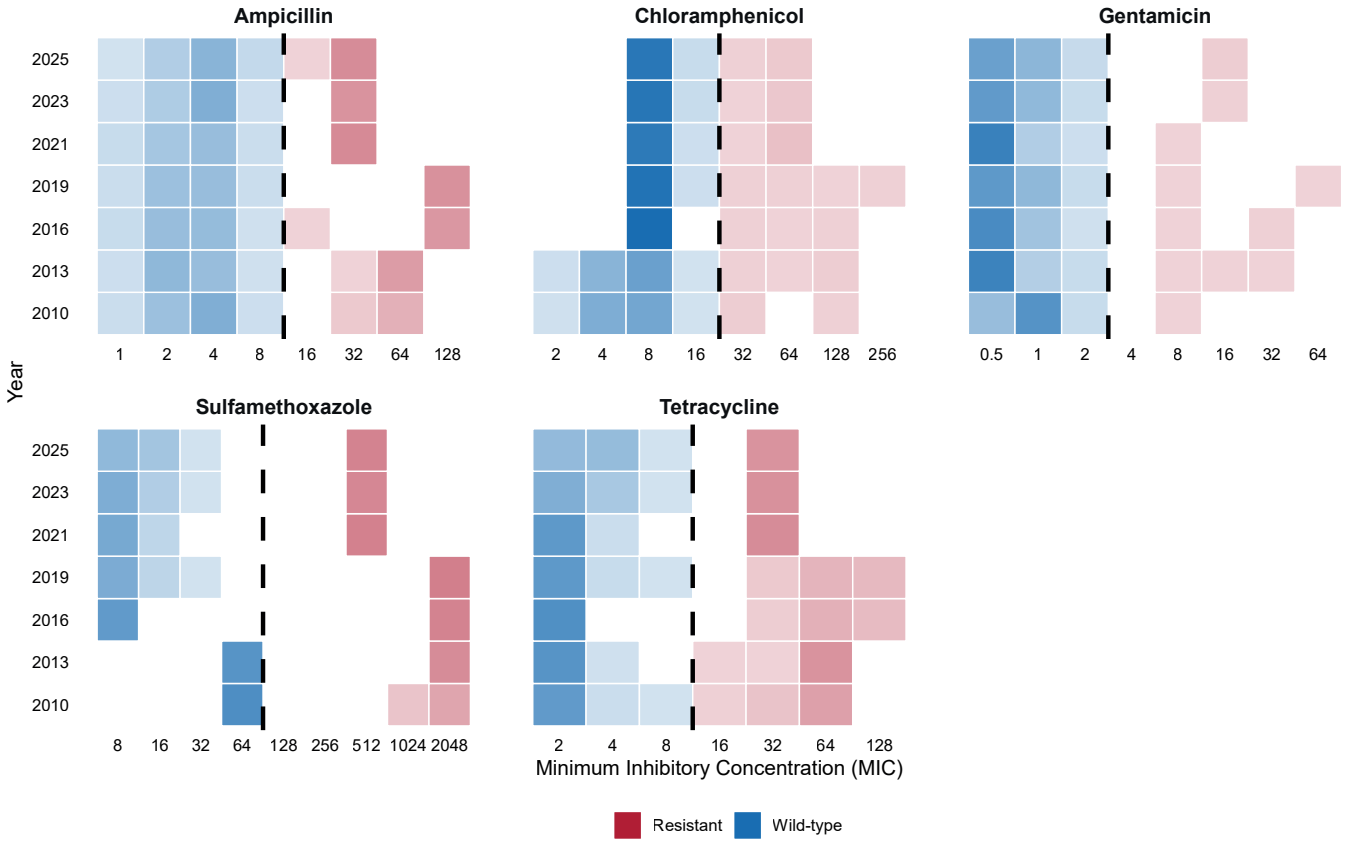


The bars show the percentage of isolates classified as ASuT (resistant to at least ampicillin, sulfamethoxazole and tetracycline), other MDR (other multidrug resistance profiles than ASuT), other resistance (resistance to one or two antimicrobial classes), or fully sensitive (sensitivity to all antimicrobial substances tested). The number of isolates included for each year is given in parentheses below each bar.

The relative distribution of antimicrobial resistance profiles varies between sample origin and year (Figure 1). Fully sensitive *E. coli* isolates were dominant in both pigs and pork across all years, ranging from 40% to 64% among pigs and from 47% to 64% among pork. Among resistant isolates from pigs, ASuT was the predominant resistance profile for most of the surveillance period. In pig isolates, the proportion of ASuT increased from 5% in 2001 to approximately 12% in 2009 and remained at a statistically similar level thereafter. However, in 2016 and 2025, other MDR accounted for a larger proportion of isolates than ASuT. A similar pattern was observed in pork, with the prevalence of ASuT increasing from 2004 to 2008 and then stabilizing (note that no data were available for the years 2005-2007, so this observation must be interpreted with caution).

[1] Although *E. coli* surveillance in DANMAP was established in 1995, MIC results are included from 2001 onwards as data from 1995-2000 was digitally unavailable at the time of writing.

Figure 2 Distribution of MIC values from *E. coli* from pigs and pork by antimicrobial substance and year DANMAP 2025



Blue indicates wild-type isolates while red indicates resistant isolates. The intensity of the colour shading represents the percentage of isolates with the respective MIC value within each year, with darker shading indicating higher percentages. The dashed line represents the ECOFF value applied for interpretation.

Among isolates from pigs, MIC distributions for ampicillin, sulfamethoxazole, tetracycline, gentamicin and chloramphenicol were examined for given years to assess changes in the distribution of MIC values over time (Figure 2). Statistical comparisons were performed separately for wild-type and resistant isolates for each antimicrobial using the Kruskal-Wallis test followed by Dunn's post hoc test with Bonferroni correction, to assess whether the MIC distributions changed across the years considered.

Among wild-type isolates, for ampicillin, the MIC distribution remained stable from 2010 to 2023, with no pairwise differences. Differences in the MIC distribution were observed in 2025 compared with 2013, 2016, 2019 and 2021 (with a slight shift towards the ECOFF). For sulfamethoxazole, the MIC distribution differed significantly between the early years (2010 and 2013) and the later part of the surveillance period. Furthermore, the MIC distribution in 2025 differed significantly from the distribution in 2016. For tetracycline, the MIC distribution remained stable from 2010 to 2021, followed by a shift towards the ECOFF in 2023 and 2025. For chloramphenicol, the MIC distribution shifted significantly towards the ECOFF from 2016 onwards compared with 2010 and 2013, after which the distribution remained stable through 2025. For gentamicin the distribution fluctuated over time, shifting away from the ECOFF in 2013 compared with 2010, followed by a shift back towards the ECOFF in 2019. The distribution then shifted away from the ECOFF again in 2021 before moving towards the ECOFF in 2023, where it remained stable through 2025.

Among resistant isolates, for ampicillin, the MIC distribution above the ECOFF had three phases, with similar distributions in 2010-2013, 2016-2019, and 2021-2025. For tetracycline, a similar pattern was observed, although the 2013 MIC distribution did not differ significantly from the distributions observed in 2010, 2016, or 2019. For sulfamethoxazole, the MIC distribution above the ECOFF shifted significantly towards the ECOFF in 2021 compared with 2010-2019 and remained stable through 2025.

continued ... Textbox 7.3

No significant differences were observed for the MIC distributions above the ECOFF for gentamicin and chloramphenicol, although the distribution appeared to shift away from the ECOFF for gentamicin and towards the ECOFF for chloramphenicol in the most recent years.

Overall, the relative occurrence of ASuT profiles in indicator *E. coli* from pigs has remained similar with minor non-significant fluctuations from 2010 to 2025, while the MIC distributions showed changes. For all five antimicrobials, the MIC distribution among wild-type isolates appeared to fluctuate over time, with distributions in the most recent years tending to be closer to the ECOFF. This shift may be indicative of future changes in the proportion of isolates classified as resistant, and hence an early signal of a possible increase in ASuT resistance in the near future. However, in 2023 and 2025 the occurrence of other MDR profiles also seems to have increased (Figure 1).

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Textbox 8.1

Long-term CPE outbreaks at Aalborg University Hospital: persistence in the hospital environment and risk factors for acquisition

A long-term outbreak of NDM-1-producing *Citrobacter freundii* ST18 was first detected at Aalborg University Hospital (AUH) in 2012. [1] The outbreak did subsequently spread to all five Danish regions and is the largest verified CPE outbreak in Denmark as of today (ID41). By the end of 2025, a total of 125 patients had been identified as part of the outbreak, including 12 new cases in 2025. In addition, an outbreak of NDM-1-producing *Klebsiella oxytoca* ST2 (ID1115) has been ongoing at the same hospital since 2022. By the end of 2025, this outbreak had affected 13 patients, including four identified in 2025. [2] Both outbreaks are classified as verified outbreaks in the national CPE surveillance programme.

The two outbreaks have persisted despite extensive infection prevention and control measures. A recent clinical study using data from 2012–2023 compared 69 cases with 552 matched controls and identified several factors associated with infection or colonisation of the *C. freundii* ST18 clone. Prolonged hospitalisation was strongly associated with infection or colonisation, with an odds ratio (OR) of 6.4 for stays exceeding 14 days compared with seven days or less. Intra-abdominal disease and biliary and pancreatic procedures were also strongly associated with infection or colonisation. In-hospital exposure to several antimicrobial classes was associated with increased odds of infection or colonisation, particularly vancomycin (OR 13.9), beta-lactam/beta-lactamase inhibitor combinations (OR 8.8), fluoroquinolones (OR 8.2) and systemic antifungals (OR 8.6). [3]

A root cause analysis investigated the *K. oxytoca* ST2 outbreak by combining repeated environmental sampling with weekly patient screening for more than 450 days. Specific NDM-1-producing *K. oxytoca* ST2 was repeatedly recovered from three toilets, with each toilet harbouring a distinct genomic sub-clade. Four patients hospitalised during the 450-day period were subsequently found to carry isolates closely related to isolates in two of the three sub-clades recovered from the toilets. Detailed hospitalisation data showed that these patients had not been hospitalised concurrently, providing no evidence for direct patient-to-patient transmission. The findings therefore support the contaminated toilets as the most plausible reservoirs for transmission to these patients. [2] Since publication of the study, a total of 13 patients have been associated with the outbreak by the end of 2025.

Several important questions remain unanswered. The precise route by which CPE is transferred from contaminated toilets or plumbing to patients is still unknown. Hypothesised transmission routes include direct contact with contaminated toilet water, transfer via surfaces, or aerosols generated during flushing. However, the available data do not allow these possibilities to be distinguished. The reason why certain CPE strains persist for years in toilets and drainage systems, and why eradication is difficult even when conventional cleaning and disinfection measures are intensified, remains unclear. Future investigations could examine the role of plumbing-associated biofilms, toilet and flushing system design, microbial and chemical conditions within the plumbing environment, and possible selective pressures that may favour long-term persistence. Understanding these factors may be important for developing more effective strategies to eliminate established environmental CPE reservoirs. [2,4]

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Textbox 8.2

Infection Prevention and Control is a cornerstone in preventing the spread of antimicrobial resistance

In Denmark, there are numerous activities concerning infection prevention and control (IPC) and antimicrobial resistance (AMR) - both on the national, regional and local level as well as at 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, and not least communication about AMR at target group level.

Danish IPC guidelines

The Danish IPC guidelines have been in place for many years. All healthcare professionals are expected to be familiar with and act in compliance with local guidelines for IPC. These are based on the national IPC guidelines published by the National Centre for Infection Control at Statens Serum Institut (SSI). The standard infection control precautions, in Danish: "*NIR Generelle forholdsregler for sundhedssektoren*"[1] is the fundament. The transmission-based precautions include specific guidance on Vancomycin-resistant enterococci (VRE), Extended-spectrum beta-lactamases (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, in Danish: "*NIR Supplerende forholdsregler ved infektioner og bærertilstand i sundhedssektoren*"[2]. In case of an outbreak, it is necessary to supplement the standard precautions with transmission-based (isolation) precautions. SSI has in addition issued specific infection control guidance for hospitals, nursing homes and home care, in Danish; "*Infektionshygiejniske retningslinjer for MRSA*"[3] and "*Infektionshygiejniske retningslinjer for CPO*"[4]. 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. The national guidelines on preventing the spread of MRSA and CPO are to be found at the Danish Health Authority website www.sst.dk.

Danish national action plan (NAP) on AMR

In Denmark, IPC is for the first time part of the Danish national action plan (NAP) on AMR issued in 2025[5]. The NAP emphasizes the importance of strengthening cooperation between hospitals and municipalities, general practitioners, and practicing specialists to ensure access to IPC guidance and rational use of antibiotics. One out of four prioritized areas are dedicated to IPC with four concrete initiatives. IPC dedicated initiatives include development of e-learning material supporting the education of nursing assistants, revision of the CPO- and MRSA guidelines and a pilot project investigating antimicrobial stewardship and point of care testing (POCT) in Long Term Care Facilities (LTCFs) as an antibiotic saving initiative.

Nordic collaboration

In 2025, as part of a Nordic collaboration, Denmark (SSI) and Norway (FHI – Folkehelseinstituttet) have developed a joint report on the screening of resistant microorganisms: "*Helhetlige vurderinger av innkomstscreening for resistente mikrober I Norge og Danmark*"[6]. The main aim of this work has been to examine the evidence base for the screening of resistant microorganisms in order to update the recommendations, focusing on a generic approach to antimicrobial resistance in Denmark and Norway.

Danish participation in European IPC initiatives

In June 2023, the European Union recommended stepping up EU actions to combat AMR with a One Health approach. Improving infection prevention and control is one of the main priorities[7]. To support the countries in stepping up the AMR actions the European Commission has invested 50 million Euros in EU-JAMRAI 2 (European Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections) which is a four-year-project (2024-2027)[8] under the EU4health programme[9].

In EU-JAMRAI 2, Denmark participates in work package (WP)5: National Action Plans, WP6: Antimicrobial Stewardship, WP7: Infection Prevention and Control, WP8: One Health Surveillance and WP9: Access to antibiotics. EU-JAMRAI 2 is progressing well, and results are being published on an ongoing basis in scientific literature and presented at the EU-JAMRAI webpage www.eu-jamrai.eu

The aim of WP7 is to improve the 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. Denmark leads the framework recommendations to support implementation of core competencies for IPC in the human sectors. The framework includes the develop-

continued ... Textbox 8.2

ment of a competency self-assessment tool (SAS) to support skills assessment and IPC development at individual health care provider level and in the organizations. Activities are carried out in close collaboration with European IPC peers, in addition to international bodies including ECDC, ESCMID/EUCIC, and WHO.

In May 2026, ECDC issued a "Proposal for EU guidance on the establishment and implementation of infection prevention and control programmes in healthcare"[10] to further emphasize the importance of implementing IPC in the countries at all levels (national, hospitals, LTCFs) and including behavior change science in the effort. WP7 provided input to the guidance.

As part of the EU-JAMRAI 2 project, SSI follows a number of IPC implementation activities from around the country. Municipalities, regions, and projects across sectors are represented. SSI is participating in a behavior change implementation project focusing on the use of gloves in close collaboration with Bispebjerg Hospital. In spring 2026, SSI launched a new inspiration site for sharing of materials and tools among healthcare professionals working with IPC in Denmark. This inspiration site supports initiative 9 – strengthening training in IPC - in the Danish NAP on AMR. Read more about the Danish EU-JAMRAI 2 IPC activities at CEI (the Danish National Center for Infection Control) SSI subsite[11].

Denmark's involvement in the EU-JAMRAI 2 - project is well aligned and supports the objectives and indicators in the Danish NAP on AMR at national and international level.

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

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4 https://hygiejne.ssi.dk/retningslinjer/infektionshygiejniske-retningslinjer-for-cpo
5 https://www.ism.dk/Media/638852182560099312/National%20handlingsplan%20for%20antimikrobiel%20resistens%20hos%20mennesker.pdf
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8 https://eu-jamrai.eu/
9 https://health.ec.europa.eu/funding/eu4health-programme-2021-2027-vision-healthier-european-union_en
10 https://www.ecdc.europa.eu/en/publications-data/proposal-eu-guidance-infection-prevention-and-control
11 https://hygiejne.ssi.dk/formidling/eu-jamrai-2

Textbox 8.3

Fungemia surveillance in Denmark – Update from 2024-2025

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Bloodstream infections with fungi (fungaemia) are most often caused by *Candida* species (candidaemia). Candidaemia occurs predominantly in immunocompromised patients, patients with gastrointestinal surgical conditions and/or critically ill individuals and has a mortality of 35% (8.7-77.3%)[1,2]. Several *Candida* species have recently been formally reclassified but for recognizability, we retain the previous nomenclature[3].

Denmark has conducted fungemia surveillance since 2004, with Departments of Clinical Microbiology submitting fungal isolates to the Mycology Reference Laboratory at Statens Serum Institut. Here we present data from 2024-2025 and compare with preceding years[4-9].

In 2024-2025, we identified 987 isolates from 954 episodes in 886 individuals. The majority of isolates were *C. albicans* and *C. glabrata*, Figure 1. Over the last two years, the incidence declined slightly, from above 9/100,000 inhabitants in preceding years to 8.1 in 2024 and 7.8 in 2025. The highest incidence was observed in elderly men (Figure 2). The decline in incidence remains unexplained and is likely multifactorial.

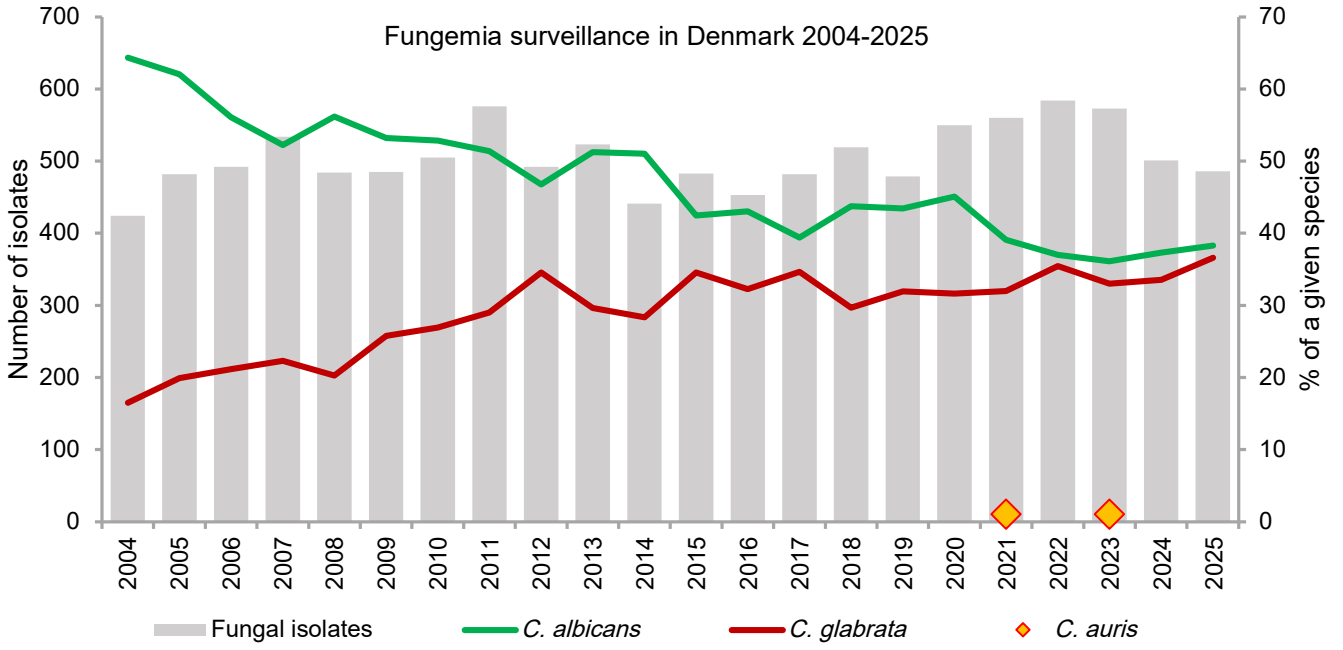
The overall fluconazole susceptibility rate has declined during the surveillance period, from 68.5% in 2004-2007 to 57.6% in 2024-2025[7]. These changes can largely be attributed to the change in species distribution over recent years from 64.4% *C. albicans* and 16.5% *C. glabrata* in 2004[6] to 38.3% *C. albicans* and 36.6% *C. glabrata* in 2024-2025 (Figure 1). Acquired antifungal resistance remain low; acquired fluconazole resistance were detected in 0.5% of *C. albicans*, 6.7% of *C. glabrata*, 6.2% of *C. tropicalis* and 0% in *C. dubliniensis*, *C. krusei* and *C. parapsilosis*. Acquired amphotericin B (AmB) resistance was not observed. However, although *C. lusitaniae* exhibits an AmB minimal inhibitory concentration (MIC) distribution similar to that of other *Candida* spp. (our 23 isolates were in the MIC range from 0.06 to 0.25), the species is not considered a good AmB target. Thus, the overall AmB coverage was 97.4% (950/975 isolates). Acquired echinocandin resistance for *C. glabrata* and *C. albicans* was 1.7% and 0.3% respectively. No bloodstream infections with *C. auris* - or azole-/echinocandin resistant *C. parapsilosis* - were observed in the two-year period.

No major changes in antifungal consumption were observed during 2024-2025, Figure 3. Fluconazole use has declined slowly over the past decade and continues that pattern - in 2025 fluconazole use was down by a third from its peak around 2013. One explanation for the species shift has been the extensive use of fluconazole compared with neighbouring countries[7], yet the beforementioned reduction in fluconazole use has, at least so far, not affected the species shift towards *C. glabrata*. Of note, the abrupt decline in overall use of mould active azoles in 2015, is largely an artifact due to the change in posaconazole DDD definition from 800 mg/day to 300 mg/day, which overinflate the earlier posaconazole use.

In conclusion, acquired antifungal resistance remains low, however, the species shift has increased the proportion of isolates with intrinsically reduced azole susceptibility. The fungemia incidence was slightly lower in 2024-25 compared to the previous years. Of note, *C. auris* candidaemia remains a rare event.

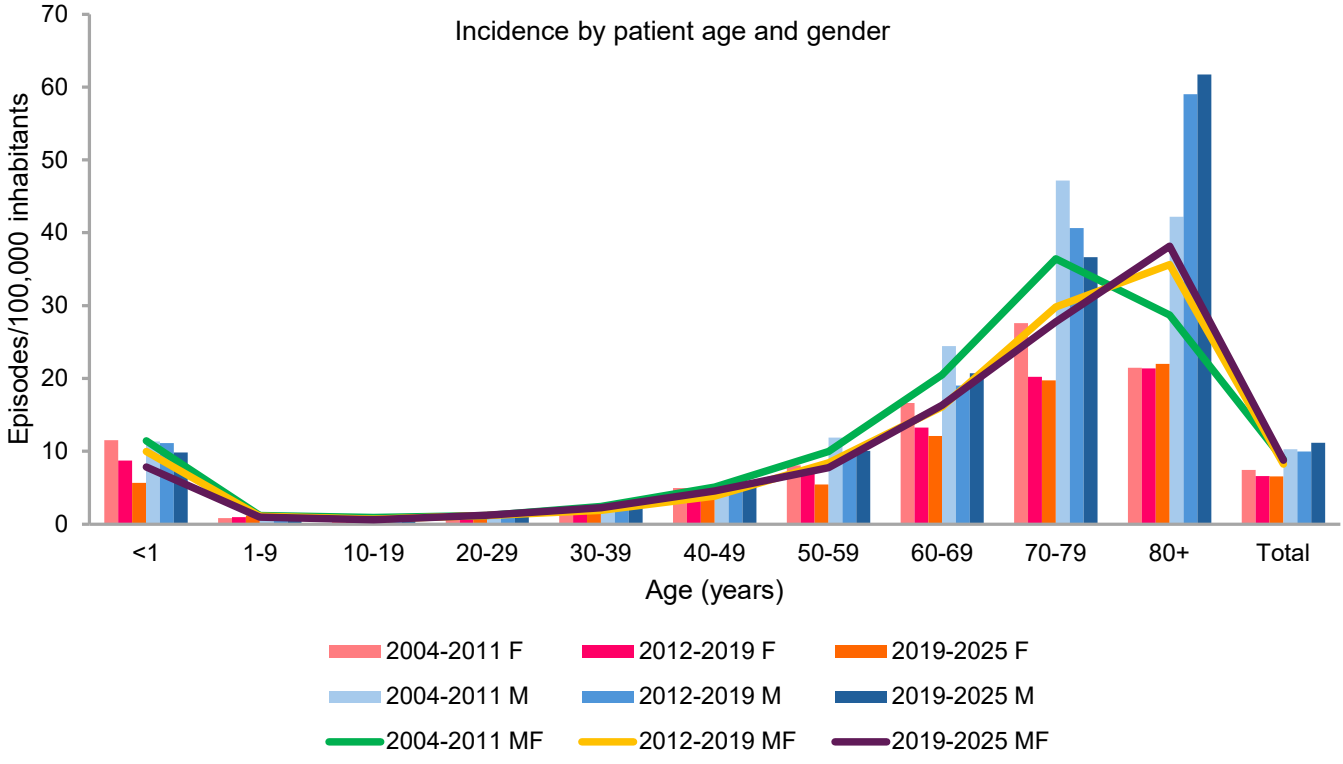
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Figure 1 Number of yearly isolates (bars) and species distribution in percentage over the years (curves) DANMAP 2025



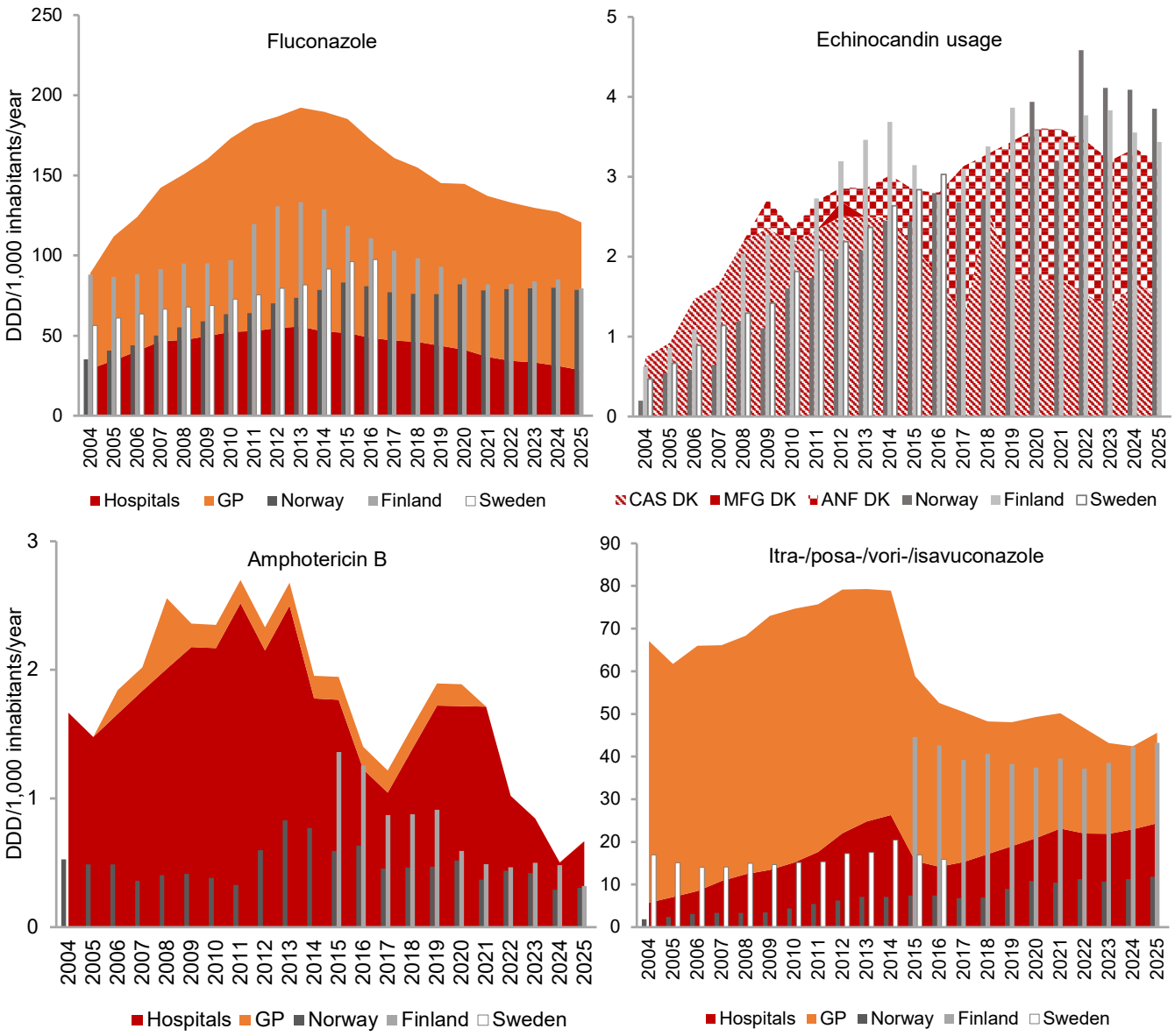
◆ Indicates one single *C. auris* episode in each of 2021 and 2023.

Figure 2 Incidence by patient age in total (curves) and by gender (bars) across two 8-year periods and a 6-year period including 2024-2025 DANMAP 2025



F = female, M = male, FM = Female & Male.

Figure 3 Systemic antifungal use in the Nordic countries. Danish data is shown for hospital and primary sector use DANMAP 2025



Abbreviations: DDD = Defined Daily Dosis. GP = General Practice. CAS = Caspofungin. MFG = Micafungin. ANF = Anidulafungin.
Data from the figures above is calculated on data from Sundhedsdatastyrelsen (www.medstat.dk), Danmarks Statistik (www.dst.dk), Folkehelseinstituttet (www.fhi.no) and Finnish Medicines Agency (www.fimea.fi). Data from Sweden is not available after 2016.
The amphotericin B DDD has recently been changed to reflect the different dose depending on the formulation; updated DDDs were not available from Sweden or from Finland prior to 2015.
The abrupt decline in azole use after 2014 largely reflects a change in posaconazole DDD definition, not an actual drop in usage (see text).

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continued ... Textbox 8.3

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Textbox 8.4

Azole resistance in clinical isolates of *A. fumigatus* (Oct 2023-Sept 2025)

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A. fumigatus is ubiquitous in the environment and can cause disease in patients with severely impaired lung function or an impaired immune system[1]. Azoles remain the most efficacious and the only orally available treatment. However, their efficacy has increasingly been challenged by resistance, which mainly arises in the environment following agri- and horticultural azole use. Environmentally selected resistance is typically characterised by specific *cyp51A* promoter tandem repeats and associated alterations, most commonly TR_{34}/L98H and TR_{46}/Y121F/T289A (with or without additional alterations), whereas various other cyp51A alterations have been observed in resistance emerging during long-term treatment. For environmentally acquired resistance, mortality may be high due to delayed appropriate treatment and the lower efficacy and poorer tolerability of second line agents[2]. An international expert guideline recommends alternative treatment when the local azole rate exceeds 10%, a threshold exceeded in the Netherlands and, more recently, in parts of Belgium[3,4]. A Danish voluntary surveillance of azole-resistant *A. fumigatus* (AR*Af*) from clinical samples was instituted in October 2018. All isolates underwent susceptibility testing using azole screening agar and/or EUCAST reference microdilution method, with *cyp51A* sequencing of resistant isolates[5]. Here, we report new data from surveillance years 6 (Oct 2023-Sept 2024) and 7 (Oct 2024-Sept 2025).

Results

A total of 1,545 isolates from 1,253 patients were included over the two-year period (Oct 2023-Sept 2025). The majority of isolates were cultured from airway samples (81.9%; 1,265/1,545) and ear samples (15.5%; 239/1,545). After a decrease in annual number of isolates during years 1-5, the number of referred isolates before exclusion increased from 750 in year 6 to 795 isolates in year 7. This may represent random variation, changes in laboratory routines or increased awareness of isolate referral. Amphotericin B susceptibility remained high (99.9%; 1,332/1,334 isolates). Azole resistance (to any azole tested) was found in 6.2% isolates, with resistance for the individual azoles ranging from 5.2%-5.6% (Table 1). 59% of resistant isolates (3.7% of all isolates) harboured an environmentally driven resistance mechanism (TR_{34} or TR_{46}, Figure 1). Patients with AR*Af* frequently had concurrent azole susceptible isolates during the same year (39%; 28/71 during the two years).

Table 1 Susceptibility classifications and MIC distributions for *A. fumigatus* isolates included during the two years DANMAP 2026

Antifungal	S	Number of isolates that were azole screening susceptible/had the given MIC (mg/L)												N tested	% R
		0.008	**0.016**	**0.03**	**0.06**	**0.125**	**0.25**	**0.5**	**1**	**2**	**4**	**8 (>4)**	**>8**		
AMB						14	342	808	168	2				1334	0,1%
ITZ	212		2	9	19	198	855	154	8	4	3	80		1544	5,6%
POS	1138	3	9	25	175	99	13	45	23	11		3		1544	5,6%
VOR	211					2	53	797	399	20	39	23		1544	5,3%
ISCO*	1141				1		8	150	153	20	31	20	21	1545	5,2%

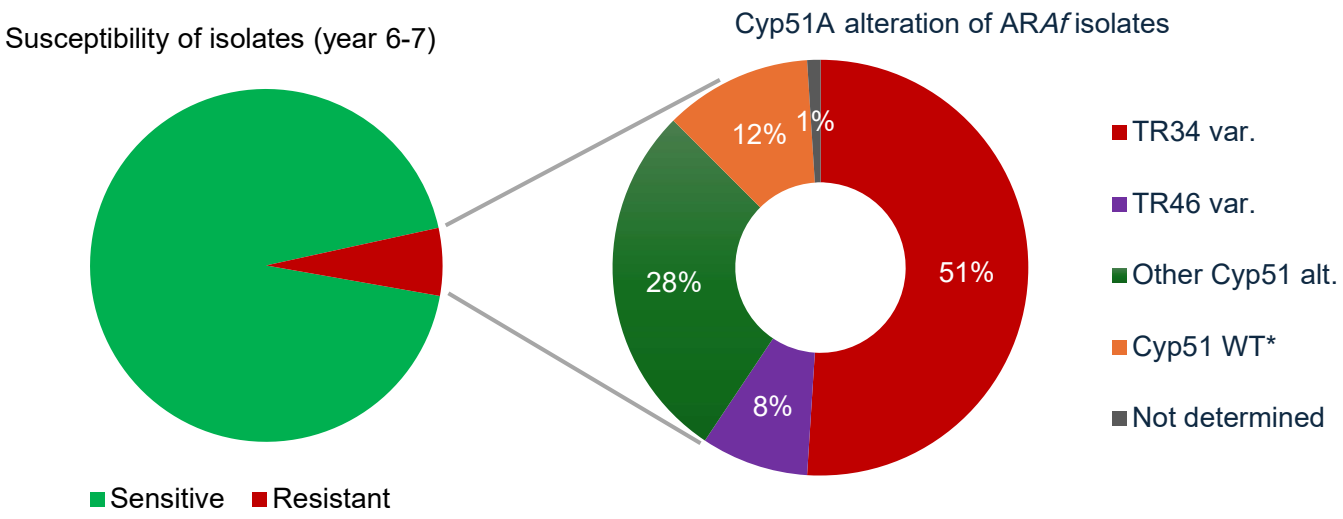
AMB: Amphotericin B. ITZ: Itraconazole. POS: Posaconazole. VOR: Voriconazole. ISA: Isavuconazole.
* All azole susceptible isolates without an ISA MIC were considered ISA susceptible.

Conclusion

The AR*Af* rate remained stable during Oct 2023-Sept 2025 compared with previous years and below the 10% threshold for changing primary therapy. The risk of potentially unexpected (environmental) resistance upon culturing *A. fumigatus* was approximately 3.7%. A large environmental study conducted in 2020-2022 detected TR_{46} only towards the end of the study period, and TR_{46} was also detected more consistently in clinical isolates in recent years, suggesting that this mechanism, which confers high-level vori- and isavuconazole resistance, may be increasing in Denmark[6]. Dual use of azoles in the environment and human medicine has recently been assessed by five European Agencies[7]. New and upcoming antifungals such as olorofim

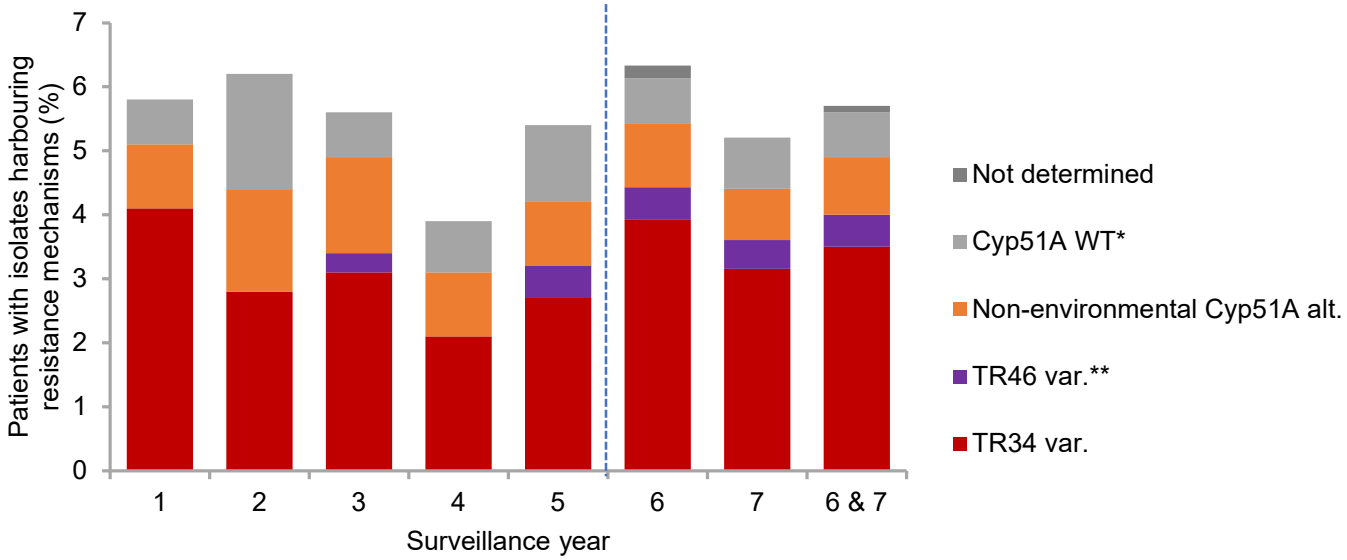
could warrant similar consideration. Ipflufenoquin shares its target with olorofim and has experimentally been shown to select for cross-resistance[8], yet is licensed for crop protection outside the EU. Resistance surveillance would therefore be advisable should ipflufenoquin be licensed in the EU, to monitor for potential emergence of olorofim resistance. ,

Figure 1 Azole susceptibility of 1,545 isolates Oct 2023-Sept 2025 (left) and associated Cyp51A alterations in resistant isolates (right) DANMAP 2025



Var: Variant. Alt: Alteration.
*) Cyp51A alterations not uniformly associated with azole resistance (e.g. F46Y/M172V/E427K) are considered as WT (wild-type) here.

Figure 2 Cyp51A-mediated resistance mechanisms in AR*Af* isolates on a patient basis. The resistance profile was categorized as environmental if both environmentally associated and other Cyp51A mechanisms were detected in isolates from the same patient. Patients could also harbour susceptible/WT isolates within the same year as resistant isolates (not detailed here) DANMAP 2025



Var: Variant. Alt: Alteration.
* Cyp51A alterations not uniformly associated with azole resistance (e.g. F46Y/M172V/E427K) are considered as WT (wild-type) here.
** One patient had AR*Af* isolates with TR34 and TR46 within the same year (grouped under TR46).

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Textbox 8.5

Nontuberculous mycobacteria – an emerging challenge of antimicrobial resistance

Background

While the number of tuberculosis (TB) cases is decreasing in Denmark, the number of drug-resistant cases has remained stable for many years, with an average of approximately three cases annually (Fig. 1). MDR- and XDR-TB therefore represent a limited public health burden in Denmark, given their low prevalence and the absence of TB-related mortality among affected patients1. In contrast, the incidence of pulmonary nontuberculous mycobacterial disease (NTM) is increasing in Denmark2 as well as globally3. This increase has been attributed to several factors, particularly an ageing population, a higher prevalence of chronic and structural lung disease, and the increasing use of immunosuppressive treatment.

In Denmark, approximately 100–150 cases of NTM disease occur annually. Approximately three quarters are pulmonary infections, while the remaining cases mainly comprise infections of lymph nodes, skin and soft tissue. Disseminated NTM disease is rare and occurs predominantly in immunocompromised patients. The annual number of unique patients with NTM isolates is approaching the number of TB cases in Denmark (Fig. 1).

NTM comprise a heterogeneous group of more than 200 *Mycobacterium* species other than those causing TB and leprosy. NTM are widely distributed in the environment, including soil and water, and only a minority of species are associated with human disease. In contrast to *Mycobacterium tuberculosis*, NTM are generally not transmitted from person to person.

Treatment of NTM disease represents a particular antimicrobial challenge. NTM display substantial intrinsic resistance to many antimicrobial agents, and resistance profiles vary considerably between species. Treatment is therefore species-dependent and typically requires combinations of several antimicrobial agents administered for many months or even years. In addition, acquired resistance may develop during treatment, further reducing the number of effective treatment options.

Diagnostic methods

In Denmark, diagnostic testing for mycobacteria is performed at the International Reference Laboratory of Mycobacteria at Statens Serum Institut (SSI), which serves as the national reference and specialist laboratory for TB and NTM.

The standard examination for mycobacteria includes microscopy, one routine PCR for *M. tuberculosis* complex, and culture. When acid-fast bacilli are detected by microscopy but PCR for the *M. tuberculosis* complex is negative, additional molecular testing for NTM is performed. Culture-positive isolates are subsequently identified to species level and, when indicated, subjected to antimicrobial susceptibility testing using both genotype and fenotypic methods.

Interpretation of NTM findings differs from that of *M. tuberculosis*. Detection of NTM in a clinical specimen does not necessarily indicate disease, as NTM are ubiquitous in the environment and may represent contamination or colonisation. Repeated microbiological samples and correlation with clinical and radiological findings may therefore be required to establish clinically significant NTM disease. Overall, more than half of all newly identified patients with NTM isolates, excluding *M. gordonae*, meet criteria for NTM-disease.

Antimicrobial resistance and clinical implications

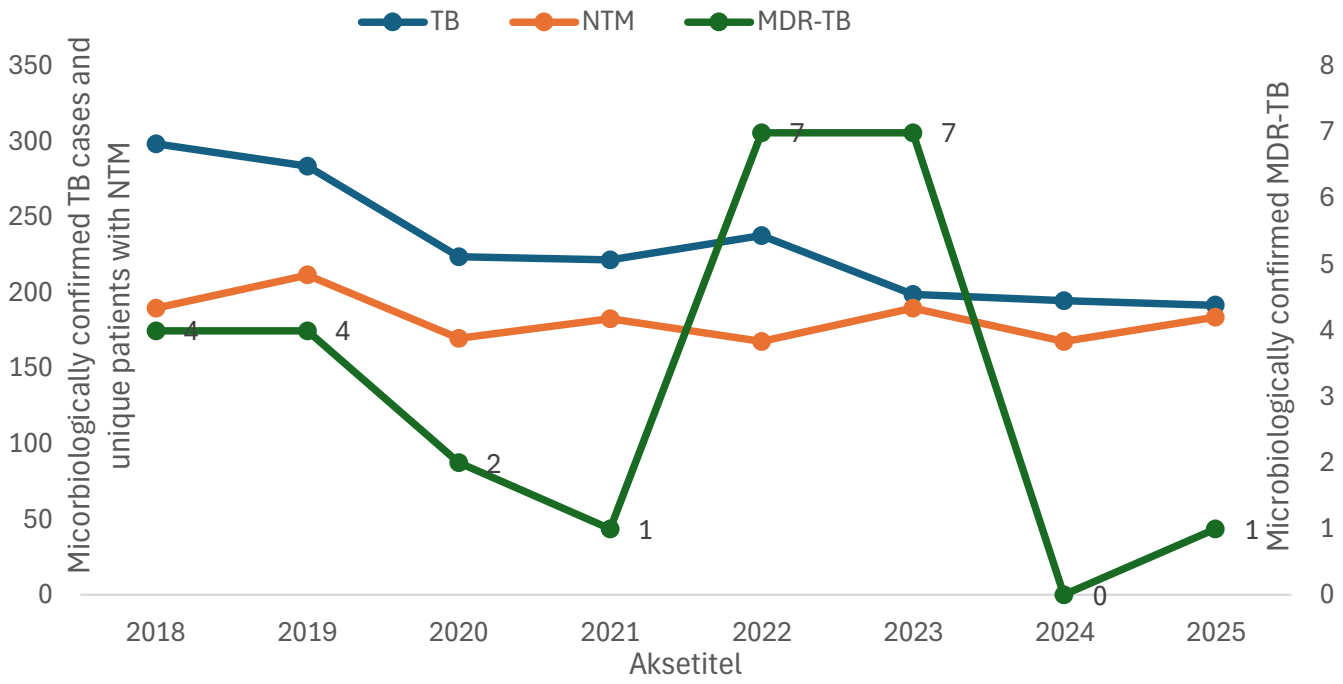
Antimicrobial susceptibility in NTM is complex. Different NTM species have markedly different intrinsic susceptibility patterns, and susceptibility testing does not predict clinical outcome equally well for all combinations of species and antimicrobial agents. Consequently, correct species identification is essential for selecting appropriate treatment and interpreting susceptibility results.

The substantial intrinsic resistance of NTM means that treatment generally is complex and requires multidrug regimens, often administered for prolonged periods and associated with substantial toxicity, drug interactions, and adverse effects. In addition, acquired resistance may develop during therapy, particularly when an effective combination of antimicrobial agents cannot be maintained.

The increasing occurrence of NTM disease, combined with intrinsic and acquired antimicrobial resistance, makes NTM an emerging challenge for clinical microbiology and antimicrobial treatment in Denmark. Continued surveillance of species distribution and antimicrobial resistance is important to monitor changes in the epidemiology of NTM and to support appropriate treatment of these often difficult-to-treat infections. Pulmonary NTM disease is associated with substantial mortality, with an overall five-year mortality of approximately 50% reported.

Figure 1 Microbiologically confirmed TB and MDR-TB cases and unique patients with NTM isolated, Denmark 2018-2025

DANMAP 2025



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