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NORM
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Usage of Antimicrobial Agents and Occurrence of Antimicrobial Resistance in Norway

Norsk overvåkingssystem for antibiotikaresistens hos mikrober (NORM)

Veterinærinstituttet
Norwegian Veterinary Institute

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CONTENTS

INTRODUCTION

Antimicrobial resistance is an emerging problem worldwide. It reduces the effectiveness of antimicrobial treatment of infectious diseases in humans and animals thereby leading to increased morbidity and mortality, as well as higher costs. It is well established that there is a strong association between the usage of antimicrobial agents and the occurrence of resistance. The selective pressure exerted following use of antimicrobial agents is a key issue in the epidemiology of resistance. In this report the term antimicrobial resistance is used synonymously with antibiotic resistance, although the term actually includes resistance in other microbes as well. Antimicrobial resistance can be disseminated through the spread of resistant pathogenic organisms themselves or by horizontal transfer of resistance genes from one type of organisms to another. Such transfer is not limited to closely related organisms; it can also take place between organisms of different evolutionary origins and/or ecological niches. Thus, antimicrobial drug usage and resistance in one ecological compartment can have consequences for the occurrence of resistance in another compartment. When addressing antimicrobial resistance – the occurrences, causes, consequences and preventive measures – a holistic approach is needed, encompassing both data on usage and resistance in human and veterinary medicine, as well as organisms in the food production chain.

In response to the growing concern about antimicrobial resistance, the Norwegian Ministry of Health and Social Affairs issued the first national action plan against antimicrobial resistance in March 2000. The importance of monitoring the human and animal health sectors as well as food production, was emphasised. The action plan recognised the need for ongoing surveillance as a fundamental component of the strategy. The NORM and NORM-VET programmes were consequently established in order to provide and present data on the occurrence and distribution of antimicrobial resistance over time. The first national action plan formally expired by the end of 2004. However, the need for continued surveillance of both resistance and antimicrobial usage was emphasised at subsequent consultations and an integrated national strategy for prevention of infections in the health service and antibiotic resistance (2008-2012) was issued in the summer of 2008. A new national strategy (2015-2020) was launched by the Norwegian government in 2015 including an explicit target of 30% reduction in antibiotic consumption in human medicine by 2020 compared to 2012. For food-producing terrestrial animals and companion animals the target was 10% and 30% reduction in the usage, respectively, by 2020, with 2013 as reference year. Additional specific targets in the food production chain were that livestock associated MRSA should not be established in the Norwegian pig population, and that ESBL in the poultry production should be reduced to a minimum. Also, the action plan stated that the government would carry out mapping of reservoirs of antimicrobial resistant bacteria in humans, in food and in relevant animal populations and in sentinel environments. Due to the coronavirus pandemic, renewal of the national strategy was delayed until 2024 when a National One Health Strategy Against Antimicrobial Resistance (2024-2033) was launched. Sector specific action plans are presently under development.

The NORM surveillance programme for antimicrobial resistance in human pathogens was established in 1999 and is coordinated by the Department of Microbiology and Infection Control at the University Hospital of North Norway in Tromsø. The NORM-VET monitoring programme for antimicrobial resistance in animals, food and feed was established in 2000 and is coordinated by the Norwegian Veterinary Institute commissioned by the Norwegian Food Safety Authority. The NORM/NORM-VET reports also present data on the usage of antimicrobial agents in humans and animals in Norway. The NORM and NORM-VET programmes are valuable tools for setting policies, assessing risks and evaluating interventions.

This report, which is the twenty-fifth annual joint report from NORM and NORM-VET, presents data on resistance and usage for 2024. The editors would like to thank all those who contributed to data collection and the writing of this report, for excellent work.

Tromsø / Ås / Oslo, September 2025

ABBREVIATIONS

AMEG	Antimicrobial Advice Ad Hoc Expert Group
AMR	Antimicrobial resistance
ASP	Antibiotic Centre for Primary Care
AST	Antimicrobial susceptibility testing
ATC	Anatomical Therapeutic Chemical
ATCvet	Anatomical Therapeutic Chemical veterinary
ATU	Area of technical uncertainty
AWaRe	Access, watch, reserve
cgMLST	Core genome multilocus sequence typing
CPE	Carbapenemase-producing *Enterobacterales*
CPO	Carbapenemase-producing organisms
CRE	Carbapenem resistant *Enterobacterales*
DDD	Defined daily doses
ECDC	European Centre for Disease Prevention and Control
ECOFF	Epidemiological cut-off values
EEA	European Economic Area
EFSA	European Food Safety Authority
EMA	European Medicine Agency
ESAC-Net	European Surveillance of Antimicrobial Consumption Network
ESBL	Extended spectrum beta-lactamase
ESC	Extended spectrum cephalosporin
ESCMID	European Society for Clinical Microbiology and Infectious Diseases
ESUAvet	European Sales and Use of Antimicrobials for Veterinary Medicine
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption
EU	European Union
EUCAST	European Committee on Antimicrobial Susceptibility Testing
GLASS	Global Antimicrobial Resistance and Use Surveillance System
GP	General practitioner
GR	Genotypic resistance
HAI	Healthcare-associated infections
HMP	Human medicinal product
K-res	Norwegian Centre for Detection of Antimicrobial Resistance
LIMS	Laboratory Information Management System
LOS	Length of stay
LRE	Linezolid resistant enterococci
LVRE	Linezolid and vancomycin resistant enterococci
MDR	Multi-drug resistant
MIC	Minimum inhibitory concentration
MRL	Maximum residue level
MRSA	Methicillin resistant *Staphylococcus aureus*
MRSP	Methicillin resistant *Staphylococcus pseudintermedius*
MSIS	Norwegian Surveillance System for Communicable Disease
NDHRS	Norwegian Dairy Herd Recording System
NFSA	Norwegian Food Safety Authority
NSAS	National Centre for Antibiotic Use in Hospitals
NIPH	Norwegian Institute of Public Health
NorPD	Norwegian Prescribed Drug Registry
NRL	National reference laboratory
NVI	Norwegian Veterinary Institute
NWT	Non-wild type
OPAT	Outpatient parenteral antimicrobial therapy
PCU	Population correction unit
PPS	Point prevalence survey
QRDR	Quinolone resistance-determining region
Rx	Prescription
SAP	Surgical antibiotic prophylaxis
SSI	Surgical site infection
ST	Sequence type
VetReg	Veterinary Prescription Register
VMP	Veterinary medicinal product
VRE	Vancomycin resistant enterococci
WGS	Whole genome sequence
WT	Wild type

SAMMENDRAG

Norsk overvåkingssystem for antibiotikaresistens hos mikrober (NORM) og Norsk overvåkingsprogram for antibiotikaresistens i mikrober fra fôr, dyr og næringsmidler (NORM-VET) utgir en felles årlig rapport. Årets rapport presenterer data om forekomst av antibiotikaresistens og forbruk av antibiotika til mennesker og dyr i 2024. Data fra relevante prosjekter som ikke er med i de kontinuerlige overvåkingsprogrammene, presenteres også. NORM og NORM-VET ble etablert som deler av Regjeringens tiltaksplan mot antibiotikaresistens offentliggjort i 2000. NORM koordineres av Avdeling for mikrobiologi og smittevern, Universitetssykehuset Nord-Norge i Tromsø. NORM-VET koordineres av Veterinærinstituttet.

Forbruk av antibiotika til dyr

I 2024 utgjorde salget av antibakterielle veterinærpreparater til landdyr totalt 4 341 kg som er 121 kg lavere enn i 2023 (-3 %) og det laveste salget som er rapportert siden datainnsamlingen startet i 1993. Salget av antibakterielle veterinærpreparater til matproduserende landdyr, inkludert hest, var på 3 984 kg. Data rapportert til Veterinært legemiddelregister (VetReg) viser at til storfe, gris og fjørfe ble det i all hovedsak brukt penicilliner, og av disse var det nesten utelukkende beta-laktamaseømfintlige penicilliner som ble benyttet. Estimert salg av antibakterielle veterinærpreparater som i hovedsak benyttes til de viktigste matproduserende artene (storfe, gris, sau, geit og fjørfe), var uendret (under 1 prosent endring) siden 2023, målt i mg aktivt stoff relatert til dyrepopulasjonen (mg/kg dyrebiomasse). Til hest ble det i hovedsak brukt trimetoprim-sulfa som oralpasta. Salget av antibakterielle veterinærpreparater til flokkbehandling er fortsatt lavt; i 2024 representerte salg av slike preparater 3 % av totalsalget til matproduserende landdyr, inkludert hest.

Forbruket av veterinære antibakterielle midler til oppdrettsfisk (forbruk til rensefisk inkludert) var fortsatt svært lavt i 2024 og utgjorde 709 kg. Dette representerer en nedgang på 99 % sammenlignet med 1987 da forbruket var på sitt høyeste. I 2024 ble det foretatt behandling med antibiotika i 2,1 % av sjølokalitetene for laks og regnbueørret.

Til kjæledyr (hund og katt) ble det i 2024 solgt 357 kg veterinære antibakterielle midler. Dette var en liten (4 %) reduksjon sammenliknet med året før. Data rapportert (i kg) til VetReg for hund og katt for perioden 2015-2024 viser en reduksjon på totalt 36 % i forskrivningen av antibakterielle humanpreparater til hund og katt, noe som indikerer at redusert salg av veterinære antibakterielle midler ikke har blitt erstattet av forskrivning av antibakterielle humanpreparater.

Det europeiske legemiddelbyrået (EMA) har anbefalt å begrense bruken av enkelte antibakterielle midler til dyr, dvs. 3.-4. generasjon cefalosporiner, kinoloner (fluorokinoloner og andre kinoloner) og polymyksiner, på grunn av den potensielle risikoen for folkehelsa. Av disse antibakterielle midlene selges det kun kinoloner til matproduserende landdyr og oppdrettsfisk. Salget av kinoloner utgjorde en svært liten andel (0,3 %) av totalsalget av veterinære antibakterielle midler til dyr, inkludert fisk, i 2024.

Forbruk av antibiotika hos mennesker

I 2024 var det totale salget av antibakterielle midler til systemisk bruk (her benevnt som antibiotika; dvs J01 unntatt metenamin) hos mennesker 13,1 DDD/1000 innbyggere/døgn. Siden 2012 har det vært en markant nedgang i total antibiotikabruk, i alt en reduksjon på 23 %. Under covid-19-pandemien ble det observert en signifikant reduksjon i bruken av antibiotika, men forbruket er nå tilbake til noenlunde samme nivå som før pandemien. Norge har et relativt lavt forbruk av antibiotika sammenliknet med andre land. Vi har også et fordelaktig forbruksmønster med stor andel av smalspektrede antibiotika, både i primærhelsetjenesten og i sykehussektoren.

Rundt 85 % av totalt antall DDD av antibakterielle midler brukes i primærhelsetjenesten, dvs. utenfor helseinstitusjoner. Av dette blir 5,5% forskrevet i tannhelsetjenesten. Penicilliner (J01C) er oftest forskrevet i primærhelsetjenesten. Fra høst 2023 og i 2024 har det vært en pågående epidemi av *Mycoplasma pneumoniae*, og dette har ført til endring av terapimønsteret med økt bruk av tetracykliner og makrolider. Penicillin (J01C)-andelen av totalbruken i primærhelsetjenesten i 2024 er derfor lavere enn tidligere år; 39 % av alle antibiotika DDD.

De tre hyppigst foreskrevne antibiotika i 2024 var metenamin, fenoksymetylpenicillin og doksycyklin. I Norge er luftveisinfeksjoner vanligste indikasjon for smalspektret penicillin og i 2024 utgjorde fenoksymetylpenicillin 17 % av alle DDD mens metenamin utgjorde 23 %. Det har vært en økning av bruk i primærhelsetjenesten etter pandemien; bruken ligger på nesten samme nivå som 2019, men sett over det siste tiåret har antibiotikabruk i primærhelsetjenesten hatt en generell jevn nedgang. Etter innføringen av regjeringens handlingsplan mot AMR i 2016 har det vært økt oppmerksomhet mot antimikrobiell resistens, både blant helsepersonell og i befolkningen for øvrig. I primærhelsetjenesten har det vært fokus på oppdaterte retningslinjer for antibiotikabruk. Etter innføringen av regjeringens handlingsplan mot AMR i 2016 har en stor andel allmennleger gjennomført kvalitetsforbedrende kurs om riktig antibiotikaforskrivning, og fra 2024 har det vært mulig for allmennleger å hente ut automatiserte rapporter om egen forskrivningspraksis. Dette tenker en vil kunne bidra til økt fokus på riktig antibiotikaforskrivning. Selv om mye er oppnådd, er det sannsynligvis fremdeles forbedringsområder i primærhelsetjenesten, f.eks. å unngå antibiotikaforskrivning ved virale infeksjoner, individualisering og riktig valg av type antibiotika, dose og varighet av kur.

Antibiotikasalg (i DDD) til sykehus utgjorde 7,3 % av totalt salg av antibakterielle midler til mennesker i 2024. Salget er redusert med 3 % i DDD/1000 innbyggere/dag sammenliknet med 2019, men økt med 7 % siden 2012. I norske sykehus ble det gjennomsnittlig brukt 81 DDD/100 liggedøgn i 2024. Dette er en økning siden 2019 og 21 % mer enn i 2012. I samme periode økte DDD/innleggelse med 5 %. Terapimønsteret for antibakterielle midler på sykehus endrer seg ikke mye fra ett år til et annet, men det er en klar trend mot mer bruk av antibiotika anbefalt i retningslinjene. Bruken av bredspektrede antibiotika er redusert siden 2012. De utgjorde 20 % av bruken målt i DDD/100 liggedøgn i 2024 og 26 % i 2012. Denne gunstige utviklingen kan

forklares med opprettelse av antibiotikastyringsprogram i sykehus, kontinuerlig god oppfølging av antibiotika-teamene og oppdaterte retningslinjer. I sykehus ble penicilliner (J01C) mest brukt (nesten halvparten av bruken målt i DDD), mens cefalosporiner er den neststørste antibiotikagruppen; 18 % av alle DDD. Det er store variasjoner mellom sykehus, både målt i volum (DDD/100 liggedøgn) av antibiotika som brukes og i terapiprofil. Variasjonene kan ikke forklares med forskjeller i aktivitet eller pasientsammensetning alene.

Antibiotikaresistens i dyr og i mat

Resistens hos kliniske isolater fra dyr

Fra infeksjoner hos dyr, ble det i 2024 undersøkt *Escherichia coli* fra kylling og kalkun, samt *Streptococcus canis* og *Campylobacter upsaliensis* fra hund.

Majoriteten av *E. coli* isolatene (73,3 % av 225 kyllingisolater og 83,0 % av 47 kalkunisolater) var fullt følsomme for de antibakterielle midlene de ble testet for. Ingen av isolatene var multiresistente (MDR), dvs. resistente mot tre eller flere antibakterielle klasser.

Av *S. canis* var 80 isolater fra lokale øreinfeksjoner og 61 isolater fra systemiske infeksjoner. Alle isolatene var følsomme for benzylpenicillin.

Majoriteten (94,5 %) av 75 undersøkte *C. upsaliensis* isolater var fullt følsomme for de antibiotika de ble testet for, og ingen var MDR.

Resistens hos indikator- og meldepliktige bakterier fra dyr og i mat

Resultatene fra 2024 bekrefter at situasjonen angående antibiotikaresistens hos bakterier fra dyr og mat i Norge er god. Forekomsten av MDR og spesielle resistente bakterier/ resistensmekanismer av særlig interesse, slik som ekstendert-spektrum cefalosporin (ESC)-resistente *E. coli*, er fremdeles lav.

NORM-VET følger de krav til overvåking av antibiotikaresistens i indikatorbakterier og i zoonotiske bakterier som er satt i EU-regelverket (2020/1729/EU). I tillegg undersøkes det prøver av dyr og matvarer ut ifra nasjonale hensyn. *E. coli* og *Enterococcus* spp. benyttes som indikatorbakterier, dvs. sensitivitetstesting av *E. coli og Enterococcus* spp. benyttes som indikator for forekomst av antibiotikaresistens. Selektive metoder brukes til overvåking av meldepliktige bakterier slik som ESC-resistente *E. coli*, karbapenemresistente *Enterobacterales* (CRE), vankomycinresistente *Enterococcus* spp. (VRE), linezolidresistente *Enterococcus* spp. (LRE), meticillinresistente *S. aureus* (MRSA) og meticillinresistente *Staphylococcus pseudintermedius* (MRSP). MRSA i svinepopulasjonen er overvåket via et eget omfattende program, som har som mål å identifisere MRSA-positive besetninger. Resultatene fra dette programmet oppsummeres også i denne rapporten.

I 2024 ble det undersøkt blindtarmsprøver fra flokker av slaktekylling for isolering og sensitivitetsundersøkelse av *E. coli* og *Enterococcus* spp., samt isolering av ESC-resistente *E. coli*, CRE og VRE. Svaberprøver fra hest var også inkludert for sensitivitetsundersøkelse av *E. coli*, samt for undersøkelser for forekomst av ESC-resistente *E. coli* og CRE. Fra hest ble det også undersøkt nesesvabre for påvisning av MRSA. Prøvene av mat var kylling- og kalkunkjøtt som ble undersøkt for forekomst av ESC-resistente *E. coli*, CRE og MRSA, samt sukkererter og tørkede frukter for sensitivitetsundersøkelse av *E. coli*, og forekomst av ESC-resistente *E. coli*, CRE og kolistin-resistente *Enterobacterales*.

I prøvene fra slaktekylling var majoriteten av de 336 *E. coli* isolatene fullt følsomme for de antibakterielle substansene de ble sensitivitetstestet for (84,8 %), og kun 0,9 % av isolatene var MDR. Andelen fullt følsomme isolater har vært relativt stabilt rundt 80 % de siste årene (2014-2024). Det har vært en nedgang i resistens mot kinoloner fra 12,6 % i 2020 til 5,4 % i 2024. CRE ble ikke påvist fra noen av prøvene i den selektive screeningen, mens ESC-resistente *E. coli* ble påvist fra ni av prøvene (alle forårsaket av kromosomale mutasjoner). Av *Enterococcus faecalis* isolatene (n=100) fra slaktekylling var 56,0 % fullt følsomme for de antibakterielle midlene de ble testet for, mens tilsvarende tall for *Enterococcus faecium* (n=312) var 59,9 %. Andelen fullt følsomme *E. faecium* har vært relativt stabil i årene 2014-2024, mens det har vært noe svingninger i andelen av fullt følsomme *E. faecalis*, hovedsakelig pga. variasjoner i forekomst av tetrasyklin-resistens. Ingen av isolatene var MDR. VRE ble ikke påvist i den selektive screeningen, og dette er i samsvar med resultatene fra 2018-2022.

I prøvene fra hest var majoriteten (79,2 %) av 250 *E. coli* isolater fullt følsomme for de antibakterielle substansene de ble sensitivitetstestet for. MDR ble påvist hos 0,4 % av isolatene. Andelen fullt følsomme isolater har vært relativt stabil i årene 2017-2024. MRSA og CRE ble ikke påvist i de selektive screeningene, men *E. coli* resistente mot ESC ble påvist fra tre av 251 prøver. Disse var forårsaket av hhv. $bla_{\text{CTX-M-1}}$, $bla_{\text{CTX-M-15}}$ og $bla_{\text{SHV-12}}$. Disse resultatene fra hest er i samsvar med resultater fra 2017 og 2021.

Det ble ikke påvist MRSA eller CRE i de selektive screeningene av kjøttprøvene, mens ESC-resistente *E. coli* ble påvist fra hhv. én prøve av kyllingkjøtt (n=325) og én prøve av kalkunkjøtt (n=114). Begge disse var forårsaket av kromosomale mutasjoner. Dette er i samsvar med resultater fra tidligere år, dvs. 2018, 2020 og 2022.

Totalt ble det undersøkt prøver av 315 sukkererter og 345 tørkede frukter. *E. coli* ble kun påvist fra 23 prøver av sukkererter, hvorav 15 isolater var fullt følsomme for de antibakterielle substansene de ble sensitivitetstestet for, og tre isolater var MDR. CRE og kolistinresistente *Enterobacterales* ble ikke påvist i de selektive screeningene, mens det fra én sukkerertprøve ble påvist ESC-resistente *E. coli* forårsaket av $bla_{\text{CTX-M-15}}$-genet.

Resistens hos zoonotiske bakterier og andre enteropatogene bakterier

Zoonosebakterier isolert fra dyr og fra mat

Den norske husdyrpopulasjonen er regnet som tilnærmet fri for *Salmonella*. I 2024 ble det sensitivitetstestet 28 *Salmonella* spp. fra hhv. ni villsvin, tre hunder, tre kyllingflokker, to storfe, to hester og ni katter (20 *S.* Typhimurium isolater hvorav ett var monofasisk (4,[5],12 : i : -), to *S. enterica* subsp. *diarizonae*, to *S*. Abony, og ett hver av hhv. *S*. Hessarek, *S*. Mbandaka, *S*. Enteritidis, og *S.* Anatum). I tillegg, ble det undersøkt sju *Salmonella* spp. isolater (*S*. Kinondoni, *S.* Münster, *S.* Newport, *S*. Tennessee og tre *S*. Kisarawe) fra kjøtt som ikke var av

norsk opprinnelse eller andre matvarer. Alle isolatene, både fra dyr og fra kjøtt, var fullt følsomme for de antibakterielle midlene de ble sensitivitetstestet for.

Majoriteten (87,5 %) av 56 undersøkte *Campylobacter jejuni* isolater fra kylling var fullt følsomme for de antibakterielle substansene de ble sensitivitetstestet for. Ingen av isolatene var MDR.

Kliniske isolater av tarmpatogene bakterier fra mennesker

Referanselaboratorium for enteropatogene bakterier (NRL) utfører årlig testing av antimikrobiell følsomhet for isolater av *Salmonella, Campylobacter, Yersinia* og *Shigella*. Siden 2020 har NRL også screenet alle *Enterobacterales* isolater for antimikrobielle resistensgener etter helgenom-sekvensering, for å påvise genotypisk resistens. I 2020 og 2021 ble det innført reiserestriksjoner som en del av smitteverntiltakene under covid-19-pandemien, noe som førte til en betydelig reduksjon i antallet reiseassosierte infeksjoner. Trender innen antibiotikaresistens må derfor tolkes med dette i betraktning..

For *Salmonella* Typhimurium og den monofasiske varianten av *S*. Typhimurium var det totale resistensnivået høyere for stammer fra reiseassosierte infeksjoner sammenlignet med isolater fra innenlands smitte. Multi-resistens (MDR) var en karakteristisk egenskap for et betydelig antall av de monofasiske *S.* Typhimurium (71,8 %). Totalt ble 18 isolater identifisert som ESBL-produserende, med følgende genotyper: $bla_{\text{CTX-M}}$ (n=11), $bla_{\text{TEM-52}}$ (n=4), $bla_{\text{CMY-2}}$ (n=2) og bla_{DHA} (n=1).

Hos *Campylobacter jejuni* var det generelle resistensnivået for ciprofloksacin og tetracyklin høyere hos stammer fra reiseassosierte infeksjoner enn hos isolater fra innenlands smitte. Antibiotikaresistens i *Yersinia enterocolitica* forblir lav. En økende trend for resistens mot ciprofloksacin og bredspektrede cefalosporiner ble observert både hos *Shigella sonnei* og *Shigella flexneri*. Totalt ble 23 ESBL-produserende *S. sonnei* stammer og 6 *S. flexneri* stammer identifisert, med følgende resistensgener: $bla_{\text{CTX-M}}$ (n=25) og $bla_{\text{DHA-1}}$ (n=4). De fleste *Shigella* stammene (94,8 %) ble karakterisert som MDR. I tillegg ble mutasjoner i *pmrB*-genet, assosiert med colistinresistens, identifisert i samtlige *S. flexneri* stammer.

Resistens hos kliniske isolater fra mennesker

Forekomsten av antibiotikaresistens hos bakterier i kliniske prøver fra mennesker var fortsatt lav i 2024. *Staphylococcus aureus* fra blodkultur og sårprøver var stort sett følsomme for alle relevante antibiotika. Det ble påvist 18 tilfeller av meticillinresistente *S. aureus* (MRSA) blant 1 614 blodkulturisolater (1,1 %). Resultatet er litt lavere enn tall fra laboratorienes datasystemer som rapporterte 50 MRSA isolater blant 2 321 *S. aureus* (2,2 %) fra blodkultur og spinalvæske i 2024. Dette er en svak økning fra 1,8 % i 2023. Meldesystemet for infeksjonssykdommer (MSIS) registrerte 1 222 tilfeller av MRSA infeksjon i 2024. De fleste tilfellene var pasienter med overfladiske sår-infeksjoner og abscesser. MRSA utgjør fortsatt en svært liten andel av *S. aureus* isolater fra sårprøver (16 av 841; 1,9 %) slik de også har gjort i tidligere år (1,6 % i 2022; 1,3 % i 2023). MSIS registrerte videre 1 689 tilfeller av MRSA kolonisering i 2024. I alt ble det meldt funn av MRSA hos 2 942 personer i 2024 mot 2 544 i 2023 (+15 %). Dette utgjør en insidensrate på 53 per 100 000 personår sammen-liknet med 38 i 2022 og 46 i 2023. Insidensen av MRSA er nå høyere enn den var før covid-19 pandemien (2 568 personer registrert i 2017). Det månedlige antall MRSA infeksjoner har ikke endret seg signifikant gjennom de siste åtte årene, og insidensen av invasive infeksjoner har holdt seg stabil på et lavt nivå. En betydelig andel av tilfellene (20 %) ble smittet i utlandet, men for mange (55 %) var smittested ukjent. Det påvises svært få tilfeller av landbruksassosiert MRSA i Norge.

Blodkulturisolater av *E. coli* viste svakt økende forekomst av resistens mot bredspektrede antibiotika i 2024. Andelen av gentamicinresistente *E. coli* isolater var 5,7 % i 2024 sammenliknet med 5,1 % i 2022 og 5,4 % i 2023, mens forekomsten av resistens mot ciprofloxacin var uendret på 9,7 % (10,0 % i 2023). *Klebsiella* spp. hadde omtrent samme forekomst av resistens mot gentamicin (4,5 %) og ciprofloxacin (8,9 %) som *E. coli*. Produksjon av ESBL er et utbredt problem i mange land, og forekomsten har også vært økende i Norge. Til sammen 155 av 2 297 (6,7 %) *E. coli* og 77 av 1 230 (6,3 %) *Klebsiella* spp. fra blodkultur ble rapportert som ESBL-positive i 2024. Forekomsten har økt både for *E. coli* (6,0 % i 2022; 5,8% i 2023) og *Klebsiella* spp. (5,5 % både i 2022 og 2023). Andelen av ESBL-positive isolater var fortsatt høyere blant *E. coli* fra blodkulturer (6,7 %) enn fra urinprøver (3,9 %). Karbapenemaseproduserende *Enterobacterales* (CPE), *Pseudomonas aeruginosa* og *Acinetobacter* spp. har vært meldepliktige til MSIS siden 2012. Antall pasienter med CPE økte fra 237 tilfeller i 2023 til 265 i 2024, mens antallet med karbapenemase-produserende *P. aeruginosa* (n=24) og *Acinetobacter* spp. (n=39) var ganske stabilt (henholdvis n=27 og n=31 i 2023). Multiresistente Gram-negative bakterier kan ofte knyttes til import fra land med høy forekomst av slike mikrober. Også i 2024 utgjorde isolater fra ukrainske pasienter ved norske sykehus en betydelig andel av totalen.

Antall systemiske isolater av *Haemophilus influenzae* og *Neisseria meningitidis* var lavere i 2024 enn i 2023, og de er fortsatt på et historisk lavt nivå etter pandemien. Det var lavere andel systemiske *H. influenzae* isolater med produksjon av beta-laktamase i 2024 (11,6 %) enn i 2023 (15,7 %), men dette kan skyldes tilfeldig variasjon. Fore-komsten av kromosomal beta-laktamresistens var høyere i 2024 (17,2 %) enn i 2023 (10,7 %). Det var omtrent samme antall *Neisseria gonorrhoeae* isolater i 2024 (1 471) som i 2023 (1 500), mens antallet kliniske tilfeller meldt til MSIS økte svakt fra 2 985 i 2023 til 3 150 i 2024. Det var utbredt resistens mot penicillin G (21,2 %), og bare 4,8 % var følsomme for standard dosering av penicillin G svarende til villtype-populasjonen. Hele 57,0 % var resistente mot ciprofloxacin. Seks isolater (0,4 %) var resistente mot ceftriaxon og/eller det perorale cefalosporinet cefixim. Alle isolater var fullt følsomme for spectinomycin.

Det ble påvist to enterokokkisolater fra blodkultur med klinisk signifikant vankomycinresistens (VRE) i 2024 (en *vanA* og en *vanB E. faecium*). Forekomsten av resistens mot ampicillin i *E. faecium* var som tidligere rundt 70-80 %, mens høygradig gentamicinresistens stort sett var uendret hos både *E. faecalis* (6,4 % i 2023; 6,2 % i 2024) og *E. faecium* (50,7 % i 2023; 43,4 % i 2024). Nesten alle *E. faecium* isolater med høygradig gentamicinresistens var også resistente mot ampicillin. Det ble funnet to *E. faecium* isolater med genetisk verifisert linezolidresistens (LRE). Både VRE og LRE er meldepliktige til MSIS. Nasjonalt

senter for påvisning av antibiotikaresistens (K-res) kunne bekrefte funn av VRE hos 239 personer i 2024 (74 i 2022; 89 i 2023), og insidensraten har dermed økt fra 0,6 per 100 000 personår i 2021 til 4,4 per 100 000 personår i 2024. Antallet LRE var derimot stabilt med 64 meldte tilfeller i 2024 sammenliknet med 38 i 2022 og 66 i 2023. Tolv isolater var resistente mot både vankomycin og linezolid. Forekomsten av VRE varierer med utbrudd fra år til år, og den betydelige økningen i 2024 skyldtes i stor grad spredning på sykehus i Helse Sør-Øst.

Overvåkingen av resistens hos *Streptococcus pneumoniae* (pneumokokker) viste at 1,1 % av isolatene fra blodkultur og spinalvæske var resistente mot penicillin G (0,3 % i 2023). I tillegg var 5,6 % bare følsomme for økt eksponering av dette middelet (7,9 % i 2023), og åtte isolater (1,3 %) hadde nedsatt følsomhet for ett eller flere 3.-generasjon cefalosporiner. Forekomsten av makrolid-resistens blant pneumokokker fra blodkultur var 6,0 % i 2024 sammenliknet med 6,5 % i 2023. Alle isolater av *S. pyogenes* (beta-hemolytiske streptokokker gruppe A) fra blodkultur, halsprøver og sår var følsomme for penicillin G, mens forekomsten av resistens mot erytromycin (3,9-6,8 %) og tetracyklin (7,6-14,4 %) varierte mellom materialene. Systemiske isolater av *Streptococcus agalactiae* (beta-hemolytiske streptokokker gruppe B) var også følsomme for penicillin G, men hadde utbredt resistens mot erytromycin (24,0 %) og tetracyklin (71,3 %). *Streptococcus dysgalactiae* (beta-hemolytiske streptokokker gruppe C og G) fra blodkultur, halsprøver og sår var følsomme for penicillin G, og andelen med resistens mot erytromycin (10,7-14,9 %) og tetracyklin (23,2-28,7 %) lå på et intermediært nivå.

I alt 181 pasienter med tuberkulose ble meldt til MSIS i 2024. Tretten isolater (8.3 %) ble definert som multiresistente (MDR) mot både rifampicin og isoniazid sammenliknet med 12.0 % i 2023. Pasientene var født i Europa utenom Norge (n=11) og i Afrika (n=2).

Det ble utført resistensbestemmelse av 238 *Candida* blod-kulturisolater fra 223 ulike pasienter. De vanligste artene var *C. albicans* (n=134), *C. glabrata* (n=37), *C. tropicalis* (n=24), *C. dubliniensis* (n=19) og *C. parapsilosis* complex (n=17). Alle *C. albicans* var følsomme for de undersøkte midlene med unntak av to echinocandin-resistente isolater. Det ble kun påvist enkelte non-*albicans* isolater med ervervet resistens, men som forventet var det en del resistens mot azoler hos *C. glabrata* (5,4 %). Nøyaktig speciesbestemmelse er nødvendig for å forutsi iboende resistens og velge effektiv behandling. Resultatene samsvarer med tidligere studier fra Norge.

Konklusjon

I Norge er forekomsten av antibiotikaresistens fortsatt lav i bakterier fra mennesker og dyr. Dette skyldes lavt forbruk av antibiotika, et fordelaktig forbruksmønster, og effektive tiltak mot spredning av resistente bakterier. Resultatene som presenteres i rapporten, viser at strategiene mot antibiotikaresistens har vært vellykkede både i husdyr-holdet og i helsevesenet. Det er imidlertid nødvendig med kontinuerlig innsats for å bevare den gunstige situasjonen slik at antibiotika også i fremtiden vil være effektive for de som trenger det. NORM/NORM-VET-rapporten er viktig for å dokumentere utviklingen av antibiotikaforbruk og resistens hos mennesker og dyr, og for å evaluere effekten av tiltak.

SUMMARY

This joint report from the surveillance programme for antimicrobial resistance in human pathogens (NORM) and the monitoring programme for antimicrobial resistance in bacteria from feed, food and animals (NORM-VET) presents data on the occurrence of antimicrobial resistance and the usage of antimicrobial agents in humans and animals for the year 2024. The NORM and NORM-VET programmes were established as part of the Norwegian Government's Action Plan against Antimicrobial Resistance issued in 2000. NORM is coordinated by the Department of Microbiology and Infection Control, University Hospital of North Norway, Tromsø. NORM-VET is coordinated by the Norwegian Veterinary Institute.

Usage of antimicrobial agents in animals

The total sales of antibacterial veterinary medicinal products (VMPs) for terrestrial animals in Norway were 4,341 kg antibacterial ingredients in 2024, which is 121 kg lower than in 2023 (-3%) and the lowest annual level reported (data available since 1993).

Sales of antibacterial VMPs for use in terrestrial food-producing animals, including horses, were 3,984 kg in 2024. Penicillins continued to be the most-selling antibacterial class for cattle, pigs and poultry - and were almost exclusively accounted for by beta-lactamase sensitive penicillins. Estimated sales of antibacterial VMPs for the largest food-producing species (cattle, pigs, sheep, goats and poultry) were unchanged (less than one percent difference) from 2023 when measured in mg related to population size (mg/kg animal biomass). For horses, the sales were mainly accounted for by trimethoprim-sulfa (oral paste). The sales (kg) of antibacterial VMPs applicable for group treatment of terrestrial food-producing animals in Norway continued to be very low; in 2024 such products accounted for only 3% of the total sales.

In 2024, the sales (kg) of antibacterial VMPs for farmed fish (cleaner fish included) were 709 kg. This is a reduction of 99% compared to 1987, when the sales were at its highest. For Atlantic salmon and rainbow trout, fish in 2.1% of the on-grower locations were subjected to antibacterial treatment in 2024.

The sales (kg) of antibacterial VMPs marketed for companion animals were 357 kg in 2024; compared to 2023 a minor reduction (4%) was observed. The prescription (in kg) for dogs and cats of human antibacterial medicinal products reported to the Veterinary Prescription Register declined by 36% from 2015 to 2024. This indicates that the decline in the sales of antibacterial VMPs for these species has not been substitutet by prescribing of human products.

The European Medicines Agency (EMA) has suggested to restrict the use of some antibacterial classes in animals due to the potential risk to public health – i.e. 3rd-4th generation cephalosporins, quinolones (fluoroquinolones and other quinolones) and polymyxins. In Norway, only quinolones are sold for use in food-producing terrestrial animals and farmed fish. The proportion sold of quinolones of the total sales of antibacterial VMPs was very low (0.3%).

Usage of antimicrobial agents in humans

Total sales of antibacterial agents for systemic use (here referred to as antibiotics, i.e. J01 excluding methenamine) in humans were 13.1 DDD/1,000 inhabitants/day in 2024. Since 2012, there has been a marked decrease in total antibiotic use; a total reduction of 23%. During the Covid-19 pandemic, a significant fall in antibiotic use was observed, but consumption has now returned to roughly the same level as before the pandemic. Norway has a relatively low consumption of antibiotics compared to other countries. We also have an advantageous consumption pattern with a large proportion of narrow-spectrum antibiotics, both in primary healthcare and in the hospital sector. Around 85% of the total amount of DDD of antibacterial agents is used in primary healthcare, i.e. outside healthcare institutions. Of this, 5.5% is prescribed by dentists. Penicillins (J01C) are most often prescribed in primary healthcare. From autumn 2023 and into 2024, there has been an ongoing epidemic of *Mycoplasma pneumoniae*, and this has caused the therapy pattern to change somewhat, with increased use of tetracyclines and macrolides. The penicillin (J01C) share of total use in primary healthcare in 2024 was therefore lower than in previous years; 39% of all antibiotic DDD.

The three most frequently prescribed antibiotics in primary care in 2024 were methenamine, phenoxymethylpenicillin and doxycycline. In Norway, respiratory tract infections are the most common indication for narrow-spectrum penicillin and in 2024, phenoxymethylpenicillin accounted for 17% of all DDD while methenamine accounted for 23%. There has been an increase in use in primary care after the pandemic; use is at almost the same level as in 2019, but over the past decade there has generally been a steady decline in antibiotic use in primary care. Following the introduction of the government's action plan against AMR in 2016, attention has been increased to antimicrobial resistance, both among healthcare professionals and the general population. In primary healthcare, there has been a focus on updated guidelines for antibiotic use. Following the introduction of the government's AMR action plan, a large proportion of general practitioners have completed quality improvement courses on correct antibiotic prescribing and from 2024, it has been possible for general practitioners to obtain automated prescribing reports for their own practices, which could contribute to increased focus on correct antibiotic prescribing. Although much has been achieved, there are probably still areas for improvement in primary healthcare, e.g. avoiding antibiotic prescription for viral infections, individualisation and correct choice of type of antibiotic, dose and duration of treatment.

Antibiotic sales (in DDD) to hospitals accounted for 7.3% of total sales of antibacterial agents to humans in 2024. Sales have decreased by 3% in DDD/1,000 inhabitants/day compared to 2019 but have increased by 7% since 2012. In Norwegian hospitals, antibiotics accounted for 81 DDD/100 bed-days in 2024. This is an increase since 2019, and an increase of 21% since 2012. During the same period, DDD/admission increased by 5%. The therapy pattern for antibacterial agents in hospitals does not change much from one year to another, but there is a clear trend towards more

use of antibiotics recommended in the guidelines. The use of broad-spectrum antibiotics has decreased since 2012. They accounted for 20% of use measured in DDD/100 bed-days in 2024 and 26% in 2012. This favorable development can be explained by updated guidelines, the establishment of antibiotic stewardship programs in hospitals and continuously good follow-up of the antibiotic stewardship teams. In hospitals, penicillins (J01C) were the most used (almost half of use measured in DDD), cephalosporins are the second largest antibiotic group; 18% of all DDD. There are large variations between hospitals, both measured in volume (in DDD/100 bed-days) of antibiotics used and in therapy profile. The variations cannot be explained by differences in activity or patient composition alone.

Antimicrobial resistance in animals and food

Resistance in animal clinical isolates

The isolates included in 2024 were *Escherichia coli* from infections in broilers and turkey, and *Streptococcus canis* and *Campylobacter upsaliensis* from infections in dogs.

The majority of the *E. coli* isolates (73.3% of 225 broiler isolates and 83% of 47 turkey isolates) were fully susceptible to the antimicrobial classes in the test panel, and none were multi-drug resistant (MDR), i.e. resistance to three or more antimicrobial classes.

Of the *S. canis*, 80 isolates were from local ear infections and 61 isolates were from systemic infections. All the isolates were susceptible to benzylpenicillin.

The majority (94.5%) of the 75 *C. upsaliensis* isolates were fully susceptible to the antimicrobial classes in the test panel, and none were MDR.

Resistance in indicator and notifiable bacteria in animals and food

The 2024 data confirm that the situation regarding antimicrobial resistance in bacteria from animals and food in Norway is good. The occurrence of MDR, and specific emerging resistant bacteria/ mechanisms, such as resistance to extended spectrum cephalosporins (ESC), are low.

NORM-VET is following the requirements set in the Commission Implementing Decision 2020/1729/EU on the monitoring and reporting of antimicrobial resistance in zoonotic and commensal bacteria. In addition, antimicrobial susceptibility testing of bacteria from sources other than those covered by this legal requirement are included. *Escherichia coli* and *Enterococcus* spp. are used as indicator bacteria, i.e. susceptibility testing of these bacteria is used as an indicator for the occurrence of antimicrobial resistance in the bacterial population. In addition, *Staphylococcus* spp. is included as an indicator for the occurrence of antimicrobial resistance in horses and pets. Selective screening methods are used for detection of notifiable bacteria such as ESC resistant *E. coli*, carbapenem resistant *Enterobacterales* (CRE), vancomycin resistant *Enterococcus* spp. (VRE), linezolid resistant *Enterococcus* spp. (LRE), methicillin resistant *S. aureus* (MRSA) and methicillin resistant *S. pseudintermedius* (MRSP). MRSA in the Norwegian pig population is investigated thoroughly through a separate specially designed surveillance programme aimed at identifying positive herds. The results from this separate MRSA programme are summarised in the NORM/NORM-VET report as well.

In 2024, animal samples included caecal samples from broiler flocks for susceptibility testing of *E. coli* and *Enterococcus* spp., and detection of emerging resistant bacteria/resistance mechanisms such as ESC resistant *E. coli*, CRE and VRE. Faecal swab samples from horses were also included for susceptibility testing of *E. coli*, and for detection of *E. coli* resistant to ESC and CRE. Nasal swabs were included for isolation of MRSA. Food samples consisted of broiler and turkey meat for detection of *E. coli* resistant to ESC and CRE, and sugar peas and dried fruit for susceptibility testing of *E. coli*, as well as *E. coli* resistant to ESC, CRE and colistin resistant *Enterobacterales*.

The majority (84.8%) of *E. coli* (n=336) from broiler flocks were fully susceptible to all the antimicrobial agents in the test panel, and only 0.9% were MDR. The proportion of fully susceptible isolates has been relatively stable around 80% in the last years (2014-2024). There has been a decrease in resistance to quinolones (i.e. ciprofloxacin and/or nalidixic acid) from 12.6% in 2020 to 5.4% in 2024. CRE were not detected from any of the samples in the selective screenings, while ESC resistant *E. coli* were detected from nine of the samples, all due to chromosomal mutations. Full susceptibility to all the antimicrobial agents was also present in 56.0% of *Enterococcus faecalis* (n=100) and 59.9% of *Enterococcus faecium* (n=312). The proportion of susceptible *E. faecium* isolates has been relatively stable over the years 2014-2024, while there has been some fluctuation in the proportion of fully susceptible *E. faecalis* isolates mainly due to variations in tetracycline resistance. None of the isolates were MDR. VRE was not detected in the selective screening, and this latter is in concordance with the 2018-2022 results.

From the horse samples, the majority (79.2%) of the detected *E. coli* isolates (n=250) were fully susceptible to the antimicrobial agents in the test panel. MDR was detected in 0.4% of the isolates. The proportion of fully susceptible isolates has been relatively stable in the years 2017-2024. No MRSA, nor CRE, were detected from these horses in the selective screenings, while *E. coli* resistant to ESC were detected from three out of 251 samples. The genes responsible were $bla_{\text{CTX-M-1}}$, $bla_{\text{CTX-M-15}}$ and $bla_{\text{SHV-12}}$, respectively. These results are in concordance with results from 2017 and 2021.

No CRE, nor MRSA, were detected in the selective screenings from the meat samples, while ESC resistant *E. coli* were detected from one of the broiler meat (n=325) and one of the turkey meat (n=114) samples, both due to chromosomal mutations. This is in concordance with results from previous years, i.e. 2018, 2020 and 2022.

A total of 315 sugar peas and 345 dried fruit samples were investigated. *E. coli* was only detected from 23 sugar peas samples. Of these, 15 isolates were fully susceptible to all antimicrobial agents in the test panel and three isolates were MDR. No CRE, nor colistin resistant *Enterobacterales*, were detected from these samples using selective methods, while one ESC resistant *E. coli* isolate was detected from the sugar pea samples and this was due to presence of the $bla_{\text{CTX-M-15}}$ gene.

Resistance in zoonotic bacteria and non-zoonotic enteropathogenic bacteria

Animal and meat isolates

In 2024, 28 *Salmonella* spp. isolates from nine wild boars, three dogs, three chicken, two cattle, two horses, and nine cats were susceptibility tested (20 *S*. Typhimurium isolates, of which one was monophasic (4,[5],12 : i : -), two *S. enterica* subsp. *diarizonae*, two *S*. Abony, and one each of *S*. Hessarek, *S*. Mbandaka, *S*. Enteritidis, and *S*. Anatum). Additionally, seven *Salmonella* spp. isolates (i.e. serovars *S*. Kinondoni*, S.* Münster, *S.* Newport, *S*. Tennessee and three *S*. Kisarawe) from non-domestic meat or other food products were included. All these isolates, both from animals and food, were fully susceptible to the antimicrobial agents included in the susceptibility test panel.

The majority (87.5%) of the *Campylobacter jejuni* from broiler flocks (n=56) were fully susceptible to the antimicrobial agents included in the test panel, and none were MDR.

Human clinical enteropathogenic isolates

The National Reference Laboratory for Enteropathogenic bacteria (NRL) conducts annual antimicrobial susceptibility testing for isolates of *Salmonella*, *Campylobacter*, *Yersinia,* and *Shigella*. Since 2020, the NRL has also screened all *Enterobacterales* isolates for antimicrobial resistance genes following whole genome sequencing, in order to detect genotypic resistance. In 2020 and 2021, travel restrictions were implemented as part of the infection control measures during the Covid-19 pandemic, leading to a significant reduction in the number of travel associated infections. Trends in antibiotic resistance should therefore be inter-preted with this in mind.

For *Salmonella* Typhimurium and its monophasic variant, the overall resistance level was higher in strains from travel associated infections compared to those acquired domestically. Multi-drug resistance (MDR) was a characteristic feature of a significant proportion of the monophasic *S*. Typhimurium (71.8%). In total, 18 isolates were identified as ESBL-producing, with the following genotypes: $bla_{\text{CTX-M}}$ (n=11), $bla_{\text{TEM-52}}$ (n=4), $bla_{\text{CMY-2}}$ (n=2), and bla_{DHA} (n=1).

In *Campylobacter jejuni*, the overall resistance levels to ciprofloxacin and tetracycline were higher among strains from travel associated infections than those acquired domestically. Antimicrobial resistance in *Yersinia enterocolitica* remains low.

An increasing trend of resistance to ciprofloxacin and extended spectrum cephalosporins was observed in both *Shigella sonnei* and *Shigella flexneri.* A total of 23 ESBL-producing *S. sonnei* strains and 6 *S. flexneri* strains were identified, carrying the following resistance genes: $bla_{\text{CTX-M}}$ (n=25) and $bla_{\text{DHA-1}}$ (n=4). Most *Shigella* strains (94.8%) were characterised as MDR. In addition, mutations in the *pmrB* gene associated with colistin resistance were identified in all *S. flexneri* strains.

Resistance in human clinical isolates

The prevalence of antimicrobial resistance in human clinical isolates was still low in Norway in 2024. *Staphylococcus aureus* from blood cultures and wound specimens were generally susceptible to all relevant antibiotics. Only 18 methicillin resistant *Staphylococcus aureus* (MRSA) blood culture isolates were detected among 1,614 strains included in NORM in 2024 (1.1%). This is somewhat lower than 50/2,321 (2.2%) blood culture and cerebrospinal fluid *S. aureus* isolates reported from the laboratory information systems, which is a minor increase from 1.8% in 2023. The Norwegian Surveillance System for Communicable Diseases (MSIS) registered 1,222 cases of MRSA infection in 2024. The majority of MRSA cases were reported as superficial wound infections and/or abscesses. The proportion of MRSA among non-invasive *S. aureus* isolates is still very low at 1.9% (16/841) and comparable to previous years (1.6% in 2022; 1.3% in 2023). Furthermore, MSIS registered 1,689 MRSA colonisations in 2024. A total of 2,942 persons were reported with MRSA in 2024 compared to 2,544 in 2023 (+15%). This corresponds to an incidence rate of 53 per 100,000 person-years compared to 38 in 2022 and 46 in 2023. The incidence of MRSA is now higher than before the Covid-19 pandemic (2,568 persons registered in 2017). The monthly number of MRSA infections has not changed significantly over the last eight years, and the incidence of invasive disease has remained stable at a low level. A large proportion of MRSA cases are still infected abroad (20%), but for many (55%) the location of acquisition was unknown. Very few cases of livestock-associated MRSA are detected in Norway.

The rates of resistance to broad-spectrum antimicrobials in *E. coli* blood culture isolates increased slightly in 2024. The prevalence of gentamicin resistance was 5.7% in 2024 compared to 5.1% in 2022 and 5.4% in 2023, while the prevalence of ciprofloxacin resistance remained unchanged at 9.7% (10.0% in 2023). *Klebsiella* spp. isolates demonstrated approximately the same rates of resistance to gentamicin (4.5%) and ciprofloxacin (8.9%) as *E. coli*. Extended spectrum beta-lactamases (ESBL) have emerged as a significant clinical problem in many countries, including Norway. A total of 155/2,297 (6.7%) *E. coli* and 77/1,230 (6.3%) *Klebsiella* spp. blood culture isolates were reported with this phenotype in 2024. The prevalence has increased for both *E. coli* (6.0% in 2022; 5.8% in 2023) and *Klebsiella* spp. (5.5% in both 2022 and 2023). The proportion of ESBL positive isolates is still higher among *E. coli* from blood cultures (6.7%) than from urine (3.9%). Carbapenemase-producing *Enterobacterales* (CPE), *P. aeruginosa* and *Acinetobacter* spp. have been notifiable to MSIS since 2012. The number of CPE patients increased from 237 in 2023 to 265 in 2024, whereas the number of patients with carbapenemase-producing *P. aeruginosa* (n=24) and *Acinetobacter* spp. (n=39) remained relatively stable (n=27 and n=31 in 2023, respectively). Many multi-drug resistant Gram-negative isolates were imported from countries with high prevalences of these organisms. Also, in 2024, isolates from hospital patients transferred from Ukraine represented a significant proportion of the total.

The number of *Haemophilus influenzae* and *Neisseria meningitidis* isolates from blood cultures and cerebrospinal fluids was lower in 2024 than in 2023, and is still at a historically low level in the aftermath of the Covid-19 pandemic. The proportion of systemic *H. influenzae* demonstrating beta-lactamase production decreased from 15.7 % in 2023 to 11.6% in 2024, but this may be due to random variation. The frequency of chromosomally encoded beta-lactam resistance was higher in 2024 (17.2%) than in 2023 (10.7%). The number of *Neisseria gonorrhoeae* isolates was approximately the same in 2024 (1,471)

as in 2023 (1,500), whereas the number of clinical cases reported to MSIS increased slightly from 2,985 in 2023 to 3,150 in 2024. Many isolates displayed resistance to penicillin G (21.2%), and only 4.8% were susceptible to standard penicillin G dosage corresponding to the wild type population. Ciprofloxacin resistance was detected in 57.0% of isolates. Six isolates (0.4%) were resistant to ceftriaxone and/or the oral cephalosporin cefixime. All isolates were susceptible to spectinomycin.

Two enterococcal blood culture isolates with clinically relevant vancomycin resistance (VRE) were detected in 2024 (one *vanA* and one *vanB E. faecium*). The prevalence of ampicillin resistance in *E. faecium* has stabilised around 70-80%. High-level gentamicin resistance (HLGR) was essentially unchanged in both *E. faecalis* (6.4% in 2023; 6.2% in 2024) and *E. faecium* (50.7% in 2023; 43.4% in 2024). Almost all HLGR *E. faecium* isolates were also resistant to ampicillin. Two linezolid resistant *E. faecium* isolates (LRE) were genetically confirmed in the NORM surveillance programme in 2024. Both VRE and LRE should be reported to the national notification system (MSIS). The Norwegian Centre for Detection of Antimicrobial Resistance (K-res) confirmed the presence of VRE in 239 persons in 2024 (74 in 2022; 89 in 2023), and the incidence rate has thus increased from 0.6 per 100,000 person-years in 2021 to 4.4 per 100,000 person-years in 2024. The number of LRE remained stable with 64 reported cases in 2024 compared to 38 in 2022 and 66 in 2023. Twelve isolates were resistant to both vancomycin and linezolid. The VRE prevalence varies over time due to outbreaks, and the large increase in 2024 was mainly due to spread in hospitals in the South-Eastern Health Region.

Surveillance of resistance in *Streptococcus pneumoniae* (pneumococci) revealed penicillin G resistance in 1.1% of isolates from blood cultures and cerebrospinal fluids (0.3% in 2023). In addition, 5.6% would require increased exposure to this agent (7.9% in 2023). Eight isolates (1.3%) isolates displayed reduced susceptibility to one or more 3rd generation cephalosporins. The prevalence of macrolide resistance was 6.0% in 2024 compared to 6.5% in 2023. All *S. pyogenes* (beta-haemolytic group A streptococci) isolates from blood cultures, respiratory samples and wounds were susceptible to penicillin G, but resistance to erythromycin (3.9-6.8%) and tetracycline (7.6-14.4%) varied between specimen types. Systemic *Streptococcus agalactiae* (beta-haemolytic group B streptococci) isolates were also susceptible to penicillin G, but had high rates of resistance to erythromycin (24.0%) and tetracycline (71.3%). *Streptococcus dysgalactiae* (beta-haemolytic group C and G streptococci) from blood cultures, respiratory samples and wounds were penicillin G susceptible, but displayed intermediate rates of resistance to erythromycin (10.7-14.9%) and tetracycline (23.2-28.7%).

A total of 181 patients with tuberculosis were reported to MSIS in 2024. Thirteen isolates (8.3%) were defined as multi-drug resistant (MDR) to both rifampicin and isoniazid compared to 12.0 % in 2023. The patients were born in Europe outside Norway (n=11) and in Africa (n=2).

Susceptibility testing was performed on 238 *Candida* spp. blood culture isolates from 223 unique patients. The most common species were *C. albicans* (n=134), *C. glabrata* (n=37), *C. tropicalis* (n=24), *C. dubliniensis* (n=19) and *C. parapsilosis* complex (n=17). All *C. albicans* were susceptible to the substances examined with the exception of two echinocandin resistant isolates. Only single non-*albicans* isolates with acquired resistance were detected, but as expected there was a significant prevalence of azole resistance among *C. glabrata* (5.4%). Precise species identification is essential to predict inherent resistance and select appropriate antifungal therapy.

Conclusion

Antimicrobial resistance is still a limited problem among humans and food-producing animals in Norway. This reflects the low usage of antibacterial agents in human and veterinary medicine, a favourable usage pattern, as well as effective infection control measures. The data presented in this report show that strategies for containment of antimicrobial resistance have been successful both in the food-producing animal sector and in the healthcare sector. Continuous efforts and awareness rising are needed to preserve the favourable situation and ensure that antimicrobials are effective when needed. The NORM/ NORM-VET report is vital in order to document the trends in antibiotic usage and occurrence of resistance in humans and animals, and to evaluate the effectiveness of interventions.

POPULATION STATISTICS

Hege Salvesen Blix and Kari Olli Helgesen

Population statistics for animal and human populations are published in order to present data used for analyses of sales and use of antimicrobial agents. The population data can further be used for comparison of Norwegian data with corresponding figures from other countries. The data are collected by Norwegian authorities as shown in the tables below.

TABLE 1. Animal population in Norway in 2023 and 2024. All population categories are measured in heads, except finfish that are measured in tonnes. For details on weights per population category: For European Sales and Use of Antimicrobials for Veterinary Medicine (ESUAvet) denominators see relevant guideline (1). For European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) denominators see relevant protocol (2). Y means included and N means not included in the denominator. All data from the Register of Production Subsidies are from the counting date March 1.

Animal species	Population category	2023	2024	Source	ESUAvet denominator	ESVAC denominator
Cattle	Male bovine animals, 1 to less than 2 years old*	570,020	542,589	3	Y	N
	Non-dairy cows	108,424	106,337	3	Y	N
	Dairy cow	202,876	202,771	3	Y	Y
	Slaughtered bullocks and bulls**	192,238	186,087	4	N	Y
	Slaughtered calves and young cattle	15,933	16,648	4	Y	Y
	Slaughtered cow	110,698	102,234	4	N	Y
Chickens	Laying hens producing eggs for human consumption	4,088,541	4,082,751	3	Y	N
	Slaughtered broilers	72,028,454	72,684,385	5	Y	Y
Turkeys	Slaughtered turkeys	913,650	871,521	5	Y	Y
Other poultry	Slaughtered duck	371,992	342,101	5	Y	N
	Slaughtered goose	2,735	2,058	5	Y	N
Sheep	Slaughtered lamb	944,240	932,805	5	Y	N
	Live sheep	909,914	889,615	3	Y	Y
	Sheep for fattening – In	0	31	5	Y	Y
	Slaughtered sheep and goat	1,140,408	1,104,717	4	N	Y
Goats	Live goats	75,394	77,375	6	Y	N
	Slaughtered goat	27,823	26,638	5	Y	N
Finfish (in tonnes)	Atlantic salmon	1,517,515.82	1,552,887.32	7	Y	Y
	Rainbow trout	86,338.17	95,863.46	7	Y	Y
	Other farmed fish produced	15,111.04	16,734.29	7	N	Y
Pigs	Breeding sows > 50 kg	69,255	66,474	8	Y	Y
	Pigs for Fattening – Out	1,106	1,227	5	Y	Y
	Slaughtered Pig	1,528,740	1,525,637	4	Y	Y
Horses	Living horses***	125,000	78,528	9	Y	Y

*Aggregated data for all live cattle except for dairy and non-dairy cows, due to only aggregated data collected in Register of Production Subsidies. **Aggregated data including slaughtered heifers, due to only aggregated data collected in Delivery Register for Carcasses. ***The data source was changed from 2023 to 2024 to the National Horse Registry. 2024-data are all horses below 35 years in the registry per March 1 2025.

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TABLE 2. Human population in Norway as of 25.02.2025. Data provided by Statistics Norway; Table 12871: Population by age, year and sex.

Age group	All	Males	Females
0 to 4 years	275,034	140,991	134,043
5 to 14 years	627,536	322,784	304,752
15 to 24 years	674,589	347,439	327,150
25 to 44 years	1,524,821	779,263	745,558
45 to 64 years	1,431,997	728,481	703,516
65 years and older	1,060,363	500,239	560,124
All age groups	5,594,340	2,819,197	2,775,143

USAGE OF ANTIMICROBIAL AGENTS

USAGE IN ANIMALS

Kari Olli Helgesen and Leif Lukas Löfling

Sales data for 1993-2024 of antibacterial veterinary medicinal products (VMP) for terrestrial animal species obtained at wholesaler's level, have been stratified into sales of antibacterial VMPs approved for terrestrial food-producing animals including horses and VMPs approved solely for companion animals, respectively. Further, sales data for food-producing animals have been stratified to reflect sales for the major food-producing species; terrestrial food-producing animals excluding horses (see Appendix 1 for methodology). The data are based on sales to Norwegian pharmacies from medicine wholesalers of VMPs. This includes all pharmaceutical formulations approved for food-producing terrestrial animals, including horses, and for companion animals as well as VMPs used on special lisence (products approved in another European Economic Area (EEA) country). In addition, data obtained from the Veterinary Prescription Register (VetReg) have been used for some use data analyses, including for supplementary information (see Appendix 1).

Calculation of kg active substance per VMP presentation follows the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) protocol for data up till 2022 and thereafter the European Sales and Use of Antimicrobials for Veterinary Medicine (ESUAvet) protocol from 2023 and onwards (see Appendix 1 and text box on ESUAvet). The shift from ESVAC to ESUAvet methodology for data from 2023 means that for this year data are slightly different from what was presented in the NORM/NORM-VET 2023 report.

Sales of veterinary antibacterial agents

All animals

Overall, the sales in Norway of antibacterial VMPs for therapeutic use in food producing terrestrial animals, including horses, and companion animals in 2024 were 4,341 kg active substance. A decline of the sales (kg) of such VMPs of 52% in the period 1993-2024 is observed (Figure 1).

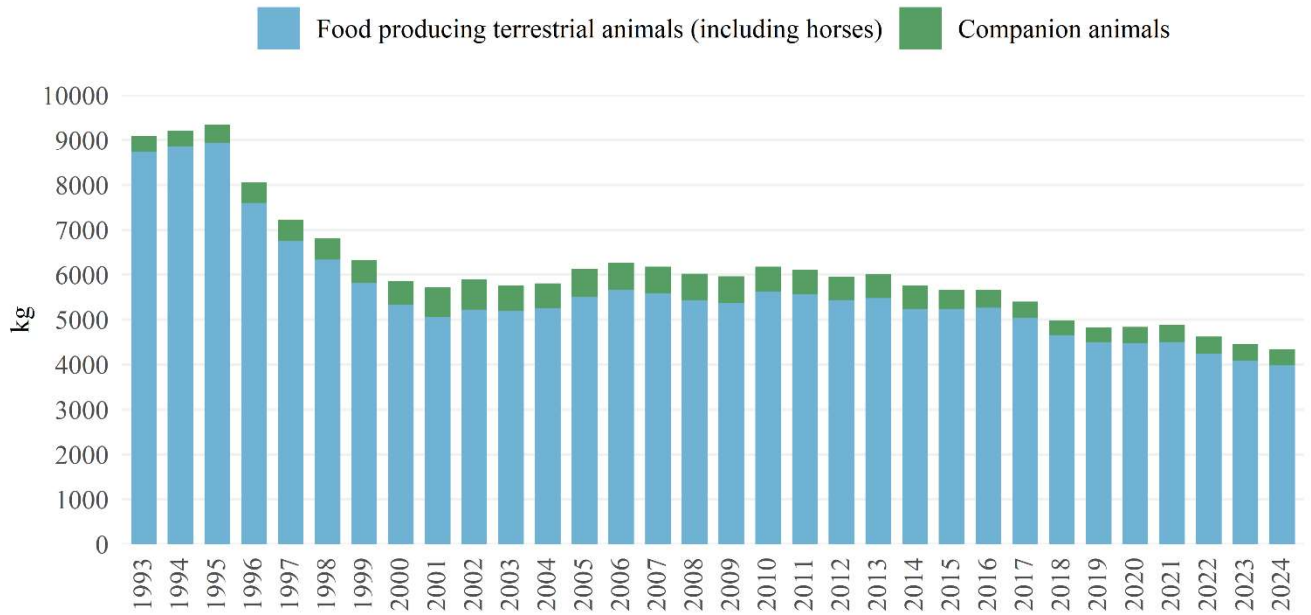

FIGURE 1. Total sales, in kg active substance, for food-producing terrestrial animals (including horses) and companion animals, of antibacterial veterinary medicinal products for therapeutic use in Norway in 1993-2024.

Food-producing terrestrial animals, including horses

In 2024 the sales, in kg active substance, of antibacterial VMPs sold for use in terrestrial food-producing animals, including horses, were 3,984 kg and compared to 1993 a decrease in the sales of such VMPs of 54% is observed (Figure 2). In total, 62% of the sales (kg) of antibacterial VMPs for this animal category in 2024 contained penicillins only, of which 95% was beta-lactamase sensitive penicillins. Of the total sales for use in terrestrial food producing animals in 2024, 27% was sales of oral paste containing trimethoprim-sulfa marketed for horses.

The proportion of sales of VMPs for terrestrial food-producing animals containing only penicillins increased from 18% to 63% during the period 1993-2024. This is mainly due to reduced sales of injectable and intramammary combination VMPs of penicillins and an aminoglycoside (dihydrostreptomycin) that has been gradually replaced by VMPs containing penicillins as the sole antibacterial agents.

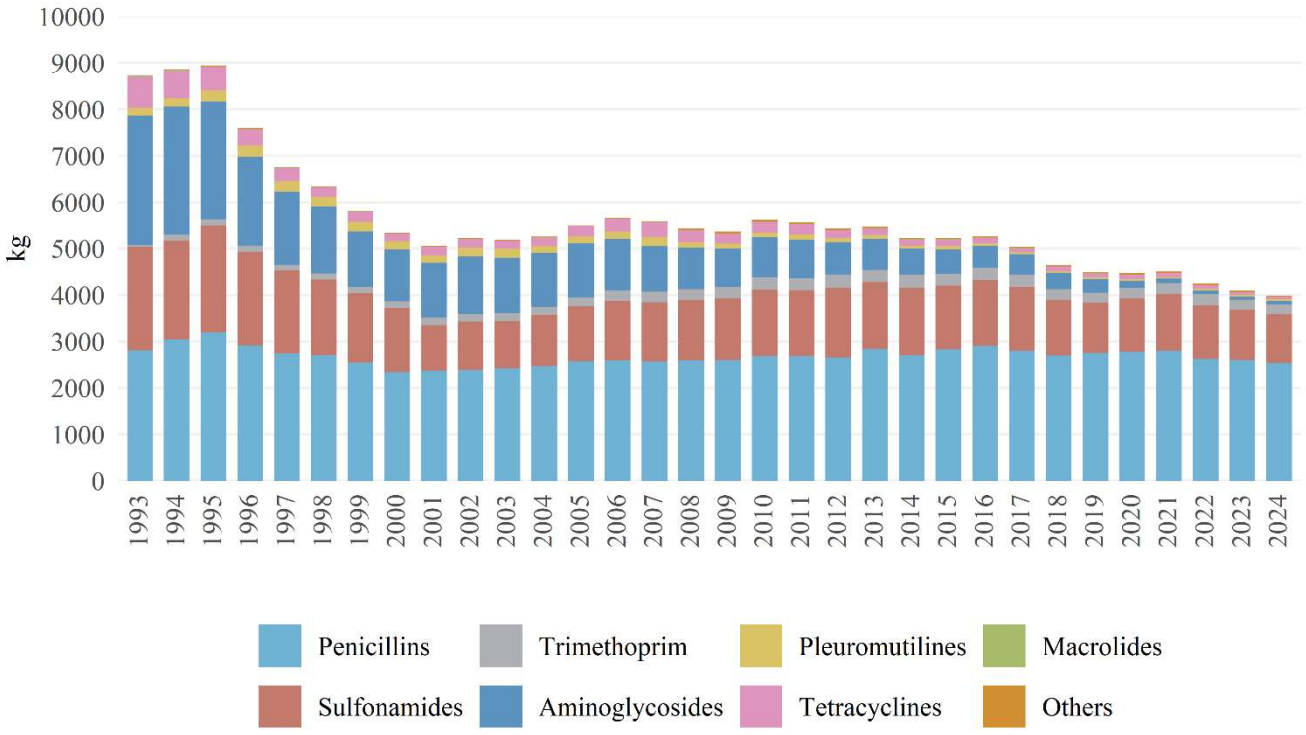

FIGURE 2. Sales, in kg active substance, of antibacterial veterinary medicinal products (VMPs) for therapeutic use in food-producing terrestrial animals (including horses) in Norway in 1993-2024. "Others" consist of minor sales of baquiloprim in 1994-2000 (range 0.2-1.8 kg), 3rd generation cephalosporines in 2012-2023 (range 0.001-0.07 kg), amphenicols in 2008-2024 (range 16-27 kg) and fluoroquinolones in 1993-2024 (range 6-19 kg).

Of the antibacterials for which restriction of use in animals is recommend at EU/EEA level due to potential public health risks – i.e. 3rd and 4th generation cephalosporins, polymyxins and quinolones (fluroquinolones and other quinolones) (1, 2), only fluoroquinolones are marketed in Norway for food-producing terrestrial animals. From 1993 to 2024, the proportion of sales of fluoroquinolones for food-producing terrestrial animals has been very low and stable varying between 0.1% and 0.3% of the total sales (Figure 2). During 1993-2024 no VMPs containing 3rd and higher generations of cephalosporins have been approved for food-producing animals in Norway via national procedures. Several 3rd generation cephalosporin VMPs have been approved via community procedures, but they are not marketed in Norway. Applications for special permits to use such VMPs marketed in other EEA countries for food-producing animals are normally not approved, and approval would only be given for specific animals if sensitivity testing precludes all other options. This is the case also for polymyxins (Knud Torjesen, Norwegian Medicines Agency, personal communication). Glyco-peptides and carbapenems are not allowed to be used for food-producing animals in EU/EEA countries.

In Norway, sales of antibacterial VMPs for treatment of food-producing terrestrial animals are predominately pharmaceutical forms for treatment of individual animals (Figure 3) and primarily by injectables. This reflects that the livestock is characterised by small herds, but it can also partly be explained by type of infections and therapeutic traditions. In 2024, only 2.8% of the sales of antibacterial VMPs for food-producing terrestrial animals was for VMPs applicable for group treatment (oral treatment).

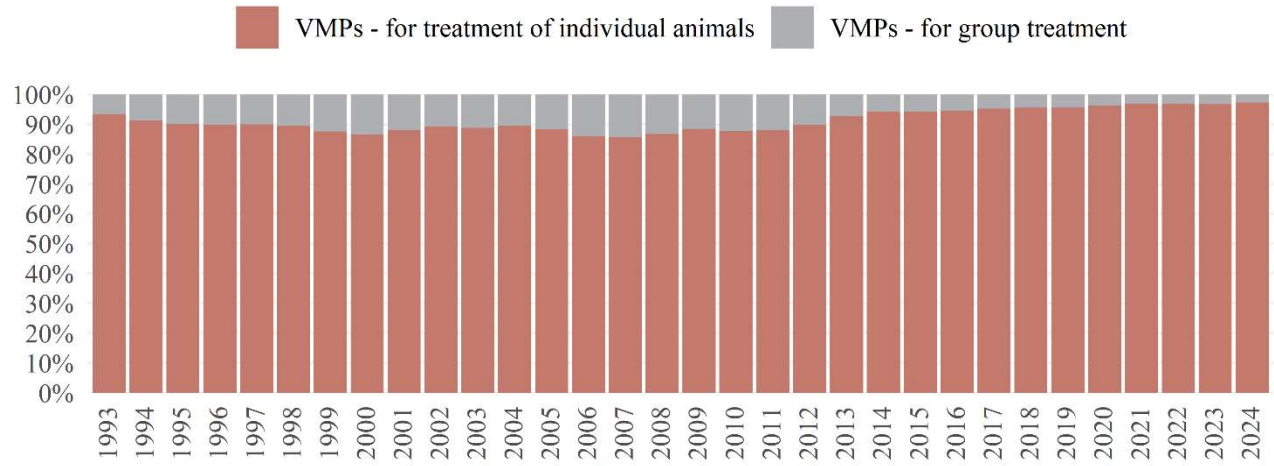

FIGURE 3. Proportion of sales in Norway, 1993-2024, (in kg active substance), of antibacterial veterinary medicinal products (VMPs) marketed for treatment of individual food-producing terrestrial animals, including horses (bolus, injectables, intramammary preparations, intrauterine preparations, oral paste and tablet VMP presentations – see Appendix 1) and applicable for group treatment through feed or drinking water (oral solution and oral powder. No premixes were sold for terrestrial food-producing animals).

Major food-producing terrestrial animal species

Antibacterial VMPs predominantly sold to food-producing terrestrial animals, excluding horses, are shown as mg per kg animal biomass in Figure 4. The methodology is described in Appendix 1. From 2013 to 2023 the sales for this group of species were reduced by 27% (given in mg/kg biomass), while the sales were stable from 2023 to 2024 (below 1% change).

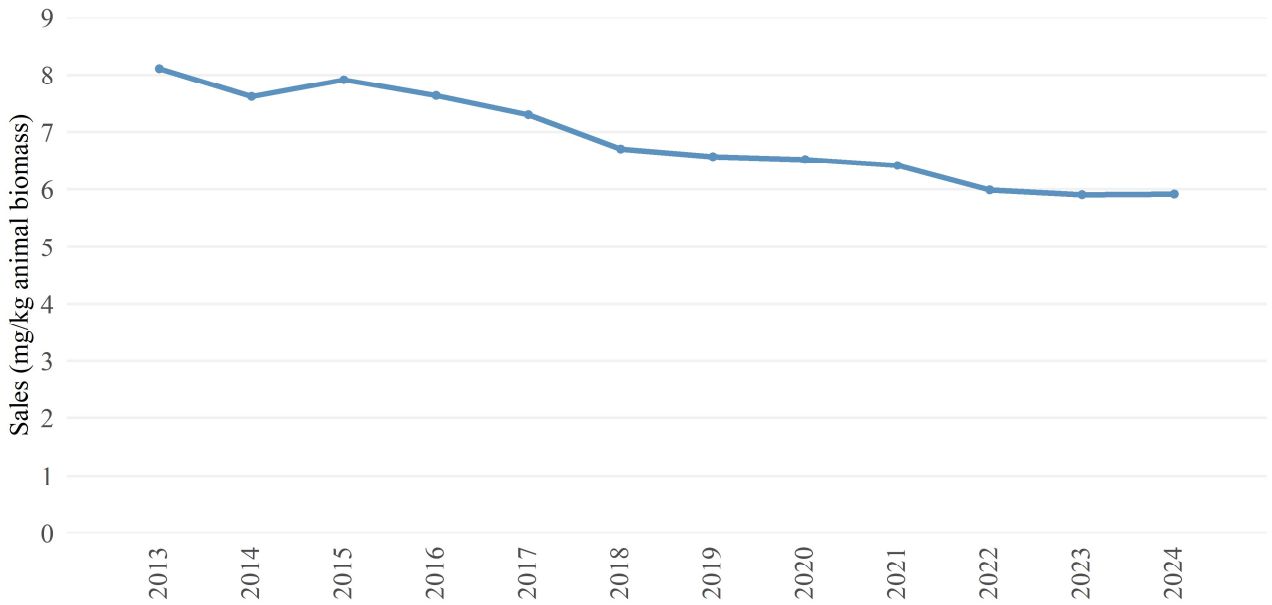

FIGURE 4. Annual sales in Norway, 2013-2024, (in mg/kg animal biomass), of antibacterial veterinary medicinal products (VMPs) marketed for treatment of food-producing terrestrial animals, stratified to exclude sales for horses (all VMP presentations included, except oral pastes – see Appendix 1). The denominator is annual animal biomass using the ESVAC-methodology for animal biomass calculation (see Appendix 1 and Text box on ESUAvet) for food-producing terrestrial animals, excluding the biomass for horses.

Use patterns - cattle, pigs, chickens and turkeys (VetReg data)

The use patterns presented represent data reported to VetReg for 2024 (see Appendix 1). The data were extracted from the VetReg database 18 March 2025. Data cover use of VMPs reported to VetReg for the four species cattle, pigs, chicken and turkey, for which use is mandatory to report to EMA according to EU 2019/6 (see Appendix 1). In addition, minor amounts of human medicinal products (HMPs) were used, and this is presented in the text per species.

Cattle

Of the prescribed (VetReg data) antibacterial VMPs (in kg active substance) for cattle in 2024, 91.2% was for penicillins; 88.1% was beta-lactamase sensitive penicillins (Figure 5). Of the total antibiotics prescribed (in kg active substance) for cattle, HMPs accounted for less than 1% (not included in Figure 5).

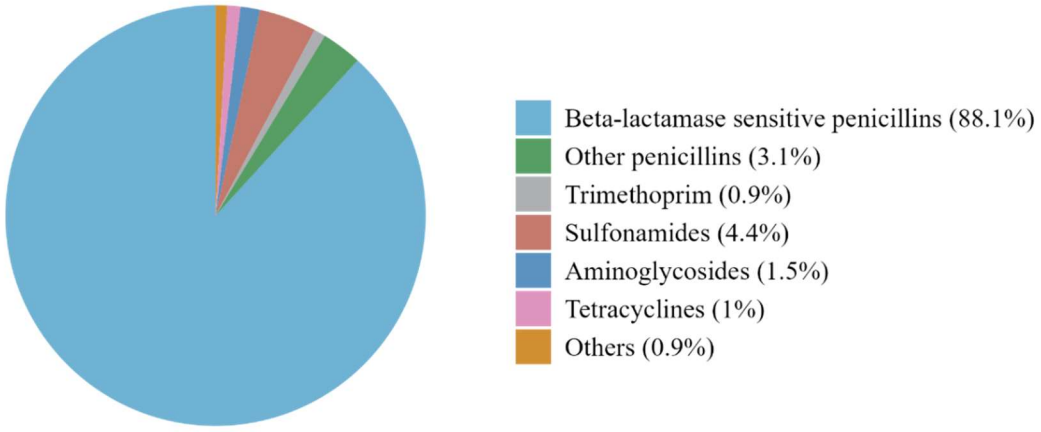

FIGURE 5. Prescribing patterns, in percentage of kg active substance, of antibacterial veterinary medicinal products (VMPs) for cattle in Norway in 2024. Data were obtained from the Veterinary Prescription Register and represent all ATCvet codes for which use data are mandatory to report to the European Medicines Agency. Others consist of florfenicol and enrofloxacin. In addition, minor amounts of HMPs (less than 1% of total use) were prescribed for cattle (not included in the figure).

Pigs

Of the antibacterial VMPs reported to VetReg (in kg active substance) as prescribed for treatment of pigs in 2024 (Figure 6), 87.0% was penicillins; 79.5% was for beta-lactamse sensitive penicillins only. Of the total antibiotics prescribed (in kg active substance) for pigs, HMPs accounted for less than 0.1% (not included in Figure 6).

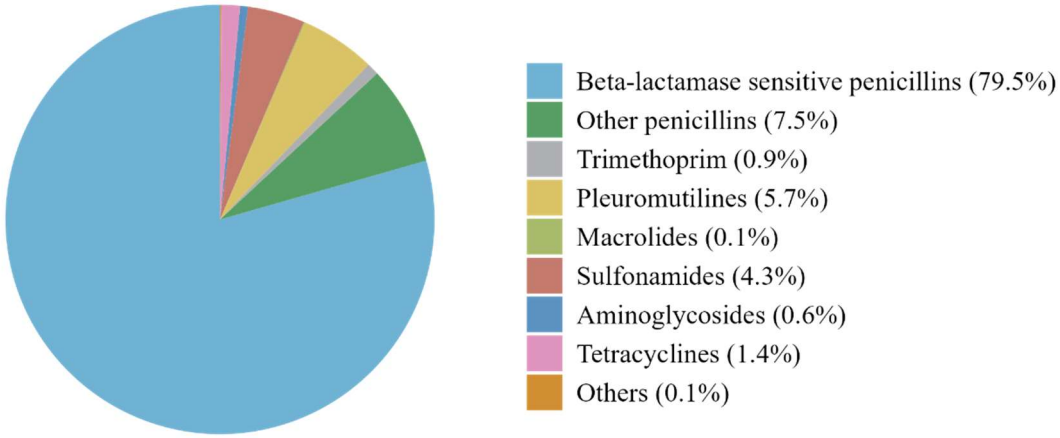

FIGURE 6. Prescribing patterns, in percentage of kg active substance, of antibacterial veterinary medicinal products (VMPs) for pigs in Norway in 2024. Data are obtained from the Veterinary Prescription Register and represent all ATCvet codes for wich use data are mandatory to report to the European Medicines Agency. Others consist of enrofloxacin. In addition, minor amounts of HMPs (less than 0.1% of total use) were prescribed for pigs (not included in the figure).

Chickens

Of the antibacterial VMPs reported to VetReg (in kg active substance) as prescribed for treatment of chicken (Figure 7), 91.6% of the total amount reported to VetReg was penicillins; 91.2% was VMPs containing only beta-lactamase sensitive penicillins. Of the total antibiotics prescribed for chicken, HMPs accounted for 6% (not included in Figure 7).

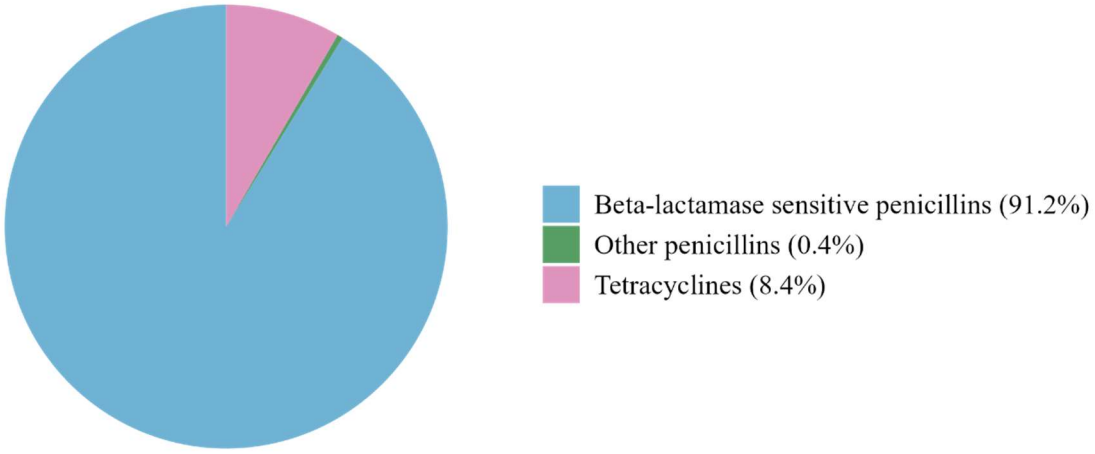

FIGURE 7. Prescribing patterns, in percentage of kg active substance, of antibacterial veterinary medicinal products (VMPs) for chickens in Norway in 2024. Data are obtained from the Veterinary Prescription Register and represent all ATCvet codes for wich use data are mandatory to report to the European Medicines Agency. In addition, total use consisted of 6% use of HMPs for chicken (not included in the figure).

Turkeys

Of the antibacterial VMPs reported to VetReg as prescribed for treatment of turkeys; all use was of beta-lactamase sensitive penicillins. No HMPs were used for turkeys.

Farmed fish

In 2024, the total amount of antibacterial VMPs dispensed for use in farmed fish in Norway was 709 kg (active substance) (Table 3); of this 2.1 kg was dispensed for use in cleaner fish. The data for farmed fish were extracted from the VetReg database 3 March 2025. Of the antibacterials for which restriction of use in animals is recommended in EU/EEA countries, adviced due to potential public health risk (1, 2), only other quinolones are used for farmed fish. From 2015 to 2024, the proportion of sales of quinolones has fluctuated; in 2024 this proportion was less than 1% (6 kg) (Table 3).

TABLE 3. Use, in kg of active substance, of antibacterial veterinary medicinal products (VMPs) for farmed fish in Norway in 2015-2024[1]. Data represent dispensed prescriptions obtained from the Veterinary Prescription Register (VetReg) (see Appendix 1). Note that data include antibacterials for use in cleaner fish.

Active substance	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Tetracyclines										
Oxytetracycline	0	0	0	20	0	0.16	0	0	0	0.04
Amphenicols										
Florfenicol	183	134	264	857	152	113	531	397	516	703
Quinolones										
Flumequine	0	0	0	0	0	0	0	0	0	0
Oxolinic acid	84	66	343	54	66	107	57	28	32	6
Enrofloxacin	0.02	0.050	0.01		0.01	0.12	0.44	0.10	0.05	0.06
Total	**267**	**199**	**607**	**930**	**218**	**220**	**588**	**425**	**548**	**709**

[1] The total amounts (kg) given may be deviating due to rounding of each single value.

From 2015 to 2021 the major proportion of dispensed prescriptions of antibacterials was for fish in the pre-ongrowing phase. However, since 2022 this trend has discontinued and in 2024 59% of the dispensed prescriptions for fish (all species combined) were for the ongrower phase (Figure 8). The number of dispensed prescriptions of antibacterial VMPs for Atlantic salmon ongrowers were, however, low during the period 2015-2024 (range 5-29 prescriptions), considering that Atlantic salmon production in this period varied between 1.3 and 1.7 million tonnes per year. This is a strong indication that the vaccines used in Atlantic salmon are efficient and that the coverage of vaccination of fingerlings is very high.

Of the antibiotics dispensed in 2024 (114 prescriptions), 65% (74 prescriptions) were for marine species, mainly halibut (66 prescriptions) and cod (five prescriptions). These 74 dispensed prescriptions accounted for 26% (187 out of 709 kg) of all antibiotic use in farmed fish.

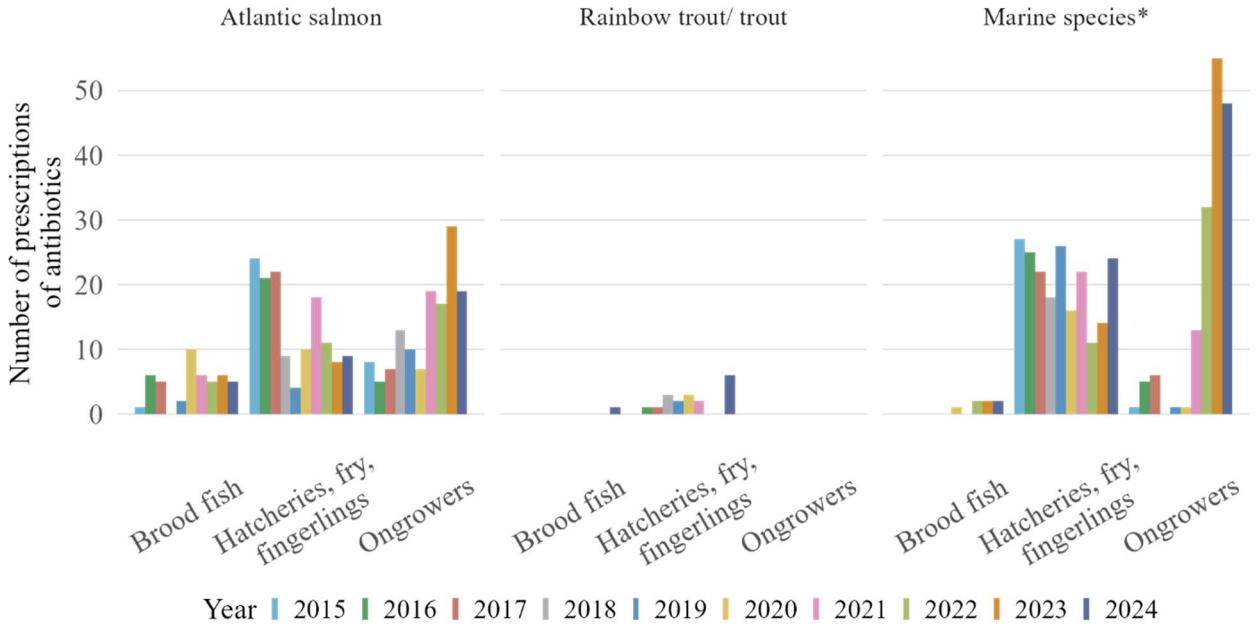

FIGURE 8. Number of dispensed prescriptions of antibiotic VMPs by fish species (aggregated for marine fish), split into production stages/types, in Norway in 2015-2024. Data were obtained from the Veterinary Prescription Register. *Arctic char, cod, halibut, pollack and/or wolffish. Note that cleaner fish are not included.

The annual sales of antibacterial VMPs for use in aquaculture peaked in 1987 when it amounted to 48 tonnes (Figure 9) – i.e. 876 mg/kg animal biomass; the corresponding figure in 2024 was 0.43 mg/kg animal biomass. Thus, the sales in mg/kg animal biomass have declined by 99%. The significant decrease in the sales of antibacterial agents in Norwegian aquaculture from 1987 is mainly attributed to the introduction of effective vaccines against bacterial diseases in Atlantic salmon and rainbow trout, but also prevention of bacterial diseases and their spread.

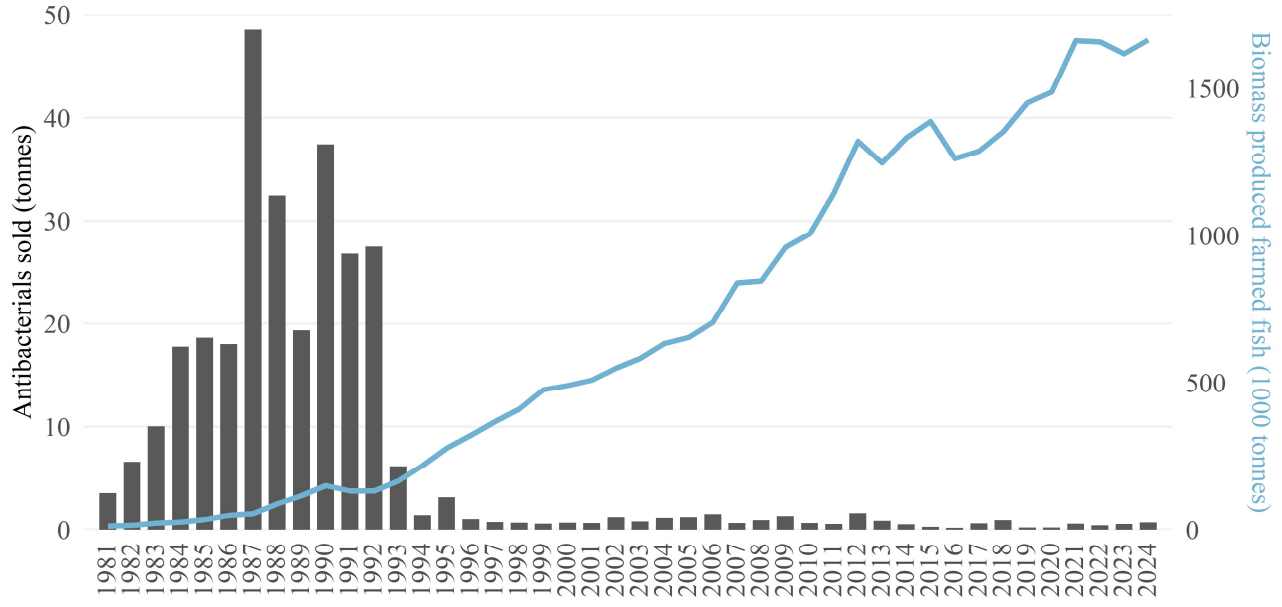

FIGURE 9. Sales, in tonnes of active substance, of antibacterial veterinary medicinal products for therapeutic use in farmed fish (including cleaner fish) in Norway in 1981-2024 versus tonnes produced (slaughtered) farmed fish. For the years 1981-2012 the data represent sales data provided by the Norwegian Institute of Public Health; for 2013-2024 data represent prescription data obtained form the Veterinary Prescription Register (VetReg). Data on slaughtered biomass farmed fish (Atlantic salmon, rainbow trout, other salmonid and marine species) were obtained from Norwegian Directorate of Fisheries [Akvakulturstatistikk (fiskeridir.no)]. Note differences in the scales of the Y-axes.

In 2013-2017 only a low percentage of Atlantic salmon and rainbow trout ongrower farms were subjected to treatment with antibiotics (range 0.6%-1.5%) (3). This was also the case for the years 2018-2023; this figure was between 0.8% and 3.3%. In 2024 this figure was 2.1%.

Companion animals (dogs and cats)

The sales in 2024 of antibacterial VMPs approved solely for companion animals (includes VMPs formulated as tablets, oral solution, injectable and oral paste) was 357 kg (active substance); in 2023 this figure was 372 kg. As shown in Figure 10, a steady increase in the sales from 1993 to 2001 was observed. This can in part be explained by an increase in the availability of antibacterial VMPs marketed for dogs and cats during that period. When the availability of VMPs for dogs and cats was lower, it is likely that antibacterial HMPs were prescribed for dogs and cats. In 1993, only eight antibacterial VMP presentations (name, pharmaceutical form, strength and pack size) were approved and sold in Norway for dogs and cats only, while in 2024 the corresponding number was 36.

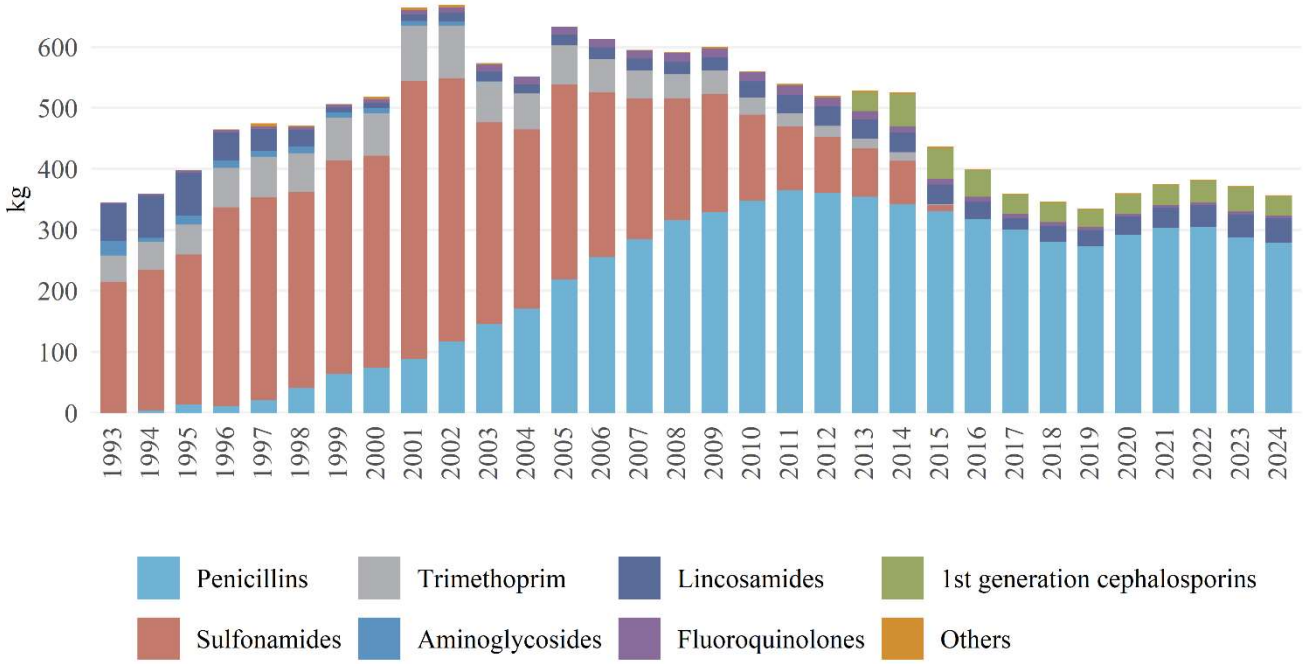

FIGURE 10. Sales, in kg active substance, of antibacterial veterinary medicinal products marketed solely for use in companion animals (see Appendix 1) in Norway for the period 1993-2024. Others include minor annual sales of a 3rd generation cephalosporin injectable VMP (range 0.3-1.1 kg) during 2008-2024, tetracycline VMPs (range 0.04-1.9) during 1995-2024, macrolide VMPs (0.4-5 kg) during 1996–2003, and baquiloprim VMPs (0.2-0.4 kg) during 1995-1999.

The sales patterns of antibacterial VMPs marketed solely for companion animals (dogs and cats) have changed significantly during the period 1993-2024 (Figure 10). The first penicillin VMP as tablets – i.e. amoxicillin (an aminopenicillin) were marketed for dogs and cats in 1994; since then, the proportion belonging to the penicillins (only aminopenicillin VMPs marketed) sold of total sales of antibacterial VMPs approved for such animals has increased from 1% to 78% (Figure 10). Among penicillin VMPs, amoxicillin combined with clavulanic acid accounted for 80% of the sales in 2024 (Figure 11).

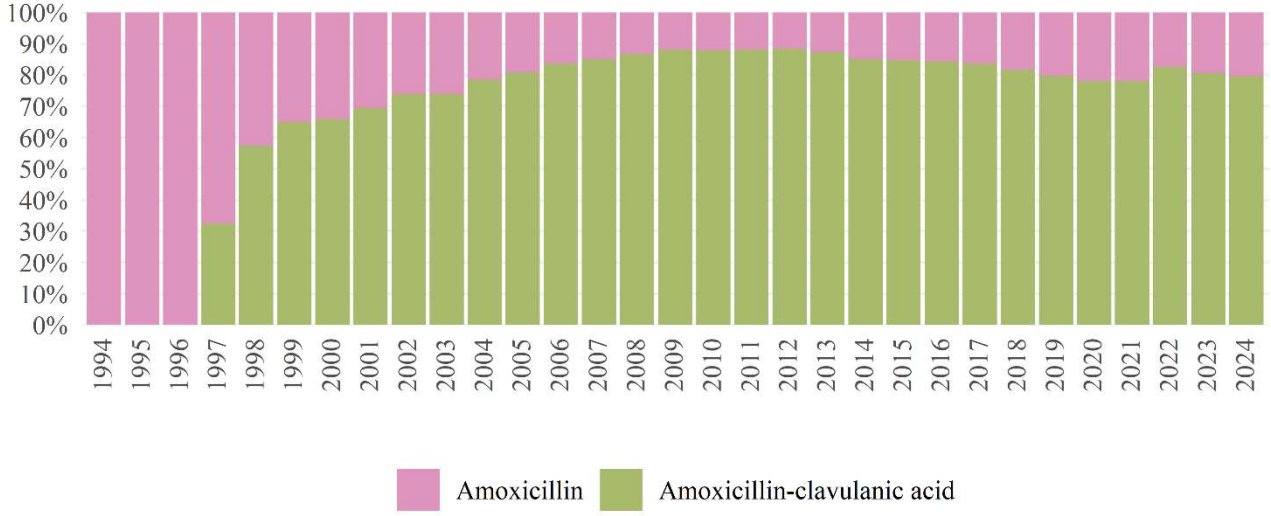

FIGURE 11. Proportions of sales (in kg active substance), of VMPs with amoxicillin combined with clavulanic acid versus amoxicillin for dogs and cats in Norway during 1994-2024.

From 1993 to 2023 the proportion of sales of fluoroquinolones have been very low, accounting for 0.5% of the total sales for this animal category in 1993, increasing marginally to 2.8% in 2011, and since then this proportion has decreased slightly to 1.3% in 2024 (Figure 10). The proportion of the total sales for dogs and cats of 3rd generation cephalosporins have been low since such VMPs were marketed in Norway in 2008; this figure was 0.2% in 2008 and 0.1% in 2024 (Figure 10).

Antibacterials for which use in animals is adviced to be restricted

In 2019, EMA's Antimicrobial Advice Ad Hoc Expert Group (AMEG) published a categorisation (1,2) of antibiotics for use in animals for prudent and responsible use at EU/EEA level. AMEG category B contains certain classes – i.e. quinolones (fluoroquinolones and other quinolones), 3rd- and 4th-generation cephalosporins and polymyxins – where it is advised that the potential risk to public health resulting from veterinary use needs to be mitigated by specific restrictions. Figure 12 shows the amounts sold, in kg of the antibacterials belonging to AMEG category B compared to the total sales of antibacterial VMPs, stratified by animal categories. In total, 0.3% of the total sales of antibacterial VMPs in 2024 belonged to the AMEG category B. For companion animals the VMPs represent 3rd generation cephalosporins and fluoroquinolones, for farmed fish other quinolones and for food-producing animals fluoroquinolones. Of note is that apart from two VMPs for local ear treatment, other pharmaceutical forms of VMPs containing polymyxins are not marketed in Norway.

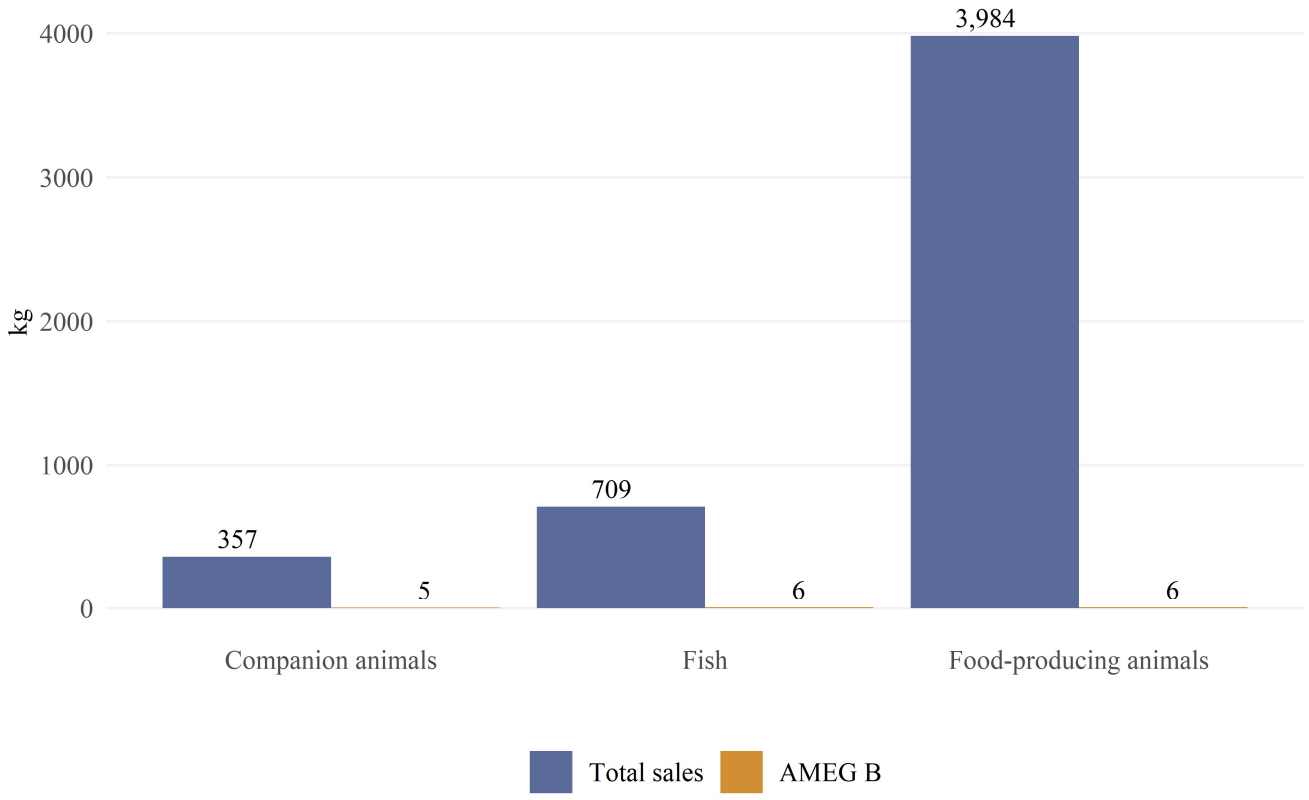

FIGURE 12. Total sales and sales of antibacterial veterinary medicinal products (VMPs) in Norway in 2024, for which the Antimicrobial Advice Ad Hoc Expert Group (AMEG) of the European Medicines Agency advises to restrict the use (AMEG category B), stratified by animal category (1, 2). For companion animals the VMPs represent 3rd generation cephalosporins and fluoroquinolones, for farmed fish other quinolones, and for food-producing animals fluoroquinolones. Of note, VMPs for topical treatment are not included.

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National Strategy against Antibiotic Resistance

1996-2001: Norwegian livestock industry

In 1996, the Norwegian livestock industry set a target for reduction of the sales of antibacterial VMPs, in weight of active substance, by 25% within five years with 1995 as the reference year. This target was reached already after two-three years. After five years the observed reduction was 40% and up to 2012 the sales for this animal category remained approximately on the same level – i.e. on average the sales for the period 1999 to 2012 were 39% lower than in 1995 (Figure 2). For more details on evaluation of reduction targets see the NORM-VET 2023 report.

2015-2020: National Strategy

In 2015, a National Strategy against Antibiotic Resistance (2015-2020) was agreed upon (1). The strategy was later prolonged until 2023. Among others, this strategy set four targets for reduction of sales of antibacterials in terrestrial animals and farmed fish:

1. To reduce the sales of antibacterials in food-producing terrestrial animals by 10% by 2020, with 2013 as reference year.
2. In 2020, sales of antibacterials in farmed fish should be at the same level or lower than the average for the period 2004-2014.
3. To reduce the sales of antibacterials in companion animals by 30% by 2020, with 2013 as reference year.
4. Phasing out use of narasin and other coccidiostat feed additives with antibacterial properties in the broiler production without
   a. compromising animal health or animal welfare
   b. increasing the therapeutic use of antibacterials

To achieve Target 1 of the national strategy, Animalia, whose role is to provide Norwegian farmers with knowledge and expertise, initiated and coordinated the development and implementation of a joint action plan against antibiotic resistance (2). The suggested key measures to reduce the use of antibacterials in the livestock industry were prevention of diseases, biosecurity, as well as optimising the use of antibiotics. This action plan covered cattle, pigs, sheep, goats and poultry. The detailed methodology used to analyse to what degree the targets were achieved during the period covered by the action plan is described in the NORM-VET 2023 report.

For Target 1 the reduction in sales of VMPs for cattle, pigs, sheep, and poultry was estimated as these accounted for almost all meat production in Norway during the period covered by the action plan (approximately 99% of the production in 2023; https://www.ssb.no/slakt).

The estimated sales of antibacterial VMPs for these species was reduced from 2013 to 2023 with 31% and 27% (see Appendix 1 for methods used for estimation/stratification of sales data), when measured in kg and in mg/kg animal biomass (kg animal biomass is calculated using ESVAC-methodology), respectively. Sales of antibacterial VMPs for farmed fish were below the maximum level set for all years 2015-2023. For companion animals the reduction target was reached by 2017, and sales kept below the target for all years except 2021 and 2022 (slightly above the target). Narasin was gradually phased out as coccidiostat feed additive by the Norwegian broiler industry during the period from February 2015 to June 2016 (see NORM-VET 2019, Table 5). This happened without increasing the sales of antibacterials for therapeutic use.

2024-2033: National One Health Strategy

In 2024, a new National One Health Strategy Against Antimicrobial Resistance 2024-2033 was agreed upon (3). The strategy did not include any targets for reduction of antibacterial use for animals in Norway. The need to ensure restrictive and prudent use is however highlighted. Moreover, surveillance of use of antimicrobials should be improved as such data is the key basis for advice and management measures.

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European Sales and Use of Antimicrobials for veterinary medicine (ESUAvet)

From 2010 to 2022, the European Medicines Agency (EMA) collected sales data of antimicrobial veterinary medicinal products (VMPs) from EU countries, Iceland, Norway and Switzerland through the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project. While it was voluntary to participate in the ESVAC project, a new EU regulation on veterinary medicinal products (Regulation (EU) 2019/6, Article 57) made it mandatory for EU countries, Iceland and Norway to submit sales data of antimicrobial VMPs but also use data of antimicrobials per animals species to EMA. The first report from the European Sales and Use of Antimicrobials for veterinary medicine (ESUAvet report) was published in March 2025 and covers 2023 data.

The antimicrobials for which it is mandatory to report sales and use of are listed in Annex 1 and 3 of Regulation (EU) 2021/578, respectively. Annexes 2 and 4 of the same regulation list antimicrobials for which it is voluntary to submit sales and use data, respectively. Substances to be included are defined by ATC/ATCvet codes. A brief description of the antimicrobials included in the mandatory and voluntary scope is as follows:

- All the antimicrobial substances in the medicinal products for sales and use data that fall under the mandatory scope have antibiotic activity.
- The antimicrobial substances in the medicinal products for sales and use data that fall under the voluntary scope include antivirals, antifungals, topical antibacterials, antiprotozoals and antiinfectives.

Food-producing animals: ESUAvet sales (mandatory scope) versus ESVAC sales

The ESUAvet sales mandatory scope incudes three additional ATCvet codes compared to ESVAC. However, sales of VMPs with these ATCvet codes were not reported for 2023 as no such products were marketed. This implies that the ESUAvet mandatory data cover the same ATCvet codes as for ESVAC during the period 2010-2022. However, because of certain modifications in the methodology regarding the calculation of weight of active substance sold as well as some minor changes in the stratification of animal species (i.e. inclusion in the category food-producing animals), comparison of the overall sales and sales by country (numerator) between ESUAvet and ESVAC sales for food producing animals should be done with care.

In 2023, EMA published a guideline describing a methodology for calculating animal biomass denominators for presenting population-adjusted sales and use data in the ESUAvet reports. The animal biomass for food-producing animals includes more species and categories, as well as different and typically higher weights, than those used for ESVAC for calculating the denominator – i.e. the Population Correction Unit (PCU). The ESUAvet biomass of food-producing animals, mg/kg animal biomass, is considerably higher than the ESVAC PCU. Consequently, the values of the indicator for sales reporting sales in the ESUAvet reports are not comparable to the indicator values in ESVAC reports (mg/PCU).

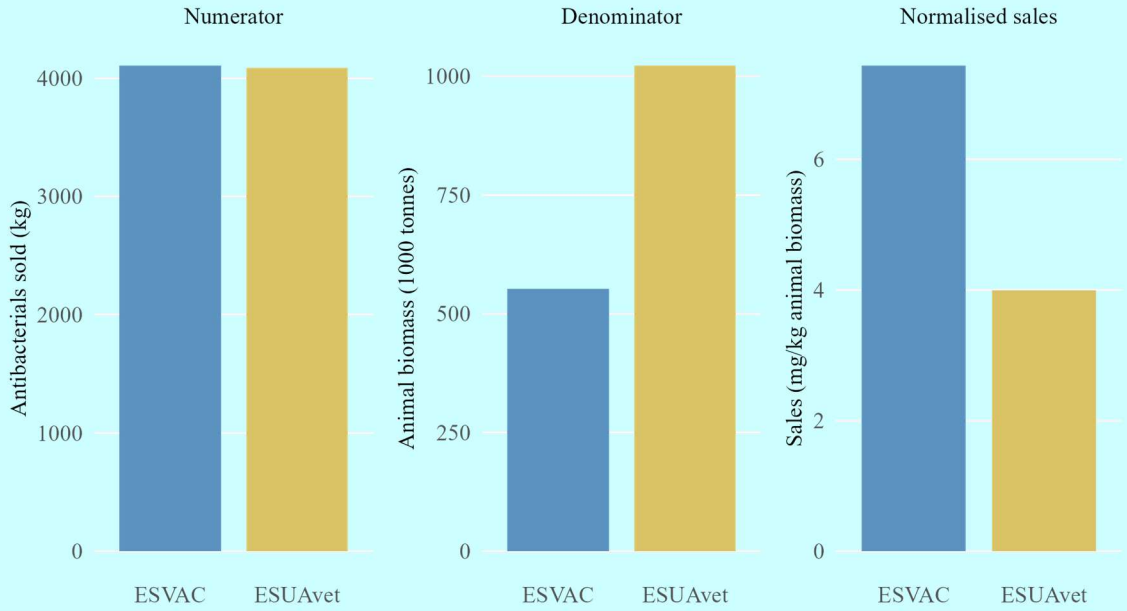

FIGURE 13. Sales of antibacterial veterinary medicinal products for food-producing animal species in Norway in 2023, reported by use of the ESVAC and ESUAvet material and methodology, respectively; sales numerators (kg active substance), denominators (biomass animals at risk of being treated) and indicators (sales normalised by the weight of the animal biomass at risk of being treated).

Figure 13 shows how the sales data for Norway for 2023 reported by use of the ESVAC and the ESUAvet material and methodology, respectively, are impacted for 2023. Compared to ESVAC the ESUAvet sales, in kg active substance, is almost identical – i.e. only minimally affected by the change of the stratification of animal species included, while the denominator (animal biomass) is almost doubled and the value of the indicator (mg/kg animal biomass) for ESUAvet therefore only about half of the ESVAC value. The ESUAvet report will also present sales data with the ESVAC indicator mg/PCU until for the year 2030 due to a target set for the 27 EU countries to reduce the sales of antimicrobials by 50% with 2018 data as the reference year.

Non-food-producing animals: ESUAvet Sales versus ESVAC sales

The ESUAvet report also introduces a biomass denominator for non-food-producing animals, enabling the reporting of normalised sales also for other animals kept or bred (dogs, cats and fur animals). The main indicator for population-adjusted ESUAvet sales for non-food-producing animals under the mandatory scope is mg/kg animal biomass.

Use data

Data on use were collected for four main food-producing animal species for 2023: cattle, pigs, chickens and turkeys. Veterinarians played a key role in gathering data, as they were selected as the sole data providers by 16 reporting countries. The remaining 13 reporting countries used other data providers in addition to veterinarians, including pharmacies, feed mills, farmers or breeders, and retailers. As this is the first time that data on use have been collected across the EU, many countries are still in the process of setting up or improving their data collection systems for antimicrobial use. For most EU/EEA countries the use data for 2023 were therefore not complete and accurate and thus quantitative information by country was not included in the ESUAvet report.

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Use of antifungals across multiple sectors in Norway

Azoles are widely utilised across multiple sectors, including human and veterinary medicine, food production, horticulture, and the wood industry. A recent report has recommended heightened awareness and increased attention to azole usage due to its broad application and potential implications for resistance development (1). The emergence of antifungal resistance - specifically, azole resistance in *Aspergillus fumigatus* and terbinafine resistance in *Trichophyton indotineae* - has recently attracted significant global concern as a serious medical challenge. The use of antifungals is believed to be an important driver of antifungal resistance development: the use of triazoles in agriculture is associated to azole resistance in *A. fumigatus* and over-the-counter use of terbinafine for the development of terbinafine resistance in *T. indotineae*. Consequently, understanding the overall use of antifungals in both humans, animals and in agriculture is essential. This report therefore examines antifungal consumption in the different sectors in Norway since the turn of the millennium.

We collected data on the volume of all sales of antifungals in three sectors: humans, animals and agriculture with a special focus on the azoles and terbinafine. Data were collected from the Norwegian drug wholesales statistics database (see appendix 2). This database contains information on total sales of antifungals for medical purposes for humans and animals, both prescription-only and over-the-counter use. All antifungals were included, both for topical and systemic use. The weights (in kilograms) of active ingredient were calculated. In addition, we have collected sales data (weight in kg) from the Norwegian Food Safety Authority on antifungals sold for use in the agriculture sector in the same period (2).

In 2024, a total of 109 tonnes of antifungals were sold. Of this amount, 1.6 tonnes (1.5%) were used in human medicine, while 0.7 tonnes were utilised in the veterinary sector, including aquaculture. Of the total antifungal use in 2024, 16 tonnes consisted of azoles while terbinafine accounted for 0.76 tonnes of the total. The majority of azoles are used in agriculture. In 2024, only 4% of the total azole volume was used in human medicine and 0.1% were for veterinary applications. Since 2018-2019 the use of azoles has increased in humans and animals, whereas usage in agriculture appears to decrease 2022-2024 (Figures 14-15). The azoles accounted for almost half (46%) of the total human weight of antifungals (as measured in kilograms). Terbinafine is almost only used in humans and represented 47% of total human antifungal weight (Figure 16). Among antifungal products intended for human use, dermatological preparations represented 32% of the total by weight (measured in kilograms). In contrast, for veterinary use (excluding fish), dermatological preparations accounted for 59% of the total weight.

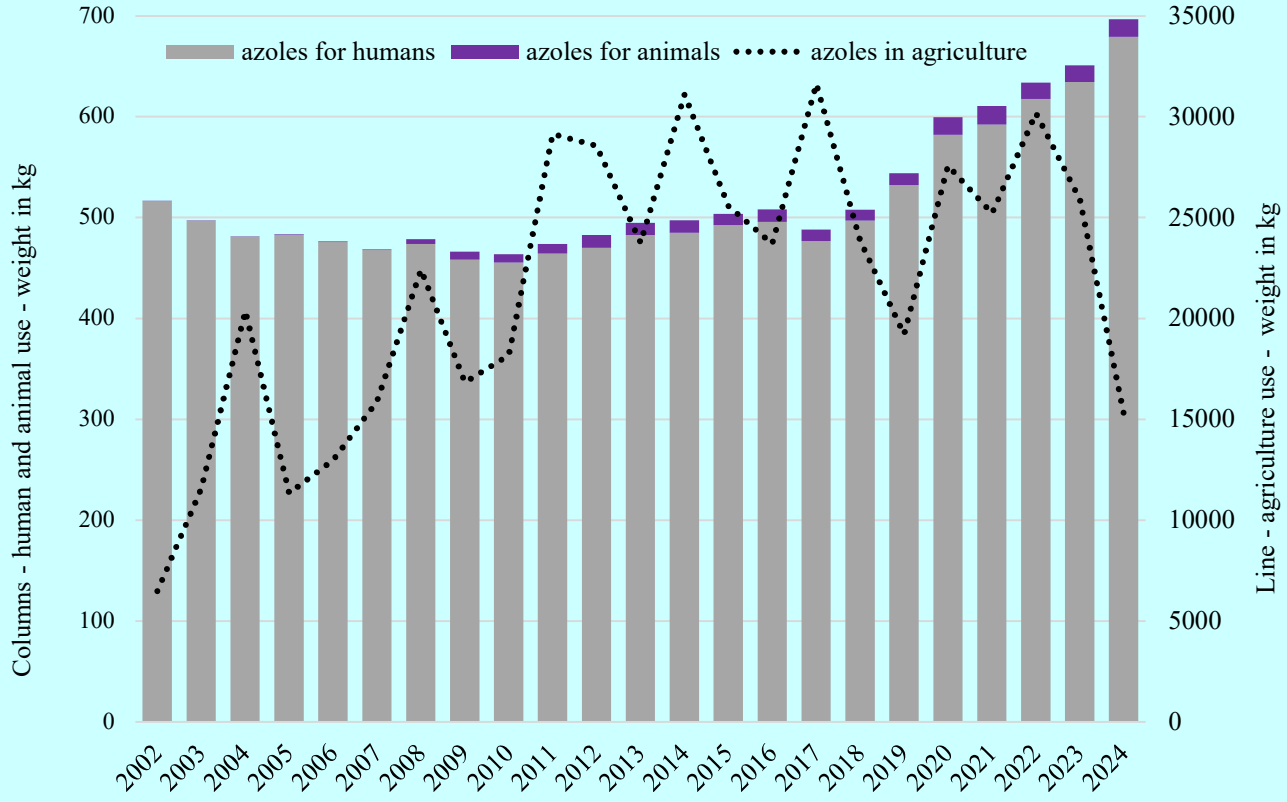

FIGURE 14. Total sales of azoles in Norway, as measured in weight (kg) of active ingredient per year, 2002-2024. Dotted line shows azole fungicides sold in agriculture for crop protection and columns show azole fungicides for medical use in the human and veterinary fields.

The azoles used in human and veterinary medicine differ from those applied in agriculture. In total, nine azoles have been utilised in humans, with ketoconazole and clotrimazole being the most used. For veterinary purposes six azoles have been sold, with miconazole as the predominant agent (Figure 15). Enilconazole is exclusively used in animals, whereas isavuconazole, voriconazole, econazole and fluconazole are only used in human medicine.

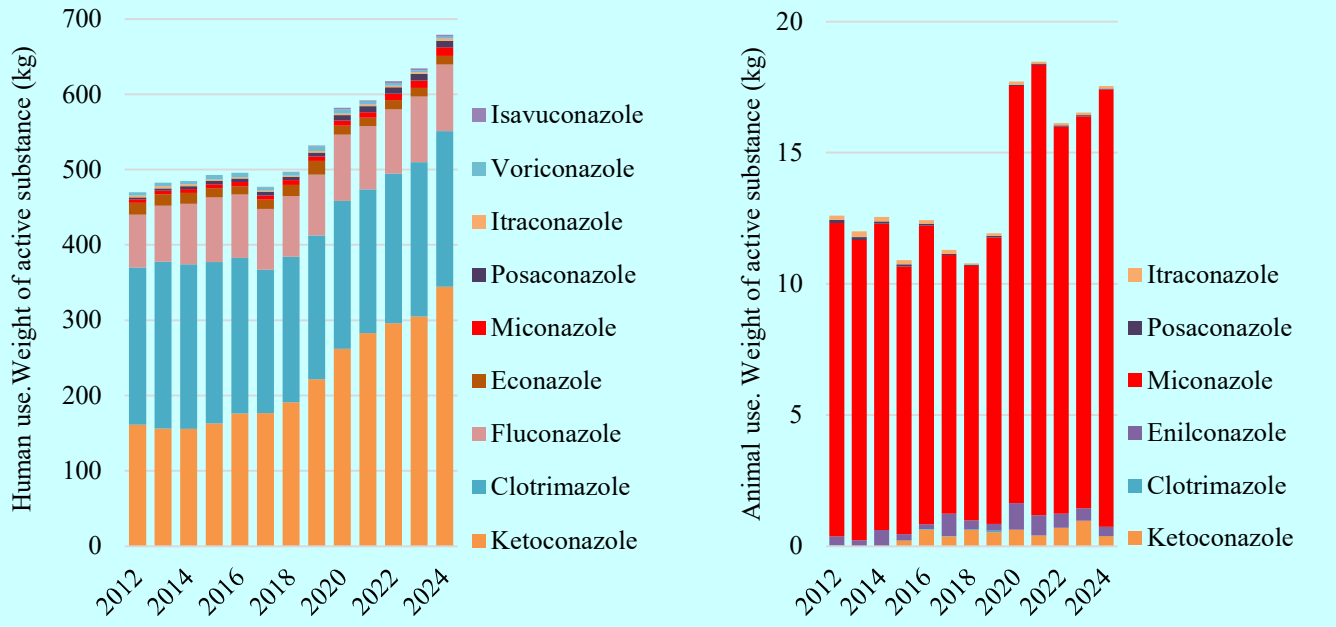

FIGURE 15. Total sales of azoles used in human and veterinary medicine, measured as kilograms of active ingredient, 2012-2024.

Terbinafine is not used in agriculture and the increased use is driven by increased prescribing of oral forms for humans. Sales of topical terbinafine are low and have shown a stable pattern over years, Figure 16. For animals, terbinafine is available in combination with corticosteroids as eardrops, but there is very little use, and animal use represents less than 0.02% of total annual weight.

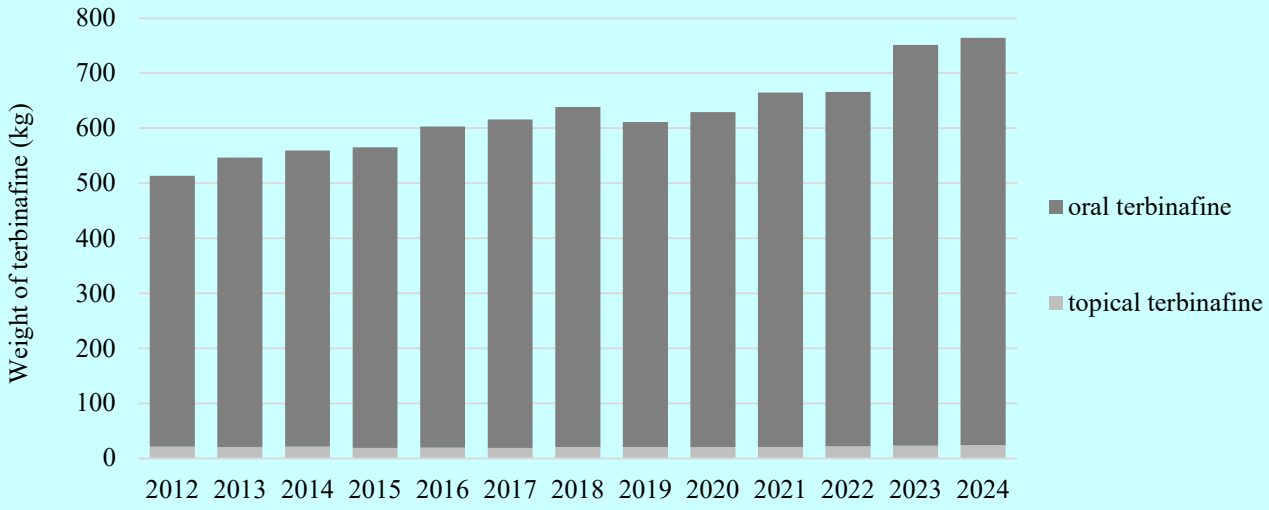

FIGURE 16. Total sales of terbinafine used in human and veterinary medicine, measured as kilograms of active ingredient, 2012-2024.

Conclusion

This short report highlights the extensive use of azole antifungals across human, veterinary, and agricultural sectors in Norway from 2002-2024. While far more of the azole usage occurs in agriculture (tonnes vs. kilograms), recent years have seen a relative increase in human and veterinary consumption, alongside a decline in agricultural use. For terbinafine, the situation is different, and it is probably only in humans that consumption needs to be followed further. Given the established link between azole application - particularly in agriculture - and the emergence of antifungal resistance in clinically important pathogens such as *Aspergillus fumigatus*, these trends warrant close monitoring. Continued collaboration and data sharing between health, veterinary, and agricultural authorities will be essential for informed policymaking.

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USAGE IN HUMANS

Hege Salvesen Blix, Marion Neteland, Eli Leirdal Hoem, Sigurd Høye, Live Storehagen Dansie, Ragnhild Raastad

Overall antibiotic sales

In 2024, the total sales of antibacterials for systemic use in humans (J01, excl. methenamine) remained relatively unchanged compared to 2023; 13.1 DDD/1,000 inhabitants/ day (Table 4, Figure 17). Since 2012, there has been a stable decrease in the use of antibacterials. A large drop (13%) was seen from 2019-2020 due to the Covid-19 pandemic. During this period, there was a significant reduction in the use of systemic antibiotics, mainly due to reduced use of antibiotics indicated for respiratory tract infections (RTI-AB), Figure 18. During the Covid-19 pandemic, the societal lockdown, higher threshold for consulting general practitioners, combined with enhanced infection control contributed to a lower incidence of infections treated within the healthcare system. Especially respiratory tract infections were sparsely reported during the Covid-19 pandemic. This is now normalised.

In 2024, the increased use of tetracyclines and macrolides can be explained by a *Mycoplasma pneumoniae* epidemic in addition to an ongoing *Bordetella pertussis* epidemic. In 2012, a *Mycoplasma pneumoniae* epidemic led to a very high prescription rate of macrolides and tetracyclines. In 2024 a similar number of positive cases of *Mycoplasma pneumoniae* as compared to 2012 was reported but the overall consumption in 2024 (J01, excl. methenamine) was much lower; 22% lower than in 2012 (Figure 17). This suggests improved adherence to treatment guidelines in 2024 compared to 2012.

Recent international and national shortage situations have caused fluctuations in sales from wholesalers. The main fluctuations in 2022 and 2023 were caused by shortage of penicillins and erythromycin. During shortage periods, generics were made available, and the shortage situations do not seem to have impacted the antibiotic consumption patterns significantly.

During the last decade, significant progress has been made in reducing the overall volume of use and increasing the use of guidelines-recommended antibiotics. However, there is still room for improvement, e.g. in adherence to guidelines; by choosing narrow-spectrum and targeted antibiotics and optimising treatment duration. These efforts could further reduce consumption rates and promote a more favourable narrow-spectrum profile. Still, more research is needed to explore patient related risk factors, especially in primary care. Questions like “How do polypharmacy, multi-morbidity, age-related and socioeconomic factors influence the need for antibiotics?” should be elucidated. Furthermore, the reasons for non-compliance to guidelines should be explored. Identifying which patients require antibiotics and which do not, will enable development of targeted interventions towards more appropriate prescribing practices.

In Norway, antibiotics are prescription-only drugs. Overall antibiotic consumption includes all sales of antibiotics to humans in Norway across primary care, hospitals and long-term care facilities. Approximately 85% of antibacterial use in humans occurs outside healthcare institutions. In 2024, hospitals accounted for 7.3% of total DDDs of systemic antibiotics (ATC group J01), while long-term care facilities contributed around 6-7%.

In recent years, decreased sales are observed for many of the main antibiotic subgroups and especially the decreased use of fluoroquinolones should be mentioned – as this is a group of resistance driving antibiotics where environmental contamination has been a concern (Table 4 and Figure 17).

In Norway, narrow-spectrum penicillins are first-line treatment when antibiotics are warranted for respiratory tract infections. Over years the proportion of narrow-spectrum penicillins (J01CE) of the total antibiotic sales (J01, excl. methenamine) has remained relatively stable at around 27%, with a small drop during the pandemic. From 2023 to 2024, the proportion decreased from 29% to 25% due to increased use of tetracyclines and macrolides, driven by outbreaks of *Mycoplasma pneumoniae* and *Bordetella pertussis*.

TABLE 4. Human usage of antibacterial agents in Norway 2012, 2014, 2016, 2018, 2020, 2022 and 2024 by ATC groups. The usage is presented as DDD (Defined Daily Doses)/1,000 inhabitants/day and in % change 2023-2024. Data from the Norwegian drug wholesales statistics database. Methodology for collection of data on human usage of antimicrobial agents is described in Appendix 2.

		Year							Change (%)
ATC	Groups of substances	2012	2014	2016	2018	2020	2022	2024	2023-2024
J01A	Tetracyclines	3.87	3.46	3.16	2.86	2.65	2.82	3.41	+17
J01B	Amphenicols	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	-
J01CA	Penicillins with extended spectrum	2.79	2.90	2.62	2.46	2.22	2.35	2.31	-4
J01CE	Beta-lactamase sensitive penicillins	4.31	3.88	3.73	3.43	2.77	3.50	3.31	-12
J01CF	Beta-lactamase resistant penicillins	0.90	0.91	0.90	0.90	0.95	1.04	1.10	+3
J01CR	Combination of penicillins, incl. beta-lactamase inhibitors	0.04	0.07	0.10	0.08	0.11	0.15	0.17	+8
J01D	Cephalosporins, monobactams, carbapenems	0.53	0.46	0.42	0.39	0.37	0.37	0.34	-3
J01E	Sulfonamides and trimethoprim	0.87	0.88	0.85	0.88	0.90	0.92	0.92	-
J01F	Macrolides, lincosamides and streptogramins	2.26	1.68	1.33	1.05	0.80	0.75	0.81	+15
J01G	Aminoglycosides	0.08	0.08	0.08	0.09	0.10	0.10	0.09	+1
J01M	Quinolones	0.74	0.67	0.53	0.42	0.30	0.29	0.24	-15
J01X*	Other antibacterials	0.47	0.43	0.38	0.32	0.34	0.37	0.40	+4
J01	**Total excluding methenamine**	**16.9**	**15.4**	**14.1**	**12.7**	**11.5**	**12.7**	**13.1**	**-**
J01XX05	Methenamine	3.57	3.86	4.09	4.08	3.85	3.96	4.21	+3
J01	**Total all antimicrobial agents**	**20.4**	**19.3**	**18.2**	**16.9**	**15.3**	**16.6**	**17.3**	**+1**

*J01X incl. glycopeptides, colistin, fusidic acid, metronidazole (i.v.), nitrofurantoin, fosfomycin, linezolid, daptomycin and tedizolid. Methenamine is excluded.

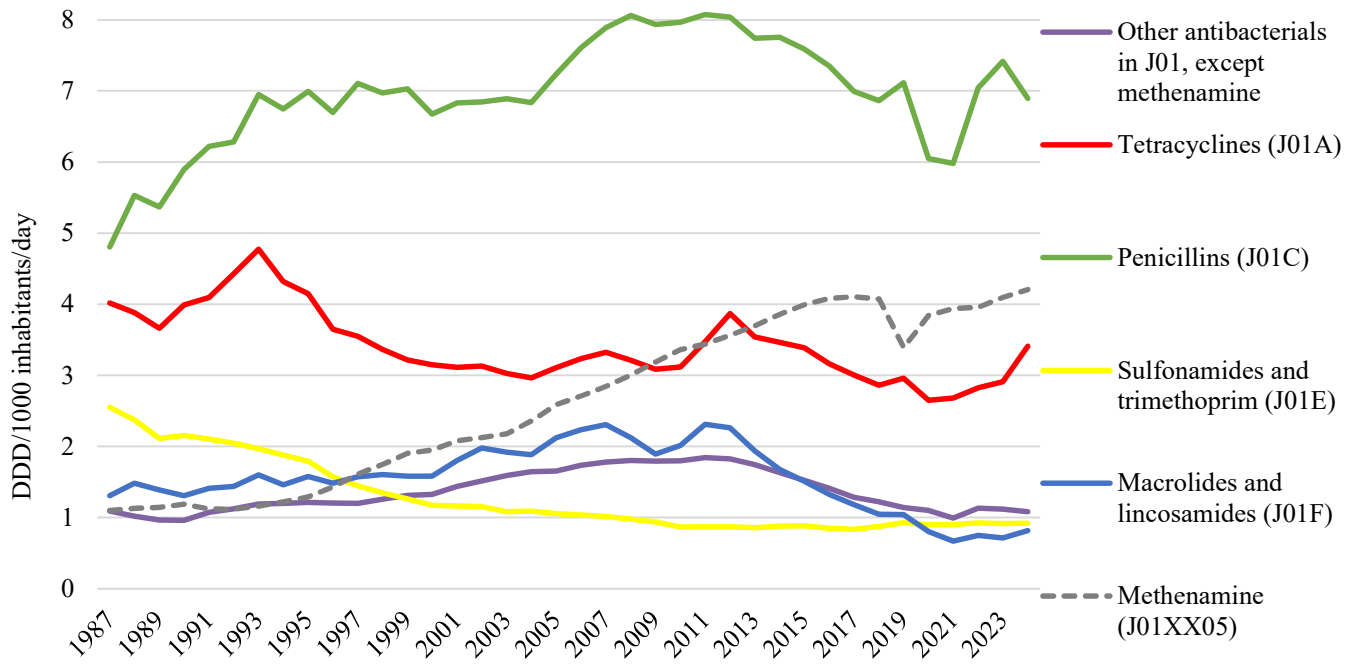

FIGURE 17. Sales of penicillins (J01C), tetracyclines (J01A), macrolides, lincosamides and streptogramines (J01F), sulfonamides and trimethoprim (J01E), methenamine and other antibacterials in Norway 1987-2024. Other types of antibacterials include all other antibacterials in ATC group J01, except methenamine (J01XX05). Data from the Norwegian drug wholesales statistics database.

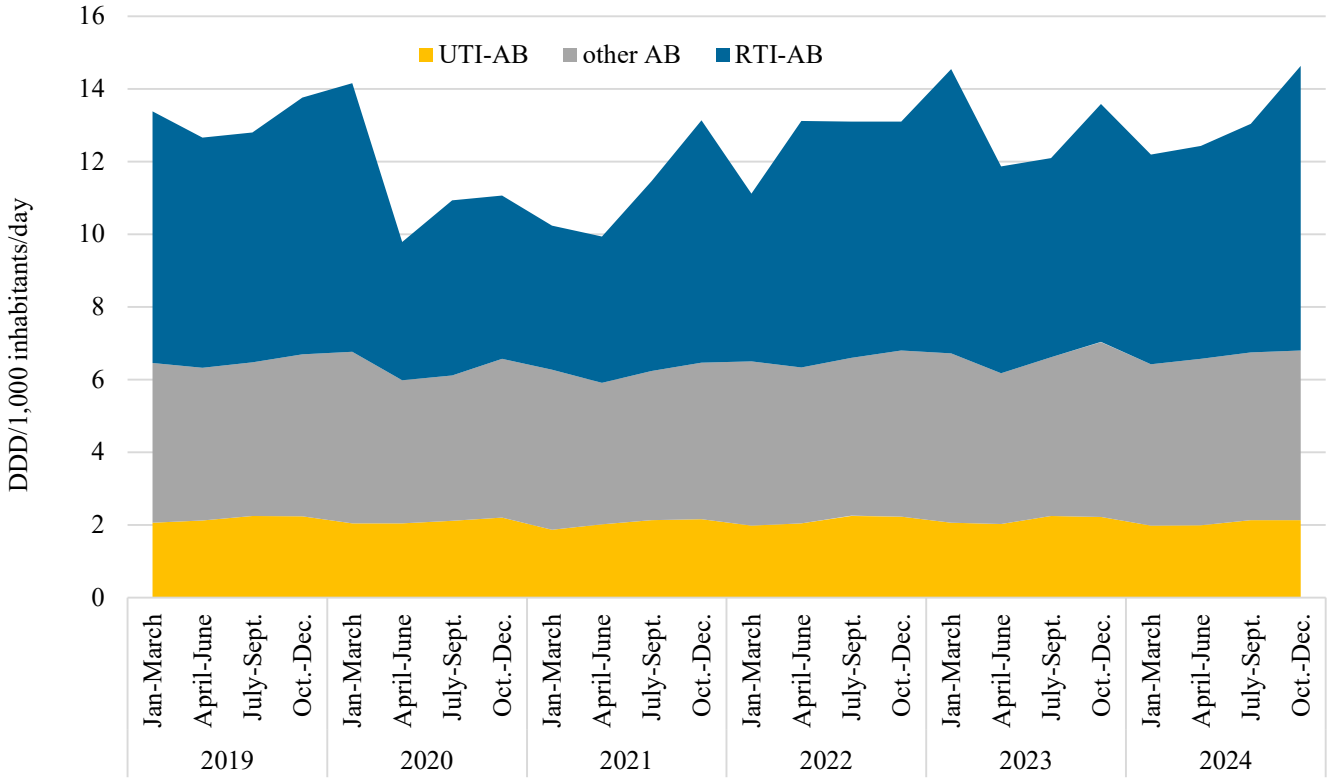

FIGURE 18. Quarterly sales of antibiotics in 2019-2024 as measured in DDD/1,000 inhabitants/day. Sales of antibiotics for respiratory tract infections (RTI-AB) is defined as amoxicillin, phenoxymethylpenicillin, macrolides and doxycycline, whereas sales of antibiotics for urinary tract infections (UTI-AB) is defined as pivmecillinam, trimethoprim and nitrofurantoin. Other antibiotics (AB) is defined as all other antibiotics in ATC group J01, excl. methenamine. Data from the Norwegian drug wholesales statistics database.

In 2024, the three most used antibacterial groups in Norway were beta-lactamase sensitive penicillins (J01CE), tetracyclines (J01A), and penicillins with extended spectrum (J01CA) (Table 4). Methenamine, a urinary prophylactic agent, generated the highest number of DDDs of all antibiotics used in Norway, mainly due to its continuous daily use. During a major shortage in the spring of 2019, methenamine use declined significantly. In 2024 the use was at the same level as in 2016 (Figure 17, Table 4), accounting for 24% of total antibacterial use (Figure 19). Among the tetracyclines (J01A), doxycycline is the most frequently used, followed by lymecycline, which is primarily used for acne treatment (Table 5).

In 2024, the penicillins (ATC group J01C) accounted for 40% of the total antibacterial use in Norway (Figure 19). Over the years there has been a shift towards increased use of broad-spectrum penicillins. In 2024, beta-lactamase sensitive penicillins accounted for 48% of total penicillin use, measured in DDDs. Penicillins with extended spectrum (J01CA) represent 33% of the J01C group. This is mainly due to the increased use of amoxicillin and pivmecillinam. Beta-lactamase resistant penicillins (J01CF) now represent 16% of total J01C use, twice the proportion recorded 20 years ago. Use of penicillins with beta-lactamase inhibitors (J01CR) has also increased in recent years (Table 4). Since the approval of oral co-amoxiclav in Norway in May 2017, its use has increased significantly, although it is only recommended for a few specific indications in the Norwegian primary care guidelines. Pivmecillinam is the most commonly used antibiotic for urinary tract infections, but pivmecillinam, trimethoprim and nitrofurantoin are all equal recommendations for acute cystitis in primary care. Trimethoprim has shown a decreasing trend over many years, possibly because GPs are aware of the relatively high resistance level for trimethoprim and hence choose other options. Total use of the sulfonamides and trimethoprim subgroup has increased due to increasing use of the combination product co-trimoxazole (Figures 17 and 19, Table 5).

Macrolide use has declined significantly since 2012, (Tables 4-5, Figures 17 and 19). The total use of the group J01F, macrolides, lincosamides and streptogramins, has followed a wavy pattern over the years. These shifts in use could partly be explained by the recurrent epidemics of *M. pneumoniae* in Norway, which tend to occur every four to six years, with the most recent outbreak in 2023-2024. Furthermore, until 2014, azithromycin and doxycycline were both recommended for genital chlamydia infection in the primary care treatment guidelines. Since then, doxycycline has been the only first-line treatment. Reducing macrolide use has been a focus in the primary care part of the former AMR National Action Plan. The use of macrolides has now declined to levels comparable to those observed in the 1970s.

In the latest years, sales of ATC group J01D (cephalosporins, monobactams and carbapenems) have decreased, primarily due to decreased use of 1st and 2nd generation cephalosporins (Tables 4-5, Figure 19). Since 2019, there has also been a slight reduction in the sales of cefotaxime, which may have at least two causes. First, reduction in the use of cefotaxime and other 3rd generation cephalosporins was specifically targeted in the National Action Plan. Secondly, since 2019 the European breakpoint committee EUCAST has recommended 1g x 3 as the standard dose for cefotaxime, whereas the most common dose in Norway has been 2g x 3. The new dosage has gradually been incorporated into guidelines and other recommendations in Norway.

In 2024, quinolones accounted for only 1% of total antibacterial sales in 2024 (Tables 4-5, Figure 19), and their use has steadily declined since 2012. This decrease is largely due to increased awareness of the resistance-driving potential of quinolones, combined with increasing warning information, such as "dear doctor" letters, on severe adverse effects associated with fluoroquinolones. In 2024, ciprofloxacin was the predominant substance within this group, accounting for 92% of the quinolones.

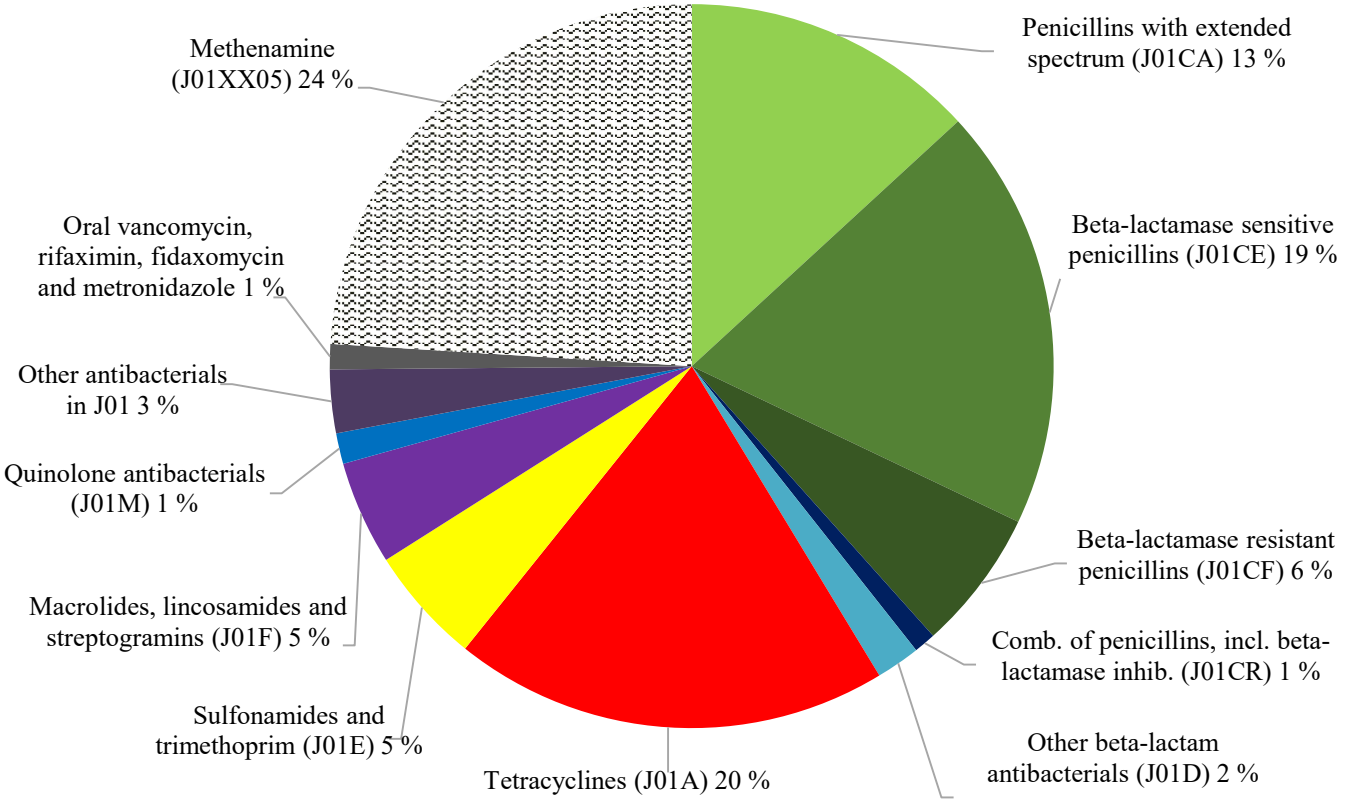

FIGURE 19. Relative amounts of antibacterial agents for systemic use in 2024 in Defined Daily Doses (DDD) (total sales in the country). Data from the Norwegian drug wholesales statistics database.

TABLE 5. Total human usage of single antibacterial agents for systemic use in Norway. Sales for overall use are given in DDD/1,000 inhabitants/day. Data from the Norwegian drug wholesales statistics database. ATC-version 2025 is used. The methodology for collection of data on human usage of antibacterial agents is described in Appendix 2.

ATC group	ATC code	Substance	2012	2014	2016	2018	2020	2022	2024
J01A - Tetracyclines	J01A A02	Doxycycline	2.36	1.99	1.82	1.60	1.38	1.51	1.96
	J01A A04	Lymecycline	0.90	0.96	0.94	0.93	1.08	1.12	1.26
	J01A A06*	Oxytetracycline		<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
	J01A A07	Tetracycline	0.62	0.50	0.40	0.32	0.19	0.20	0.18
	J01A A08*	Minocycline	0.006	0.003	0.002	0.001	0.001	0.001	0.001
	J01A A12	Tigecycline	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
J01B - Amphenicols	J01B A01*	Chloramphenicol	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
J01CA - Penicillins with extended spectrum	J01C A01	Ampicillin	0.03	0.04	0.04	0.05	0.05	0.05	0.06
	J01C A04	Amoxicillin	0.97	0.97	0.88	0.84	0.65	0.74	0.76
	J01C A08	Pivmecillinam	1.78	1.87	1.69	1.57	1.52	1.56	1.49
	J01C A11	Mecillinam	0.008	0.008	0.005	0.002	0.003		
J01CE - Beta-lactamase sensitive penicillins	J01C E01	Benzylpenicillin	0.24	0.24	0.23	0.24	0.23	0.18	0.17
	J01C E02	Phenoxymethyl-penicillin	4.07	3.64	3.50	3.18	2.53	3.32	3.14
	J01C E08*	Benzathine benzylpenicillin	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
J01CF - Beta-lactamase resistant penicillins	J01C F01	Dicloxacillin	0.76	0.72	0.74	0.74	0.78	0.84	0.88
	J01C F02	Cloxacillin	0.14	0.19	0.17	0.16	0.16	0.19	0.22
	J01C F05*	Flucloxacillin	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
J01CR - Combination of penicillins, incl. beta-lactamase inhibitors	J01C R01*	Ampicillin and enzyme inhibitor							<0.001
	J01C R02	Amoxicillin and enzyme inhibitor	0.00	0.01	0.01	0.03	0.05	0.09	0.10
	J01C R05	Piperacillin and enzyme inhibitor	0.03	0.07	0.09	0.05	0.06	0.07	0.07
J01DB – 1st generation cephalosporins	J01D B01	Cefalexin	0.18	0.14	0.10	0.09	0.07	0.06	0.06
	J01D B03	Cefalotin	0.08	0.09	0.09	0.07	0.02	0.02	0.02
	J01D B04	Cefazolin				0.03	0.08	0.09	0.09
J01DC – 2nd generation cephalosporins	J01D C02	Cefuroxime	0.08	0.06	0.04	0.03	0.03	0.02	0.01
J01DD – 3rd generation cephalosporins	J01D D01	Cefotaxime	0.12	0.12	0.12	0.12	0.11	0.13	0.12
	J01D D02	Ceftazidime	0.01	0.01	0.01	0.008	0.006	0.004	0.003
	J01D D04	Ceftriaxone	0.03	0.02	0.02	0.02	0.03	0.02	0.02
	J01D D08*	Cefixime			<0.001	<0.001	<0.001	<0.001	
	J01D D52	Ceftazidime and avibactam				<0.001	<0.001	<0.001	<0.001
J01DF - Monobactams	J01D F01	Aztreonam	<0.001	0.001	0.001	<0.001	<0.001	0.001	0.003
J01DH - Carbapenems	J01D H02	Meropenem	0.03	0.03	0.03	0.02	0.03	0.03	0.02
	J01D H03	Ertapenem	0.002	0.002	0.002	0.002	0.002	0.002	0.002
	J01D H51	Imipenem and enzyme inhibitor	0.002	0.002	0.002	0.002	0.002	0.001	<0.001
	J01D H52*	Meropenem and vaborbactam						<0.001	<0.001
	J01D H56	Imipenem, cilastatin and relebactam						<0.001	<0.001

ATC group	ATC code	Substance	2012	2014	2016	2018	2020	2022	2024
J01DI – Other cephalo-sporins and penems	J01D I02	Ceftaroline fosamil		<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
	J01D I04	Cefiderocol						<0.001	<0.001
	J01DI54	Ceftolozane and enzyme inhibitor			<0.001	<0.001	0.001	<0.001	<0.001
J01E - Sulfonamides and trimethoprim	J01E A01	Trimethoprim	0.51	0.46	0.38	0.34	0.33	0.29	0.26
	J01E B02*	Sulfamethizole					<0.001	<0.001	
	J01E C02*	Sulfadiazine			0.001	<0.001	<0.001	<0.001	<0.001
	J01E E01	Sulfamethoxazole and trimethoprim	0.36	0.40	0.44	0.53	0.57	0.63	0.66
J01F - Macrolides, lincosamides and streptogramins	J01F A01	Erythromycin	1.06	0.75	0.60	0.44	0.29	0.21	0.25
	J01F A02	Spiramycin	0.01	0.005	0.003	0.002	0.002	0.001	<0.001
	J01F A06*	Roxithromycin		<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
	J01F A09	Clarithromycin	0.39	0.23	0.14	0.11	0.09	0.09	0.12
	J01F A10	Azithromycin	0.48	0.35	0.30	0.24	0.19	0.21	0.23
	J01FS15	Telithromycin	<0.001	<0.001	<0.001				
	J01F F01	Clindamycin	0.33	0.34	0.28	0.25	0.23	0.23	0.23
	J01F G01*	Pristinamycin							<0.001
J01G - Aminoglycosides	J01GA01*	Streptomycin	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
	J01G B01	Tobramycin	0.03	0.02	0.02	0.01	0.01	0.01	0.01
	J01G B03	Gentamicin	0.05	0.05	0.06	0.08	0.09	0.09	0.08
	J01G B06	Amikacin	0.001	0.001	0.001	0.001	0.001	<0.001	<0.001
J01M - Quinolones	J01M A01*	Ofloxacin	0.02	0.01	0.01	0.01	0.01	0.004	<0.001
	J01M A02	Ciprofloxacin	0.71	0.64	0.51	0.39	0.28	0.27	0.22
	J01MA12	Levofloxacin	0.002	0.002	0.003	0.004	0.005	0.006	0.008
	J01MA14*	Moxifloxacin	0.004	0.007	0.009	0.011	0.009	0.01	0.01
J01X - Other antibacterials	J01X A01	Vancomycin	0.01	0.02	0.02	0.02	0.02	0.02	0.02
	J01X A02*	Teicoplanin	0.001	<0.001	<0.001	<0.001		<0.001	<0.001
	J01X A04	Dalbavancin							<0.001
	J01X B01	Colistin	0.004	0.005	0.006	0.006	0.008	0.01	0.01
	J01X C01	Fusidic acid	0.005	0.004	0.003	0.003	<0.001	<0.001	<0.001
	J01X D01	Metronidazole	0.07	0.05	0.03	0.04	0.04	0.04	0.04
	J01X E01	Nitrofurantoin	0.37	0.35	0.31	0.25	0.26	0.29	0.32
	J01XX01	Fosfomycin	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
	J01X X05	Methenamine	3.57	3.86	4.09	4.08	3.85	3.96	4.21
	J01XX08	Linezolid	0.01	0.007	0.010	0.009	0.009	0.009	0.009
	J01XX09	Daptomycin	0.001	<0.001	0.001	0.001	0.001	0.001	0.001
	J01X X11	Tedizolid			<0.001	<0.001	0.001	0.002	0.003
Antibiotics in other ATC groups	A07A A09	Vancomycin	0.002	0.002	0.002	0.002	0.003	0.004	0.005
	A07AA11	Rifaximin	0.00	0.01	0.04	0.08	0.10	0.13	0.14
	A07A A12	Fidaxomicin	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.002
	P01A B01	Metronidazole	0.23	0.24	0.23	0.21	0.21	0.20	0.19

*Drugs not licensed in the Norwegian market in 2024.

Antibiotic use in primary care

Approximately 84% of the total human sales of antibacterials are dispensed as prescriptions from pharmacies, that is - primarily prescribed to persons in ambulatory care, most of whom live at home. These data are derived from the Norwegian Prescribed Drug Registry (NorPD) that includes all dispensed antibacterial prescriptions issued to persons living in Norway. This also covers antibiotics prescribed from hospitals to discharged patients and outpatients, see Appendix 2.

The overall reduction in antibacterial use during the Covid-19 pandemic was mainly driven by decreased use in primary care. In 2024, the use of antibacterials (J01 excl. methenamine) in primary care was 10.8 DDD/1,000 inhabitants/day, equivalent to the level seen in 2017. In primary care in 2024, penicillins (J01C) was the most commonly used antibiotic group, accounting for 39% of total DDDs within ATC group J01. Tetracyclines (J01A) was the second most used group at 21%, and sulfonamides and trimethoprim (J01E) made up 5% of all DDDs in primary care. The six antibiotic substances most often prescribed for outpatients in 2024 were methenamine, phenoxymethylpenicillin, doxycycline, pivmecillinam, lymecycline, and dicloxacillin (Table 6). Together, these six antibiotics accounted for 81% of all DDDs of the antibacterial group J01. Phenoxymethylpenicillin represented 20% of DDDs while methenamine represented 27% of the DDDs.

Antibacterial use in primary care is now slightly higher than during the pandemic but remains close to the level observed in 2019; the year before the Covid-19 pandemic. It is currently uncertain whether the decrease observed between 2012 and 2019 will resume. However, there is strong focus on antimicrobial resistance, both among the general public and healthcare personnel. Since the launch of the Government's Action Plan against AMR in 2016, a large proportion of general practitioners have completed quality improvement courses. Additionally, from 2024, automated feedback reports on individual prescribing practices have been made available to GPs, further supporting efforts to promote appropriate antibiotic prescribing.

The usage of antibacterials varies among the Norwegian regions, Table 6. The ranking is similar in all regions, except for azithromycin being somewhat more prevalent in health regions West and South-East. Lymecycline, used for acne, is now the fifth most used antibiotic in primary care in all regions. Nitrofurantoin has climbed on the list since 2022 at the expense of trimethoprim. In addition to pivmecillinam, these two substances are recommended as first-line treatment for urinary tract infections.

None of the regions have reached the prescription target set in the former National Strategy against Antibiotic Resistance of 250 Rx/1,000 inhabitants/year when excluding methenamine (Figure 20). The North Region has the lowest Rx/1,000 inhabitants/year and the lowest DDD/1,000 inhabitants/day, Figure 20. The South-East Region had the highest proportion of phenoxymethylpenicillin in 2024; 20.4% of all DDDs and the North region had the lowest; 16.6%. Moreover, the North region had the highest proportion of urinary tract antibiotics (pivmecillinam, trimethoprim and nitrofurantoin); 14.2% of all DDDs and South-East had the lowest (11.5%).

Females use more antibiotics than males; in 2024, 24.2% of all females purchased at least one antibiotic prescription (methenamine excluded) compared to 16.8% of males (Figure 21). The prevalence is higher than in 2023 and higher than in 2019 (pre-pandemic year). Young children, young women and the elderly are high users of antibiotics (Figure 21). Between 2012 and 2019, there was a reduced prevalence of use in all age groups. In 2023 and 2024 there has been increased use in children (0-9 and 10-19 years), Figure 22. In the older age-groups the prevalence is decreased compared to 2019. The dramatic reduction during the pandemic in 2020 was mainly due to lower prescribing of antibiotics for respiratory tract infections, Figure 21. The prevalence varies somewhat from one year to another according to the burden of infection. The increase in 2023 and 2024 may be explained by increased reporting of *Bordetella pertussis* and *Mycoplasma pneumoniae* from autumn 2023. The epidemic of *Bordetella pertussis* peaked during 2024 and seems to fade during spring 2025. The age group most often reported was elderly children. The decreased use of phenoxymethylpenicillin in 2024 can be explained by increased use of the other respiratory tract antibiotics being effective towards *Mycoplasma pneumoniae* and *Bordetella pertussis.* The share of phenoxymethylpenicillin decreased in all health regions of Norway, Figure 23. These epidemics can also partly explain the increased use of antibiotics in primary care in 2023 and 2024 compared to 2022.

Among those who are prescribed antibacterials, the elderly population is prescribed more; for those above 75 years; 2.2 prescriptions/user for females and 2.1 prescriptions/user for males are dispensed every year compared to around 1.5 prescriptions/user for younger persons (men and women together), Figure 24. This has been stable over years. The mean number of antibacterial prescriptions delivered from pharmacies was reduced between 2012 and 2019 for men and women and in all age groups. Compared to the prepandemic year 2019 there has been an increase in younger age groups, but a decrease in the group of elderly people, more so for women than men, however, the differences are small, Figure 25. It is difficult to predict the future consumption, but if we want to achieve appropriate use of antibiotics it is important to continuously remind the population and prescribers that antibiotics should only be used when necessary and with caution. The differences according to age and gender groups indicate that interventions should be focused on the vulnerability in different population groups to achieve optimal treatment patterns.

Over the years there are differences in the therapy patterns according to recommendations in guidelines. In Norway, narrow-spectrum antibiotics are first-line antibiotics. Figure 26 shows variation in use of antibiotics (as measured in DDD/1,000 inhabitants/day), recommended as first-line versus not first-line treatment, and the figure indicates a higher prescribing of recommended antibiotics in recent years. This could be caused by increased attention towards AMR as well as increased adherence to guidelines by healthcare workers in the period. Prescriptions (Rx) per 1,000 inhabitants per year (J01, excl. methenamine) are reduced by 24% since 2012 and in 2024 the number was 346 Rx/1,000 inhabitants/year for the general population (Figure 20).

TABLE 6. Human usage of the 15 antibacterial agents for systemic use with the highest volume in ambulatory care in the four health regions in Norway in 2024. Sales are given in DDD/1,000 inhabitants/day. Data from the Norwegian Prescribed Drug Registry (NorPD).

	Health region				Norway
	Mid	North	South-East	West	
Methenamine	4.57	4.15	3.79	3.82	3.93
Phenoxymethylpenicillin	2.88	2.26	3.00	2.96	2.94
Doxycycline	1.64	1.44	1.79	1.76	1.74
Pivmecillinam	1.42	1.30	1.24	1.28	1.29
Lymecycline	1.17	1.08	1.22	1.40	1.24
Dicloxacillin	0.76	0.75	0.80	0.72	0.78
Amoxicillin	0.57	0.53	0.64	0.54	0.60
Sulfamethoxazole and trimethoprim	0.54	0.57	0.51	0.52	0.52
Nitrofurantoin	0.34	0.37	0.25	0.32	0.29
Trimethoprim	0.27	0.27	0.20	0.19	0.21
Azithromycin	0.16	0.15	0.21	0.24	0.20
Erythromycin	0.15	0.10	0.21	0.19	0.19
Tetracycline	0.17	0.15	0.19	0.17	0.18
Ciprofloxacin	0.17	0.17	0.18	0.16	0.17
Clindamycin	0.15	0.16	0.18	0.16	0.17

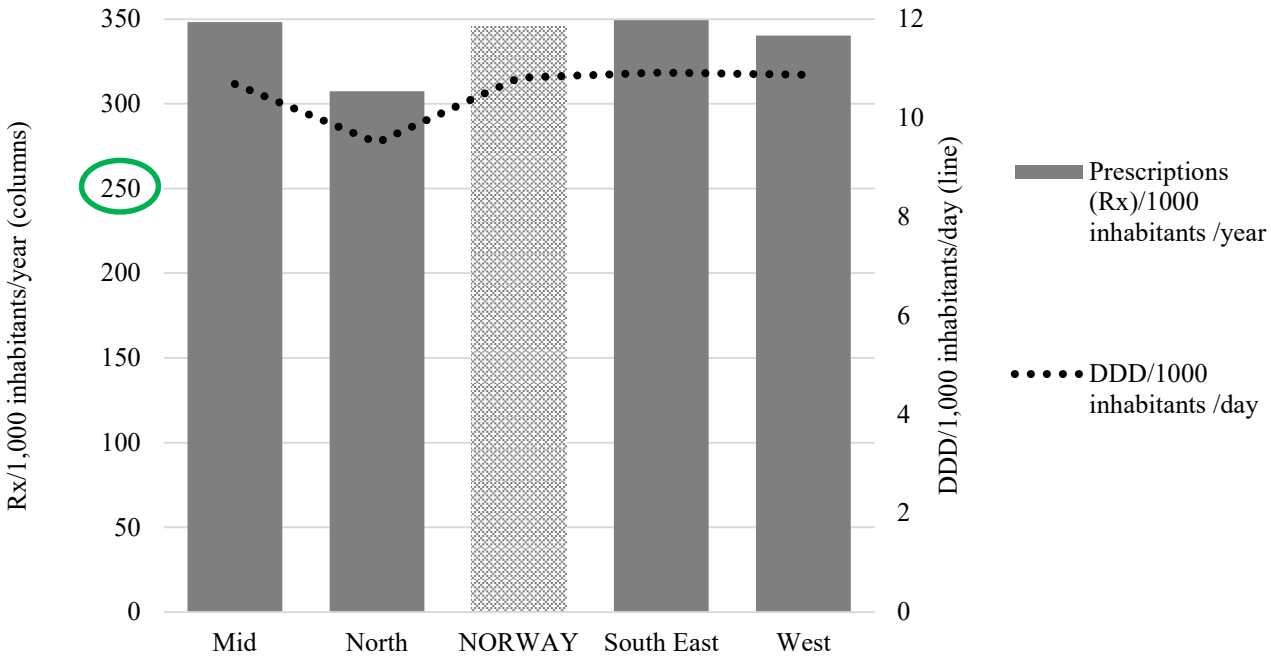

FIGURE 20. Consumption of antibacterial agents for systemic use (ATC group J01, excl. methenamine) in outpatients in the different regions of Norway in 2024. Measured as number of prescriptions (Rx)/1,000 inhabitants/year and in DDD/1,000 inhabitants/day. Prescription target set in National Strategy against Antibiotic Resistance is 250 Rx/1,000 inhabitants/year (green ring). Data from the Norwegian Prescribed Drug Registry (NorPD).

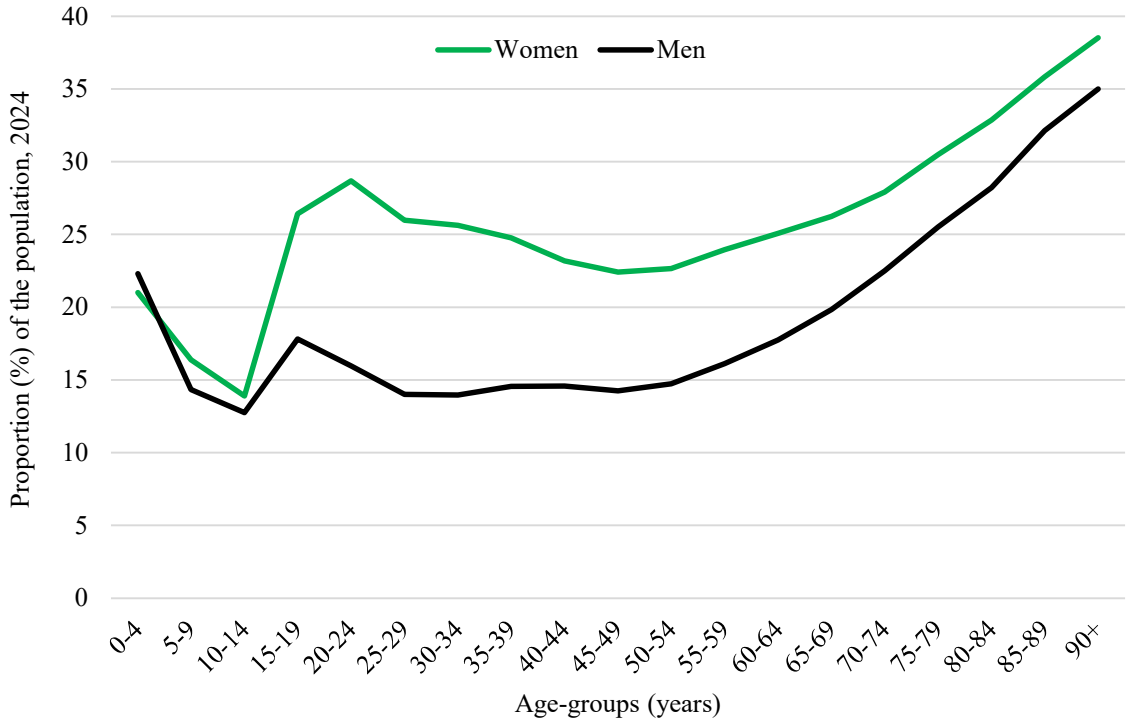

FIGURE 21. Proportion (%) of the population having dispensed at least one prescription of antibacterials (one-year prevalence) in primary care by gender and age in Norway, 2024. Antibacterials included are antibacterials for systemic use (ATC group J01, excl. methenamine), vancomycin (A07AA09), fidaxomicin (A07AA12) and metronidazole (P01AB01). Prevalence in age groups above 65+ is adjusted according to persons from these age groups living in long-term care institutions. Data from the Norwegian Prescribed Drug Registry (NorPD).

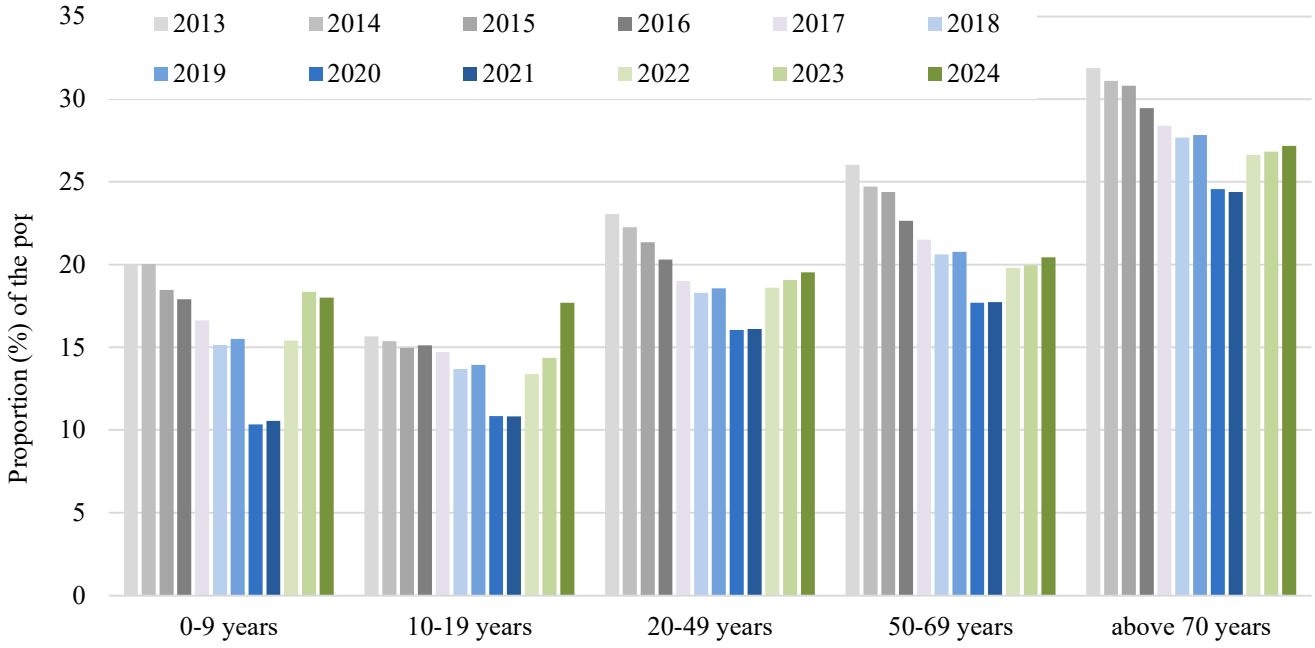

FIGURE 22. Proportion (%) of the population having dispensed at least one prescription of antibacterials (one-year prevalence) in primary care in Norway, 2013-2024. Antibiotics included are antibacterials for systemic use (ATC group J01, excl. methenamine). Data from the Norwegian Prescribed Drug Registry (NorPD).

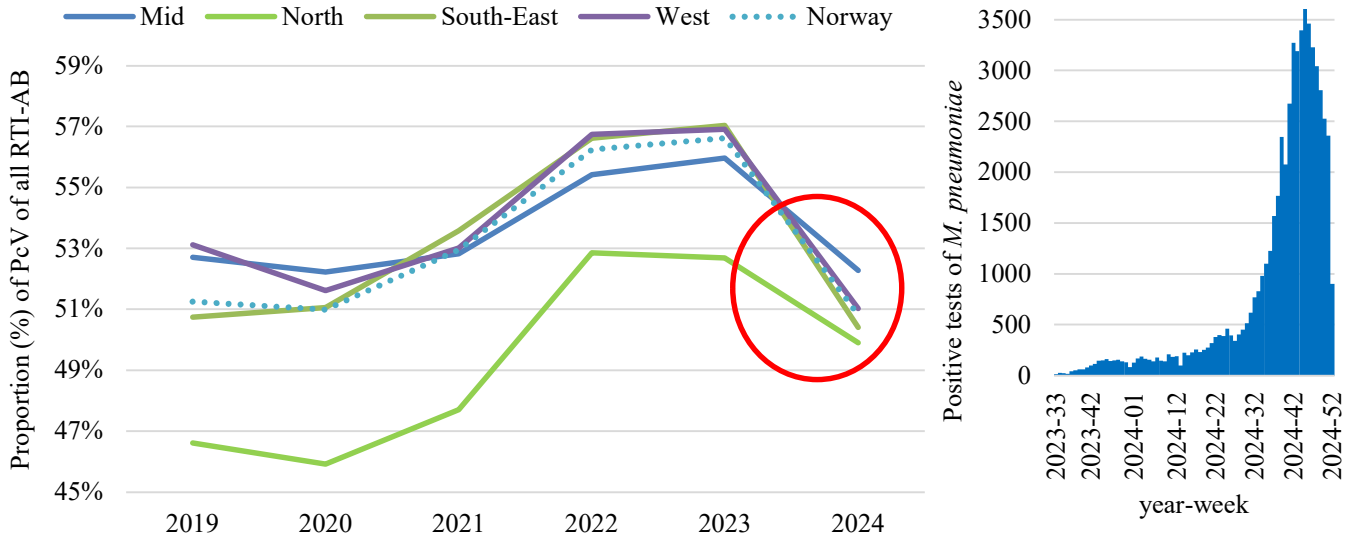

FIGURE 23. The use (in DDDs) of penicillin V (phenoxymethylpenicillin) as the proportion (%) of all antibiotics for respiratory tract infections (amoxicillin, phenoxymethylpenicillin, macrolides (J01FA01, -02, -06, -09, -10), and doxycycline) in primary care in Norway, 2019-2024. Data from the Norwegian Prescribed Drug Registry (NorPD). The inserted graph is reported positive tests of *Mycoplasma pneumoniae* to the MSIS laboratory database August 2023 – December 2024. Data from the Norwegian Institute of Public Health.

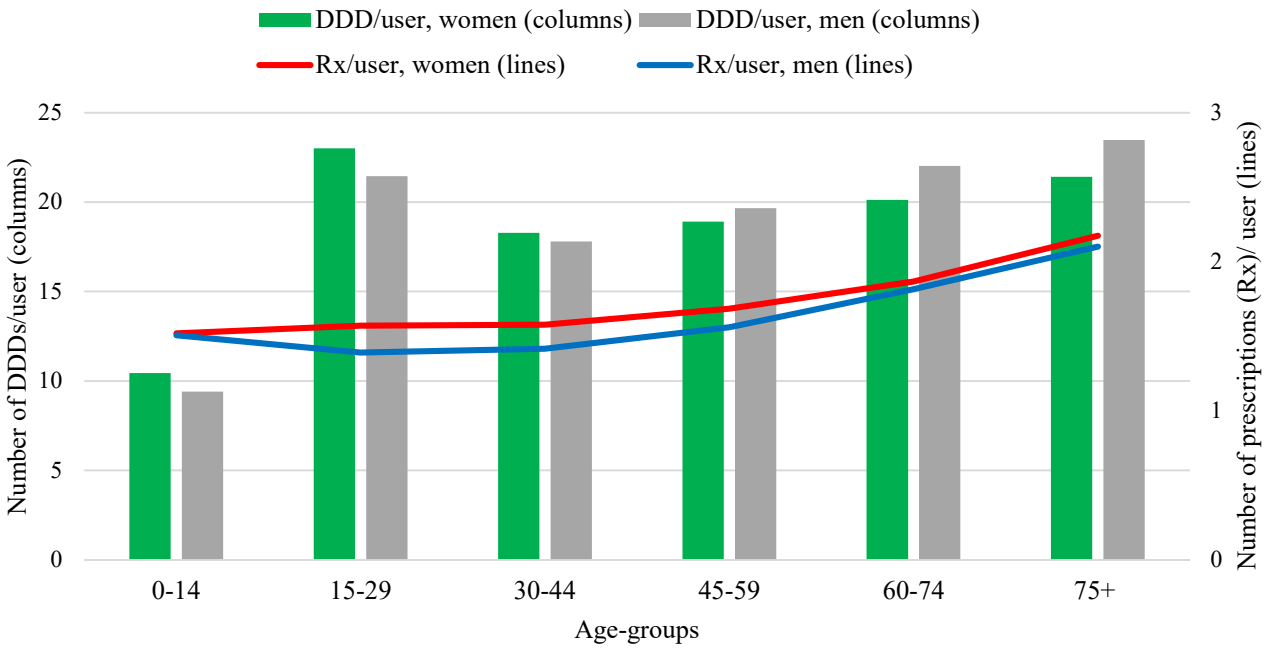

FIGURE 24. Mean number of prescriptions (Rx) per person and mean number of DDDs per person among users of antibacterials in ambulatory care by gender and age in Norway, 2024. Antibacterials included are antibacterials for systemic use (ATC group J01, excl. methenamine). Data from the Norwegian Prescribed Drug Registry (NorPD).

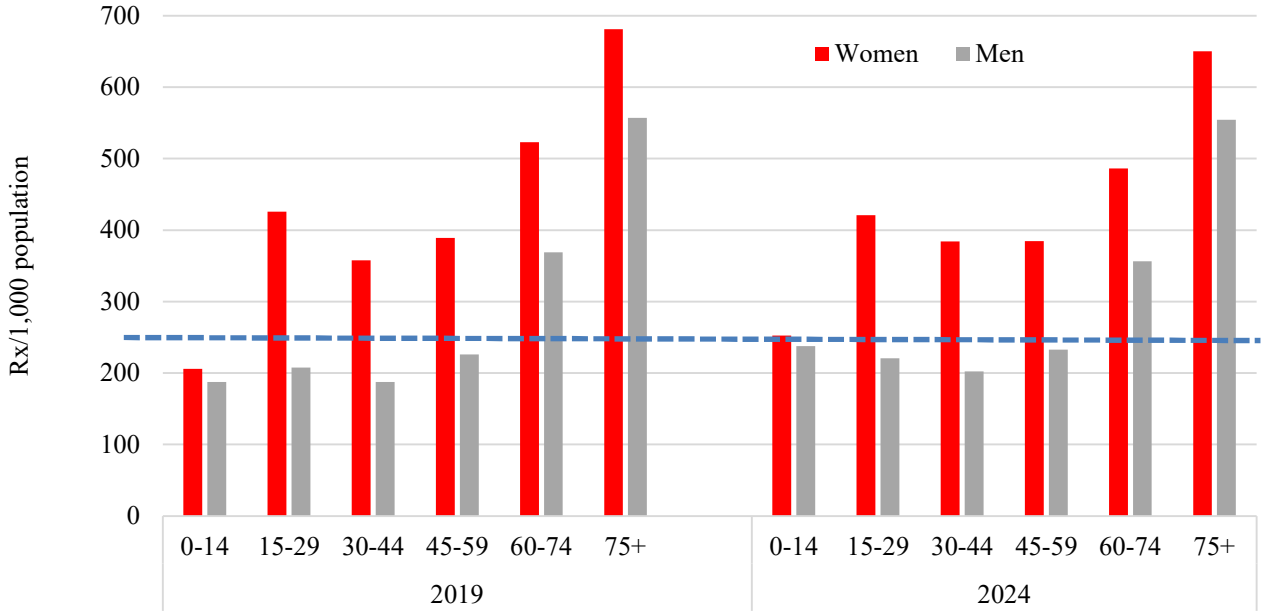

FIGURE 25. Mean number of prescriptions (Rx)/1,000 population of antibacterials (J01, excl. methenamine) in ambulatory care by gender and age groups; 2019 and 2024. The blue line indicates the target of 250 prescriptions/1,000 population/year. Data from the Norwegian Prescribed Drug Registry (NorPD).

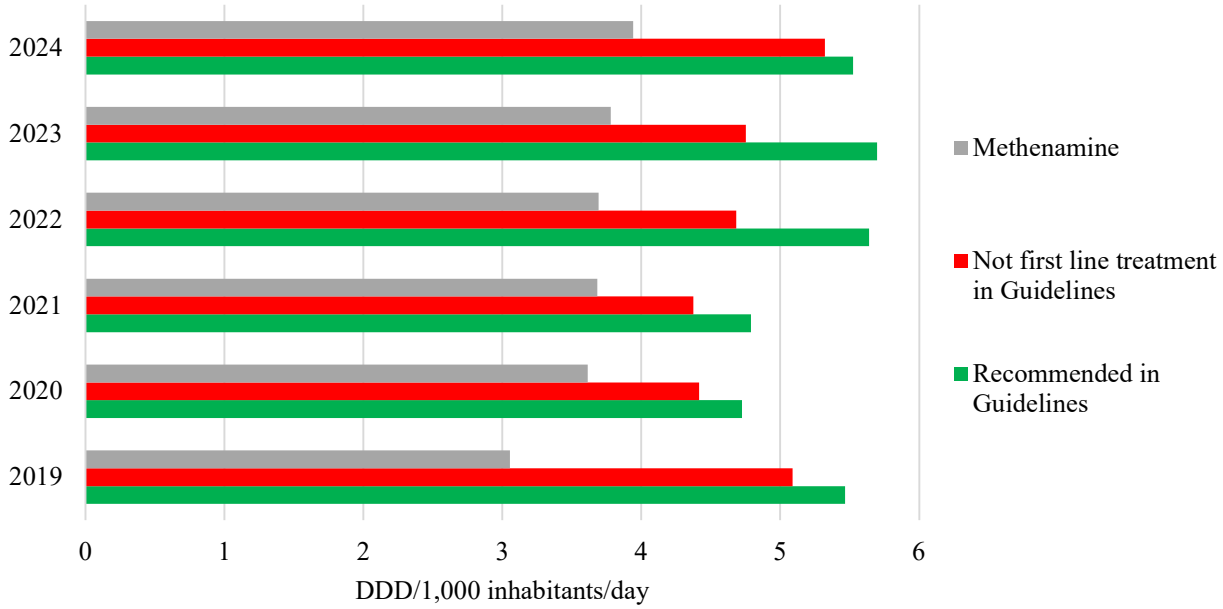

FIGURE 26. Consumption of antibacterial agents for systemic use (ATC group J01) in outpatients. Aggregated in three groups; a) recommended as first-line treatment in the guidelines for primary care (phenoxymethylpenicillin for respiratory tract infections, pivmecillinam, trimethoprim and nitrofurantoin for urinary tract infections and dicloxacillin for skin infections), b) not first-line treatment includes all other antibiotics in J01, and c) methenamine. Measured as number of DDD/1,000 inhabitants/day. Data from the Norwegian Prescribed Drug Registry (NorPD) (i.e. healthcare institutions and sales to prescriber own practice not included).

Antibiotic prescribing in dentistry

The sales of antibiotics to dentists and/or to dental clinics in 2024 measured in DDD/1,000 inhabitants/day decreased by 2% since 2012 but have increased by 18% compared with 2019, Figure 27. Phenoxymethylpenicillin is most commonly prescribed followed by amoxicillin, oral metronidazole and clindamycin. In 2024, these antibiotic substances represented 79%, 9%, 5% and 4% of all DDDs of antibiotics prescribed by dentists, respectively.

The phenoxymethylpenicillin share has increased; the proportion of DDDs has been around 75% for many years, but since 2019, this share has increased, possibly due to adherence to guidelines.

The prevalence of use has been stable; around 2.2% of the population are prescribed at least one antibiotic a year from a dentist and in 2024, more than 130,000 unique individuals were prescribed an antibiotic from dentists.

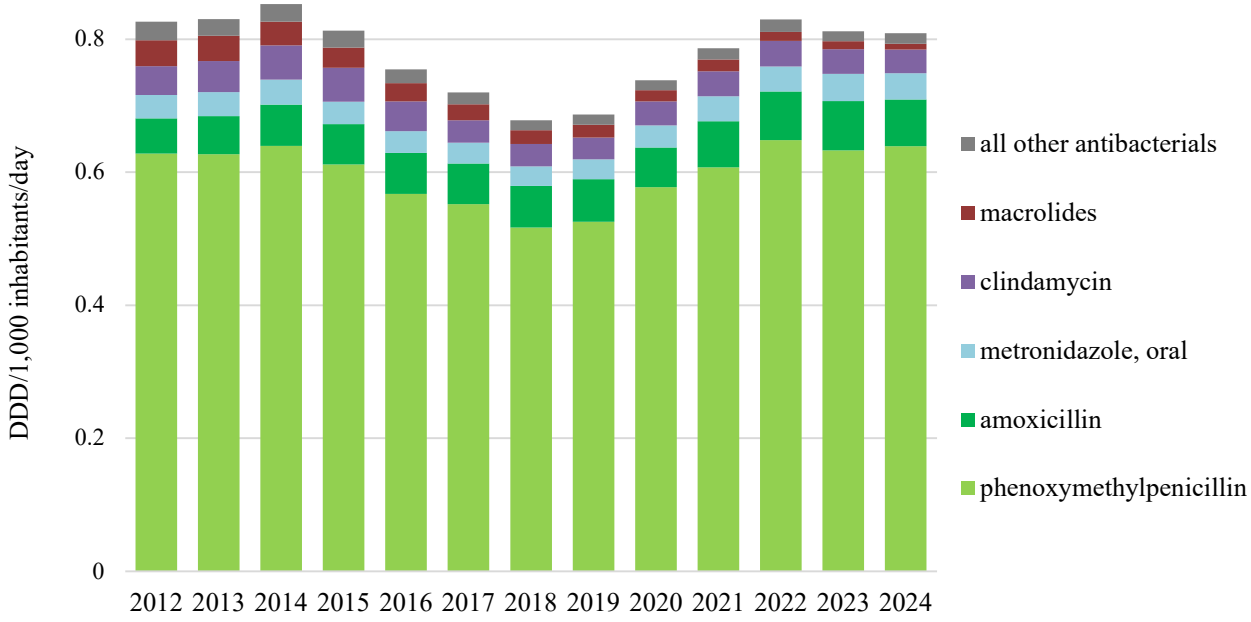

FIGURE 27. Antibiotics (J01 and oral metronidazole (P01AB01)), prescribed by dentists in Norway for the years 2012-2024, measured in DDDs per 1,000 inhabitants per day. Data from the Norwegian Prescribed Drug Registry (NorPD).

Antibiotic consumption in hospital care

In 2024, hospitals accounted for approximately 7.3 % of total antibacterial sales (measured in DDDs) for human use in Norway. When considering only antibacterials for systemic use (J01 excl. methenamine, A07AA09, A07AA12 and P01AB01), the hospital proportion was 9.4%. Figure 28 shows that this proportion has increased slightly over time. Figure 29 shows that antibiotic use in hospitals (measured in DDD/1,000 inhabitants/day) decreased by 3% compared to 2019 but was 7% higher than in 2012. The temporary drop in 2020 and 2021 was due to the Covid-19 pandemic, when hospitals reorganised and postponed elective surgeries as preparation for the expected high numbers of Covid-19 admissions. This led to fewer admissions and bed-days, as most hospitals turned out to actually have surplus capacity.

Prior to the Covid-19 pandemic, total hospital antibiotic use remained stable in volume (i.e. in DDD/1,000 inhabitants/day). However, the patterns of use changed, with increased consumption of narrow-spectrum antibiotics, a trend that has continued after the pandemic. Narrow-spectrum penicillins in particular, recommended in national guidelines, are widely used. It is important to consider that the DDDs for these agents are lower than the therapeutic doses usually prescribed in Norway. As a result, DDD-based metrics may underestimate the actual quantity of antibiotics administered. Furthermore, when narrow-spectrum penicillins are combined with aminoglycosides, the result is a higher total number of DDDs compared to monotherapy with a broad-spectrum antibiotic such as a cephalosporin or a carbapenem. This may give a misleading impression of excessive or inappropriate antibiotic use, when in fact it reflects more guideline-adherent and rational prescribing.

The pattern of antibiotic use in hospitals tends to be stable year-to-year. However, since 2012, there has been a decline in the use of selected “indicator” broad-spectrum antibiotics. In 2024, these broad-spectrum antibiotics (defined as J01_CR/DC/DD/DI/DF/DH/MA) accounted for 20% of total hospital antibiotic use, down from 26% in 2012. Beta-lactamase sensitive penicillins (J01CE) made up 14% of total use in 2024, the lowest share in the period 2012-2024 (Figure 29).

Overall, penicillins (J01C) accounted for 48% of hospital antibiotic use, measured in DDDs (J01CE 14%, J01CA 11%, J01CF 17% and J01CR 6%). Cephalosporins were the second-largest group, making up 18% of use, the dominant subgroup being 3rd generation cephalosporins (J01DD). In

2024, seven antibiotics accounted for 75% of all systemic antibiotic use in hospitals (i.e. J01 excl. methenamine, A07AA09, A07AA12 and P01AB01). These were ampicillin, benzylpenicillin, cefotaxime, piperacillin-tazobactam, cloxacillin, gentamicin and co-trimoxazole. Three of these made up 55% of all hospital antibiotic use; ampicillin (40%), benzylpenicillin (8%), and cefotaxime (7%).

The proportion of antibiotics used for medical and preoperative prophylaxis has remained stable. National point prevalence surveys (PPS) show that more than 95% of cefazolin and cefalotin is used for prophylaxis, and about 40% of parenteral metronidazole and co-trimoxazole is used for prophylaxis. This pattern has been consistent since 2015. When extrapolated to sales data (Figure 30) prophylaxis accounted for approximately 8% of hospital antibiotic use, rising to 11% in 2024.

The classification of antibacterials into access-, watch- or reserve- antibiotics (the WHO AWaRe classification) helps guide responsible antibiotic use. The WHO recommends that the access group antibiotics should account for at least 60% of total antibiotic use at the national level. In Norwegian hospitals, the access group has increased from 70% in 2012 to 77% in 2024. During the same period, the use of reserve antibiotics has doubled and increased from 1% of total use in 2012 to 2% in 2024. Among these, linezolid is the most frequently used reserve antibiotic, representing 43% of total DDDs in this category, followed by aztreonam (21%), Figure 31.

Hospital antibiotic use is often presented as DDD/1,000 inhabitants/day, but activity-adjusted metrics such as DDD/100 bed-days and DDD/100 admissions are more informative for comparing hospitals (Figure 32). Although length of stay (LOS) in Norwegian hospitals has remained stable in recent years, the number of admissions and bed-days has declined. This is likely due to a shift toward day-care and outpatient treatments, rather than a decrease in overall hospital activity. Figure 33 illustrates how reduction in bed-days influences antibiotic use statistics.

Figure 34 shows trends for seven antibiotic groups, primarily used in hospitals. The use of piperacillin-tazobactam has been increasing for many years but was markedly reduced in 2017 and 2018 due to nationwide shortage, followed by an increase in 2020 and 2021. In 2024, there was increased use of penicillins with beta-lactamase inhibitors, 2nd generation cephalosporins, amino-glycosides, quinolones and glycopeptides compared to 2023. At the same time, use of 3rd generation cephalo-sporins and carbapenems decreased. Compared to 2016, the use of aminoglycosides increased by 58%, which is in line with guideline recommendations. Moreover, the use of glycopeptides increased by 35%. The use of carbapenems peaked in 2014, and has since stabilised, likely due to the implementation of antibiotic stewardship programs in Norwegian hospitals from 2016. Mainly parenteral formulations of 2nd, 3rd and higher generation cephalo-sporins as well as carbapenems are licensed in Norway, and parenteral forms are primarily used in hospitals. Antibiotic therapy in hospitals differs from outpatient therapy due to the severity of the infections treated. However, almost none of the antibiotics commonly used in hospitals are solely used in this setting. Figure 35 illustrates the hospital share of selected ATC 4th level antibiotic groups. Substances with a high share in hospitals are used to treat severe infections and are thus particularly important in the view of antibiotic stewardship outside hospitals. For aminoglycosides, colistin and aztreonam, inhalation therapy is used for a small number of patients in ambulatory care; and of all DDDs used outside hospitals 99% of total colistin DDDs, 90% of total aminoglycoside DDDs and 84% of total aztreonam DDDs were inhalation therapy. However, for antibiotic stewardship the parenteral forms are more important, hence in Figure 35 only parenteral DDDs of aztreonam, aminoglycosides and colistin are included. One explanation for the observed parenteral share outside hospitals is the increasing practice of outpatient parenteral antimicrobial therapy (OPAT) - the administration of intravenous (IV) antibiotics outside the hospital setting, e.g. at home or an outpatient clinic. This is a wanted development, but – at the same time – it is important that OPAT is practiced by personnel trained in antibiotic stewardship.

Figure 36 shows the distribution between “preferred antibiotics” (which largely reflects standard treatment regimens in national guidelines) and antibiotics considered to be drivers of antibiotic resistance across Norwegian hospitals. The share of preferred antibiotics varies between hospitals, from 58 % to 80%. There are large variations between hospitals in both the volume of antibiotics used (measured in DDD/100 bed-days), and the types of antibiotics used.

The five selected groups of broad-spectrum antibiotics that were targeted in the former National Action Plan have been used as quality indicators for antibiotic stewardship programs in Norwegian hospitals/health trusts, Figures 36-38. Overall use in 2024 was 4% lower than in 2016. The drop in 2017-2021 was mainly due to the piperacillin-tazobactam shortage. During that time, hospitals used more beta-lactamase sensitive- and resistant penicillins (J01CE and J01CF) instead. The low use in 2020 and 2021 was influenced by the Covid-19 pandemic and case-mix changes. The reasons for the low use of the five indicator groups in 2019 remain speculative but may indicate better compliance with established guidelines. The variations observed among hospitals cannot be explained by differences in activity or patient composition alone, but are likely influenced by local prescribing practices, Figure 38.

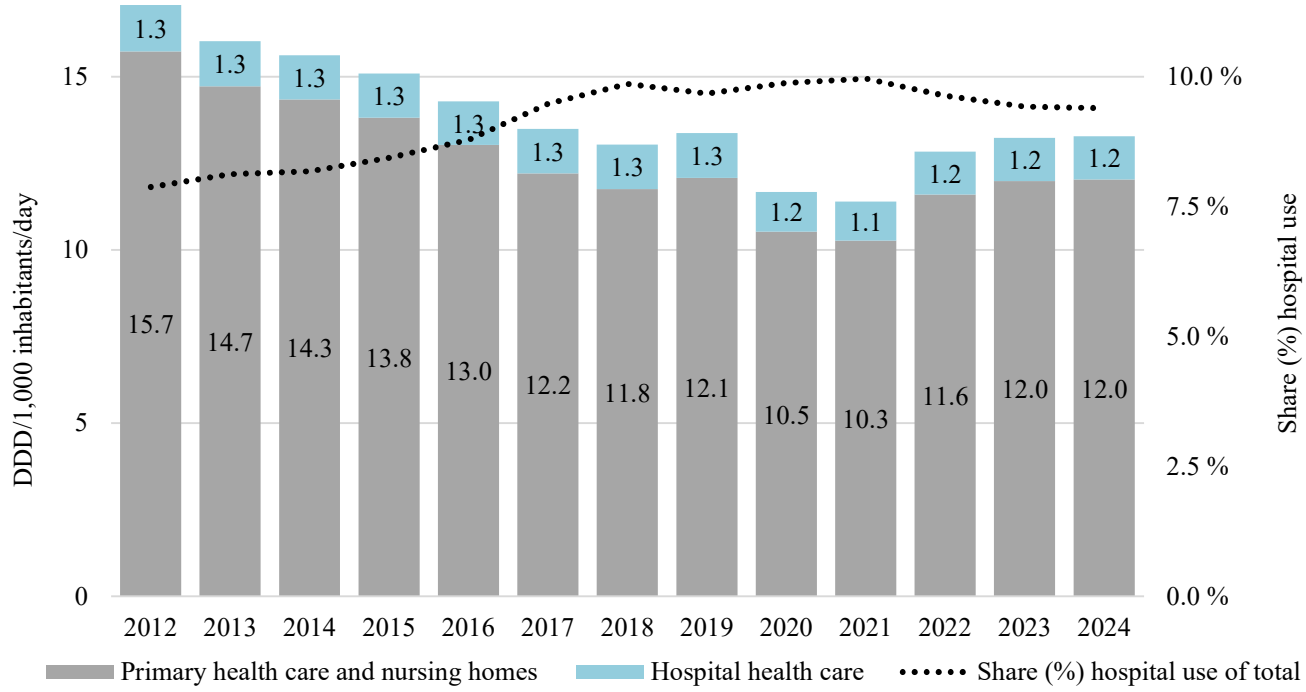

FIGURE 28. Consumption of antibacterial agents for systemic use (J01 excl. methenamine, A07AA09, A07AA12 and P01AB01) in Norway in primary healthcare and in hospitals 2012-2024, measured in DDD/1,000 inhabitants/day. Data source; Norwegian drug wholesales statistics database and the hospital pharmacies drug statistics database

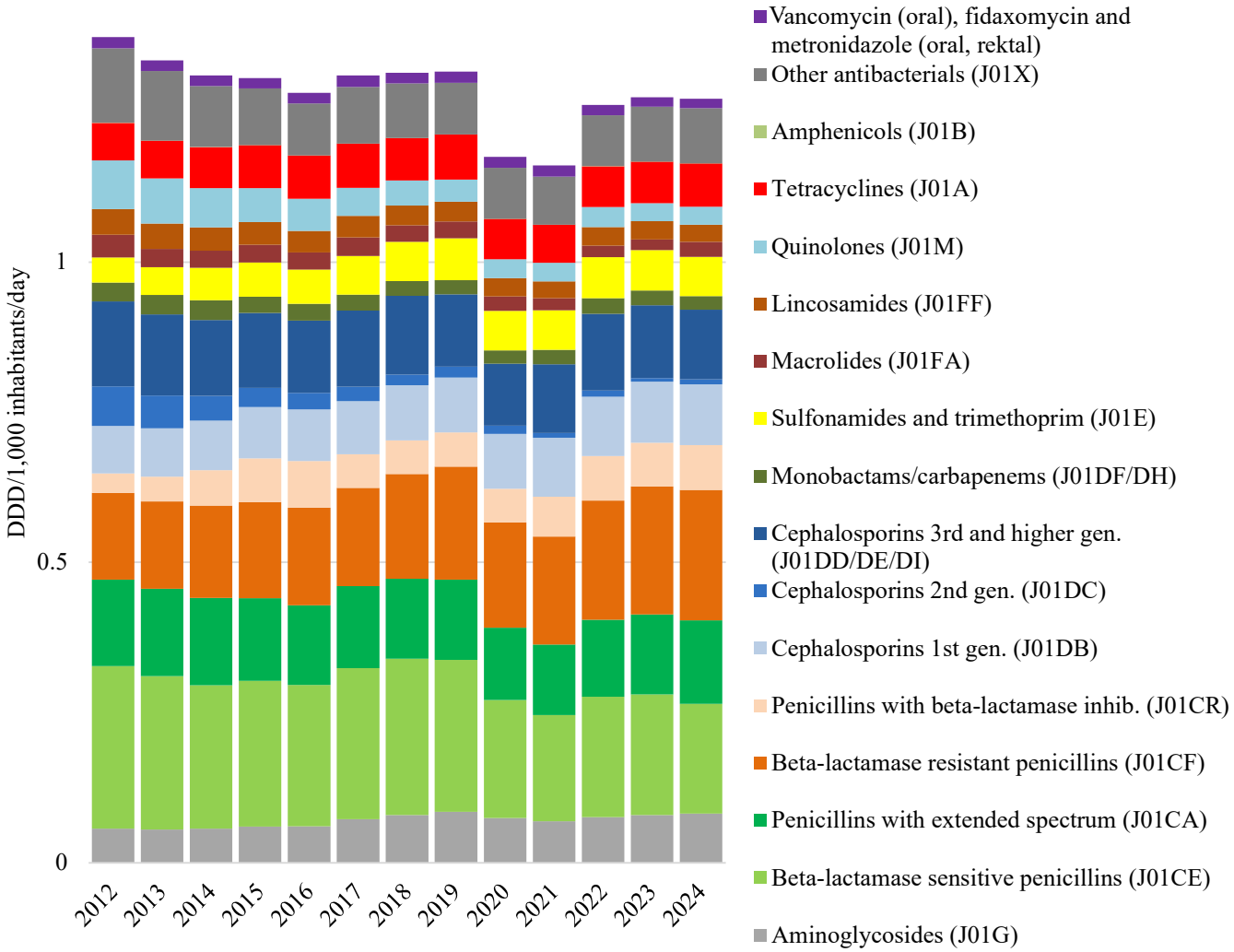

FIGURE 29. Proportions of antibacterial agents for systemic use (J01), vancomycin (A07AA09), fidaxomicin and oral metronidazole (P01AB01) in Norwegian hospitals 2012-2024, measured as DDD/1,000 inhabitants/day. Data source; hospital pharmacies drug statistics database.

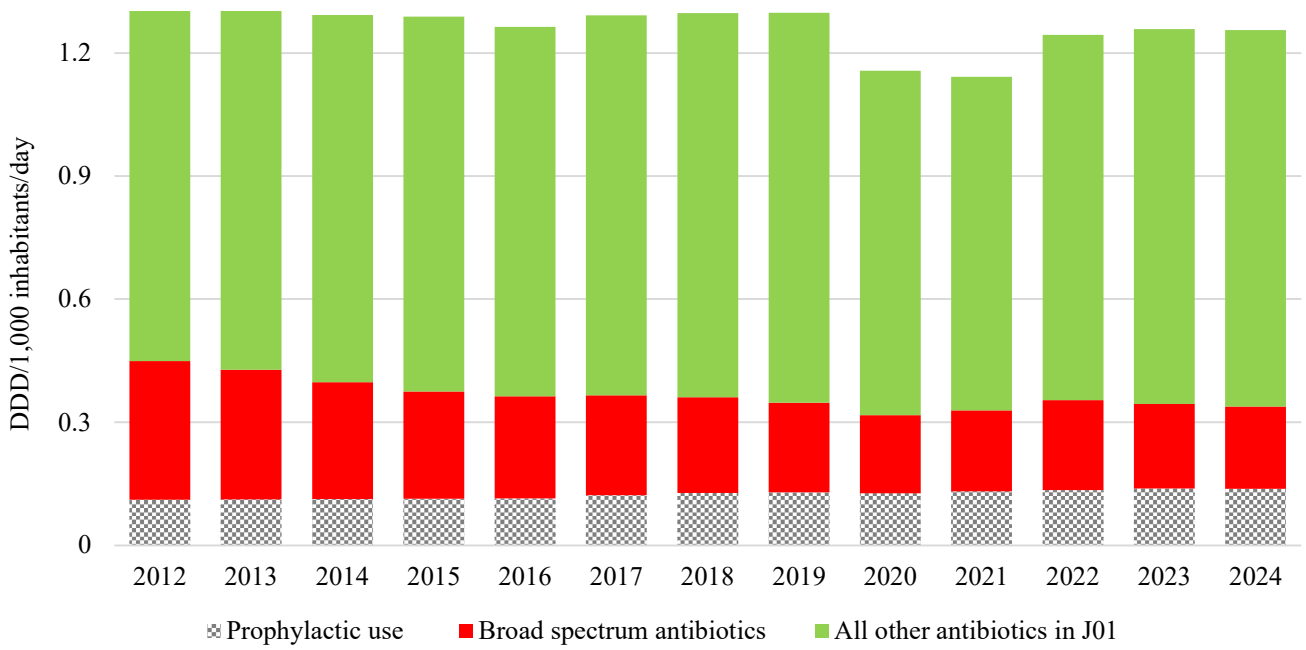

FIGURE 30. Proportions of prophylactic antibacterial agents for systemic use, broad-spectrum and other antibiotics in Norwegian somatic hospitals 2012-2024, measured as DDD/1,000 inhabitants/day. The volume of antibiotics for prophylactic use is estimated. Information on prescribing indications from the national point prevalence surveys were used to recalculate the sales data. Included in prophylactic use are all DDDs of the 1st generation cephalosporins cefazolin and cefalotin and 40% of the DDDs from metronidazole i.v. and co-trimoxazole, respectively. Broad-spectrum antibiotics are defined as J01CR, J01DC/DD/DI/DH, J01M, J01XA, J01XX-08, -09, -11 and J01AA12. Data source; hospital pharmacies drug statistics database.

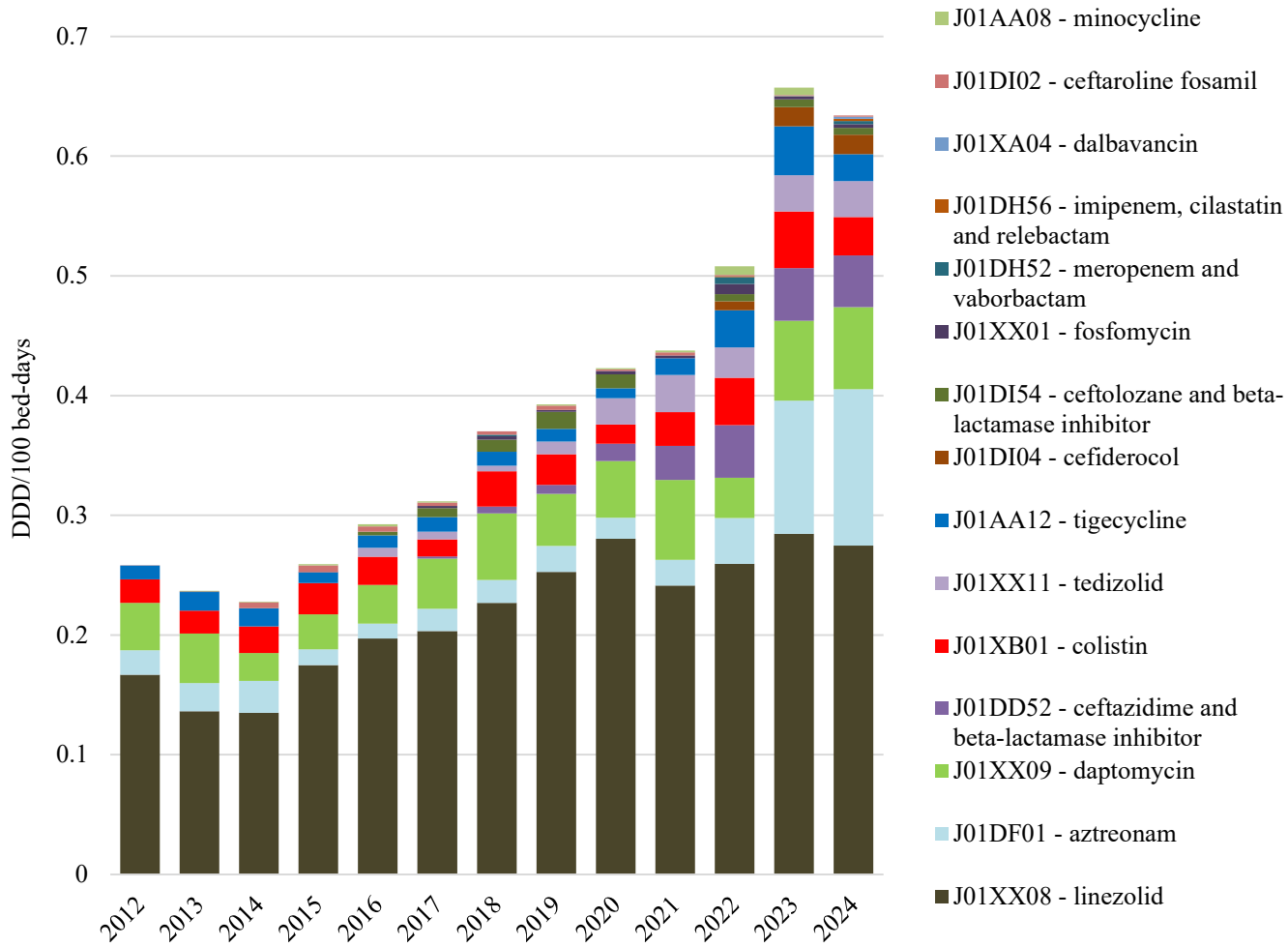

FIGURE 31. Reserve antibiotics (as defined according to the AWaRe 2023 classification) used in Norwegian hospitals (somatic) 2012-2024, in DDD/100 bed-days. Data source; hospital pharmacies drug statistics database.

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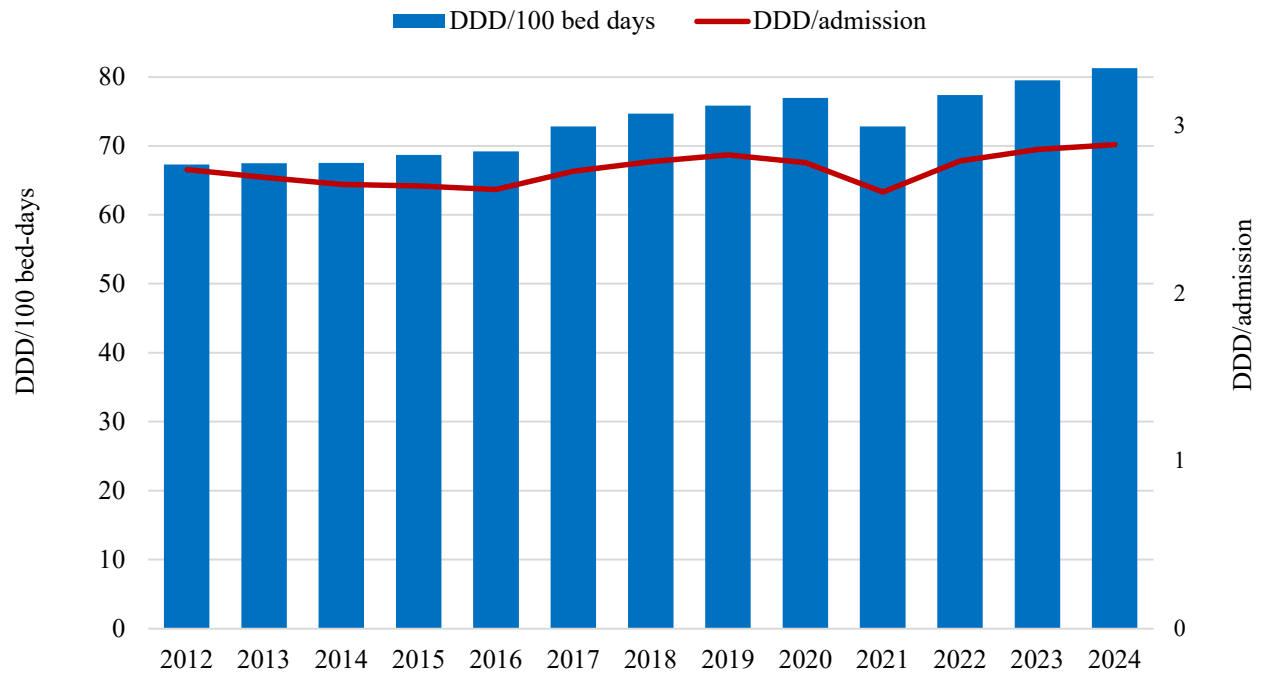

FIGURE 32. Total use of antibiotics in Norwegian hospitals (somatic) 2012-2024, in DDD/100 bed-days and in DDD/admission. Antibiotics are defined as J01 antibacterials for systemic use, A07AA09 vancomycin (oral), A07AA12 fidaxomycin and P01AB01 metronidazole (oral and rectal). Data source; hospital pharmacies drug statistics database.

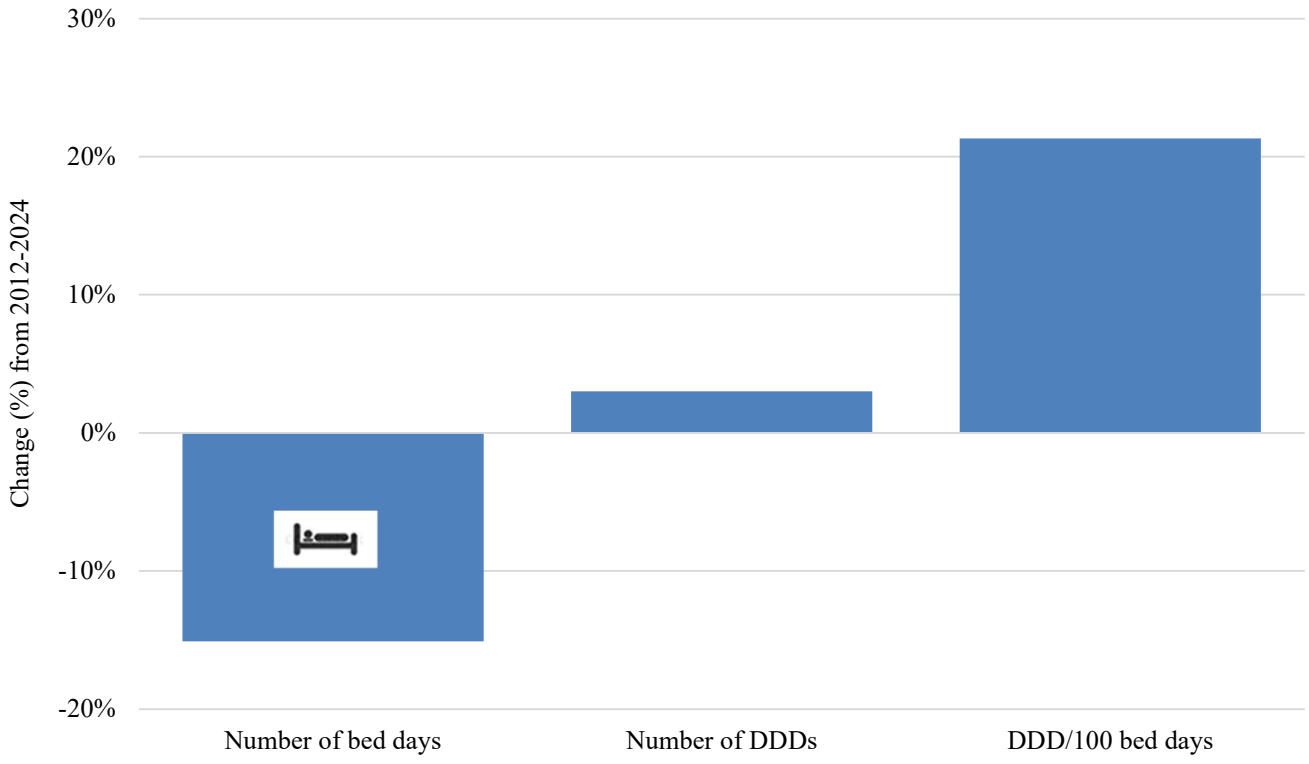

FIGURE 33. Proportional change will vary according to the measures used. Antibiotic usage in hospitals is often presented as DDD/100 bed-days, but total number of DDDs may also be used as a measure. The number of bed-days in Norwegian hospitals has been reduced by 15% since 2012. The figure visualises the impact of the reduction in bed-days on antibiotic consumption statistics of antibacterial agents for systemic use (J01 antibacterials for systemic use, A07AA09 vancomycin (oral), A07AA12 fidaxomycin and P01AB01 metronidazole (oral and rectal)) in Norwegian hospitals 2012-2024, measured as % change either as change of total DDDs (3% increase) or change of DDD/100 bed-days (20% increase).

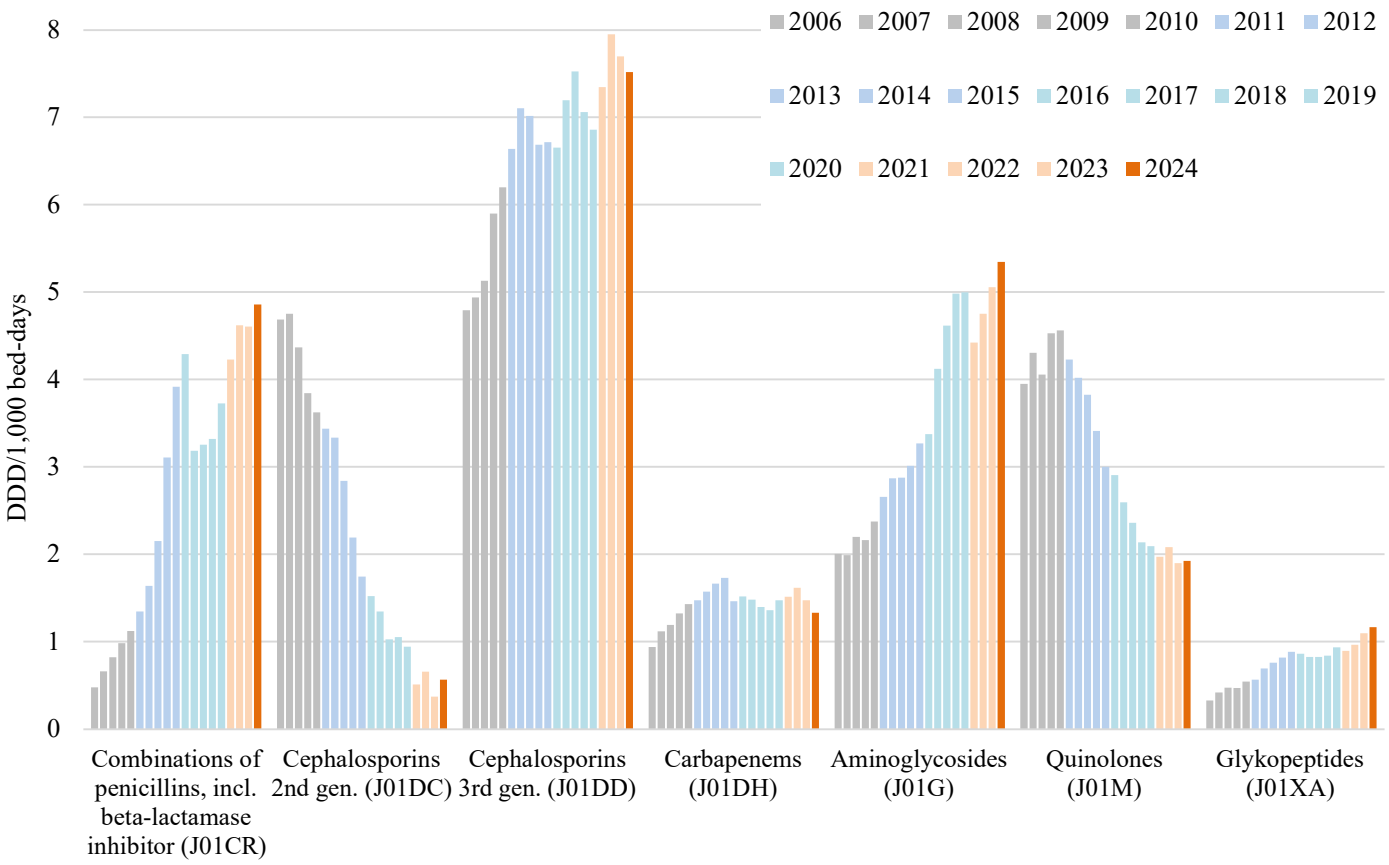

FIGURE 34. Consumption of seven antibacterial agents for systemic use (ATC J01CR, ATC group J01DC, J01DD, J01DH, J01G, J01M and J01XA) in Norwegian hospitals 2006-2024, measured in DDD/100 bed-days. Data source; hospital pharmacies drug statistics database.

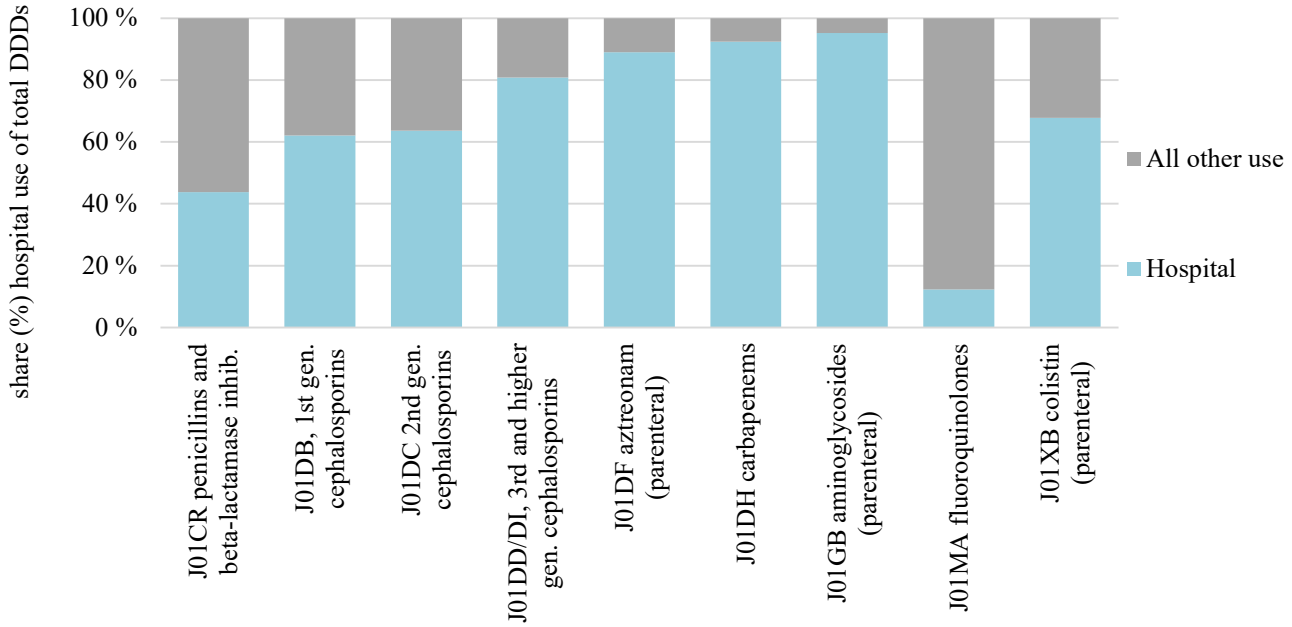

FIGURE 35. Proportion (%) of total sales as measured in defined daily doses (DDD) attributable to hospitals in 2024 shown for selected antibiotic groups; the five groups defined as broad-spectrum antibiotics in Norway (J01CR, J01DC, J01DD/DI, J01DH and J01M), in addition J01DB, J01DF, J01GB and J01XB. For ATC groups J01DF, J01GB and J01XB only parenteral forms are included. Data source; Norwegian drug wholesales statistics database and the hospital pharmacies drug statistics database.

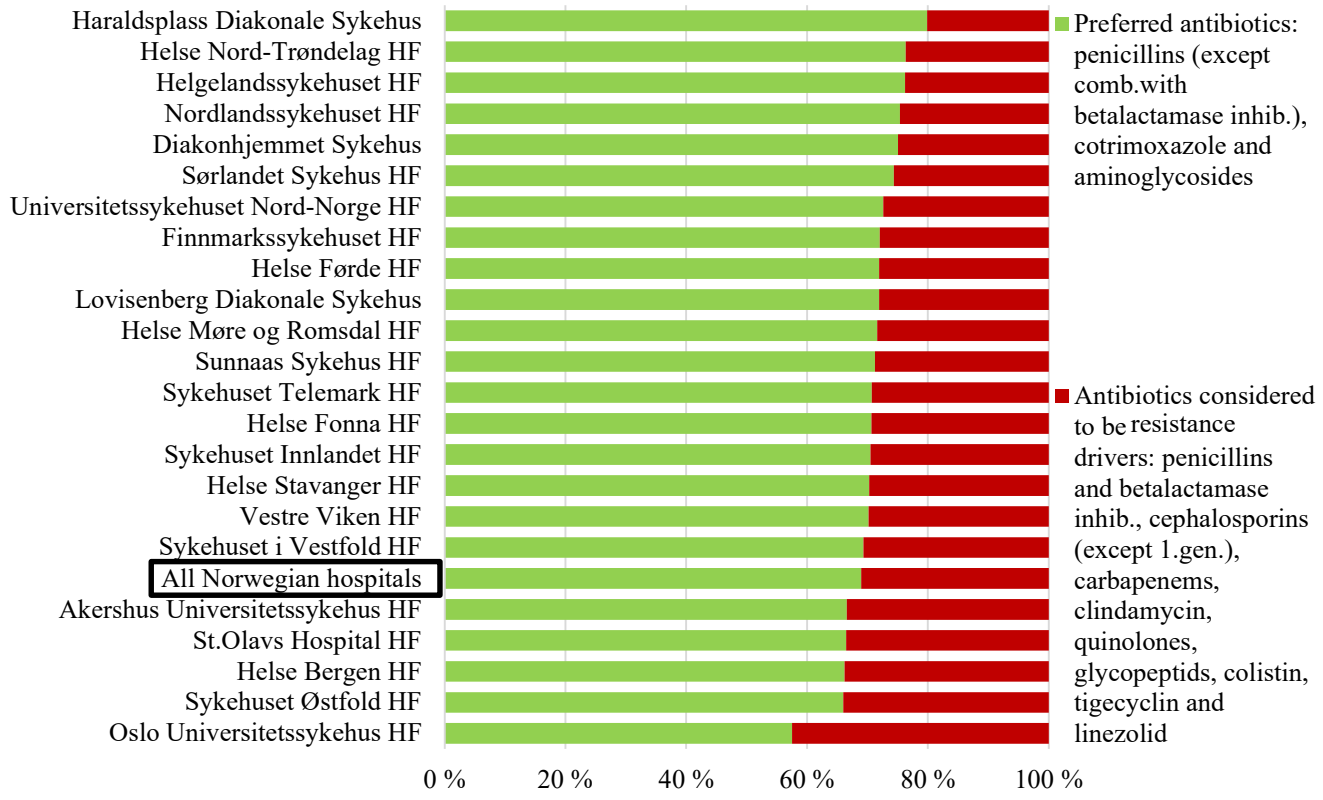

FIGURE 36. Proportions (% of DDDs) of preferred antibiotics (green part of the columns) and antibiotics that are considered to be drivers of antibiotic resistance (red part i.e. belonging to ATC groups J01CR, J01DC, J01DD, J01DE, J01DI, J01DH, J01M, J01XA, J01XB, J01AA12, J01FF01 and J01XX08) in Norway, presented per hospital/health trust in 2024. 1st generation cephalosporins and tetracyclines are not included as they in hospitals are mainly used for surgical prophylaxis. Metronidazole is also excluded from the figure because it does not readily fit either of the descriptions "preferred" or "resistance driver", and there are no alternative drugs specifically targeting anaerobic bacteria. Data source; hospital pharmacies drug statistics database.

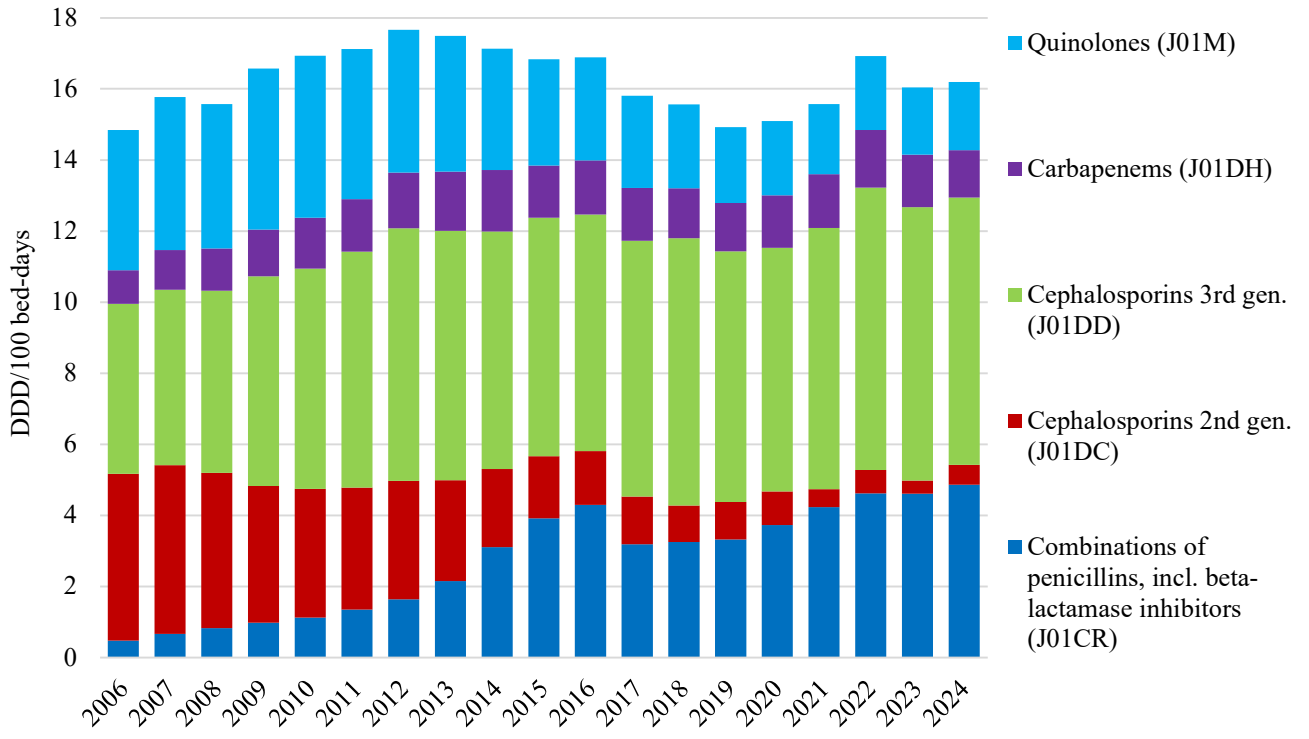

FIGURE 37. Consumption of selected antibacterial agents for systemic use (belonging to ATC-groups J01CR, J01DC, J01DD, J01DH and J01M) in Norwegian hospitals 2006-2024, in DDD/100 bed-days. Data source; hospital pharmacies drug statistics database.

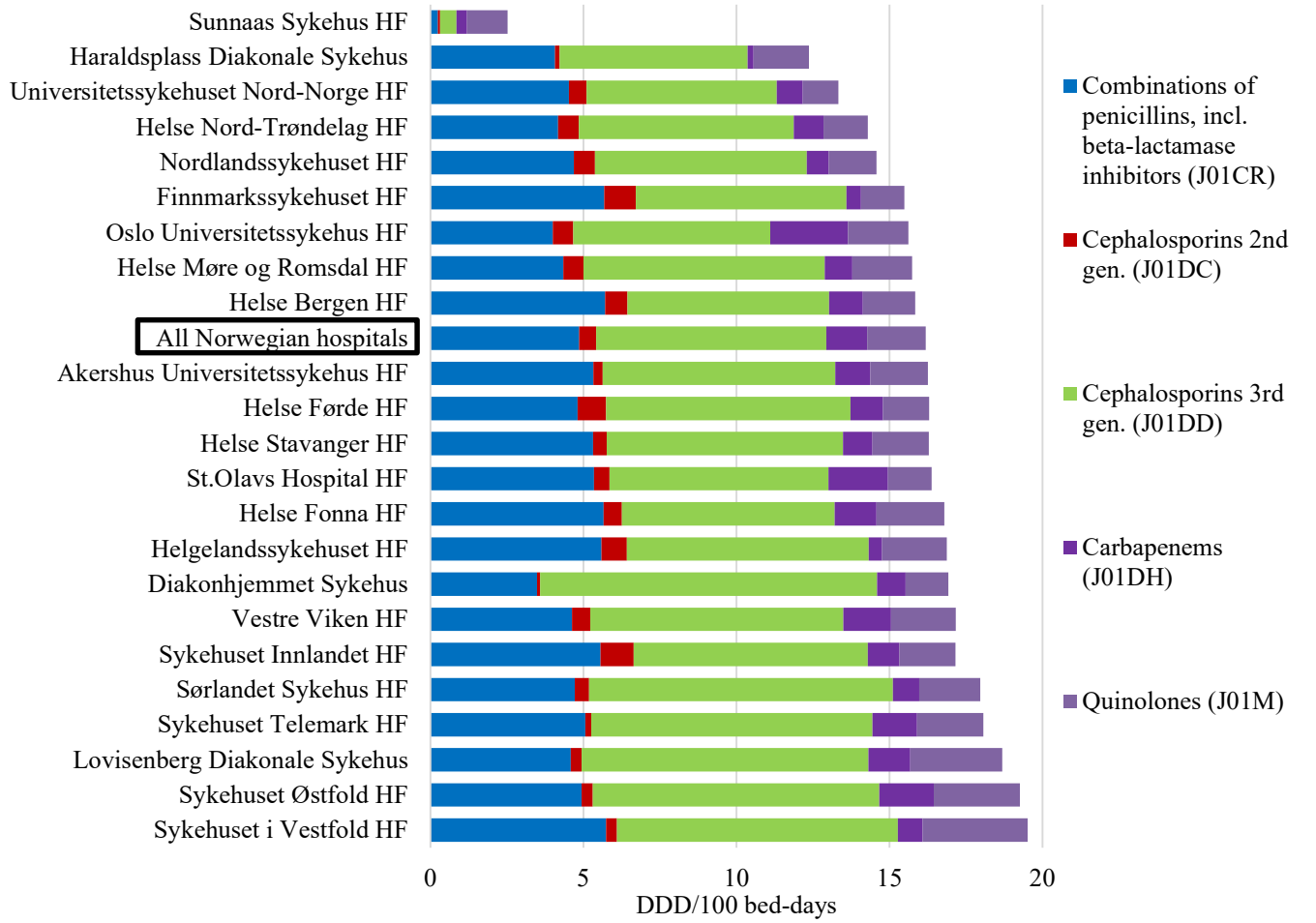

FIGURE 38. Consumption of selected antibacterial agents for systemic use (belonging to ATC groups J01CR, J01DC, J01DD, J01DH and J01M) in Norway, presented per hospital/health trust, in 2024, measured in DDD/100 bed-days. All hospitals, except one (Sunnaas Sykehus) are acute care hospitals. Data source; hospital pharmacies drug statistics database.

Surgical prophylaxis and antimicrobial resistance – consequences for treatment

Background

Surgical site infections (SSIs) are among the most common healthcare-associated infections (HAIs), and are associated with increased morbidity, mortality and cost (1). Preventing SSIs requires a range of measures, one of which is surgical antibiotic prophylaxis (SAP). SAP is effective in certain procedures (2), notably when the risk of infection is high, such as in colorectal surgery, or when an SSI can have devastating consequences, such as in cardiothoracic- or orthopaedic prosthetic surgery (3). However, SAP is frequently used inappropriately, unnecessarily and for too long (4).

Antibiotics used for surgical prophylaxis comprise a significant share of antibiotic use in Norwegian hospitals, at an estimated 12 % in 2023 (5). Appropriate use of surgical prophylaxis is therefore an important target for antimicrobial stewardship. Norwegian guidelines for the use of surgical prophylaxis are currently being updated (6), and may contribute to more rational use of SAP in Norway.

Choice of antibiotic prophylaxis

The ideal prophylactic antibiotic should have a narrow spectrum, cover the most relevant pathogens causing SSIs, have low toxicity, be easy to administer, achieve optimal concentrations at the surgical site, and have low cost. Traditionally, agents commonly used for treatment have been avoided.

In the Norwegian guidelines, cefazolin is the first-line choice when skin flora is the most likely source of SSI, in line with most international guidelines. Metronidazole is added when the alimentary or genital tract is entered. For gastrointestinal procedures doxycycline and metronidazole has been first choice for several decades, a practice particular to Norway, based on Norwegian studies (7). For urological procedures, trimethoprim-sulfamethoxazole is recommended (6).

Surgical prophylaxis as a driver of resistance

The association between antibiotic use and resistance is well established (8). Reducing antibiotic consumption is a cornerstone of antimicrobial stewardship. It is reasonable to assume that surgical prophylaxis contributes to selective pressure favouring resistance, although studies directly addressing the effects of antimicrobial prophylaxis on the development of antibiotic resistance are scarce. In a recent review, including 75 meta-analyses, antibiotic resistance was reported in only 6 scenarios (3), with increased risk of resistance with prophylaxis suggested in patients undergoing cystoscopy (9).

Choice of prophylaxis in patients colonised with multi-resistant bacteria
Some patients are known to be colonised with resistant bacteria. SSIs are usually caused by the patient's own flora. Several studies have shown higher SSI rates in patients colonised by multi-drug resistant (MDR) organisms. The clinician is faced with the question of whether to adapt the choice of SAP (10).

Patients colonised with resistant Gram-positive bacteria
Cefazolin is the first-line prophylactic agent in Norwegian and international guidelines in clean or clean-contaminated surgeries where skin flora is the primary source of SSIs. A 2013 meta-analysis including patients undergoing cardiac or orthopaedic surgery found fewer MRSA infections post-surgery when vancomycin was used as the prophylactic agent, but the overall infection rate did not decrease (11). ESCMID recently published European guidelines on preoperative prophylaxis in patients colonised with multi-drug resistant Gram-positive bacteria, recommending targeted prophylaxis with vancomycin for MRSA carriers in cardiothoracic, orthopaedic and neurosurgery (12).

MRSA screening and nasal decolonisation with mupirocin in carriers shortly (1-2 weeks) before surgery has also been recommended as part of a bundle to reduce postoperative infection risk, although evidence is derived mostly from studies on MSSA decolonisation (12). Whether screening all patients is cost effective in Norway, given the low prevalence of MRSA colonisation, remains uncertain.

Several centres already perform screening and decolonisation for *Staphylococcus aureus,* either targeted or universal, prior to high-risk surgeries, as recommended by WHO (2). However, the development of mupirocin resistance might be a concern with this approach. There is limited evidence regarding targeted prophylaxis for patients colonised with vancomycin resistant enterococci (VRE) (12).

Carriers of resistant Gram-negative bacteria
Gram-negative *Enterobacterales* are the most common pathogens in SSIs following gastrointestinal and urological surgery (13). Global rates of SSI following colorectal surgery were shown to increase from 1980 to 2005 in a 2019 meta-analysis (14). Some infections are caused by bacteria resistant to first-line prophylactic agents, and carriers of multi-drug resistant bacteria are at a higher risk of postoperative infection (13). International guidelines for preoperative prophylaxis did not address this issue (2,15), until European guidelines were published by ESCMID in 2023 (13).

For patients colonised with ESBL-producing *Enterobacterales*, European guidelines give a conditional recommendation to adapt SAP in colorectal and liver transplant surgery. Norwegian guidelines recommend doxycycline and metronidazole for these procedures, but susceptibility to doxycycline is not tested, making it difficult to apply this recommendation in clinical practice. Avoiding the cefazolin/metronidazole option seems prudent.

Screening for ESBL before high-risk surgery (e.g., colorectal and liver transplant), may be useful in high-prevalence settings, but the prevalence in Norway is still below the suggested threshold of 10%.

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National Action Plan against Antibiotic Resistance in Healthcare – National Targets for Antibiotic Use and change according to target

The former National Strategy against Antibiotic Resistance was agreed upon in 2015 and set an overarching goal of reducing the total volume of antibiotics used in Norway by 30%, by the end of 2020, compared to the baseline year of 2012. In addition to this national target, two sector specific objectives were established for ambulatory care; a reduction in the average number of prescriptions to 250 prescriptions per 1,000 inhabitants per year, and a 20% reduction in the use of antibiotics for respiratory tract infections, measured in DDD/1,000 inhabitants/day. Figure 39 shows the change in consumption of total human antibiotics (J01) and antibiotics for respiratory tract infections (amoxicillin, phenoxymethylpenicillin, macrolides and doxycycline) in Norway since 2012.

For hospitals, the work was focused on reducing the combined use of five specific groups of antibiotics by 30% compared with 2012. To support this goal, the National Action Plan mandated the implementation of antibiotic stewardship programs in all Norwegian hospitals. Figure 40 shows the annual variation of total hospital use of these targeted groups 2019-2024 according to the national target.

Between 2019 and 2024, Norwegian hospitals achieved an 8% reduction in use of the five selected groups of broad-spectrum antibiotics when adjusting for activity using bed-days. However, this indicator has limitations, as the number of bed-days has declined steadily over time while outpatient consultations have increased considerably. Relying solely on bed-days to measure clinical activity may obscure actual trends in antibiotic use, and alternative indicators could contribute to different interpretations of the data.

Norway has a beneficial pattern of antibacterial use compared to other countries. Norwegian antibiotic consumption data are shared through European Surveillance of Antimicrobial Consumption Network (ESAC-Net) at European Centre for Disease Prevention and Control (https://www.ecdc.europa.eu) and through the Global Antimicrobial Resistance and Use Surveillance System (GLASS) in WHO (https://www.who.int/ initiatives/glass). According to a target proposed by the WHO, at least 60% of total consumption should correspond to antimicrobials from the Access group, as classified by the AWaRe classification 2023. Figure 41 shows the proportion of access antibiotics in different healthcare settings in Norway: hospital care, primary care and total. In September 2024, a new policy document, National One Health Strategy Against Antimicrobial Resistance 2024–2033, was published. The corresponding National Action Plan for the human health sector is expected to be in place during autumn 2025.

Norway has established two national advisory units dedicated to antibiotic use and stewardship in humans; The Antibiotic Centre for Primary Care (ASP), founded in 2006, focuses on primary care, while the National Centre for Antibiotic Use in Hospitals (NSAS), established in 2011, serves the hospital and specialist healthcare services.

The Directorate of Health, in collaboration with the national advisory units, issues updated, evidence based National Antibiotic Treatment Guidelines for antibiotic use in ambulatory care, nursing homes, dental practices and hospitals.

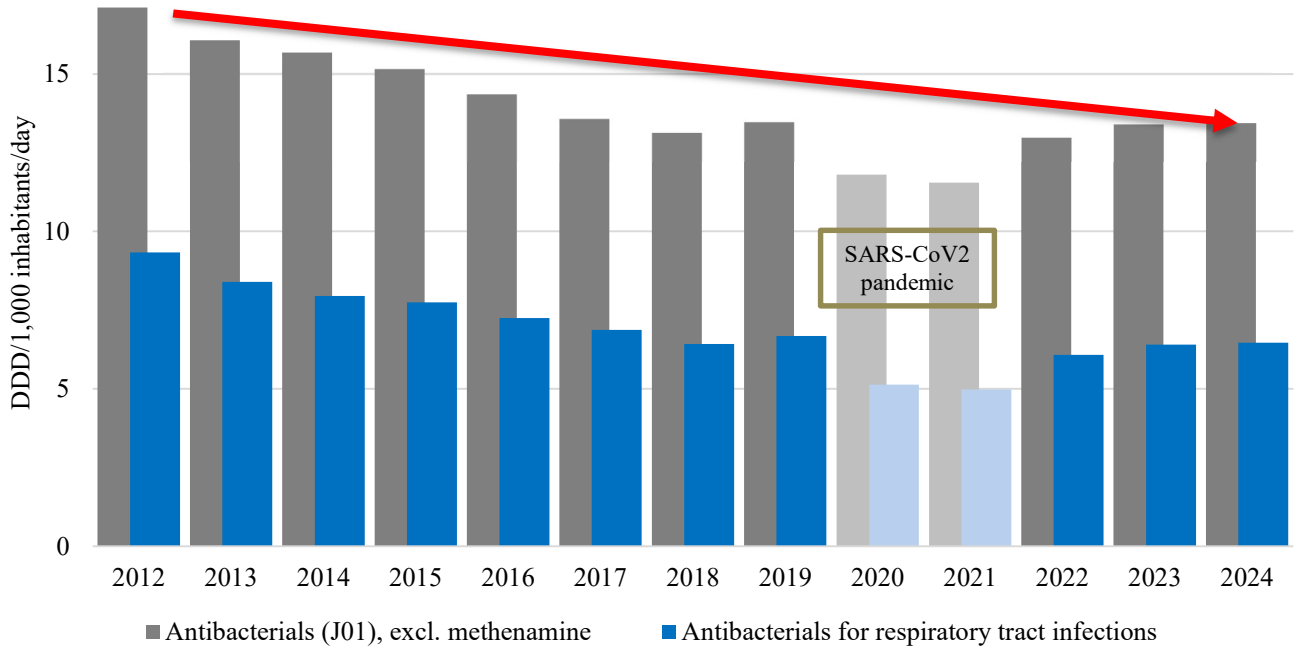

FIGURE 39. Total human sales of antibacterial agents for systemic use (ATC group J01) and sales of antibiotics for respiratory tract infections (amoxicillin, phenoxymethylpenicillin, macrolides (J01FA01, -02, -06, -09, -10), and doxycycline) in Norway in 2012-2024 measured in DDD/1,000 inhabitants/day. Reduction of total use since 2012, measured in DDDs (end of red line) was 21%, and for antibacterials for respiratory tract infections the reduction was 31%. Bars show measured use 2012-2024 (grey; J01, blue; antibiotics for respiratory tract infections). Data from the Norwegian drug wholesales statistics database.

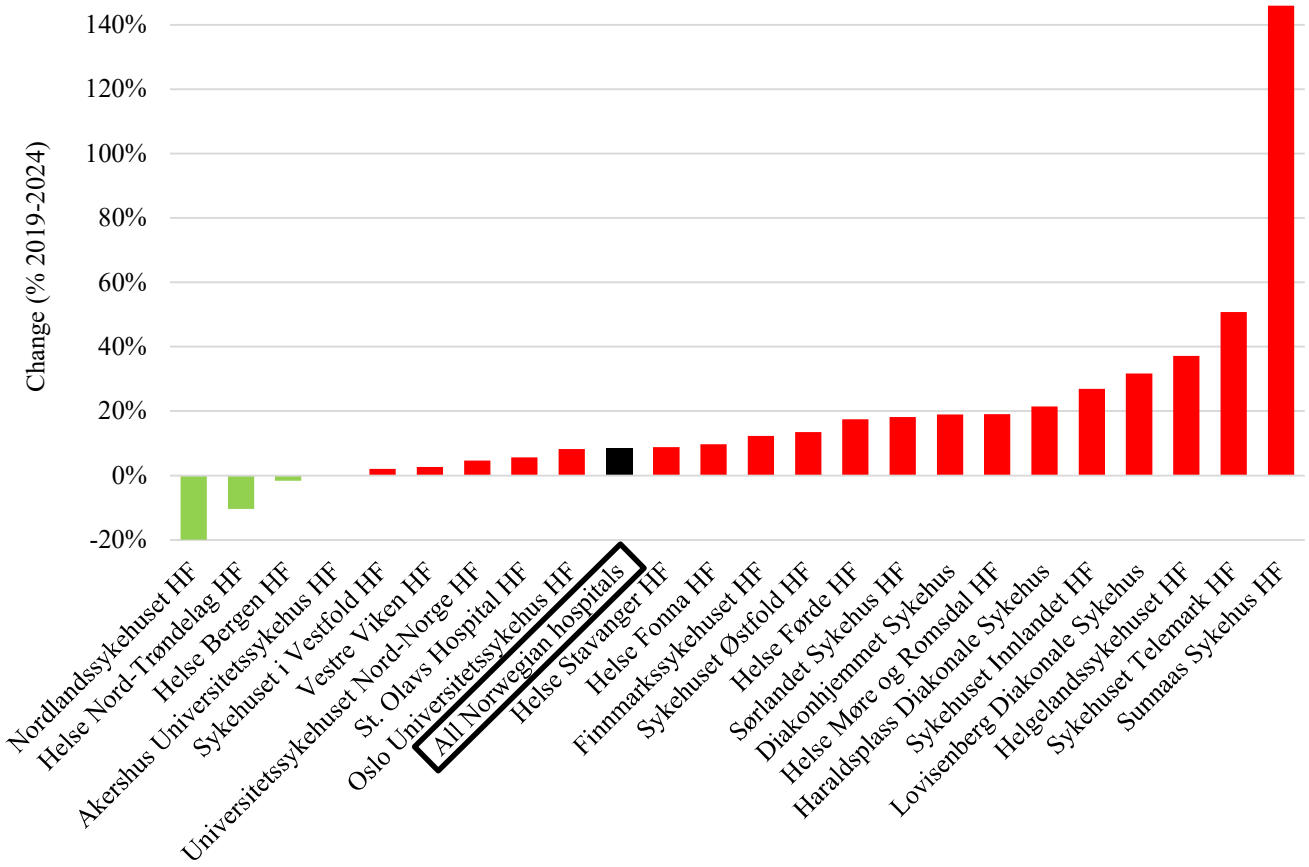

FIGURE 40. Changes in the use of selected antibacterials for systemic use (ATC-groups J01CR, J01DC, J01DD, J01DH and J01M) in Norwegian hospitals, 2019-2024. The data are presented per hospital/health trust as DDD/100 bed-days. Red columns; increase, green columns; decrease and average for all Norwegian hospitals shown in black. Data source; hospital pharmacies drug statistics database.

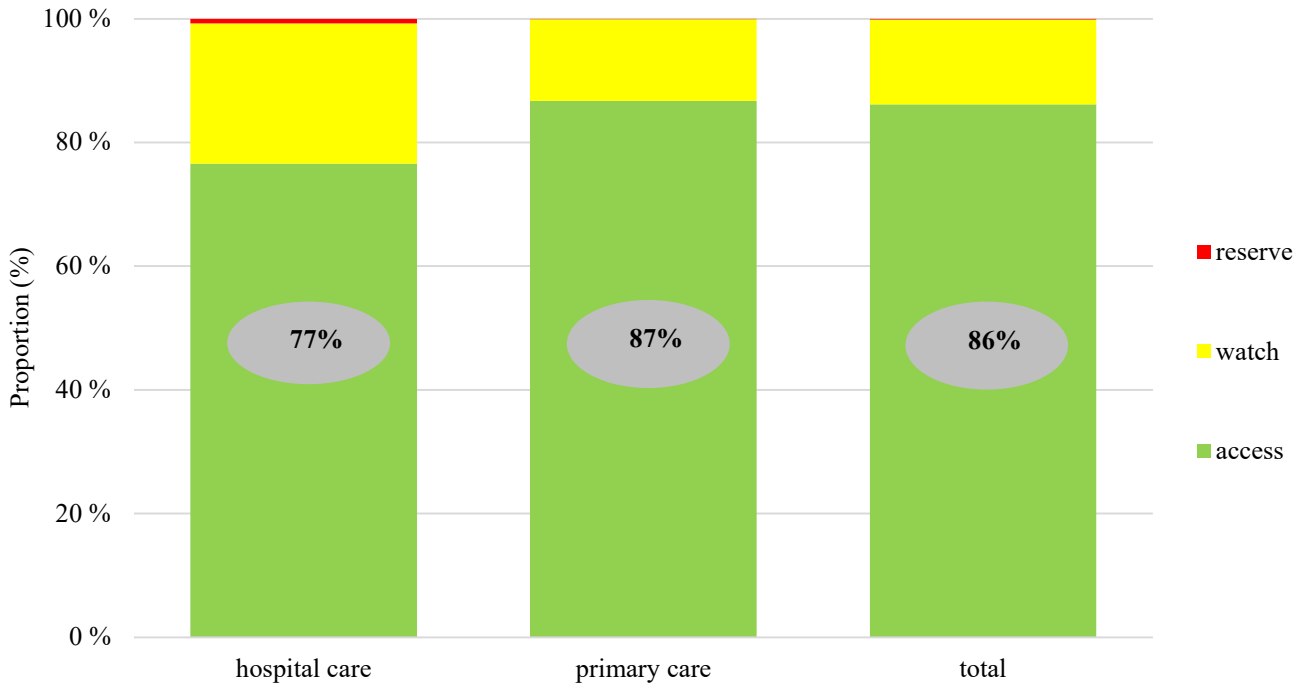

FIGURE 41. Relative consumption as measured in DDDs of Access, Watch and Reserve antibiotics in hospital care, ambulatory care and in total use in Norway 2024. Only antibiotics in ATC group J01 are included. Data source for total use, Norwegian drug wholesales statistics database; for hospitals, the hospital pharmacies drug statistics database; for primary care, the Norwegian Prescribed Drug Registry (NorPD).

Antimycotic use in hospitals and ambulatory care in Norway

The use of antimycotics for systemic use (ATC group J02) has been increasing in ambulatory care in Norway, while the use has decreased in hospitals (Figure 42). In 2018, hospital use of antimycotics represented 18% of total use of antimycotics measured in DDDs while in 2024 the percentage was 14%. Fluconazole is the most commonly used agent in both settings. In July 2013, a warning regarding the use of oral ketoconazole was issued due to increased risk of liver damage. This resulted in decreased use of ketoconazole in ambulatory care (grey part of the bars). Oral ketoconazole is available for endogenous Cushing syndrome, but not much used.

Oral antimycotic formulations represent 93% of total DDDs in 2024, and this share has increased since 2012 (88%). Oral formulations are utilised more often in ambulatory care. Of total DDDs in hospitals, 51% was parenteral use.

It should be noted that nystatin mixture for oral thrush is not included here. Nystatin mixture is mainly used by young children and in 2024, 2.5% of the 0-4-year-olds were prescribed nystatin mixture.

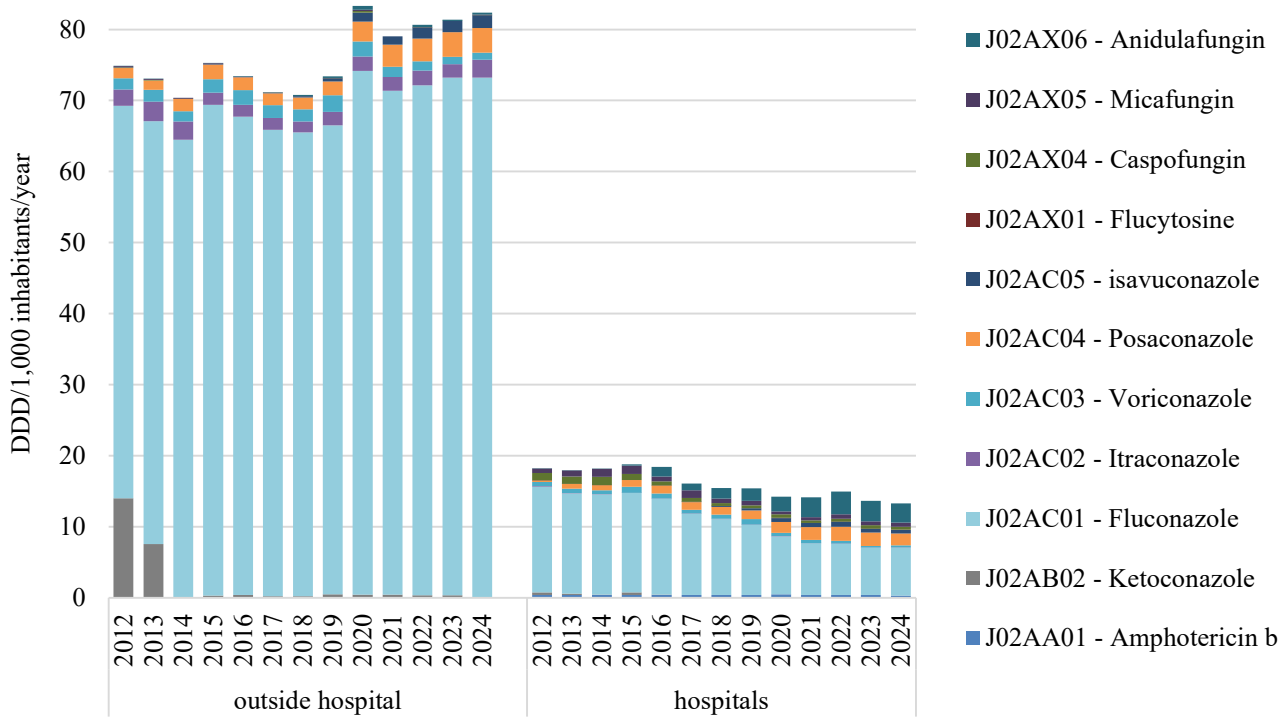

FIGURE 42. Sales of antimycotics for systemic use (ATC group J02) in Norway for ambulatory care and hospitals 2012-2024, measured in DDD/1,000 inhabitants/year.

ANTIMICROBIAL RESISTANCE IN ANIMALS AND FOOD

ANIMAL CLINICAL ISOLATES

Madelaine Norström, Jannice Schau Slettemeås, Marianne Sunde and Anne Margrete Urdahl

The clinical isolates included in NORM-VET 2024 were *Escherichia coli* from broilers and turkey, and *Streptococcus canis* and *Campylobacter upsaliensis* from dogs. Sampling, laboratory methods and data processing are described in Appendix 3.

Escherichia coli from poultry

A total of 272 isolates of *Escherichia coli* from clinical infections in poultry, collected between 2020 and 2024, were susceptibility tested. Of these, 225 were from broilers and 47 from turkey. Some isolates originated from the same flock, either from different animals or from different organs within an animal. The results are presented in Table 7, Figures 43-44, and in the text.

TABLE 7. Antimicrobial resistance in clinical isolates of *Escherichia coli* from broiler (225) and turkey (47) in 2020-2024.

Substance	Animal species	Resistance (%) [95% CI]		Distribution (%) of MIC values (mg/L)*													
				0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256
Tetracycline	Broiler	7.6	[4.5 – 11.8]							78.2	14.2			7.6			
	Turkey	4.3	[0.5 – 14.5]							89.4	6.4			4.3			
Ampicillin	Broiler	16.0	[11.5 – 21.5]							24.4	56.9	2.7		16.0			
	Turkey	12.8	[4.8 – 25.7]							31.9	53.2	2.13		12.8			
Amoxicillin-clavulanic acid	Broiler	0.4	[0.0 – 2.4]								86.7	12.9	0.4				
	Turkey	0.0	[0.0 – 7.6]								85.1	14.9					
Cefalexin	Broiler	0.0	[0.0 – 1.6]								12.9	79.1	7.1	0.9			
	Turkey	0.0	[0.0 – 7.6]								17.0	80.9	2.1				
Cefotaxime	Broiler	0.0	[0.0 – 1.6]				100										
	Turkey	0.0	[0.0 – 7.6]				100										
Meropenem	Broiler	0.0	[0.0 – 1.6		100												
	Turkey	0.0	[0.0 – 7.6]		100												
Trimethoprim-sulfamethoxazole	Broiler	3.1	[1.3 – 6.3]					96.9	0.4			2.7					
	Turkey	2.1	[0.1 – 11.3]					97.9				2.1					
Gentamicin	Broiler	0.4	[0.0 – 2.4]							99.6			0.4				
	Turkey	2.1	[0.1 – 11.3]							97.9	2.1						
Neomycin	Broiler	0.4	[0.0 – 2.4]								98.7	0.9		0.4			
	Turkey	0.0	[0.0 – 7.6]								100						
Enrofloxacin	Broiler	4.4	[2.2 – 8.0]			95.6	1.3	3.1									
	Turkey	0.0	[0.0 – 7.6]			100											
Colistin	Broiler	0.0	[0.0 – 1.6]						100								
	Turkey	0.0	[0.0 – 7.6]						97.9	2.1							
Nitrofurantoin	Broiler	0.4	[0.0 – 2.4]											95.6	4.0	0.4	
	Turkey	0.0	[0.0 – 7.6]											97.9	2.1		

*Bold vertical lines denote epidemiological cut-off values for resistance. CI=confidence interval. White fields denote range of dilutions tested for each antimicrobial agent. MIC values higher than the highest concentration tested are given as the lowest MIC value above the range. Clinical breakpoints are marked in blue vertical lines. In cases where clinical breakpoint is identical to ECOFF, only ECOFF is shown.

RESULTS AND COMMENTS

In total, 73.3% and 83.0% of the isolates from broilers and turkey, respectively, were susceptible to all antimicrobial agents included in the test panel. Among the isolates from broilers 24.4% were resistant to one antimicrobial class, and 2.2% to two antimicrobial classes. Among the isolates from turkey, 14.9% were resistant to one and 2.1% to two antimicrobial classes. Resistance towards ampicillin and tetracycline, was most common as shown in Table 7. None of the *E. coli* isolates displayed resistance to the cephalosporins cefalexin or cefotaxime, nor to the carbapenem meropenem.

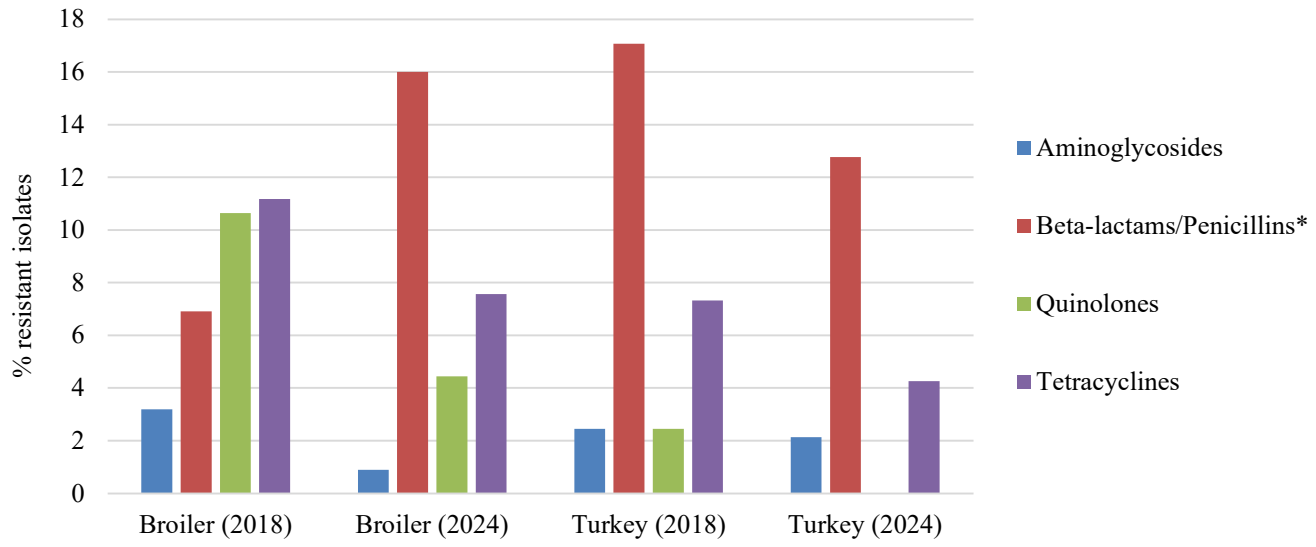

FIGURE 43. Prevalence of resistance to various antimicrobial classes in clinical *Escherichia coli* isolates from broilers (n=188 and n=225, respectively) and turkey (n=41 and n=47, respectively) reported in 2018 (i.e. 2015-2018) and 2024 (i.e. 2020-2024), respectively. *Only ampicillin/amoxicillin. NORM-VET 2024 epidemiological cut-off values were applied.

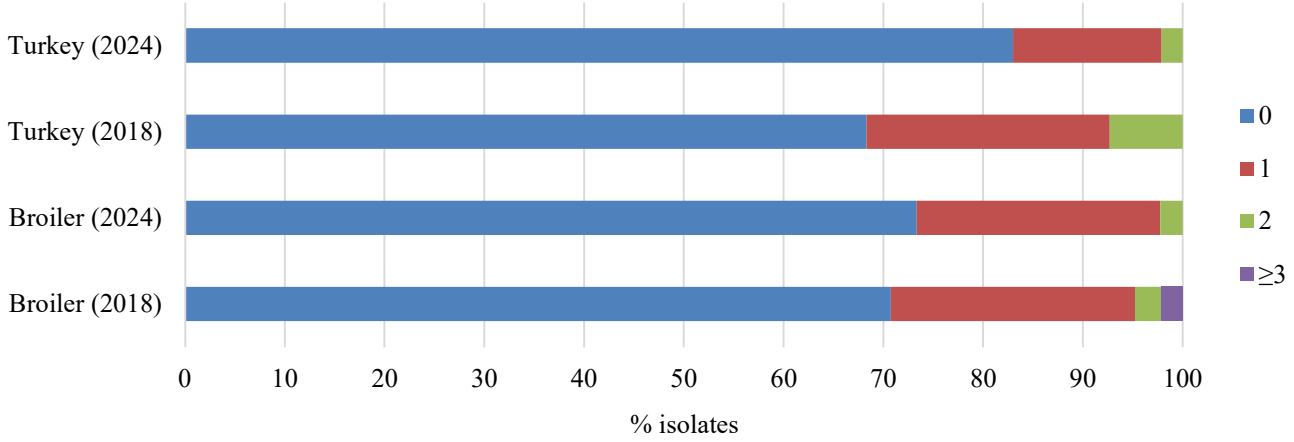

FIGURE 44. Antimicrobial resistance profiles for *Escherichia coli* from clinical infections in broilers and turkey, i.e. 188 and 41 isolates from broilers and turkey, respectively sampled between 2015 and 2018 (NORM-VET 2018) and 225 and 47 isolates from broilers and turkey, respectively between 2020 and 2024. Percentage of isolates susceptible to all (0), resistant to one (1), two (2), or three (3) or more antimicrobial classes are illustrated. NORM-VET 2024 epidemiological cut-off values were applied.

E. coli isolates from clinical submissions of poultry have been sensitivity tested previously, in 2004, 2011 and 2018. The number of isolates tested in 2004 and 2011 was, however, limited. Moreover, there has been changes made in the panel of antimicrobial agents tested for, making comparisons between the years difficult. For instance, only a few of the antimicrobial agents tested in 2018 are included in the 2024 panel (i.e. tetracycline, ampicillin, cefotaxime, meropenem and gentamicin). Among these, there has been an increase in resistance to ampicillin in broilers from 6.9% [95% CI: 3.7-11.5] in 2018, to 16.0% [95% CI: 11.5-21.5] in 2024. This is also indicated in Figure 43 showing the prevalence of resistance to various antimicrobial classes. This is, however, not a statistically significant change and further monitoring is needed to see if these are true increasing trends. As shown in Figure 44, the percent of broiler isolates being fully susceptible has been relatively stable around 70% in both the 2018 and 2024 reports. For turkey, Figure 44 indicates that there has been an increase in isolates fully susceptible. However, this increase is not statistically significant, and further monitoring is necessary to see if this is a true trend.

Epidemiological cut-off values were used for the classification of resistance in these clinical *E. coli* isolates, facilitating comparison to surveillance results for indicator *E. coli*. The indicator *E. coli* was, however, tested with the same panel as the 2018 clinical isolates, thereby only resistance to tetracycline, ampicillin, cefotaxime, meropenem and gentamicin are directly comparable. There was higher resistance to ampicillin in the clinical *E. coli* isolates from broilers than in the indicator *E. coli* ($p<0.007$). Also, there was a higher proportion of overall antimicrobial resistance in these clinical *E. coli* isolates compared to antimicrobial resistance in indicator *E. coli* from broilers as presented in Figures 45-46, page 58.

Clinical breakpoints are shown in dotted blue lines in Table 7. However, these clinical breakpoints are defined in order to indicate if treatment of a specific pathogen is likely to succeed or not, and factors like dosage, formulations and host species will affect the clinical result.

Streptococcus canis from dogs

A total of 141 *Streptococcus canis* isolates from infections in dogs were included. Of these, 80 were mainly from local ear infections, while the remaining 64 isolates were from infections in skin, urine, inner organs, etc. The isolates were collected through the years 2020-2024. The results are presented in Tables 8-9, and in the text.

TABLE 8. Antimicrobial resistance in *Streptococcus canis* from infections in skin, urine, inner organ etc. in dogs (n=61) in 2020-2024.

Substance	Resistance (%) [95% CI]		Distribution (%) of MIC values (mg/L)*													
			0.015	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128
Tetracycline	98.4	[91.2 – 100]						1.6		14.8	83.6					
Benzylpenicillin	0.0	[0.0-5.9]	95.1	4.9												
Cefalexin	ND	ND						96.7	3.3							
Trimethoprim/sulfamethoxazole	0.0	[0.0 – 5.9]				91.8	6.6	1.6								
Erythromycin	13.1	[5.8– 24.2]				85.3	1.6	1.6		11.5						
Clindamycin	11.5	[4.7– 22.2]				78.7	8.2	1.6		11.5						
Enrofloxacin	NA	NA						19.7	80.3							
Nitrofurantoin	0.0	[0.0 – 5.9]										72.1	27.9			

*Bold vertical lines denote epidemiological cut-off values for resistance. ND = not defined. NA= Not applicable. CI = confidence interval. White fields denote range of dilutions tested for each antimicrobial agent. MIC values higher than the highest concentration tested are given as the lowest MIC value above the range. Clinical breakpoints are marked in blue vertical lines. In cases where clinical breakpoint is identical to ECOFF, only ECOFF is shown. ECOFFs for group G streptococci used for tetracycline, benzylpenicillin and clindamycin, breakpoint for *S. agalactiae* used for nitrofurantoin.

TABLE 9. Antimicrobial resistance in *Streptococcus canis* mainly from local ear infections in dogs (n=80) in 2020-2024.

Substance	Resistance (%) [95% CI]		Distribution (%) of MIC values (mg/L)*													
			0.015	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128
Tetracycline	97.5	[91.3 – 99.7]						1.3	1.3	22.5	48.8	26.3				
Chloramphenicol	0.0	[0.0 – 4.5]								6.3	90.0	3.8				
Florfenicol	0.0	[0.0 – 4.5]							22.5	75.0	2.5					
Cefotaxime	ND	ND				93.8	2.5	3.8								
Enrofloxacin	1.3	[0.0 – 6.8]					1.3	28.8	61.3	7.5	1.3					

*Bold vertical lines denote epidemiological cut-off values for resistance. ND = not defined. CI=confidence interval. White fields denote range of dilutions tested for each antimicrobial agent. MIC values higher than the highest concentration tested are given as the lowest MIC value above the range. Clinical breakpoints are marked in blue vertical lines. In cases where clinical breakpoint is identical to ECOFF, only ECOFF is shown. ECOFF for group G streptococci used for tetracycline.

RESULTS AND COMMENTS

All the isolates were susceptible to benzylpenicillin. Though, the majority of the isolates seem to have reduced susceptibility to tetracycline, this high proportion of tetracycline resistance should be interpreted with caution as the breakpoint probably is suboptimal for *S. canis*. Currently there is a lack of species-specific breakpoints for the species within the *Streptococcus* groups A, B, C and G.

In total, eight (11.5%) of the isolates were resistant to clindamycin. Of these, six had growth in the well containing erythromycin/clindamycin (EM/CM) 1/0.5 to detect inducible resistance (data not shown in Table 8). One clindamycin susceptible isolate had growth in the EM/CM well and should be reported as resistant to clindamycin.

Comparison to previous results, i.e. to results for *S. canis* from the NORM-VET 2019 report is difficult due to differences in the panels used. However, for those substances included in both years, it seems to be relatively stable with no large changes in resistance.

At present there are very few specific ECOFFs established for *S. canis*, and clinical breakpoints have been used where available. Where the ECOFF may indicate emerging resistance in the bacterial populations, clinical breakpoints, shown in dotted blue lines in the tables, are defined to indicate if treatment of a specific pathogen is likely to succeed or not. Moreover, factors like dosage and formulations will affect the clinical result. Additional testing could be applied to assess whether an isolate is clinically resistant or not, but this was beyond the scope of the current monitoring.

Campylobacter upsaliensis from dogs

A total of 75 *Campylobacter upsaliensis* isolates from infections in dogs were included. The isolates were collected through the years 2018-2024. The results are presented in Table 10, and in the text.

TABLE 10. Antimicrobial resistance in *Campylobacter upsaliensis* from infections in dogs (n=75) in 2018-2024.

Substance	Resistance (%) [95% CI]		Distribution (%) of MIC values (mg/L)*													
			0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	512	≥1024
Tetracycline	0.0	[0.0 – 4.8]				98.7		1.3									
Chloramphenicol	0.0	[0.0 – 4.8]						74.7	25.3								
Ertapenem	0.0	[0.0 – 4.8]		100													
Erythromycin	0.0	[0.0 – 4.8]					96.0	4.0									
Gentamicin	1.3	[0.0 – 7.2]			85.3	13.3				1.3							
Ciprofloxacin	6.7	[2.2 – 14.9]		86.7	6.7		2.7	1.3	1.3		1.3						

*Blue vertical lines denote clinical breakpoints. CI=confidence interval. White fields show range of dilutions tested for each antimicrobial agent. MIC values higher than the highest concentration tested are given as the lowest MIC value above the range. MIC values equal to or lower than the lowest concentration tested are given as the lowest concentration tested.

RESULTS AND COMMENTS

In total, 94.5% of the isolates were susceptible to all antimicrobial agents included in the test panel, 4.1% were resistant to one antimicrobial class, and 1.4% to two antimicrobial classes. Resistance to ciprofloxacin was most commonly detected. This is the first time *Campylobacter upsaliensis* has been included in NORM-VET.

At present there are no specific ECOFFs established for *C. upsaliensis*, and therefore clinical breakpoints have been used. Where the ECOFF may indicate emerging resistance in the bacterial populations, clinical breakpoints, shown in dotted blue lines in Table 10, are defined to indicate if treatment of a specific pathogen is likely to succeed or not. Moreover, factors like dosage and formulations will affect the clinical result. Additional testing could be applied to assess whether an isolate is clinically resistant or not, but this was beyond the scope of the current monitoring.

Antimicrobial susceptibility testing of animal clinical isolates by zone diameter – a pilot project

The Norwegian Veterinary Institute retrieves samples from sick animals for bacteriological diagnostic purposes. At the laboratory such clinical isolates are susceptibility tested by disc diffusion giving zone diameter. In the internal Laboratory Information Management System (LIMS), susceptibility testing of clinical bacterial isolates is normally reported as sensitive (S), susceptible with increased exposure (I) or resistant (R) for a selection of antimicrobial substances considered as clinically relevant. However, for the purpose of surveillance, the distribution of the zone diameter as well the results for several other antimicrobial substances are of interest. Some of these substances are included in the test panel, though not reported in the internal LIMS. To accommodate this, we used BIOMIC ® V3 (Giles Scientific Inc, Santa Barbara, California, USA) for reading zone diameters and semi-automated transfer of these into the internal LIMS. The accurate zone diameters will be used for reporting data to international surveillance initiatives such as EARS-Vet (https://eu-jamrai.eu/surveillance/) that will summarise data from many European countries using epidemiological cut-off values to determine resistance. In the following tables, however, EUCAST clinical breakpoints (CBs) are given with corresponding classification of isolates as S, I or R.

Escherichia coli

A total of 15 *E. coli* isolates from infections in pigs (n=4) and dogs (n=11) in 2022-2023 were included. The dog isolates were mainly from urinary infections (n=9), while the pig isolates were from gastrointestinal infections.

TABLE 11. Antimicrobial resistance in *Escherichia coli* from infections in pigs (n=4) and dogs (n=11).

	Clinical breakpoints (mm)		No. of isolates		
Substance	S	R	S	I	R
Tetracycline*	≥ 19	< 19	12	-	3
Ampicillin	≥ 14	< 14	10	-	5
Amoxicillin-clavulanic acid	≥ 16	< 16	14	-	1
Cefotaxime	≥ 20	< 17	15	0	0
Meropenem	≥ 22	< 16	15	0	0
Trimethoprim	≥ 15	< 15	13	0	2
Trimethoprim-sulfamethoxazole	≥ 14	< 11	14	0	1
Neomycin*	≥ 13	< 12	15	0	0
Ciprofloxacin	≥ 25	< 22	14	0	1
Nalidixic acid*	≥ 16	< 16	13	-	2
Nitrofurantoin	≥ 11	< 11	15	-	0

*In house breakpoints, the Norwegian Veterinary Institute.

Staphylococcus pseudintermedius

The *S. pseudintermedius* isolates were all from dogs sampled in 2022 and 2023, mainly from ear or skin infections, though a few from urine infections. Altogether this comprised 64 isolates.

TABLE 12. Antimicrobial resistance in *Staphylococcus pseudintermedius* (n=64) from infections in dogs 2022-2023.

	Clinical breakpoints (mm)		No. of isolates		
Substance	S	R	S	I	R
Tetracycline	≥ 22	< 22	48	-	16
Florfenicol	≥ 25	< 25	63	0	1
Benzylpenicillin**	≥ 26	< 26	9	-	55
Oxacillin	≥ 20	< 20	64	-	0
Trimethoprim-sulfamethoxazole	≥ 17	< 14	63	0	1
Erythromycin	≥ 21	< 21	50	-	14
Clindamycin	≥ 22	< 22	51	-	13
Gentamicin	≥ 18	< 18	63	-	1
Neomycin	≥ 19	< 19	51	-	13
Ciprofloxacin*	≥ 21	< 21	64	-	0
Fusidic acid	≥ 24	< 24	53	-	11

*In house breakpoints, the Norwegian Veterinary Institute. **Resistance is inferred from results from beta-lactamase test and disc diffusion test.

Streptococcus canis

The *S. canis* isolates were all from skin, ear, urinary or respiratory infections in dogs sampled in 2022-2025, altogether 52 isolates. The table below comprises susceptibility testing result of these, though for some substances less than 52 isolates have been tested.

TABLE 13. Antimicrobial resistance in Streptococcus canis (n=52) from infections in dogs 2022-2025.

	Clinical breakpoints (mm)		No. of isolates		
Substance	S	R	S	I	R
Tetracycline	≥ 23	< 23	8	-	44
Benzylpenicillin	≥ 23	< 23	44	-	2
Trimethoprim- sulfamethoxazole	≥ 18	< 15	46	0	0
Erythromycin	≥ 21	< 21	49	-	3
Clindamycin	≥ 17	< 17	45	-	7

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Antimicrobial susceptibility testing in routine mastitis diagnostics in Norway 2024

Background

The Norwegian dairy co-operative TINE SA operates the TINE Mastitis Laboratory in Molde. The laboratory currently performs all bacteriological analyses for mastitis control in Norway and analysed approximately 65,000 quarter milk samples from dairy cows in 2024. The laboratory performs antimicrobial susceptibility testing of selected isolates, an important contribution to the antimicrobial resistance surveillance in milk-producing animals. Results from the mastitis diagnostics are reported to the Norwegian Dairy Herd Recording System (NDHRS) (1, 2). Statistics from the mastitis diagnostics of dairy cows are published yearly in the TINE udder health report (3). *Staphylococcus aureus* is the leading cause of mastitis of both dairy cows and goats in Norway (3, 4). Since benzylpenicillin procaine is the first choice for treatment of mastitis in Norwegian dairy cows (5), testing for beta-lactamase production of *Staphylococcus aureus* is the primary focus of the antimicrobial susceptibility testing in the mastitis diagnostics.

Methods

Results from susceptibility testing of isolates from dairy cows in 2024 were retrieved from the NDHRS. *S. aureus* isolates are routinely tested for beta-lactamase production by the clover leaf assay (6). Penicillin resistant *S. aureus* and *Enterobacteriaceae* from clinical mastitis are tested by disc diffusion for amoxicillin-clavulanic acid, ampicillin, cefoxitin (*S. aureus*) and trimethoprim-sulfamethoxazole (*Enterobacteriaceae*). Other bacterial species from clinical mastitis may also be tested. Streptococci are considered sensitive to penicillin (7) and are therefore not routinely tested.

A total of 6,728 isolates from cow milk were tested in 2024. The tested isolates were *S. aureus* (n=5,608, 83%), *Enterobacteriaceae* (n=780, 12%), non-aureus staphylococci (n=290, 4%) and other bacteria (n=50, 1%). The isolates were from 4,698 cows from 1,982 farms. The results for *S. aureus* and *E. coli* are presented here.

Results and discussion

Among the *S. aureus* from cows, 126 of 5,608 (2.2%) isolates were resistant by the clover leaf test, meaning that 97.8% of *S. aureus* from bovine mastitis in Norway were sensitive to penicillin. The proportion of penicillin resistant *S. aureus* in milk samples from Norwegian dairy cows has been low the last 20 years, ranging from 1.5-3.5% (2). Results from disk diffusion for amoxicillin-clavulanic acid and ampicillin were available for 121 *S. aureus*, whereof two and 35 isolates were resistant, respectively. Methicillin resistant *S. aureus*, i.e. MRSA, was detected in a milk sample from one cow in 2024.

Table 14 shows the results of the susceptibility testing for amoxicillin-clavulanic acid and trimethoprim-sulfamethoxazole of *E. coli* in 2024. A majority of the isolates were susceptible to trimethoprim-sulfamethoxazole. In the routine mastitis diagnostics, susceptible *E. coli* are reported as "susceptible with increased exposure (I)" to amoxicillin-clavulanic acid and ampicillin because the response to treatment is expected to be low. According to the Norwegian therapy guidelines (5), cases of *E. coli* clinical mastitis do not benefit from antimicrobial treatment and should be treated with supportive therapy only.

TABLE 14. Susceptibility testing of *Escherichia coli* from mastitis in Norwegian dairy cows in 2024. Number of isolates (%) is given for each category susceptible (S), susceptible with increased exposure (I) and resistant (R).

	Amoxicillin-clavulanic acid (n=755)		Trimethoprim-sulfamethoxazole (n=755)			Ampicillin (n = 786)	
Species	I	R	S	I	R	I	R
E. coli	594 (79%)	161 (21%)	681 (90%)	4 (0.5%)	70 (9%)	649 (83%)	137 (17%)

In conclusion, *S. aureus* remains the most common cause of mastitis in Norwegian dairy goats and cows. The level of penicillin resistance of *S. aureus* from mastitis samples is very low in dairy cows (2.3%) and slightly higher (8.5%) in dairy goats. *E. coli* is an important cause of severe clinical mastitis in Norway but does not benefit from antimicrobials and could, if identified at the time of clinical examination, be treated with supportive therapy.

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INDICATOR BACTERIA FROM ANIMALS

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The prevalence of antimicrobial resistance among certain bacteria of the normal microbiota can be used as an indicator of the selective pressure from use of antimicrobial agents. These bacteria may form a reservoir of transferrable resistance genes enabling the spread of antimicrobial resistance to other bacteria, including those responsible for infections in animals or humans. Thus, resistance monitoring of indicator bacteria from the microbiota of healthy animals is of importance in a One Health perspective, and to detect trends and evaluate effects of interventions.

Escherichia coli, *Enterococcus faecalis* and *Enterococcus faecium* are used as indicator bacteria for antimicrobial resistance surveillance in animals. In addition, *Staphylococcus* spp. is included as an indicator in horses and pets.

In 2024, samples from animals included caecal samples from broiler flocks and faecal swabs from horses for isolation of indicator bacteria. In addition, selective screening methods for detection of some notifiable resistance bacteria were implemented on the same sample material (see notifiable resistance chapter, page 67).

Only data retrieved following the requirements set in decision 2013/652/EU and 2020/1729/EU are shown for broiler. For previous data, please see the respective annual reports. Sampling, laboratory methods and data processing are described in Appendix 3.

PRODUCTION ANIMALS

Escherichia coli from broilers

Caecal samples from 336 broiler flocks were examined and *E. coli* isolates were obtained from all the samples (100%). One isolate per positive sample was susceptibility tested. The results are presented in the text, in Table 15 and Figures 45-46.

TABLE 15. Antimicrobial resistance in *Escherichia coli* isolates from caecal samples of broilers (n=336) in 2024.

Substance	Resistance (%) [95% CI]		Distribution (%) of MIC values (mg/L)*															
			0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	≥512
Tetracycline	2.7	[1.2 – 5.0]								83.6	13.4	0.3			2.7			
Tigecycline	0.0	[0.0 – 1.0]					99.7	0.3										
Chloramphenicol	0.0	[0.0 – 1.0]										95.8	4.2					
Ampicillin	7.4	[4.9 – 10.8]							1.8	35.1	51.2	4.5	1.5	0.6	5.4			
Cefotaxime	0.0	[0.0 – 1.0]					100											
Ceftazidime	0.0	[0.0 – 1.0]					97.6	2.4										
Meropenem	0.0	[0.0 – 1.0]		99.7	0.3													
Trimethoprim	1.2	[0.3 – 3.0]					60.1	37.8	0.9					1.2				
Sulfamethoxazole	5.1	[3.0 – 8.0]										34.5	42.3	15.8	2.4		5.1	
Azithromycin	0.0	[0.0 – 1.0]								11.3	72.3	16.4						
Gentamicin	1.5	[0.5 – 3.4]						72.3	25	1.2	0.3		0.6	0.6				
Amikacin	0.0	[0.0 – 1.0]									96.1	3.9						
Ciprofloxacin	5.1	[3.0 – 8.0]	84.5	10.1	0.3	0.3	1.2	2.1	1.5									
Nalidixic acid	4.7	[2.8 – 7.6]									93.8	1.5	0.9		0.6	3.3		
Colistin	0.0	[0.0 – 1.0]							99.7	0.3								

*Bold vertical lines denote epidemiological cut-off values for resistance. CI = confidence interval. White fields show range of dilutions tested for each antimicrobial agent. MIC values higher than the highest concentration tested are given as the lowest MIC value above the range. MIC values equal to or lower than the lowest concentration tested are given as the lowest concentration tested.

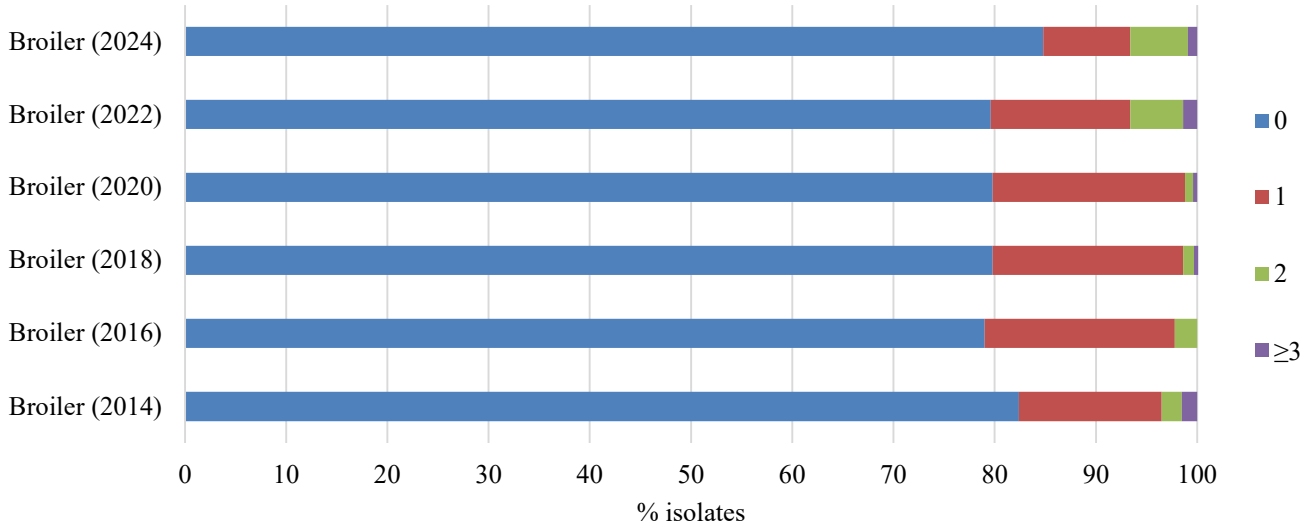

FIGURE 45. Antimicrobial resistance profile for *Escherichia coli* from caecal samples from broiler flocks in 2014-2024. Percentage of isolates susceptible to all (0) or resistant to one (1), two (2), and three or more (≥3) antimicrobial classes are illustrated. The epidemiological cut-off values used in NORM-VET 2024 were applied.

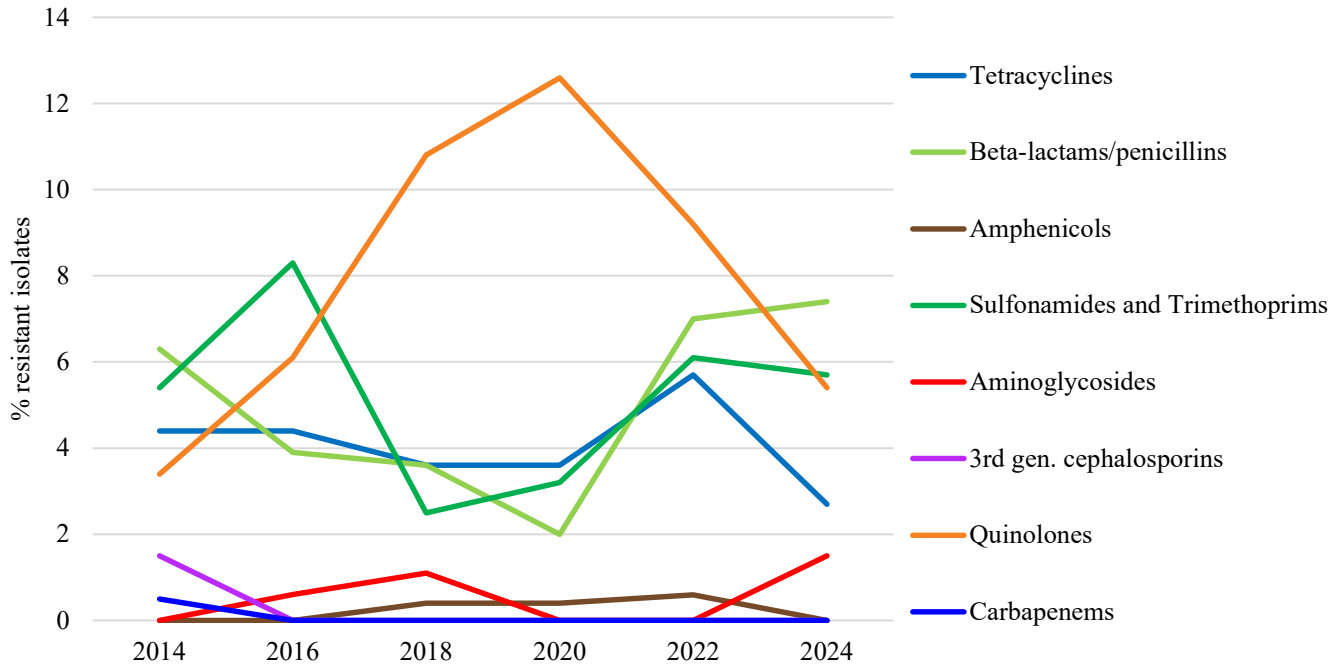

FIGURE 46. Prevalence of resistance to various antimicrobial agents in *Escherichia coli* from caecal samples from broilers collected in 2014-2024. The epidemiological cut-off values used in NORM-VET 2024 were applied.

RESULTS AND COMMENTS

BROILER

The 2024 data showed that 84.8% of the *E. coli* isolates from broiler caecal samples were susceptible to all antimicrobial agents included. Altogether, 8.6% of the isolates were resistant to one antimicrobial class (predominantly beta-lactams/penicillins), 5.7% to two and 0.9% to three or more antimicrobial classes (Figure 45). In total, 15.2% of the isolates were resistant to at least one antimicrobial, indicating a moderate occurrence of resistance in broilers according to the EFSA classification described in Appendix 6. Resistance to ampicillin was the most frequently identified resistance determinants, followed by resistance to ciprofloxacin and sulfamethoxazole.

As shown in Figure 45, the percent of isolates being fully susceptible has been relatively stable around 80% over the years 2014-2024. The antimicrobial classes for which the isolates showed resistance have changed over these years (Figure 46). There was an increase in resistance to quinolones (i.e. ciprofloxacin and/or nalidixic acid) from 2014-2020 (p=0.002) (NORM-VET 2021). In 2022, however, a decrease in quinolone resistance was registered, a decrease that has continued with 5.4% [95% CI: 3.2-8.3] of the isolates being resistant to quinolones in 2024. This is a significant decrease compared to 2020 ($p = 0.003$).

None of the *E. coli* isolates from broilers displayed resistance to the extended spectrum cephalosporins (ESC) cefotaxime or ceftazidime [95% CI: 0.0-1.0]. This is in concordance with the results from previous years. In addition, a selective method was used to investigate the occurrence of ESC resistant *E. coli* in the same broiler caecal sample material (see notifiable resistance chapter, page 67).

The occurrence of resistance among *E. coli* varies markedly between countries reporting to EFSA with the Nordic countries having the lowest resistance rates (EFSA and ECDC European Union Summary Report 2022-2023). This favorable situation in Norway is probably due to the very limited use of antibiotics in Norwegian broiler production (Figure 7, page 21 on usage in broiler production).

Enterococcus spp. from broilers

Caecal samples from 336 broiler flocks were investigated. *E. faecalis* was obtained from 100 (29.8%) and *E. faecium* from 312 (92.9%) of the broiler samples. All these *E. faecalis* and *E. faecium* isolates were susceptibility tested. The results are presented in Tables 16-17, Figures 47-50, and in the text.

TABLE 16. Antimicrobial resistance in *Enterococcus faecalis* from caecal samples from broiler flocks (n=100) in 2024.

Substance	Resistance (%) [95% CI]		Distribution (%) of MIC values (mg/L)*														
			0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	≥512
Tetracycline	41.0	[31.2 – 51.3]						58.0		1.0		1.0	21.0	11.0	8.0		
Tigecycline	0.0	[0.0 – 3.6]		37.0	55.0	8.0											
Chloramphenicol	0.0	[0.0 – 3.6]								33.0	67.0						
Ampicillin	0.0	[0.0 – 3.6]					7.0	53.0	40.0								
Erythromycin	5.0	[1.6 – 11.3]						45.0	49.0	1.0	1.0		1.0	1.0		2.0	
Quinupristin-dalfopristin	0.0	[0.0 – 3.6]							2.0	7.0	36.0	55.0					
Gentamicin	0.0	[0.0 – 3.6]									77.0	23.0					
Ciprofloxacin	0.0	[0.0 – 3.6]				2.0	25.0	64.0	9.0								
Vancomycin	0.0	[0.0 – 3.6]						61.0	39.0								
Teicoplanin	0.0	[0.0 – 3.6]					100										
Linezolid	0.0	[0.0 – 3.6]						17.0	83.0								
Daptomycin	0.0	[0.0 – 3.6]						52.0	47.0	1.0							

*Bold vertical lines denote microbiological cut-off values for resistance. CI=confidence interval. White fields show range of dilutions tested for each antimicrobial agent. MIC values higher than the highest concentration tested are given as the lowest MIC-value above the range. MIC values equal to or lower than the lowest concentration tested are given as the lowest concentration tested.

TABLE 17. Antimicrobial resistance in *Enterococcus faecium* from caecal samples from broiler (n=312) flocks in 2024.

Substance	Resistance (%) [95% CI]		Distribution (%) of MIC values (mg/L)*														
			0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	≥512
Tetracycline	7.7	[5.0 – 11.2]						91.0	1.3		0.6	1.0	0.6	4.8	0.6		
Tigecycline	0.0	[0.0 – 1.2]	25.0	52.9	22.1												
Chloramphenicol	0.0	[0.0 – 1.2]								44.9	55.1						
Ampicillin	0.6	[0.1 – 2.3]					32.4	28.9	31.1	7.1	0.6						
Erythromycin	4.5	[2.5 – 7.4]						75.3	19.2	1.0	3.9	0.6					
Quinupristin-dalfopristin	36.5	[31.2 – 42.2]					4.8	21.5	37.2	35.9	0.6						
Gentamicin	0.0	[0.0 – 1.2]									94.9	4.5	0.6				
Ciprofloxacin	0.0	[0.0 – 1.2]				1.6	2.6	16.0	37.8	35.6	6.4						
Vancomycin	0.0	[0.0 – 1.2]						90.1	9.3	0.6							
Teicoplanin	0.0	[0.0 – 1.2]					99.4	0.6									
Linezolid	0.0	[0.0 – 1.2]						6.4	92.3	1.3							
Daptomycin	0.0	[0.0 – 1.2]				0.6	3.2	15.7	49.0	29.8	1.6						

*Bold vertical lines denote microbiological cut-off values for resistance. CI=confidence interval. White fields show range of dilutions tested for each antimicrobial agent. MIC values higher than the highest concentration tested are given as the lowest MIC-value above the range. MIC values equal to or lower than the lowest concentration tested are given as the lowest concentration tested.

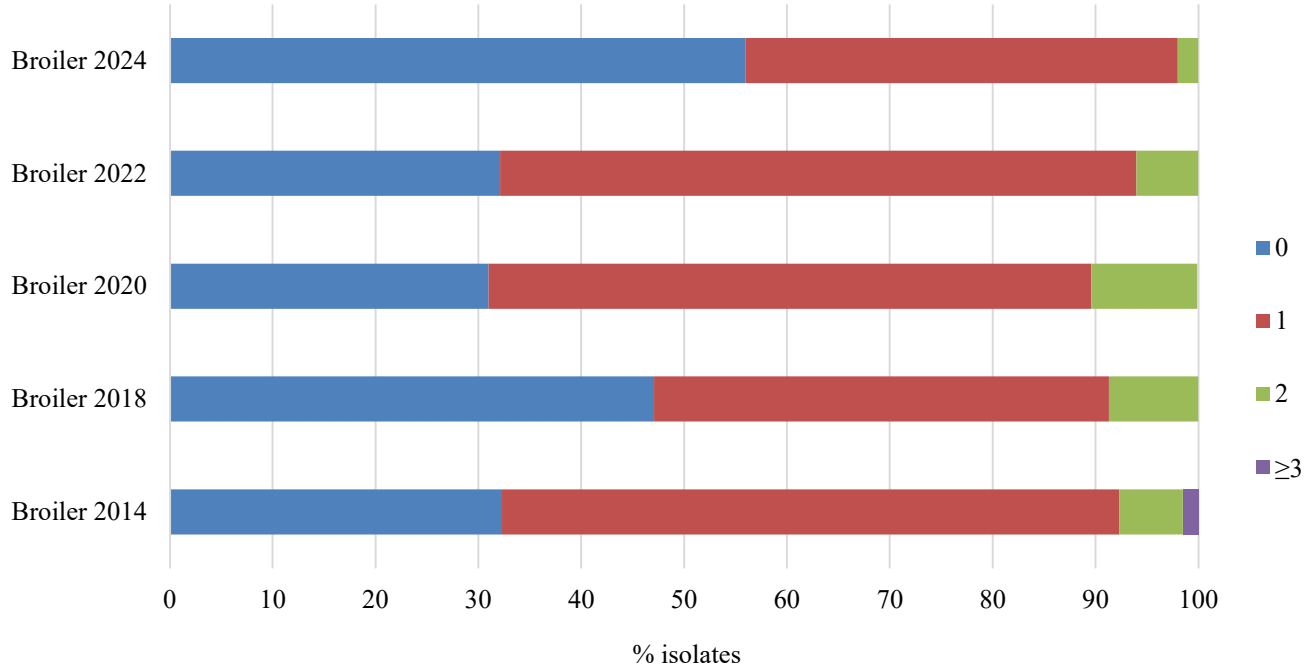

FIGURE 47. Antimicrobial resistance profile for *Enterococcus faecalis* caecal isolates from broilers in 2014-2024. Proportions of isolates (%) susceptible to all (blue), resistant to one (red), two (green) or three or more (purple) antimicrobial classes are illustrated. The epidemiological cut-off values used in NORM-VET 2024 were applied.

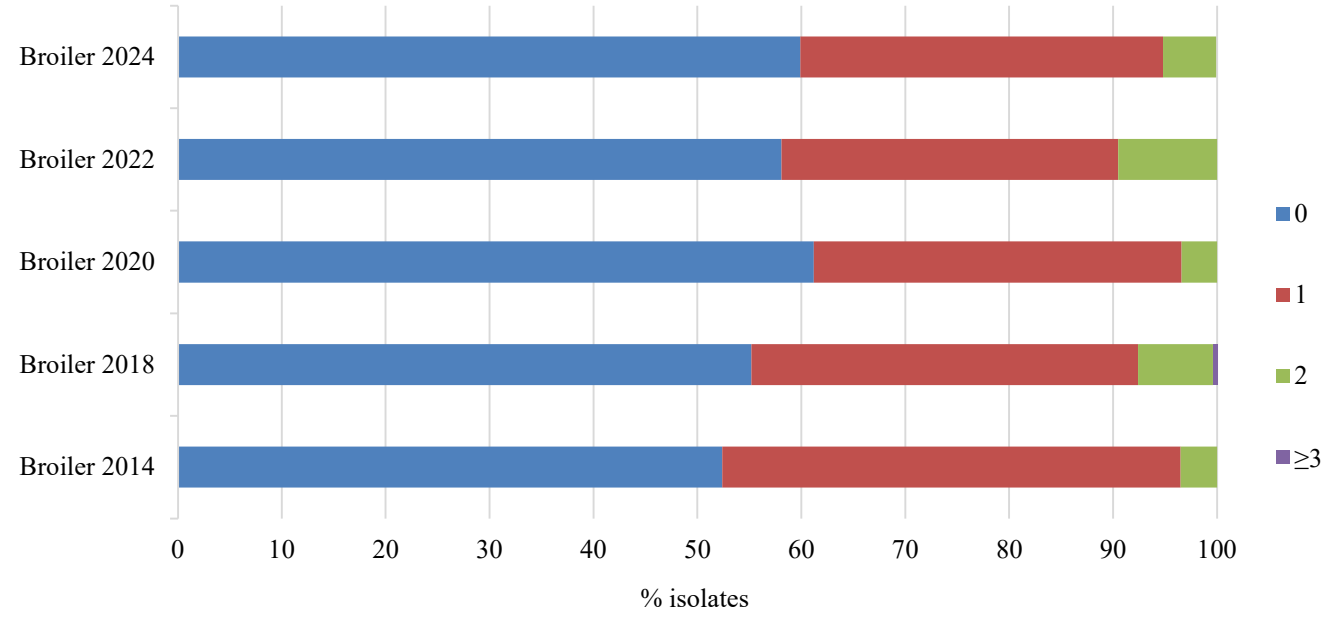

FIGURE 48. Antimicrobial resistance profile for *Enterococcus faecium* caecal isolates from broilers in 2014-2024. Proportions of isolates (%) susceptible to all (blue), resistant to one (red), two (green) or three or more (purple) antimicrobial classes are illustrated. The epidemiological cut-off values used in NORM-VET 2024 were applied.

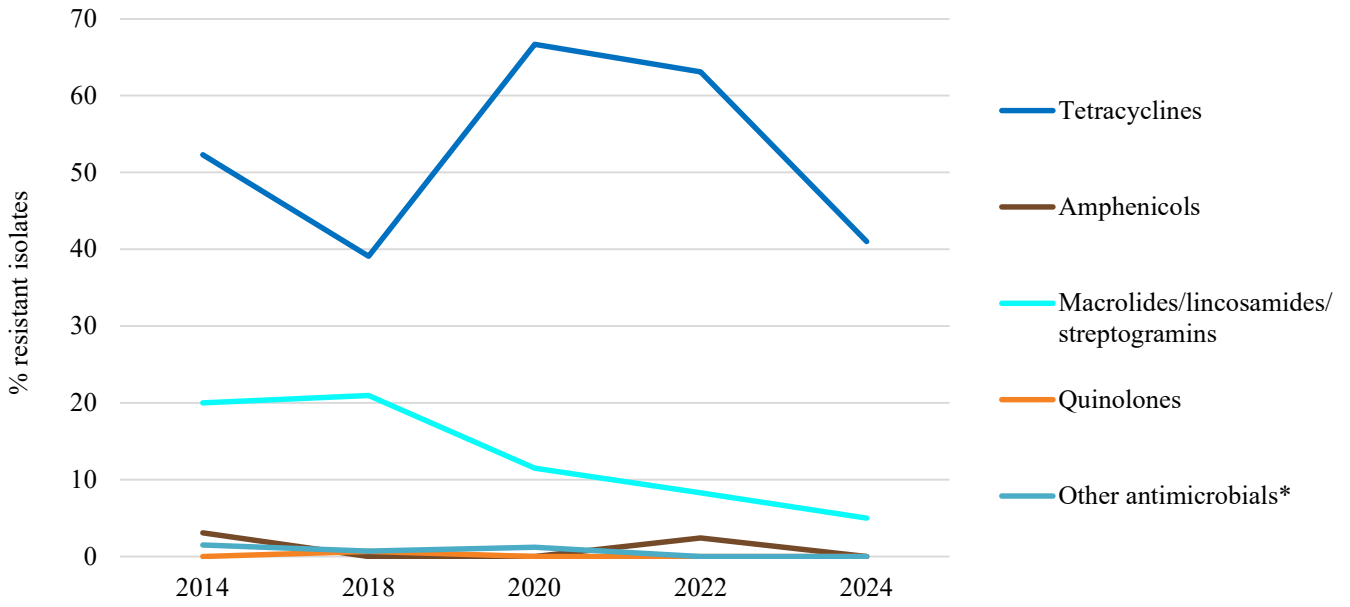

FIGURE 49. Prevalence of resistance to various antimicrobial classes in *Enterococcus faecalis* isolates from caecal samples from broilers in 2014-2024. The epidemiological cut-off values used in NORM-VET 2024 were applied. *i.e. daptomycin.

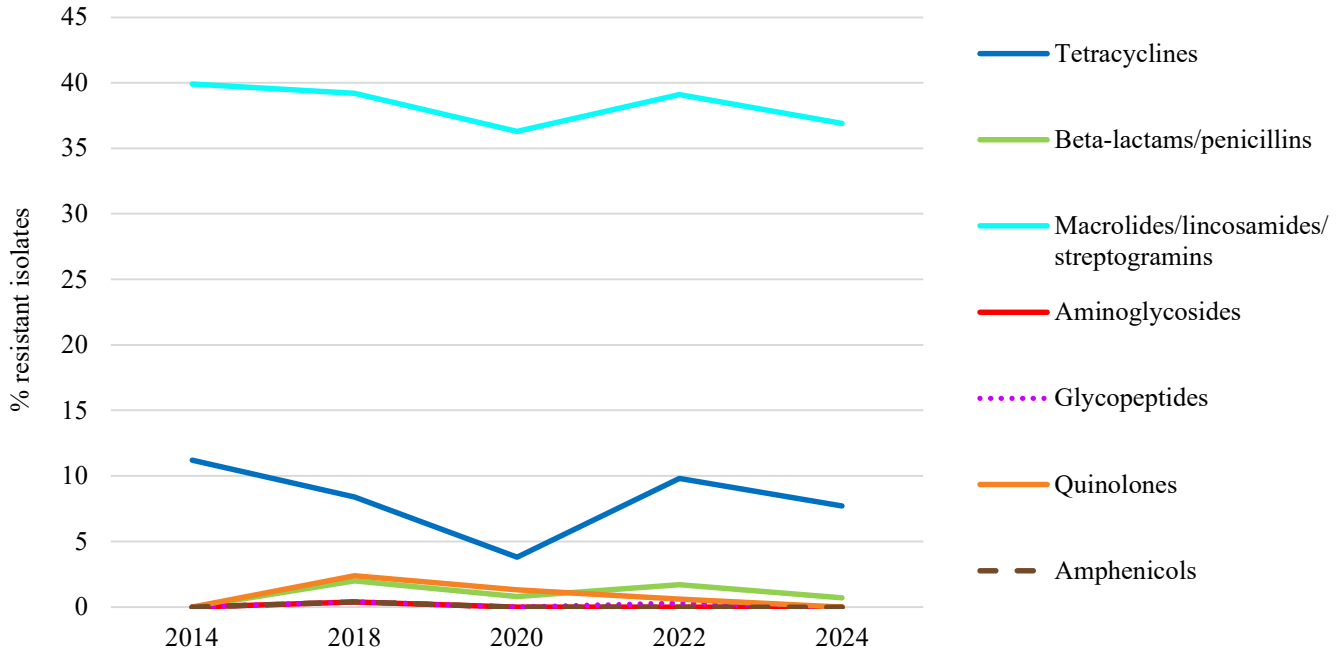

FIGURE 50. Prevalence of resistance to various antimicrobial classes in *Enterococcus faecium* isolates from caecal samples from broilers 2014-2024. The epidemiological cut-off values used in NORM-VET 2024 were applied.

RESULTS AND COMMENTS

The 2024 data showed that 56.0% of the *E. faecalis* and 59.9% of the *E. faecium* isolates from broiler caecal samples were susceptible to all antimicrobial agents included in the test panel (Figures 47-48). In total, 44.0% of the *E. faecalis* isolates and 30.1% of the *E. faecium* isolates were resistant to at least one antimicrobial agent, indicating a high occurrence of resistance according to the EFSA classification described in Appendix 6.

E. faecalis: Resistance to tetracycline was the most frequently identified resistance determinant, followed by resistance to the macrolide erythromycin. Altogether, 42.0% of the isolates were resistant to one and 2.0% to two antimicrobial classes (Figure 47). As shown in Figure 47, the number of *E. faecalis* isolates being fully susceptible was down to around 30% in 2020 and 2022, while around 50% in 2018 and 56% in 2024. This drop in fully susceptible isolates seen in 2020 and 2022 was mainly due to an increase in the occurrence of tetracycline resistance as shown in Figure 49. The occurrence increased from 36.7% [95% CI: 28.7-45.3] in 2018, to 66.7% [95% CI: 55.7-76.4] in 2020 and 63.1% [95% CI: 51.9-73.4] in 2022. The results from 2024 show that the occurrence of tetracycline resistance has now dropped down back to 2018 levels with 41.0% [95% CI: 31.2-51.3]. This rather high prevalence of tetracycline resistance among *E. faecalis* is surprising, as there is insignificant use of oxytetracycline for clinical purposes in Norwegian broiler production. Further monitoring is needed to follow this situation in the years to come.

E. faecium: Resistance to quinupristin-dalfopristin was the most frequently identified resistance determinant, followed by resistance to tetracycline and erythromycin (Figure 50). Altogether, 34.9% of the *E. faecium* isolates were resistant to one and 5.1% to two antimicrobial classes (Figure 48). The number of *E. faecium* isolates being fully susceptible has been relatively stable around 55-65% over the years 2014-2024 (Figure 48).

Reduced susceptibility to linezolid or vancomycin was not observed in any of the *E. faecalis*, nor in any of the *E. faecium* isolates. This is in concordance with the results from previous years. A selective method was applied to investigate the occurrence of vancomycin resistant *Enterococcus* spp. (VRE) in the same caecal sample material (see notifiable resistant chapter, page 68). Avoparcin, which induces cross-resistance to vancomycin, was routinely used as a growth promoter in Norwegian broiler and turkey production from 1986 until it was banned in 1995. The use selected for a reservoir of VRE in Norwegian broiler production that persisted for many years after the ban was implemented.

SPORTS AND FAMILY ANIMALS

Escherichia coli from horses

Faecal swab samples from a total of 251 horses were examined. *E. coli* isolates were obtained from 250 (99.6%) of the samples. One isolate per positive sample was susceptibility tested. The results are presented in Table 18, Figures 51-52, and in the text.

TABLE 18. Antimicrobial resistance in *Escherichia coli* isolates (n=250) from faecal samples from horses in 2024.

Substance	Resistance (%) [95% CI]		Distribution (%) of MIC values (mg/L)*															
			0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	≥512
Tetracycline	1.2	[0.2 – 3.5]								89.0	9.6				1.2			
Tigecycline	0.0	[0.0 – 1.5]					100											
Chloramphenicol	0.4	[0.0 – 2.2]										98.0	2.0		0.4			
Ampicillin	1.2	[0.2 – 3.5]							0.8	15	65	18			1.2			
Cefotaxime	0.0	[0.0 – 1.5]					100											
Ceftazidime	0.0	[0.0 – 1.5]					94.8	5.2										
Meropenem	0.0	[0.0 – 1.5]		100														
Trimethoprim	18.0	[13.4 – 23.3]					62.0	19.2	0.8					18.0				
Sulfamethoxazole	19.2	[14.5 – 24.6]										48	24	6.8	2	0.8	0.4	18.0
Azithromycin	0.0	[0.0 – 1.5]								23.0	72.0	4.8	0.4					
Gentamicin	0.4	[0.0 – 2.2]						60.8	38.0	0.4				0.4				
Amikacin	0.0	[0.0 – 1.5]									96.0	4.0						
Ciprofloxacin	0.0	[0.0 – 1.5]	90.8	8.8	0.4													
Nalidixic acid	0.0	[0.0 – 1.5]									99.0	0.8						
Colistin	0.0	[0.0 – 1.5]							100									

*Bold vertical lines denote epidemiological cut-off values for resistance. CI=confidence interval. White fields denote range of dilutions tested for each antimicrobial agent. MIC values higher than the highest concentration tested are given as the lowest MIC value above the range. MIC values equal to or lower than the lowest concentration tested are given as the lowest concentration tested.

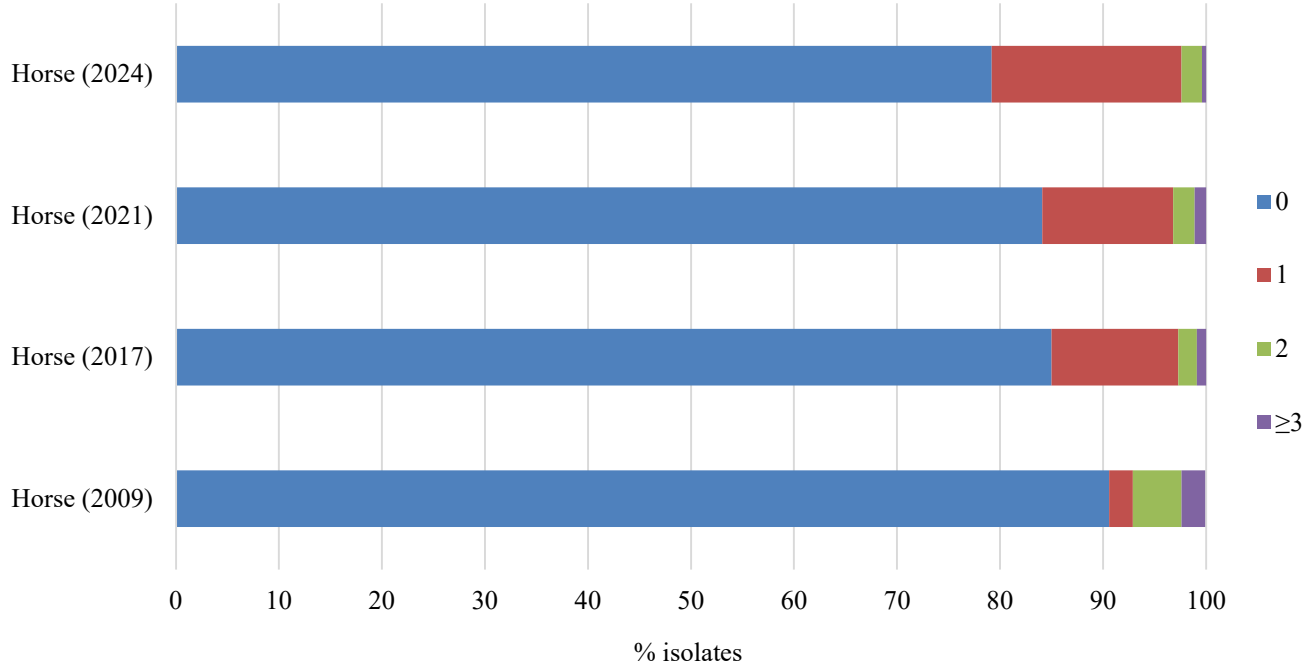

FIGURE 51. Antimicrobial resistance profile for *Escherichia coli* from faecal samples from horses collected in 2009-2024. Percentage of isolates susceptible to all (0) or resistant to one (1), two (2), and three or more (≥3) antimicrobial classes are illustrated. The epidemiological cut-off values used in NORM-VET 2024 were applied.

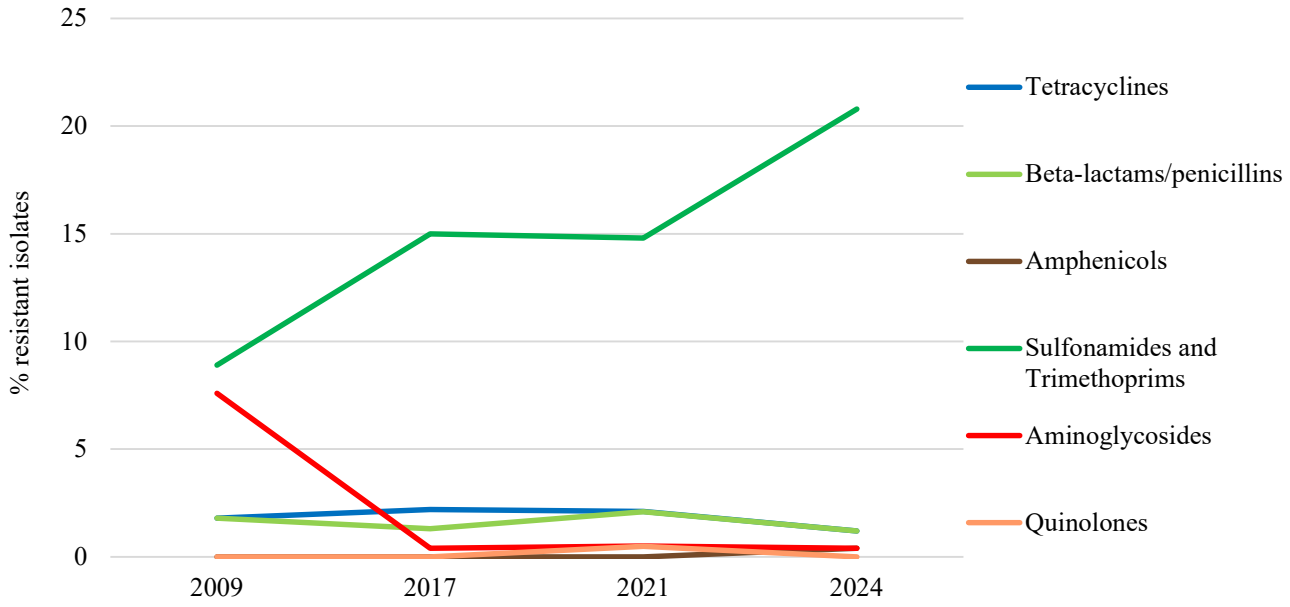

FIGURE 52. Prevalence of resistance to various antimicrobial classes in *Escherichia coli* from faecal samples from horses collected in 2009-2024. The epidemiological cut-off values used in NORM-VET 2024 were applied.

RESULTS AND COMMENTS

In total, 79.2% of the isolates were susceptible to all antimicrobial agents included in the test panel. Altogether, 18.4% of the isolates were resistant to one antimicrobial class (predominantly sulfonamides/trimethoprim), 2.0% to two, and 0.4% to three or more antimicrobial classes (Figure 51). In total, 20.8% of the isolates were resistant to at least one of the tested antimicrobial agents, indicating a high occurrence of resistance among *E. coli* from faecal samples of horses according to the EFSA classification described in Appendix 6. Resistance to sulfamethoxazole and trimethoprim were the most frequently identified resistance determinants (Figure 52).

None of the isolates displayed any resistance to the extended spectrum cephalosporins (ESC) cefotaxime or ceftazidime. This is in concordance with previous results from 2009, 2017 and 2021 (NORM/NORM-VET 2009, NORM/NORM-VET 2017, NORM/NORM-VET 2021). Selective screening methods for detection of ESC resistant *Enterobacterales* and other notifiable resistance bacteria were also used on the same sample material (see notifiable resistance chapter, page 67).

Samples from horses have been included in NORM-VET thrice before, in 2009, 2017 and 2021. Comparison to 2009 is difficult due to changes in the panel of antimicrobial agents tested. In 2009, 7.6% of the tested isolates displayed reduced sensitivity towards the aminoglycoside streptomycin. Streptomycin is no longer part of the test panel, and thereby comparison to 2009 on the overall resistance is difficult. As shown in Figure 51, the percent of isolates being fully susceptible has been realtively stable around 80% over the years 2017-2024. There has, however, been an increase in resistance to sulfonamides and trimethoprim, i.e. to both sulfamethoxazole and trimethoprim. The data from 2009 also indicate this with 7.6% [95% CI: 4.3-12.9] and 8.8% [95% CI: 5.2-14.3] resistance to sulfamethoxazole and trimethoprim, respectively. The increase from 2009 is, however, only significant for sulfamethoxazole ($p<0.006$) and further monitoring is needed to follow the situation in the years to come.

NORM-VET Utforsker - an interactive digital application for displaying NORM-VET data

Introduction

The Norwegian monitoring programme for antimicrobial resistance in the veterinary sector (NORM-VET) was established in 2000. The programme is coordinated by the Norwegian Veterinary Institute on commission from the Norwegian Food Safety Authority (Mattilsynet). Data from the programme have been recorded for more than two decades, initially using WHONET, but after some years, data were recorded in the Laboratory Information Management System (LIMS) at the Norwegian Veterinary Institute. Over the years, there have been several changes in what have been included in NORM-VET, with regards to animal species, sample material, bacterial species, susceptibility testing panels, and antimicrobial substances. In addition, the epidemiological cut-off values (ECOFFs) have changed over time. Our objectives were to: 1) simplify and transfer the relevant data into a new database, and 2) establish a digital application to enable interactive visualisation of the data.

Material and methods

We developed an R package, called “noRmvet”, with functions to handle the NORM-VET data (NorwegianVeterinary Institute/noRmvet). A shiny application, the NORM-VET Utforsker, has been developed to make the data digitally available (currently only in Norwegian). The original data were classified to groups of animal species, material categories, bacterial species and bacterial categories (e.g. indicator, zoonotic, clinical and important; i.e. notifiable AMR). Further, the variable ‘report_year’ was included to align the data with the NORM/NORM-VET reports. We also included a table for the classification of the antimicrobial agents to antimicrobial classes and individual tables for the ECOFFs. The application includes information related to the samples and programme, as well as substances and classes. Each bacterial species must be selected separately, and not more than two animal species and years can be selected simultaneously for displaying the occurrence of resistance as a figure or in tables. The resistance profile i.e. percentage of susceptible, resistant to one, two or three classes (“Resistensprofil”) and trends (“Resistensforekomst over tid”) are possible to display as well. All figures and tables can be downloaded from the application.

FIGURE 53: Interface of the digital application "NORM-VET Utforsker".

Results and comments

Currently, the application only includes the indicator bacteria *Escherichia coli*, *Staphylococcus felis* and *S. pseudintermedius* from healthy carriers. More data from the monitoring programme will be included in the future. The database is still missing data from the years where WHONET was used (2000-2003) as it has been difficult to harmonise with the data recorded in the LIMS. Further, we encountered challenges in how to manage changes of ECOFFs when previous susceptibility testing was shown not to be applicable to newer sets of ECOFFs.

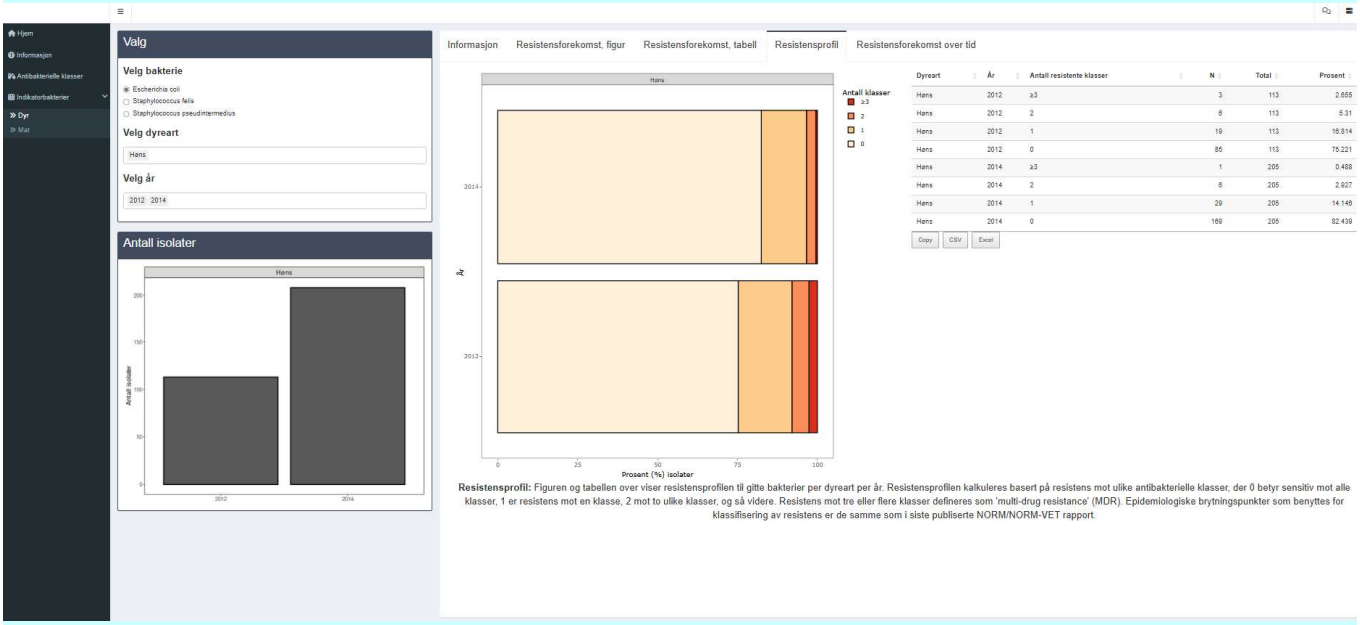

FIGURE 54. One example of how the resistance profiles are displayed.

Conclusions

Developing the NORM-VET database and its digital application NORM-VET Utforsker is an ongoing process. New data from the LIMS need to be transferred yearly. In addition, variable names and ECOFFs in the new database need to be updated annually. Overall, the new harmonised database will save time and effort in writing future NORM-VET reports. Moreover, the NORM-VET Utforsker will have an added value for several end users (governmental stakeholders, industry and other researchers) as it allows for interactive exploration and downloading of figures, aggregated data and results.

Link to the application can be found at vetinst.no, under Overvåking, Antibiotikaresistens (NORM-VET).

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NOTIFIABLE ANTIMICROBIAL RESISTANCE IN ANIMALS

Madelaine Norström, Jannice Schau Slettemeås and Anne Margrete Urdahl

Bacterial resistance to some important antimicrobials, such as extended spectrum cephalosporins (ESC) and carbapenems are defined by the WHO as critically important for antimicrobial treatment of human infections (WHO 2019). A reservoir of such resistant bacteria in food production animals and the food chain is of concern as they may have an impact on resistance development in human bacterial populations.

In 2019, some antimicrobial resistant bacteria were made notifiable to the Norwegian Food Safety Authorities by the Animal Health Regulations. This was implemented to monitor the occurrence and follow trends of these in the animal populations. The resistant bacteria included in the regulation largely corresponds to those that are notifiable in humans.

In NORM-VET, selective screening methods are used for detection of *E. coli/Enterobacterales* resistant to ESC, carbapenem resistant *Enterobacterales* (CRE), vancomycin resistant *Enterococcus* spp. (VRE), linezolid resistant *Enterococcus* spp. (LRE), methicillin resistant *Staphylococcus aureus* (MRSA) and methicillin resistant *Staphylococcus pseudintermedius* (MRSP).

In 2024, samples from animals included caecal samples from broiler flocks and faecal swabs from horses for isolation of ESC resistant *E. coli*, CRE and VRE. In addition, swabs from oral/nasal mucosa of horses were included for detecting methicillin resistant *Staphylococcus aureus* (MRSA). Results from the surveillance programme for MRSA in pigs are described as well (see page 68).

PRODUCTION ANIMALS

Extended spectrum cephalosporin resistant *E. coli* from broilers

A total of 336 broiler flocks were investigated for the presence of *E. coli* resistant to extended spectrum cephalosporins (ESC). The results are presented in the text and in Figure 55.

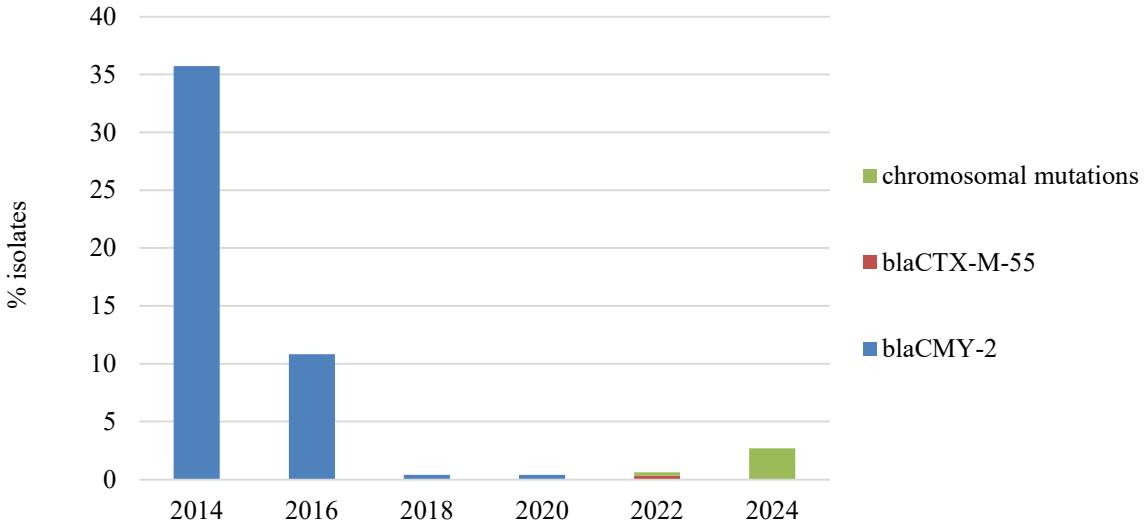

FIGURE 55. Occurrence (%) of ESC resistant *Escherichia coli* in caecal samples from broiler flocks in 2014-2024.

RESULTS AND COMMENTS

BROILER

ESC resistant *E. coli* was found in nine (2.7% [95% CI: 1.2-5.0]) of the 336 broiler flock samples. As described above, no cephalosporin resistant isolates were found using the standard non-selective procedure, indicating a low within-flock prevalence.

All nine isolates had a cephalosporin resistance profile corresponding to an AmpC beta-lactamase phenotype, and whole genome sequencing showed that resistance was due to mutations (n.-42C>T) in the promoter and attenuator regions of the chromosomally located *ampC* gene resulting in *ampC* overexpression. The isolates did not show reduced susceptibility to meropenem, the preferred carbapenem used for detecting carbapenem resistance.

As shown in Figure 55, these results with only finding of chromosomal mutations, confirm that the measures implemented by the industry to reduce the occurrence of ESC resistant *E. coli* due to the bla_{CMY-2} gene in broilers have been successful.

Also, in a European perspective, this prevalence of ESC resistant *E. coli* in Norwegian broilers is low, though the occurrence varies markedly between countries reporting to EFSA (EFSA and ECDC European Union Summary Report 2022-2023).

Carbapenem resistant *Enterobacterales* from broilers

Selective screening for carbapenem resistant *Enterobacterales* (CRE) was performed on caecal samples from a total of 336 broiler flocks. No CRE were detected. Carbapenems are not approved for use in food-producing animals in EU and EEA countries. Nevertheless, resistance to these critically important antimicrobial agents has sporadically been reported from animals in some of the EU/EEA countries, and further monitoring is recommended to follow the situation in the years to come.

Vancomycin resistant *Enterococcus* spp. from broiler

A total of 336 broiler flocks were screened for the presence of vancomycin resistant *Enterococcus* spp. (VRE). No VRE were detected [95% CI: 0.0-1.1]. This is in concordance with the result from 2018-2022. For broilers, there has been a statistically significant decrease from 2014 when 6.7% [95% CI: 3.7-10.9] of the flocks were VRE positive.

Surveillance of methicillin resistant *Staphylococcus aureus* (MRSA) in pigs

Methicillin resistant *Staphylococcus aureus* (MRSA) associated with animals, i.e. livestock associated MRSA (LA-MRSA) have become widespread in pig populations around the world, thereby representing a risk for dissemination to the human population. As the only country in the world, Norway implemented a control strategy from 2013 including measures to eradicate MRSA in pigs as described in Grøntvedt *et al.* 2016 (1). The rationale behind this strategy was to prevent the pig population from becoming a domestic reservoir of MRSA with the potential of zoonotic transmission, as MRSA is not a significant cause of disease in pig.

As part of this strategy, an extensive yearly surveillance programme was implemented from 2014. The aim of the programme is to identify MRSA positive pig herds. Each year the nucleus and multiplier herds, as well as central units of sow pool herds and the 20 biggest sow herds are sampled twice, while the remaining sow herds are sampled once. Every third year finisher pig herds are sampled instead of the sow herds. In 2024, 626 herds were investigated, of which 66 were genetic nucleus or multiplier herds, 11 herds were central units of the sow pool herds, 21 were of the largest farrow to grower or farrow to finish herds, and the remaining 528 were fattening herds. The surveillance programme did not detect any pig herds with MRSA in 2024. Further details can be found in the report "The surveillance programme for methicillin resistant *Staphylococcus aureus* in pig in Norway 2024" (2). Table 19 summarises the findings from the surveillance programme from 2013-2024 and additional MRSA findings from herds not included in the surveillance (including herds detected through contact tracing).

TABLE 19. Pig herds in Norway with methicillin resistant *Staphylococcus aureus* in 2013-2024.

Year	No. MRSA positive herds detected by the MRSA surveillance programme (Total No. of positive herds)	Herds investigated in the MRSA surveillance programme	MRSA typing*
2013	(22**)		CC398 t034 (some also with t12359) (22)
2014	1 (5)	986	CC398 t034 (2), CC398 t011 (3)
2015	4 (34)	821	CC398 t034 (25), CC1 t177 (9)
2016	1 (8)	872	CC398 t034 (8)
2017	2 (6)	826	CC7 t091 (2), CC8 t024 (2), CC130 t843 (1), CC425 t6292 (1)
2018	0	716	
2019	1 (9)	722	CC398 t034 (3), CC398 t011 (5), CC130 t843 (1)
2020	0	641	
2021	0	763	
2022	0	591	
2023	0	541	
2024	0	626	
Total	9 (84**)		CC398 t034 (60), CC398 t011 (8), CC1 t177 (9), CC7 t091 (2), CC8 t024 (2), CC130 t843 (2), CC425 t6292 (1)

**mecC*-gene detected for CC130 t843 and CC425 t6292, *mecA*-gene detected for the others. **Number of positive herds detected during 2013 before the MRSA surveillance programme was implemented.

References

1. Grøntvedt. C.A., Elstrøm. P., Stegger. M., Skov. R.L., Skytt Andersen. P., Larssen. K.W., Urdahl. A.M., Angen. Ø., Larsen. J., Åmdal. S., Løtvedt. S.M., Sunde. M., Bjørnholt. J.V. Methicillin-Resistant *Staphylococcus aureus* CC398 in Humans and Pigs in Norway: A "One Health" Perspective on Introduction and Transmission. Clin Infect Dis. 2016 Dec 1;63(11):1431-1438.
2. Urdahl AM, Norström M, Welde H, Bergsjø B, Grøntvedt CA. The surveillance programme for methicillin resistant *Staphylococcus aureus* in pigs in Norway 2024. *Surveillance programmes for terrestrial and aquatic animals in Norway. Annual report 2024.* Norwegian Veterinary Institute 2025.

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SPORTS AND FAMILY ANIMALS

Extended spectrum cephalosporin resistant *Escherichia coli* from horses

Selective screening for *E. coli* resistant to extended spectrum cephalosporins (ESC) was performed on the samples from horses. A total of 251 samples were screened. *E. coli* resistant to ESC were detected in three (1.2% [95% CI: 0.2-3.5]) of the samples. All three isolates had a cephalosporin resistance profile corresponding to an ESBL phenotype. Whole genome sequencing showed that resistance was due to different ESBL genotypes in all three isolates; $bla_{\text{CTX-M-1}}$, $bla_{\text{CTX-M-15}}$ and $bla_{\text{SHV-12}}$ (Figure 56), respectively, the two last isolates also carried the plasmid mediated quinolone resistance gene *qnrS1*.

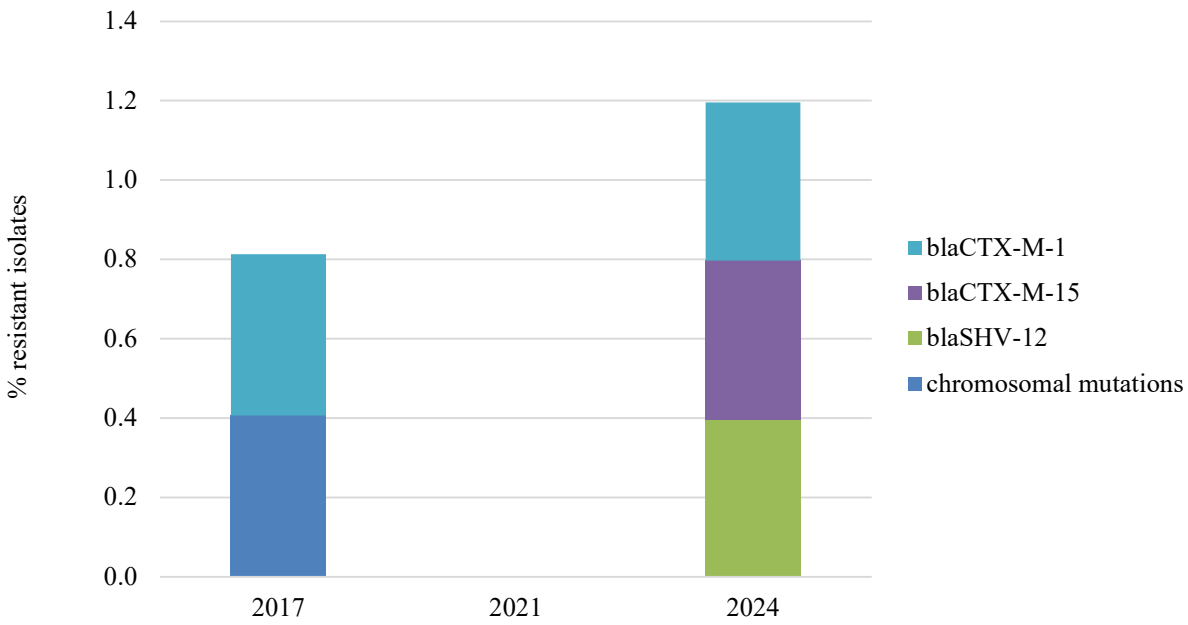

FIGURE 56. Occurrence (%) of ESC resistant *Escherichia coli* in samples from horses in 2017-2024.

Screening for *E. coli* resistant to ESC has previously been conducted in 2017 and 2021. The present findings are in concordance with previous results; i.e. none of 201 samples [95% CI: 0.0-1.8] were positive in 2021 (NORM/NORM-VET 2021), while *E. coli* resistant to ESC was detected in two of 246 samples (0.8% [95% CI: 0.1-2.9]) in 2017 (NORM/NORM-VET 2017). One of these isolates displayed an AmpC beta-lactamase phenotype due to mutations in the promoter and attenuator regions of the chromosomally located *ampC* gene (p.C-42T), and the last isolate displayed an ESBL phenotype and was genotyped as $bla_{\text{CTX-M-1}}$.

Carbapenem resistant *Enterobacterales* from horses

A total of 251 faecal samples from horses were screened for the presence of carbapenem resistant *Enterobacterales* (CRE). No CRE isolates were detected.

Methicillin resistant *Staphylococcus aureus* from horses

A total of 251 nasal swab samples from horses were screened for the presence of methicillin resistant *Staphylococcus aureus* (MRSA). MRSA was not detected from any of these horses [95% CI: 0.0-1.5%]. This result is in concordance with previous screening results in NORM-VET in 2009 and 2021 where no MRSA was detected among sampled horses, and in 2017 when MRSA CC398 *spa*-type t011 was detected from one of the 246 investigated horses (NORM/NORM-VET 2009, NORM/NORM-VET 2017, NORM/NORM-VET 2021). MRSA CC398 *spa*-type t011 is associated with MRSA findings in horses as well as other animals including pigs, and has previously been detected from clinical cases in horses in several countries, including Norway.

Notifiable antimicrobial resistant bacteria in animals – results from 2024

In 2019, some antimicrobial resistant bacteria were made notifiable to the Norwegian Food Safety Authority (NFSA) by the Animal Health Regulations. This was implemented to monitor the occurrence and follow trends in the animal populations. The resistant bacteria included in the regulation largely correspond to those that are notifiable in humans (Table 20).

TABLE 20. Overview of resistant bacteria notifiable according to the Norwegian Animal Health Regulations.

Resistant bacteria	Explanations with MIC and zone diameters
Colistin resistant *Enterobacterales*, *Acinetobacter* spp. and *Pseudomonas* spp.	*Enterobacterales* (e.g. *Escherichia coli* and *Klebsiella* spp.), *Acinetobacter* spp. and *Pseudomonas* spp. resistant to colistin (MIC ECOFF > 2 mg/L, 2 mg/L and 4 mg/L, respectively, or by detected *mcr* genes). Exempt from notification are *Enterobacterales* that are naturally resistant to colistin: *Proteus* spp., *Morganella morganii*, *Serratia* spp. and *Providencia* spp.
Enterobacterales and *Pseudomonas* spp. resistant to extended spectrum cephalosporins (ESC)	*Enterobacterales* (e.g. *Escherichia coli* and *Klebsiella* spp.) and *Pseudomonas* spp. resistant to 3rd and 4th generations cephalosporins. *E. coli*; MIC (zone diameter): • Cefotaxime MIC > 0.25 mg/L (< 21 mm) • Ceftazidime MIC > 0.5 mg/L (< 20 mm) *Salmonella* spp.; MIC (zone diameter): • Cefotaxime MIC > 0.5 mg/L (< 20 mm) • Ceftazidime MIC > 2 mg/L (< 20 mm) *K. aerogenes*; MIC (zone diameter): • Cefotaxime MIC > 0.5 mg/L (-) • Ceftazidime MIC > 1 mg/L (-) *K. oxytoca*; MIC (zone diameter): • Cefotaxime MIC > 0.125 mg/L (-) • Ceftazidime MIC > 0.5 mg/L (-) *K. pneumoniae*; MIC (zone diameter): • Cefotaxime MIC > 0.25 mg/L (< 21 mm) • Ceftazidime MIC > 0.5 mg/L (< 19 mm) *Pseudomonas aeruginosa*; MIC (zone diameter): • Ceftazidime MIC > 8 mg/L (< 16 mm) Exempt from the notification obligation is the detection of inherent/natural resistance, e.g. resistance to cefotaxime in *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Stenotrophomonas maltophilia.*
Carbapenemase-producing/ carbapenem resistant *Enterobacterales* (CPE/CRE), *Acinetobacter* spp. and *Pseudomonas* spp.	*Enterobacterales* (e.g. *Escherichia coli*, *Klebsiella* spp., *Enterobacter* spp.), *Acinetobacter* spp. and *Pseudomonas* spp. resistant to carbapenems. Enterobacterales; MIC (zone diameter): • Meropenem MIC > 0.125 mg/L (< 25 mm) *Acinetobacter baumannii* and *Pseudomonas aeruginosa*; MIC (zone diameter for *P. aeruginosa*): • Meropenem MIC > 2 mg/L (< 24 mm) Exempt from the notification obligation are *Enterobacterales* that are naturally resistant to carbapenems such as *Stenotrophomonas maltophilia.*
Linezolid resistant *Enterococcus* spp. (LRE)	*Enterococcus* spp. resistant to linezolid (MIC > 4 mg/L, zone diameter < 19 mm) and/or isolates with detected transferable linezolid resistance genes
Methicillin resistant *Staphylococcus aureus* (MRSA)	*Staphylococcus aureus* resistant to cefoxitin (MIC > 4 mg/L, zone diameter < 22 mm), and/or isolates with detected *mecA* or *mecC* genes.
Methicillin resistant *Staphylococcus pseudintermedius* (MRSP)	*Staphylococcus pseudintermedius* resistant to cefoxitin (MIC > 4 mg/L, zone diameter < 22 mm), and/or isolates with detected *mecA* or *mecC* genes.
Linezolid resistant *Staphylococcus* spp.	*Staphylococcus* spp. resistant to linezolid (MIC > 4 mg/L, zone diameter < 19 mm), and/or isolates with detected transferable linezolid resistance genes.
Vancomycin resistant *Enterococcus* spp. (VRE)	*Enterococcus* spp. resistant to vancomycin (MIC > 4 mg/L, zone diameter < 12 mm). Exempts from the notification requirement are *Enterococcus gallinarum* and *Enterococcus casseliflavus*, which are naturally resistant.
Fluoroquinolone resistant *Campylobacter* spp.	Thermophile *Campylobacter* spp. (e.g. *C. jejuni* and *C. coli*) resistant to fluoroquinolones: • Ciprofloxacin MIC > 0.5 mg/L (zone diameter < 26 mm).

Since the implementation of the notification requirement, there has been some notifications made to the NFSA. However, it is suspected that notification of antimicrobial resistant bacteria to the NFSA is underreported, especially regarding bacteria resistant to ESC, as well as MRSA and MRSP. Part of the reason for this may be explained by a poorly designed reporting system for antimicrobial resistant bacteria during the first years. However, the last couple of years a new and better system for reporting these has been implemented at the NFSA website (Melding om resistente bakterier). Moreover, there is a large number of samples from animals that are sent to laboratories abroad and these laboratories are not aware of the notification requirements. The veterinarians should then report, though probably not all are aware of their obligation to notify these bacteria.

In 2022, three dogs were reported with MRSP, one dog with VRE (i.e. *Enterococcus faecalis*), two dogs with ESC resistant *Escherichia coli*, one dog with ESCresistant *Klebsiella pneumoniae*, and one dog with ESC resistant *Pseudomonas aeruginosa*. In addition, there were reports on one ESC resistant *Escherichia coli* and one *Pseudomonas* spp., though no information on animal species was recorded. Most reported cases in 2023 were also from dogs; two MRSA, one MRSP, and seven ESC resistant bacteria (i.e. one *Escherichia coli,* one *Enterobacter cloacae*, two *Pseudomonas* spp. and three *Pseudomonas aeruginosa*). In addition, MRSA was detected from one dairy cattle herd.

Table 21 shows the antimicrobial resistant bacteria reported to the NFSA in 2024.

TABLE 21. Notifiable antimicrobial resistant bacteria reported to the Norwegian Food Safety Authorities in 2024.

	No. animals			
Notifiable resistant bacteria	**Dog**	**Turkey**	**Sheep**	**Cattle**
ESC resistant *Escherichia coli*		1*		
ESC resistant *Enterobacter cloacae*	1			
ESC resistant *Pseudomonas aeruginosa*	2		1	
ESC resistant *Pseudomonas* spp.	1			
MRSA				1*
MRSP	3			

*i.e. turkey flock and cattle herd.

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ANTIMICROBIAL RESISTANCE IN FOOD

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In 2024, food samples included broiler and turkey meat, and sugar peas and dried fruit. One isolate of interest per positive sample per category was susceptibility tested. Some of the cut-off values defining resistance applied in NORM-VET have changed over the years. To facilitate comparisons, data on prevalence of resistance presented in earlier reports have been recalculated using the cut-off values applied in 2024. Sampling, laboratory methods and data processing are described in Appendix 3.

MEAT

Extended spectrum cephalosporin resistant *Escherichia coli* from broiler and turkey meat

In total, 325 broiler and 114 turkey meat samples were examined for the presence of *E. coli* resistant to extended spectrum cephalosporins (ESC), i.e. cefotaxime and/or ceftazidime. Results are presented in the text and in Figures 57-58.

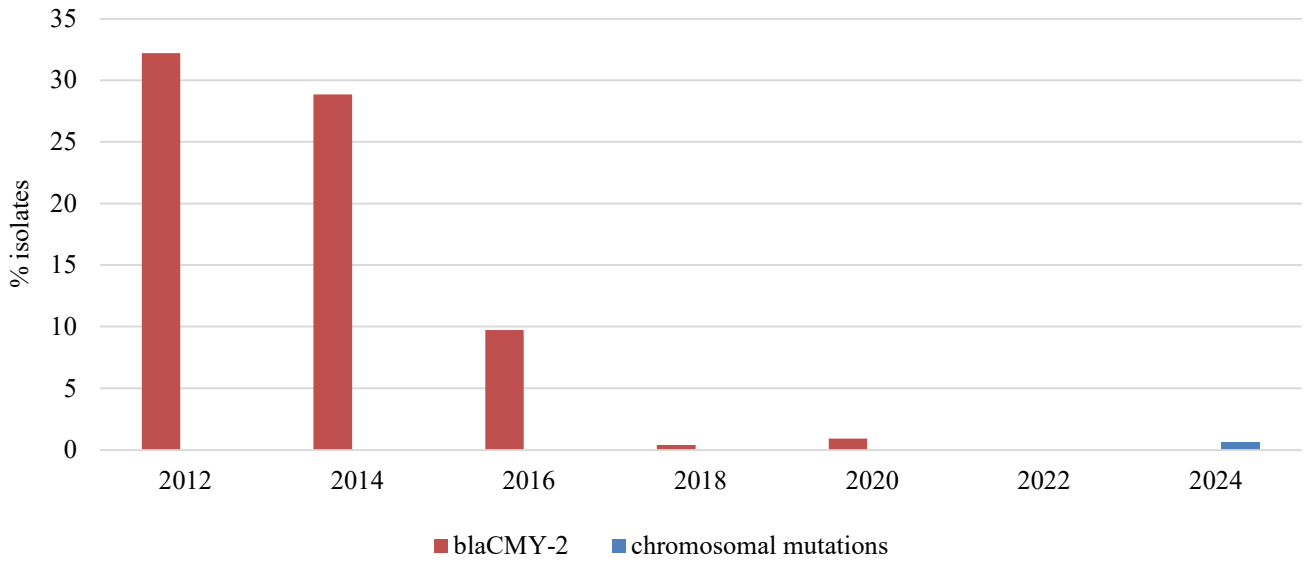

FIGURE 57. Occurrence (%) of ESC resistant *Escherichia coli* in broiler meat samples 2012-2024.

RESULTS AND COMMENTS

BROILER MEAT

ESC resistant *E. coli* was detected in one (0.3%) [95% CI: 0.01-1.7] of the 325 broiler meat samples. The isolate had a cephalosporin resistance profile corresponding to an AmpC beta-lactamase phenotype, and whole genome sequencing showed that resistance was due to mutations (n.-42C>T) in the promoter and attenuator regions of the chromosomally located *ampC* gene resulting in *ampC* overexpression. The isolate did not show reduced susceptibility to meropenem, the preferred carbapenem used for detecting carbapenem resistance.

The result from 2024 is in concordance with results from the period 2018-2022 where ESC resistant *E. coli* were detected in 0-3 samples. After the significant reduction of ESC resistant *E. coli* due to presence of bla_{CMY-2} was observed in 2018, the number of samples from which ESC resistant *E. coli* is detected has been low (Figure 57).

In a European perspective, the occurrence of ESC resistant *E. coli* detected in Norwegian broiler meat is very low, although the occurrence varied markedly between countries reporting to EFSA in 2022 (EFSA and ECDC European Union Summary Report 2022-2023). While the Nordic countries tend to report a lower prevalence of ESC resistant *E. coli* in broiler meat, a decrease in prevalence has also been observed in several other European countries.

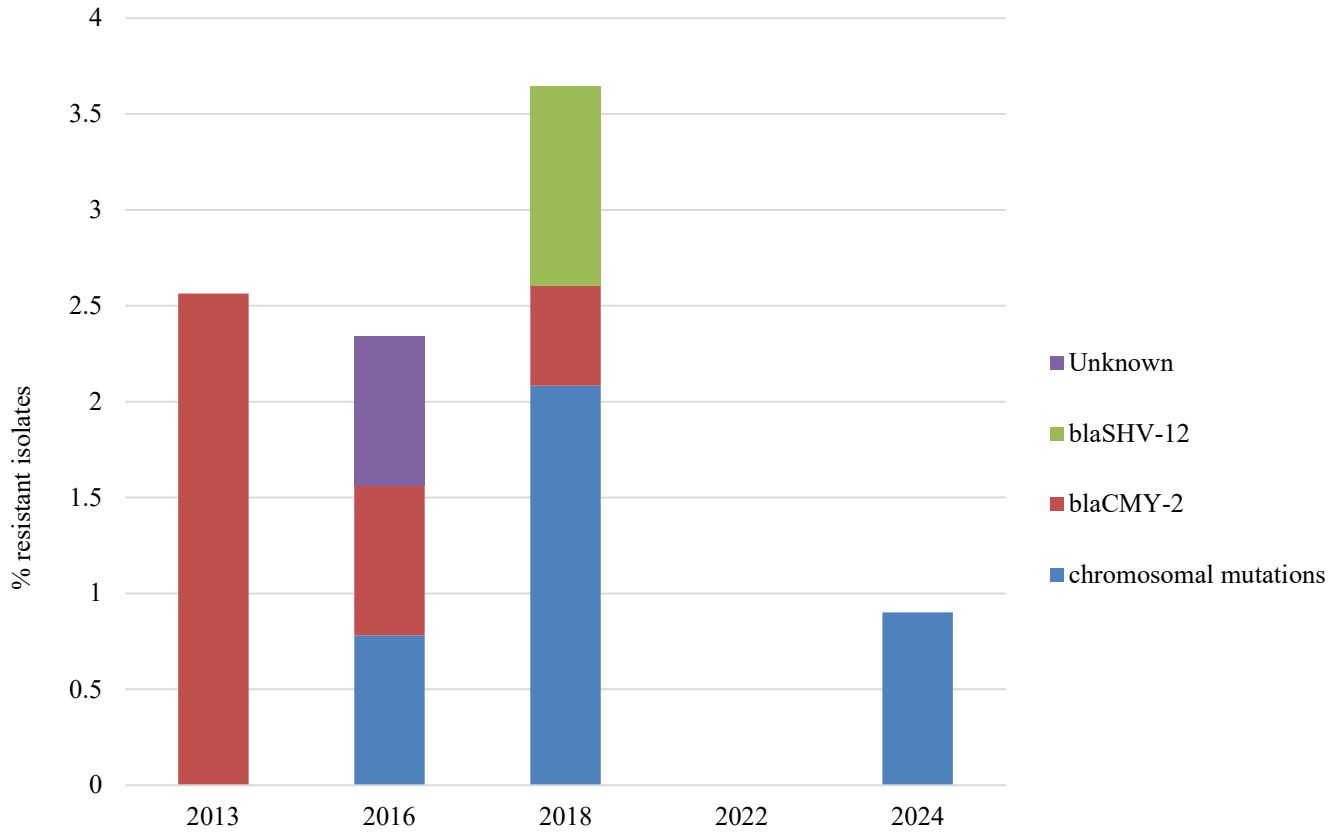

FIGURE 58. Occurrence (%) of ESC resistant *Escherichia coli* in turkey meat samples 2013-2024.

TURKEY MEAT

ESC resistant *E. coli* was detected in one (0.9%) [95% CI: 0.0-4.8] of the 114 turkey meat samples. The isolate had a cephalosporin resistance profile corresponding to an AmpC beta-lactamase phenotype, and whole genome sequencing showed that resistance was due to mutations (n.-42C>T) in the promoter and attenuator regions of the chromosomally located *ampC* gene resulting in *ampC* overexpression. The isolate did not show reduced susceptibility to meropenem, the preferred carbapenem used for detecting carbapenem resistance.

Similar to the findings in broiler meat, the occurrence of ESC resistant *E. coli* due to presence of bla_{CMY-2} in turkey meat was significantly reduced in the period from 2013 to 2022, and the occurrence of ESC resistant *E. coli* has thereafter been at the same level (Figure 58). On a European level there are large variations with respect to prevalence of ESC resistant *E. coli* in turkey meat where Norway is among the countries with lowest prevalence (EFSA and ECDC European Union Summary Report 2022-2023).

Carbapenem resistant *Enterobacterales* from broiler and turkey meat

A total of 325 broiler and 114 turkey meat samples were examined for the presence of carbapenem resistant *Enterobacterales* (CRE). No CRE were detected (broiler meat: [95% CI: 0.0-1.1] and turkey meat: [95% CI: 0.0-3.2]). This is in concordance with previous results. Carbapenems are not approved for use in food-producing animals in the EU and EEA countries. Nevertheless, resistance to these antimicrobial agents has sporadically been reported from animals in some of the EU/EEA countries. Carbapenems are defined by the WHO as critically important for treatment of human infections, and a possible development of a significant reservoir of carbapenem resistant bacteria in animals and food is therefore of concern. Further monitoring is recommended to follow the situation in the years to come.

Methicillin resistant *Staphylococcus aureus* from broiler and turkey meat

A total of 325 broiler and 114 turkey meat samples were examined for the presence of methicillin resistant *Staphylococcus aureus* (MRSA). None of the samples were positive for MRSA [95% CI: 0.0-1.1] and [95% CI: 0.0-3.2], respectively.

In one of the samples from turkey meat, we detected *Mammaliicoccus sciuri* carrying the *mecA* gene. *M. sciuri* was formerly called *Staphylococcus sciuri*, but was renamed in 2020 (Madhaijan et al, 2020). *M. sciuri* is considered the evolutionary origin of the *mecA* gene, which has later disseminated to *S. aureus* (Van der Veken et al, 2022).

OTHER FOOD CATEGORIES

Escherichia coli from sugar peas and dried fruits

A total of 315 sugar pea and 345 dried fruit samples were examined. *E. coli* isolates were obtained from 23 (7.3%) of the sugar pea samples, and none of the dried fruit samples. One isolate per positive sample was susceptibility tested. Of the 23 *E. coli* isolates, 15 (65.2%) were susceptible to all antimicrobial agents included in the test panel. Altogether, three of the isolates were resistant to one (mainly tetracyclines), two to two, and three to three or more antimicrobial classes (up to six different antimicrobial classes). None of the isolates were resistant to extended spectrum cephalosporins (ESC), nor carbapenems. In addition, selective methods were used to investigate the occurrence of ESC resistant *E. coli*, carbapenem resistant *Enterobacterales* (CRE) and colistin resistant *Enterobacterales* in the same material (see below).

This was the first survey of sugar peas and dried fruit in NORM-VET. Previously, surveys of fresh produce have been performed on domestic and imported leafy greens and imported leafy herbs (summarised in NORM-VET 2019). As for the results from sugar peas, the majority of the 93 *E. coli* isolates obtained from the leafy greens and leafy herbs surveys, i.e. 78.5%, were susceptible to all antimicrobial agents included in the test panel. However, results from the present survey on sugar peas and the previous ones on fresh produce, show that food from such categories may be contaminated with MDR *E. coli* (with resistance to up to six different antimicrobial classes).

Extended spectrum cephalosporin resistant *Escherichia coli* from sugar peas and dried fruits

In total, 315 sugar peas and 345 dried fruits samples were examined for the presence of *E. coli* resistant to extended spectrum cephalosporins (ESC), i.e. cefotaxime and/or ceftazidime. One ESC resistant *E. coli* was detected from the sugar peas and none from the dried fruit samples.

The ESC resistant isolate had a cephalosporin resistance profile corresponding to an ESBL phenotype, and whole genome sequencing showed that resistance was due the $bla_{\text{CTX-M-15}}$ gene. The isolate did not show reduced susceptibility to meropenem, the preferred carbapenem used for detecting carbapenem resistance. In addition, this isolate was resistant to several other antimicrobial classes (genes) and was considered MDR; macrolides (*mphA*), tetracyclines (*tetB*), trimethoprim (*dfrA17*) sulfonamides (*sul1*, *sul2*), and aminoglycosides (*aadA5*, *aac*(6')-*Ib-cr*, *aph*(6)-*Id*, *aph*(3")-*Ib*, *aac*(3)-*IIa*).

In previous NORM-VET surveys of domestic and imported leafy greens and imported leafy herbs, ESC was isolated from a total of five samples, all imported products (summarised in NORM NORM-VET 2019). This supports that fresh produce may be contaminated with ESC and MDR *E. coli* as also shown by the results above.

Carbapenem resistant *Enterobacterales* from sugar peas and dried fruits

A total of 315 sugar peas and 345 dried fruits samples were examined for the presence of carbapenem resistant *Enterobacterales* (CRE). No CRE were detected (sugar peas: [95% CI: 0.0-1.2] and dried fruits: [95% CI: 0.0-1.1]).

Colistin resistant *Enterobacterales* from sugar peas and dried fruits

A total of 315 sugar peas and 345 dried fruits samples were examined for the presence of colistin resistant *Enterobacterales.* No colistin resistant *Enterobacterales* were detected in any of the samples (sugar peas [95% CI: 0.0-1.2] and dried fruits: 95% CI: 0.0-1.1]).

ZOONOTIC AND NON-ZOONOTIC ENTEROPATHOGENIC BACTERIA

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Zoonotic and non-zoonotic enteropathogenic bacteria represent a considerable public health problem. The presence of acquired antimicrobial resistance in these bacteria represents a further concern. Therefore, it is of great importance to monitor the occurrence of antimicrobial resistance in zoonotic and other enteropathogenic bacteria at relevant stages in the farm-to-fork continuum.

Included from animals and food are *Salmonella* spp., *Campylobacter coli* and *Campylobacter jejuni* isolates. From human cases, all *Salmonella*, *Shigella* and *Yersinia enterocolitica* isolates are included, as well as a representative number of *Campylobacter* isolates. Sampling, laboratory methods and data processing is described in Appendix 4. One isolate of each serovar per incident was included for susceptibility testing.

SALMONELLA SPP.

Salmonella from animals and food

The situation regarding occurrence of *Salmonella* spp. in food-producing animals in Norway is very favourable, and such animal populations are considered virtually free from *Salmonella* spp.. To document and maintain this favourable situation, Norway has extensive surveillance programmes covering live animals and meat of pigs and cattle, and live poultry, poultry meat and eggs.

The *Salmonella* isolates examined in NORM-VET 2024 included those that were detected in the Salmonella surveillance programmes, as well as isolates obtained from submissions to the National Reference Laboratory for Salmonella (including isolates from non-domestic meat or other food products) and from clinical submissions or necropsies at the Norwegian Veterinary Institute (NVI). The data are presented in Tables 22-23, and in the text.

TABLE 22. Antimicrobial resistance in *Salmonella* spp. (n=28) from animals (nine wild boars, three chicken, three dogs, two cattle, two horses, nine cats); *S.* Typhimurium (n=20) and other *Salmonella* spp. (n=8) in 2024.

Substance	Distribution (n) of MIC values (mg/L)*															
	n (resistance)	0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	≥512
Tetracycline	0								28								
Tigecycline	ND					28											
Chloramphenicol	0										28						
Ampicillin	0							15	13								
Cefotaxime	0					28											
Ceftazidime	0					21	7										
Meropenem	ND		15	13													
Trimethoprim	0					24	4										
Sulfamethoxazole	ND										1	1	3	17	6		
Azithromycin	0								1	23	4						
Gentamicin	0						27	1									
Amikacin	0									28							
Ciprofloxacin	0	14	14														
Nalidixic acid	0									28							
Colistin	ND							18	10								

*Bold vertical lines denote microbiological cut-off values, i.e. for *Salmonella enterica*. ND = not defined. White fields show range of dilutions tested for each antimicrobial agent. MIC values higher than the highest concentration tested are given as the lowest MIC value above the range. MIC values equal to or lower than the lowest concentration tested are given as the lowest concentration tested.

TABLE 23. Antimicrobial resistance in *Salmonella* spp. (n=7) from different food products in 2024.

Substance	Distribution (n) of MIC values (mg/L)*																
	n (resistance)	0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	≥512
Tetracycline	0								7								
Tigecycline	ND					7											
Chloramphenicol	0										7						
Ampicillin	0							6	1								
Cefotaxime	0					7											
Ceftazidime	0					5	2										
Meropenem	ND		7														
Trimethoprim	0					7											
Sulfamethoxazole	ND											1	3	3			
Azithromycin	0									5	2						
Gentamicin	0						6	1									
Amikacin	0									7							
Ciprofloxacin	0	5	2														
Nalidixic acid	0									6	1						
Colistin	ND							7									

*Bold vertical lines denote microbiological cut-off values, i.e. for *Salmonella enterica*. ND = not defined. White fields show range of dilutions tested for each antimicrobial agent. MIC values higher than the highest concentration tested are given as the lowest MIC value above the range. MIC values equal to or lower than the lowest concentration tested are given as the lowest concentration tested.

RESULTS AND COMMENTS

In total, 28 *Salmonella* spp. isolates from animals were susceptibility tested. The animals were nine wild boars, three dogs, three chicken, two cattle, two horses, and nine cats. In total, there were 20 *S.* Typhimurium isolates (of which one was monophasic (4,[5],12 : i : -)), two *S. enterica* subsp. *diarizonae*, two *S.* Abony, and one each of *S.* Hessarek, *S.* Mbandaka, *S.* Enteritidis, and *S.* Anatum. Additionally, seven *Salmonella* spp. isolates from non-domestic meat or other food products obtained from submissions to the National Reference Laboratory for Salmonella were susceptibility tested. The serovars of these isolates were *S.* Kinondoni, *S.* Münster, *S.* Newport, *S.* Tennessee and three *S.* Kisarawe. All the isolates, both from animals and food, were fully susceptible to the antimicrobial agents included in the susceptibility test panel.

Salmonella from human clinical specimens

In 2024, 1,197 human cases of nontyphoidal salmonellosis and 12 cases of typhoid fever were notified to the Norwegian Surveillance System for Communicable Disease (MSIS). Most cases with known place of acquisition were domestically acquired (54.1%). The National Reference Laboratory (NRL) for Entero-pathogenic Bacteria at the Norwegian Institute of Public Health (NIPH) received 1,097 *Salmonella* isolates from the primary diagnostic laboratories for further characterisation. 293 isolates were linked to 9 clusters/outbreaks, and 813 unique isolates were screened for antimicrobial resistance determinants following whole genome sequencing. Antimicrobial susceptibility testing was performed on 546 isolates, including all *Salmonella* Typhi and 86% of *Salmonella* Paratyphi A and B isolates, 96% of the unique *Salmonella* Typhimurium, 64% of the unique monophasic *Salmonella* Typhimurium, 95% of the unique domestically acquired *Salmonella* Enteritidis and 98% of the domestically acquired *Salmonella* of other serovars (Table 24). Isolates were susceptibility tested against six antibiotic classes: penicillins (ampicillin), extended spectrum cephalosporins (cefotaxime and ceftazidime), carbapenems (meropenem), fluoroquinolones (ciprofloxacin/pefloxacin), phenicol (chloramphenicol) and tetracyclines (tetra-cycline).

TABLE 24. Number of *Salmonella* isolates tested for phenotypic antimicrobial susceptibility (AST) and screened for predicted genotypic resistance (GR) recovered from human clinical specimens in Norway 2024, by serovar and place of acquisition.

Salmonella serovars	No. of isolates tested in 2024		Place of acquisition					
			Norway		Abroad		Unknown	
	Phenotypic AST	Predicted GR	Phenotypic AST	Predicted GR	Phenotypic AST	Predicted GR	Phenotypic AST	Predicted GR
S. Typhimurium	89	93	46	46	31	35	12	12
S. Typhimurium monophasic	25	39	8	10	10	21	7	8
S. Enteritidis	129	262	52	55	53	177	24	30
S. Typhi	12	12	2	2	9	9	1	1
S. Paratyphi A and B	38	44	3	3	32	38	3	3
Other *Salmonella*	253	363	122	125	68	172	63	66
Total	**546**	**813**	**233**	**241**	**203**	**452**	**110**	**120**

A total of 85 isolates were recovered form blood cultures representing 16% of all *Salmonella* isolates, including 8 *S.* Paratyphi A (80%), 9 *S.* Typhi (75%), 5 Paratyphi B (17.9%), 19 *S.* Enteritidis (14.7%), 3 *S.* Typhimurium (3.4%), and 41 *Salmonella* isolates of other serovars (16.2%). The results from the antimicrobial susceptibility testing and genomic resistance screening are presented in Tables 25-39, Figures 59-70, and in the related text.

ANTIMICROBIAL RESISTANCE IN SALMONELLA TYPHIMURIUM

TABLE 25. Percentage distributions of antimicrobial susceptibility categories in domestically acquired *Salmonella* Typhimurium (n=46) from human clinical specimens in Norway 2024.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Ampicillin	≤ 8	> 8	93.5	-	6.5
Cefotaxime	≤ 1	> 2	97.8	0.0	2.2
Ceftazidime	≤ 1	> 4	97.8	0.0	2.2
Meropenem	≤ 2	> 8	100.0	0.0	0.0
Pefloxacin[1]	≥ 24 mm	< 24 mm	93.5	-	6.5
Tetracycline[2]	≥ 17 mm	< 17 mm	95.7	-	4.3
Chloramphenicol	≤ 8	> 8	95.7	-	4.3

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. [1]Low-level resistance against ciprofloxacin is underestimated using breakpoints based on ciprofloxacin disk diffusion. Susceptibility to ciprofloxacin is inferred from pefloxacin disk diffusion according to EUCAST clinical breakpoints (v.15.0). [2]Breakpoints according to national zone distributions.

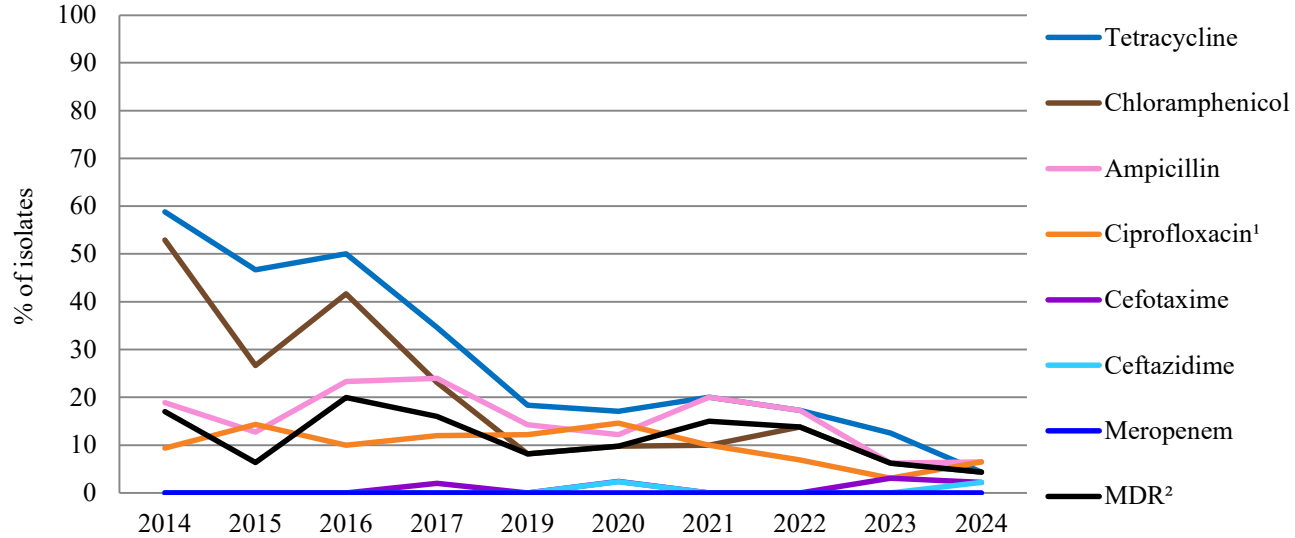


FIGURE 59. Trend 2014-2024. Percentage of domestically acquired *Salmonella* Typhimurium resistant to selected antimicrobial agents in Norway.[1]Resistance to ciprofloxacin is inferred from pefloxacin disk diffusion 2016 onwards. [2]MDR is defined as acquired non-susceptibility to antimicrobials from three or more categories.

TABLE 26. Percentage distributions of predicted genotypic resistance in domestically acquired *Salmonella* Typhimurium (n=46) compared to phenotypic wild type/non-wild type distribution (n=46) from human clinical specimens in Norway 2024.

	Phenotype[1] (%)		Predicted genotype[2] (%)	
Antibiotic	Wild type	Non-wild type	S	R
Gentamicin	-	-	100.0	0.0
Streptomycin	-	-	93.5	6.5
Ampicillin	91.3	8.7	93.5	6.5
Meropenem	100.0	0.0	100.0	0.0
Cefotaxime[3]	97.8	2.2	97.8	2.2
Ceftazidime[3]	97.8	2.2		
Colistin	-	-	100.0	0.0
Chloramphenicol	95.7	4.3	95.7	4.3
Ciprofloxacin	93.5	6.5	91.3	8.7
Sulfonamide	-	-	93.5	6.5
Tetracycline	95.7	4.3	93.5	6.5
Trimethoprim	-	-	95.7	4.3

[1]Wild type (WT) and non-wild type (NWT) categorisation according to EUCAST epidemiological cut-off values (ECOFF), and clinical breakpoints in absence of ECOFF for *Salmonella enterica* (v.15.0). [2]R and S categorisation based on presence or absence of resistance determinants. [3]Predicted genotypic resistance to cefotaxime and ceftazidime is combined to predict genotypic resistance against extended spectrum cephalosporins.

TABLE 27. Percentage distributions of antimicrobial susceptibility categories in travel associated *Salmonella* Typhimurium (n=31) from human clinical specimens in Norway 2024.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Ampicillin	≤ 8	> 8	80.6	-	19.4
Cefotaxime	≤ 1	> 2	96.8	0.0	3.2
Ceftazidime	≤ 1	> 4	96.8	0.0	3.2
Meropenem	≤ 2	> 8	100.0	0.0	0.0
Pefloxacin[1]	≥ 24 mm	< 24 mm	80.6	-	19.4
Tetracycline[2]	≥ 17 mm	< 17 mm	80.6	-	19.4
Chloramphenicol	≤ 8	> 8	87.1	-	12.9

[1]Low-level resistance against ciprofloxacin is underestimated using breakpoints based on ciprofloxacin disk diffusion. Susceptibility to ciprofloxacin is inferred from pefloxacin disk diffusion according to EUCAST clinical breakpoints (v.15.0). [2]Breakpoints according to national zone distributions.

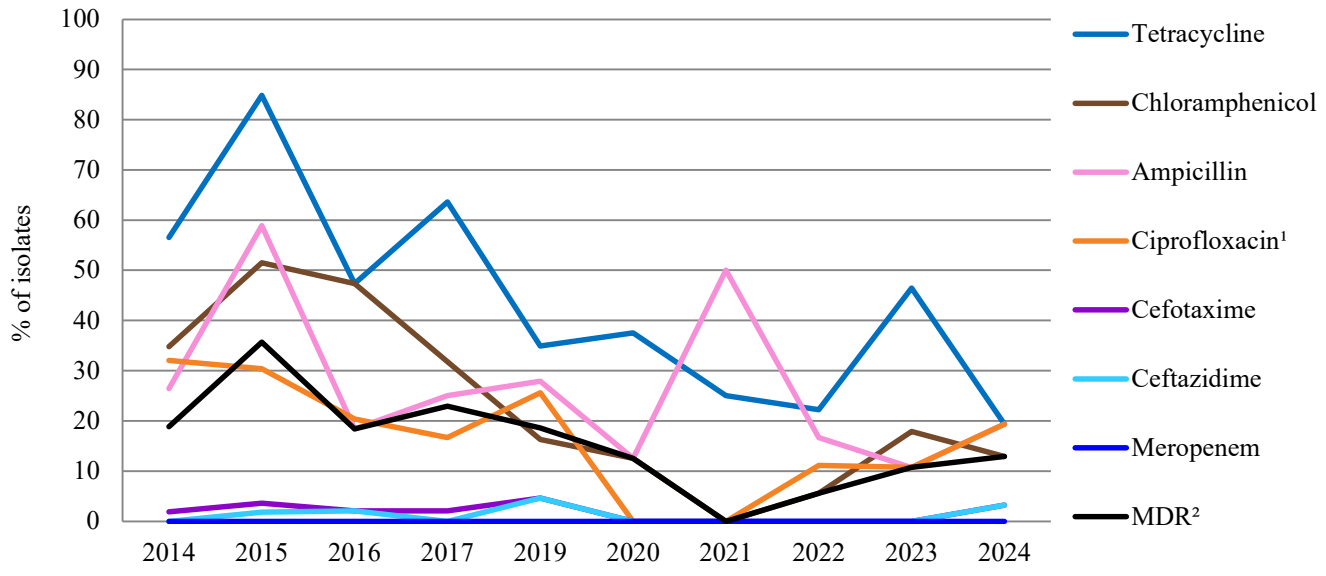


FIGURE 60. Trend 2014-2024. Percentage of travel associated *Salmonella* Typhimurium resistant to selected antimicrobial agents in Norway. [1]Resistance to ciprofloxacin is inferred from pefloxacin disk diffusion 2016 onwards. [2]MDR is defined as acquired non-susceptibility to antimicrobials from three or more categories.

TABLE 28. Percentage distributions of predicted genotypic resistance in travel associated *Salmonella* Typhimurium (n=35) compared to phenotypic wild type/non-wild type distribution (n=31) from human clinical specimens in Norway 2024.

	Phenotype[1] (%)		Predicted genotype[2] (%)	
Antibiotic	Wild type	Non-wild type	S	R
Gentamicin	-	-	100.0	0.0
Streptomycin	-	-	77.1	22.9
Ampicillin	77.4	22.6	82.9	17.1
Meropenem	100.0	0.0	100.0	0.0
Cefotaxime[3]	96.8	3.2	97.1	2.9
Ceftazidime[3]	96.8	3.2		
Colistin	-	-	100.0	0.0
Chloramphenicol	83.9	16.1	85.7	14.3
Ciprofloxacin	83.9	16.1	82.9	17.1
Sulfonamide	-	-	82.9	17.1
Tetracycline	80.6	19.4	77.1	22.9
Trimethoprim	-	-	91.4	8.6

[1]Wild type (WT) and non-wild type (NWT) categorisation according to EUCAST epidemiological cut-off values (ECOFF), and clinical breakpoints in absence of ECOFF for *Salmonella enterica* (v.15.0). [2]R and S categorisation based on presence or absence of resistance determinants. [3]Predicted genotypic resistance to cefotaxime and ceftazidime is combined to predict genotypic resistance against extended spectrum cephalosporins.

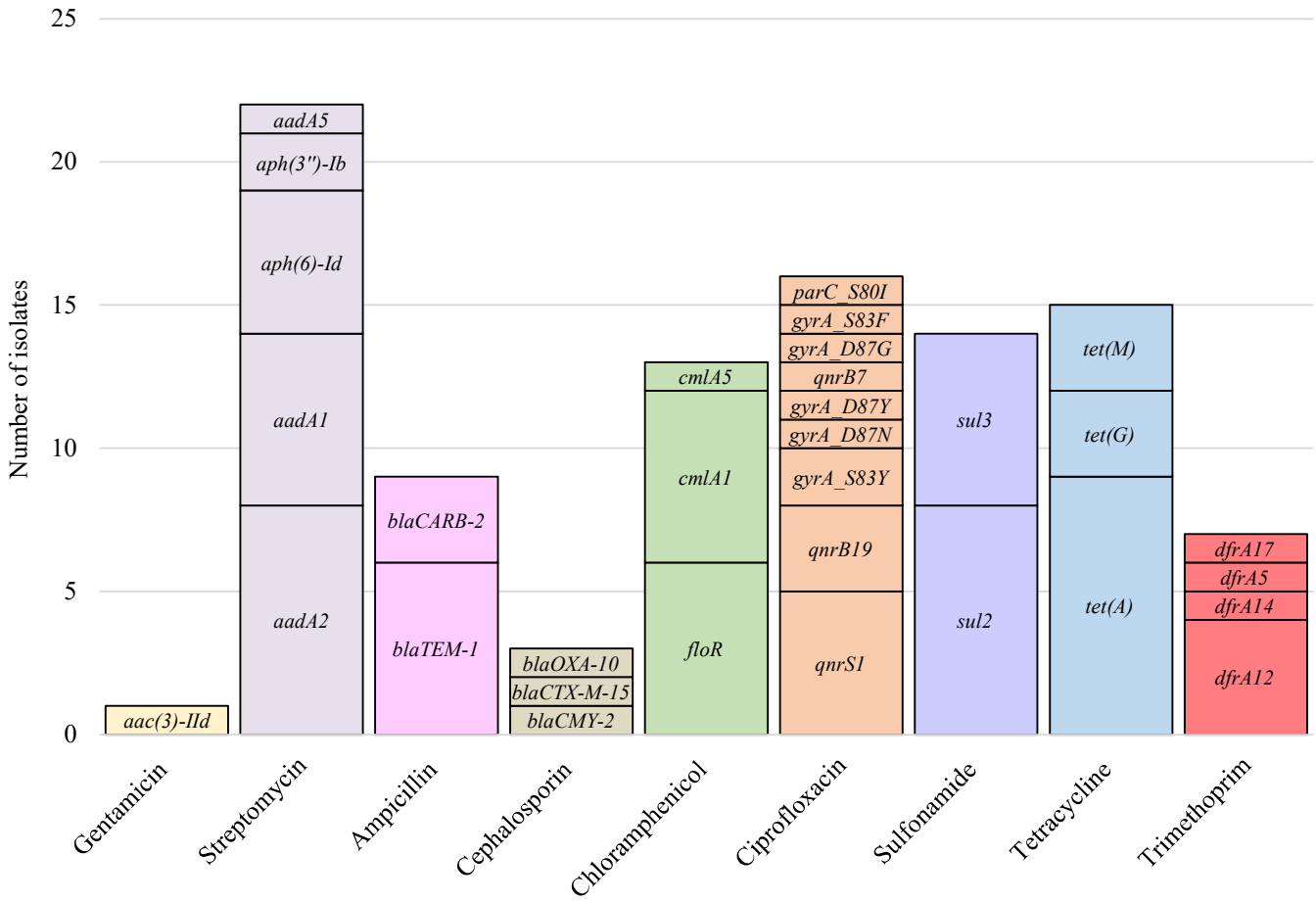


FIGURE 61. Identified resistance determinants in *Salmonella* Typhimurium (n=93) to selected antimicrobial agents in Norway 2024.

ANTIMICROBIAL RESISTANCE IN MONOPHASIC SALMONELLA TYPHIMURIUM

TABLE 29. Percentage distributions of antimicrobial susceptibility categories in domestically acquired monophasic *Salmonella* Typhimurium (n=8) from human clinical specimens in Norway 2024.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Ampicillin	≤ 8	> 8	12.5	-	87.5
Cefotaxime	≤ 1	> 2	100.0	0.0	0.0
Ceftazidime	≤ 1	> 4	100.0	0.0	0.0
Meropenem	≤ 2	> 8	100.0	0.0	0.0
Pefloxacin[1]	≥ 24 mm	< 24 mm	87.5	-	12.5
Tetracycline[2]	≥ 17 mm	< 17 mm	25.0	-	75.0
Chloramphenicol	≤ 8	> 8	75.0	-	25.0

[1] Low-level resistance against ciprofloxacin is underestimated using breakpoints based on ciprofloxacin disk diffusion. Susceptibility to ciprofloxacin is inferred from pefloxacin disk diffusion according to EUCAST clinical breakpoints (v.15.0). [2]Breakpoints according to national zone distributions.

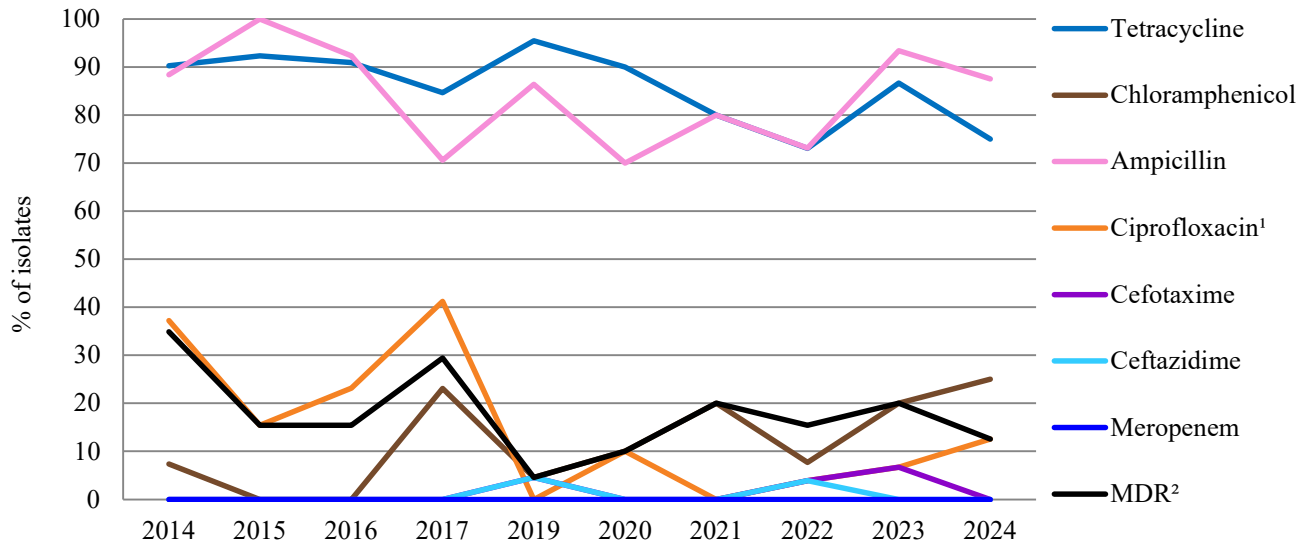


FIGURE 62. Trend 2014-2024. Percentage of domestically acquired monophasic *Salmonella* Typhimurium resistant to selected antimicrobial agents in Norway. [1]Resistance to ciprofloxacin is inferred from pefloxacin disk diffusion 2016 onwards. [2]MDR is defined as acquired non-susceptibility to antimicrobials from three or more categories.

TABLE 30. Percentage distributions of predicted genotypic resistance in domestically acquired monophasic *Salmonella* Typhimurium (n=10) compared to phenotypic wild type/non-wild type distribution (n=8) from human clinical specimens in Norway 2024.

	Phenotype[1] (%)		Predicted genotype[2] (%)	
Antibiotic	Wild type	Non-wild type	S	R
Gentamicin	-	-	100.0	0.0
Streptomycin	-	-	30.0	70.0
Ampicillin	12.5	87.5	20.0	80.0
Meropenem	100.0	0.0	100.0	0.0
Cefotaxime[3]	100.0	0.0	100.0	0.0
Ceftazidime[3]	100.0	0.0		
Colistin	-	-	100.0	0.0
Chloramphenicol	75.0	25.0	80.0	20.0
Ciprofloxacin	87.5	12.5	90.0	10.0
Sulfonamide	-	-	40.0	60.0
Tetracycline	25.0	75.0	20.0	80.0
Trimethoprim	-	-	80.0	20.0

[1]Wild type (WT) and non-wild type (NWT) categorisation according to EUCAST epidemiological cut-off values (ECOFF), and clinical breakpoints in absence of ECOFF for *Salmonella enterica* (v.15.0). [2]R and S categorisation based on presence or absence of resistance determinants. [3]Predicted genotypic resistance to cefotaxime and ceftazidime is combined to predict genotypic resistance against extended spectrum cephalosporins.

TABLE 31. Percentage distributions of antimicrobial susceptibility categories in travel associated monophasic *Salmonella* Typhimurium (n=10) from human clinical specimens in Norway 2024.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Ampicillin	≤ 8	> 8	30.0	-	70.0
Cefotaxime	≤ 1	> 2	100.0	0.0	0.0
Ceftazidime	≤ 1	> 4	100.0	0.0	0.0
Meropenem	≤ 2	> 8	100.0	0.0	0.0
Pefloxacin[1]	≥ 24 mm	< 24 mm	100.0	-	0.0
Tetracycline[2]	≥ 17 mm	< 17 mm	20.0	-	80.0
Chloramphenicol	≤ 8	> 8	80.0	-	20.0

[1]Low-level resistance against ciprofloxacin is underestimated using breakpoints based on ciprofloxacin disk diffusion. Susceptibility to ciprofloxacin is inferred from pefloxacin disk diffusion according to EUCAST clinical breakpoints (v.15.0). [2]Breakpoints according to national zone distributions.

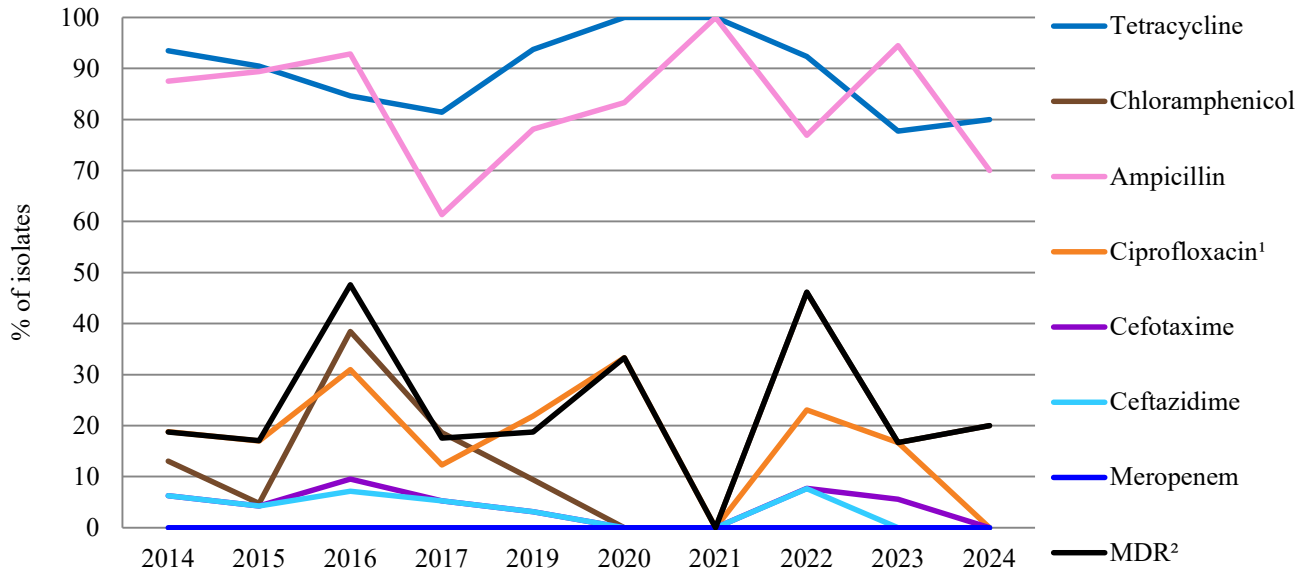


FIGURE 63. Trend 2014-2024. Percentage of travel associated monophasic *Salmonella* Typhimurium resistant to selected antimicrobial agents in Norway. [1]Resistance to ciprofloxacin is inferred from pefloxacin disk diffusion 2016 onwards. [2]MDR is defined as acquired non-susceptibility to antimicrobials from three or more categories.

TABLE 32. Percentage distributions of predicted genotypic resistance in travel associated monophasic *Salmonella* Typhimurium (n=21) compared to phenotypic wild type/non-wild type distribution (n=10) from human clinical specimens in Norway 2024.

	Phenotype[1] (%)		Predicted genotype[2] (%)	
Antibiotic	Wild type	Non-wild type	S	R
Gentamicin	-	-	85.7	14.3
Streptomycin	-	-	33.3	66.7
Ampicillin	30.0	70.0	28.6	71.4
Meropenem	100.0	0.0	100.0	0.0
Cefotaxime[3]	100.0	0.0	100.0	0.0
Ceftazidime[3]	100.0	0.0		
Colistin	-	-	100.0	0.0
Chloramphenicol	80.0	20.0	76.2	23.8
Ciprofloxacin	100.0	0.0	81.0	19.0
Sulfonamide	-	-	28.6	71.4
Tetracycline	20.0	80.0	23.8	76.2
Trimethoprim	-	-	85.7	14.3

[1]Wild type (WT) and non-wild type (NWT) categorisation according to EUCAST epidemiological cut-off values (ECOFF), and clinical breakpoints in absence of ECOFF for *Salmonella enterica* (v.15.0). [2]R and S categorisation based on presence or absence of resistance determinants. [3]Predicted genotypic resistance to cefotaxime and ceftazidime is combined to predict genotypic resistance against extended spectrum cephalosporins.

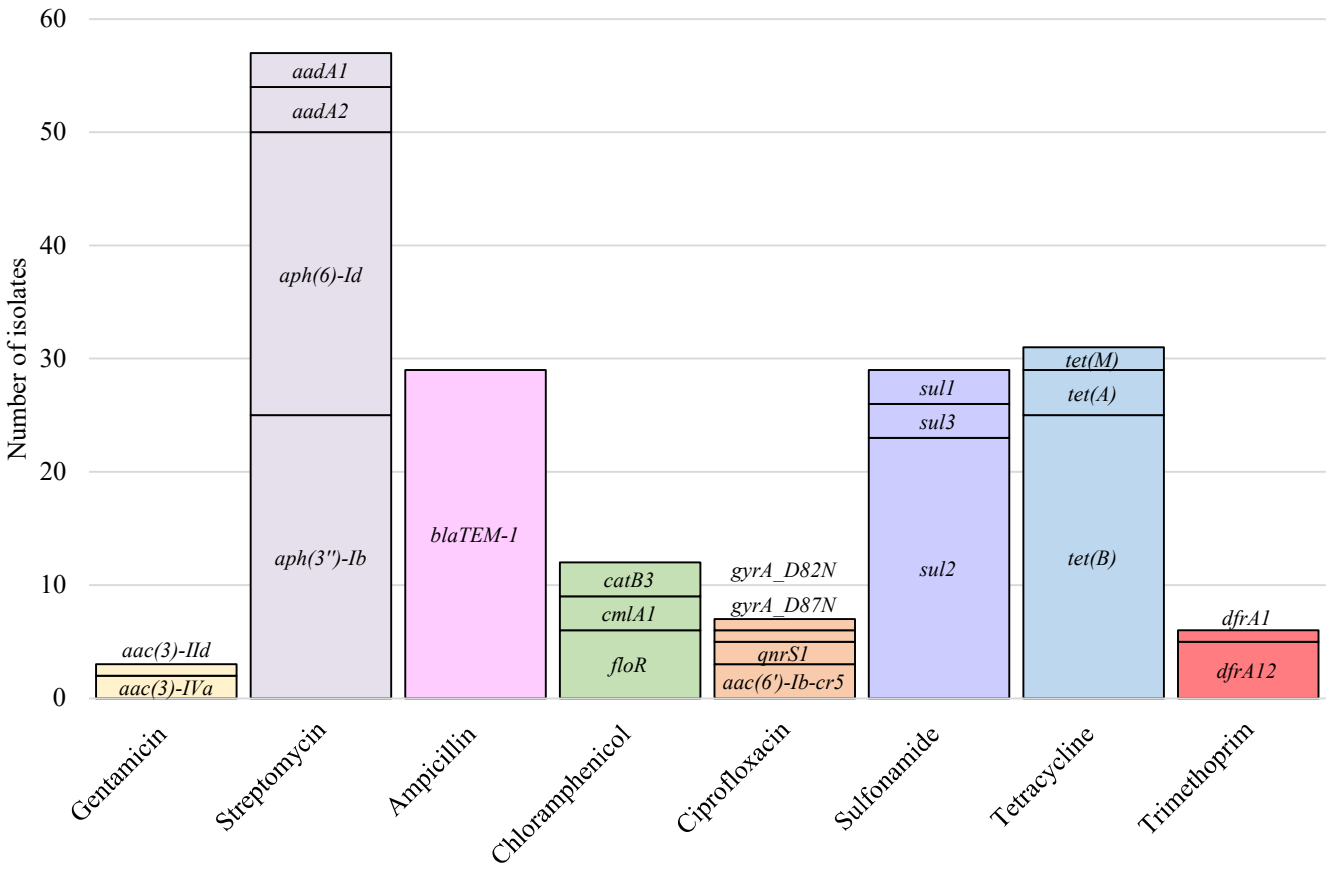


FIGURE 64. Identified resistance determinants in monophasic *Salmonella* Typhimurium (n=39) to selected antimicrobial agents in Norway 2024.

ANTIMICROBIAL RESISTANCE IN SALMONELLA ENTERITIDIS

TABLE 33. Percentage distributions of antimicrobial susceptibility categories in *Salmonella* Enteritidis (n=129) from human clinical specimens irrespective of place of acquisition, in Norway 2024.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Ampicillin	≤ 8	> 8	92.2	-	7.8
Cefotaxime	≤ 1	> 2	99.2	0.0	0.8
Ceftazidime	≤ 1	> 4	99.2	0.0	0.8
Meropenem	≤ 2	> 8	100.0	0.0	0.0
Pefloxacin[1]	≥ 24 mm	< 24 mm	73.6	-	26.4
Tetracycline[2]	≥ 17 mm	< 17 mm	94.6	-	5.4
Chloramphenicol	≤ 8	> 8	100.0	-	0.0

[1] Low-level resistance against ciprofloxacin is underestimated using breakpoints based on ciprofloxacin disk diffusion. Susceptibility to ciprofloxacin is inferred from pefloxacin disk diffusion according to EUCAST clinical breakpoints (v.15.0). [2]Breakpoints according to national zone distributions.

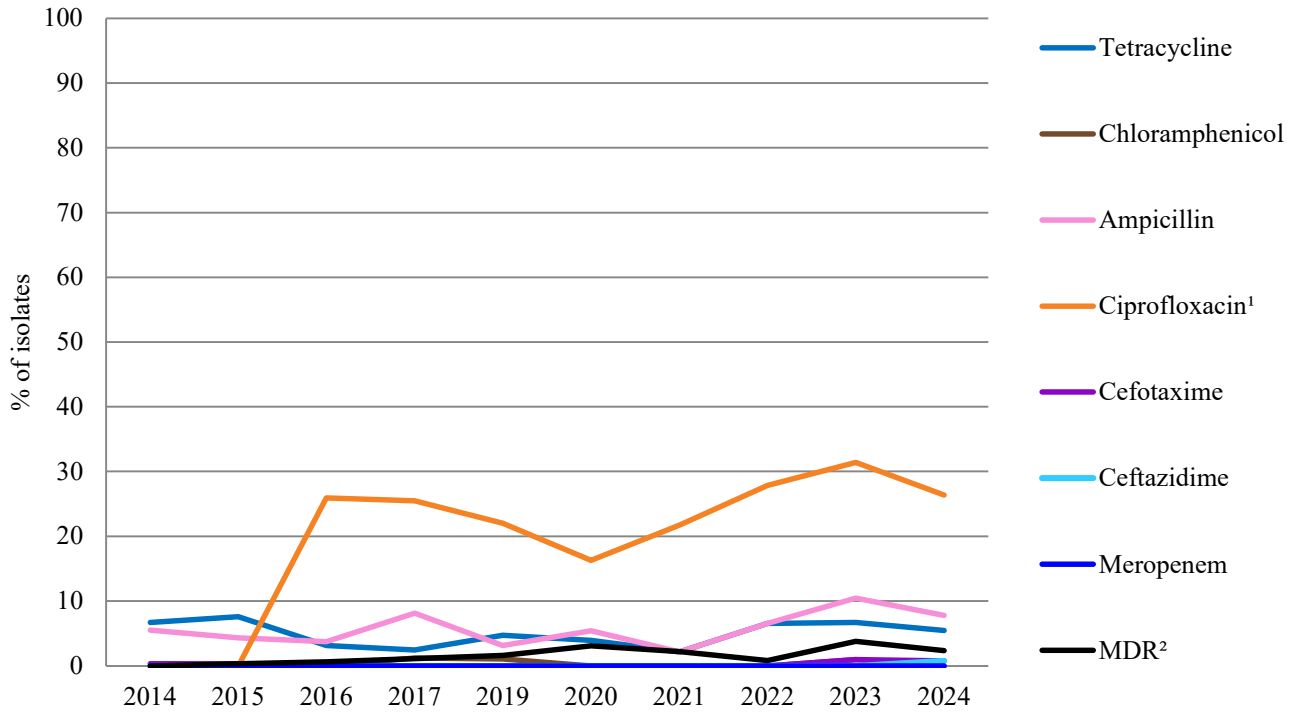


FIGURE 65. Trend 2014-2024. Percentage of *Salmonella* Enteritidis resistant to selected antimicrobial agents irrespective of place of acquisition, in Norway. [1]Resistance to ciprofloxacin is inferred from pefloxacin disk diffusion 2016 onwards. [2]MDR is defined as acquired non-susceptibility to antimicrobials from three or more categories.

TABLE 34. Percentage distributions of predicted genotypic resistance in *Salmonella* Enteritidis (n=262) compared to phenotypic wild type/non-wild type distribution (n=129) from human clinical specimens, in Norway 2024.

	Phenotype[1] (%)		Predicted genotype[2] (%)	
Antibiotic	Wild type	Non-wild type	S	R
Gentamicin	-	-	100.0	0.0
Streptomycin	-	-	99.2	0.8
Ampicillin	90.7	9.3	98.1	1.9
Meropenem	100.0	0.0	100.0	0.0
Cefotaxime[3]	99.2	0.8	98.1	1.9
Ceftazidime[3]	99.2	0.8		
Colistin	-	-	100.0	0.0
Chloramphenicol	100.0	0.0	100.0	0.0
Ciprofloxacin	73.6	26.4	69.8	30.2
Sulfonamide	-	-	99.2	0.8
Tetracycline	94.6	5.4	95.4	4.6
Trimethoprim	-	-	100.0	0.0

[1]Wild type (WT) and non-wild type (NWT) categorisation according to EUCAST epidemiological cut-off values (ECOFF), and clinical breakpoints in absence of ECOFF for *Salmonella enterica* (v.15.0). [2]R and S categorisation based on presence or absence of resistance determinants. [3]Predicted genotypic resistance to cefotaxime and ceftazidime is combined to predict genotypic resistance against extended spectrum cephalosporins.

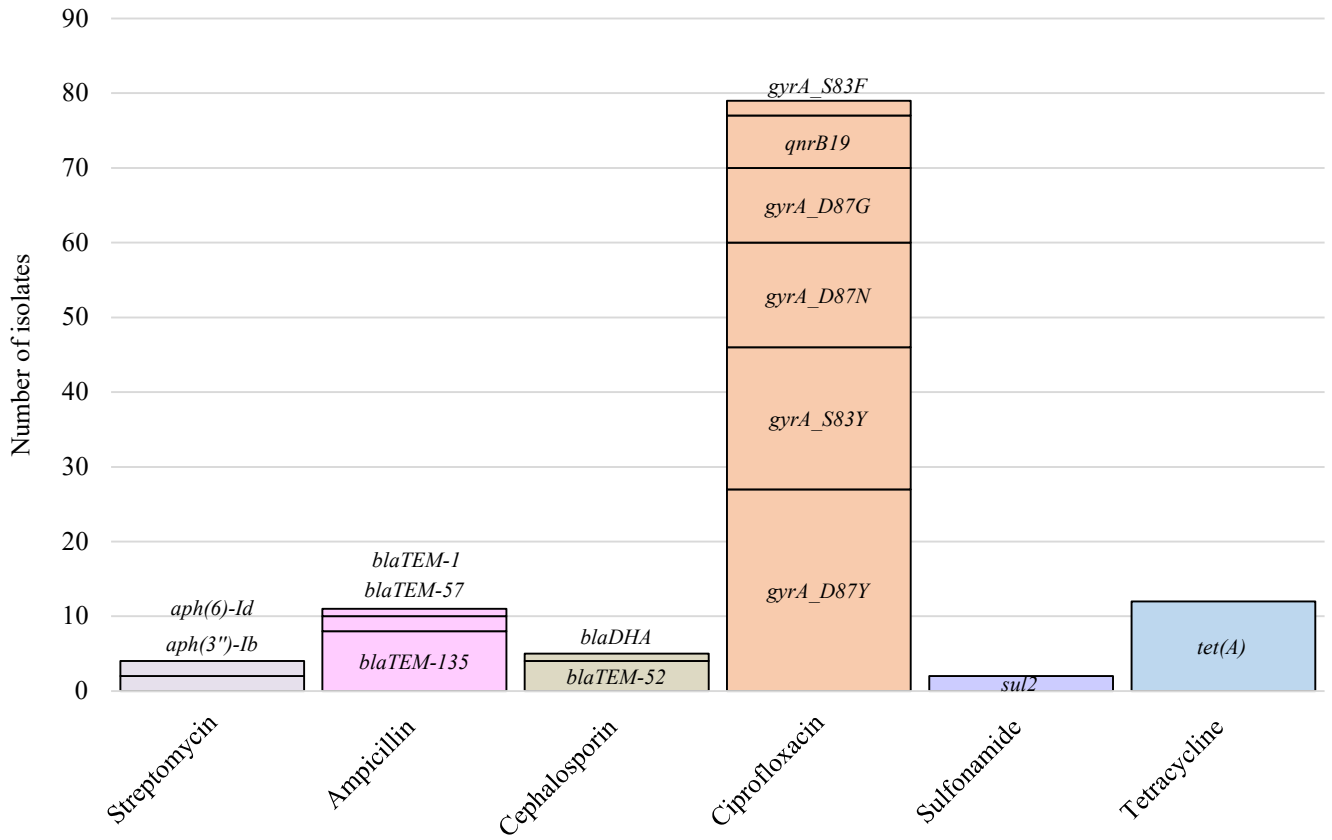


FIGURE 66. Identified resistance determinants in *Salmonella* Enteritidis (n=262) to selected antimicrobial agents in Norway 2024.

ANTIMICROBIAL RESISTANCE IN SALMONELLA TYPHI

TABLE 35. Percentage distributions of antimicrobial susceptibility categories in *Salmonella* Typhi (n=12) from human clinical specimens irrespective of place of acquisition, in Norway 2024.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Ampicillin	≤ 8	> 8	58.3	-	41.7
Cefotaxime	≤ 1	> 2	58.3	0.0	41.7
Ceftazidime	≤ 1	> 4	58.3	0.0	41.7
Meropenem	≤ 2	> 8	100.0	0.0	0.0
Pefloxacin[1]	≥ 24 mm	< 24 mm	0.0	-	100.0
Tetracycline[2]	≥ 17 mm	< 17 mm	100.0	-	0.0
Chloramphenicol	≤ 8	> 8	58.3	-	41.7

[1] Low-level resistance against ciprofloxacin is underestimated using breakpoints based on ciprofloxacin disk diffusion. Susceptibility to ciprofloxacin is inferred from pefloxacin disk diffusion according to EUCAST clinical breakpoints (v.15.0). [2]Breakpoints according to national zone distributions.

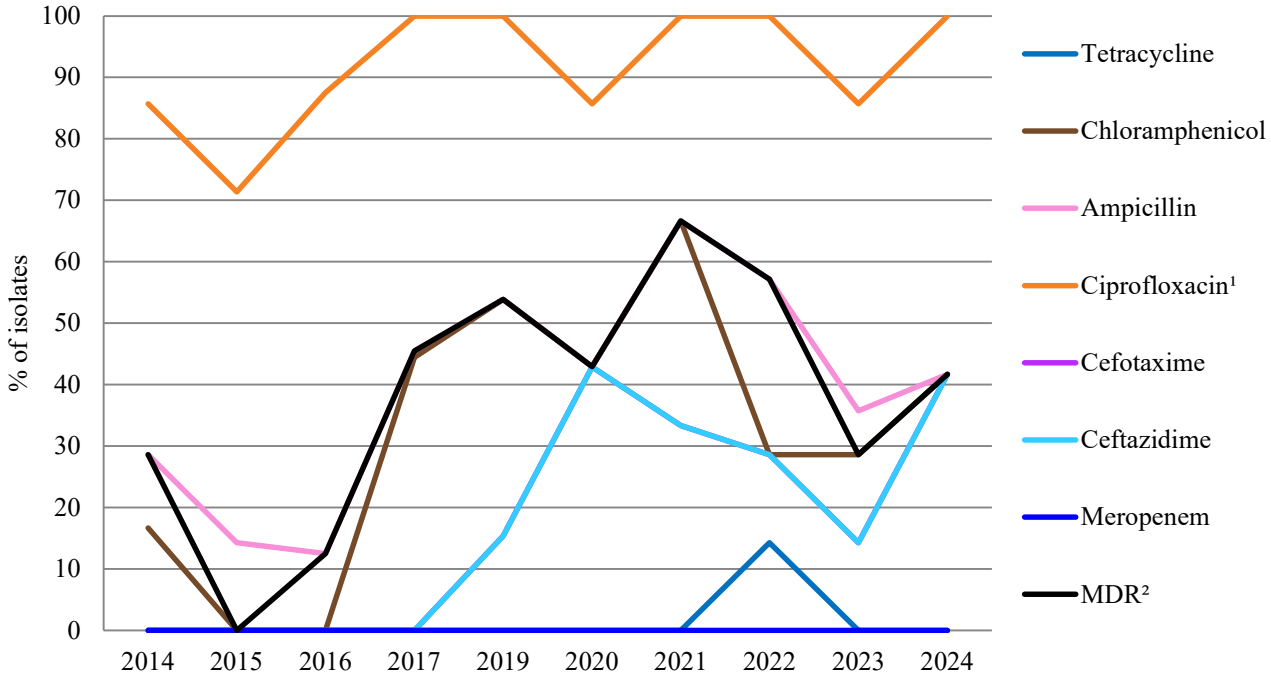


FIGURE 67. Trend 2014-2024. Percentage of *Salmonella* Typhi resistant to selected antimicrobial agents irrespective of place of acquisition, in Norway.[1]Resistance to ciprofloxacin is inferred from pefloxacin disk diffusion 2016 onwards. [2]MDR is defined as acquired non-susceptibility to antimicrobials from three or more categories.

TABLE 36. Percentage distributions of predicted genotypic resistance in *Salmonella* Typhi (n=12) compared to phenotypic wild type/non-wild type distribution (n=12) from human clinical specimens in Norway 2024.

	Phenotype[1] (%)		Predicted genotype[2] (%)	
Antibiotic	Wild type	Non-wild type	S	R
Gentamicin	-	-	100.0	0.0
Streptomycin	-	-	75.0	25.0
Ampicillin	58.3	41.7	58.3	41.7
Meropenem	100.0	0.0	100.0	0.0
Cefotaxime[3]	58.3	41.7	58.3	41.7
Ceftazidime[3]	58.3	41.7		
Colistin	-	-	100.0	0.0
Chloramphenicol	58.3	41.7	58.3	41.7
Ciprofloxacin	0.0	100.0	0.0	100.0
Sulfonamide	-	-	58.3	41.7
Tetracycline	100.0	0.0	100.0	0.0
Trimethoprim	-	-	58.3	41.7

[1]Wild type (WT) and non-wild type (NWT) categorisation according to EUCAST epidemiological cut-off values (ECOFF), and clinical breakpoints in absence of ECOFF for *Salmonella enterica* (v.15.0). [2]R and S categorisation based on presence or absence of resistance determinants. [3]Predicted genotypic resistance to cefotaxime and ceftazidime is combined to predict genotypic resistance against extended spectrum cephalosporins.

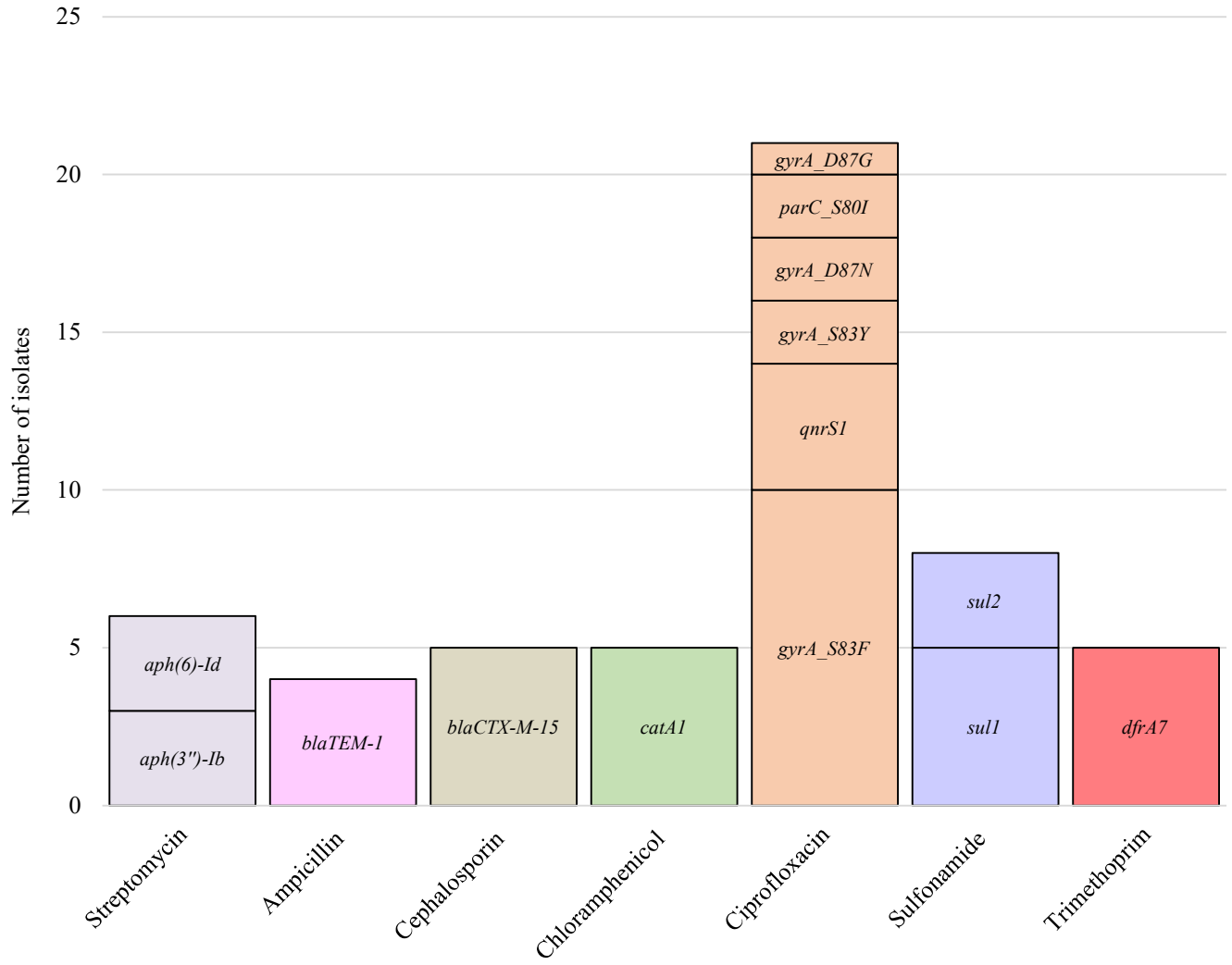


FIGURE 68. Identified resistance determinants in *Salmonella* Typhi (n=12) to selected antimicrobial agents in Norway 2024.

ANTIMICROBIAL RESISTANCE IN OTHER SALMONELLA SEROTYPES

TABLE 37. Percentage distributions of predicted genotypic resistance in other *Salmonella* serotypes (n=363) to phenotypic wild type/non-wild type distribution (n=253) from human clinical specimens in Norway 2024.

	Phenotype[1] (%)		Predicted genotype[2] (%)	
Antibiotic	Wild type	Non-wild type	S	R
Gentamicin	-	-	98.1	1.9
Streptomycin	-	-	89.0	11.0
Ampicillin	91.3	8.7	90.9	9.1
Meropenem	100.0	0.0	100.0	0.0
Cefotaxime[3]	99.2	0.8	98.6	1.4
Ceftazidime[3]	99.2	0.8		
Colistin	-	-	100.0	0.0
Chloramphenicol	94.9	5.1	95.3	4.7
Ciprofloxacin	84.6	15.4	81.0	19.0
Sulfonamide	-	-	90.6	9.4
Tetracycline	88.9	11.1	87.1	12.9
Trimethoprim	-	-	93.1	6.9

[1]Wild type (WT) and non-wild type (NWT) categorisation according to EUCAST epidemiological cut-off values (ECOFF), and clinical breakpoints in absence of ECOFF for *Salmonella enterica* (v.15.0). [2]R and S categorisation based on presence or absence of resistance determinants. [3]Predicted genotypic resistance to cefotaxime and ceftazidime is combined to predict genotypic resistance against extended spectrum cephalosporins.

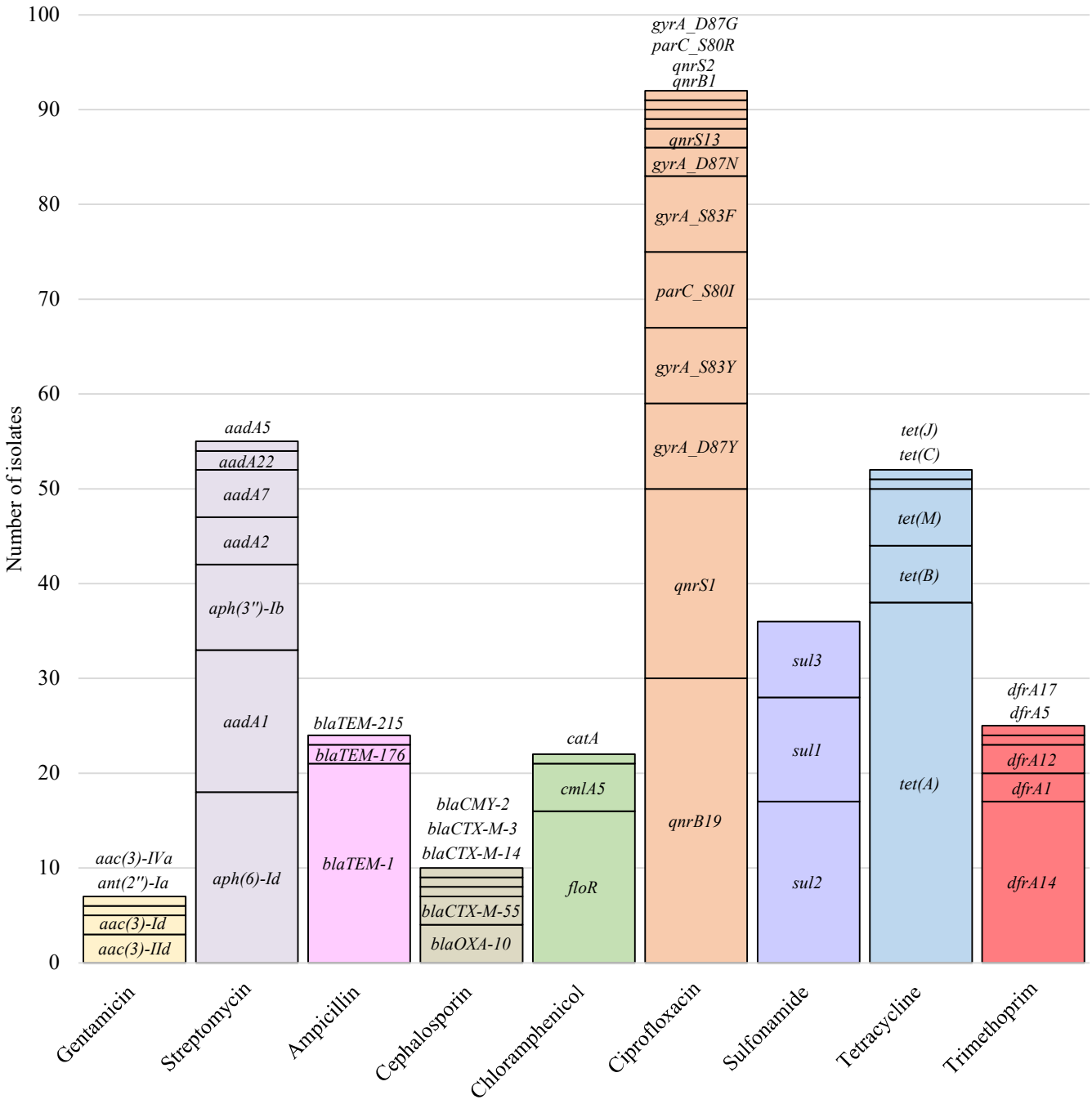


FIGURE 69. Identified resistance determinants in other *Salmonella* serotypes (n=363) to selected antimicrobial agents in Norway 2024.

MULTI-DRUG RESISTANCE IN SALMONELLA

TABLE 38. Number of predicted genotypic multi-drug resistant (MDR) *Salmonella* isolates identified in Norway 2024, stratified according to serotype and resistance to different antibiotic categories.

Salmonella serotypes	MDR[1]	Antibiotic categories[2]							
		STR	AMP	ESC	CHL	CIP	SUL	TET	TMP
monophasic *Salmonella* Typhimurium	28	27	27	0	8	6	27	26	6
Salmonella Typhimurium	16	15	11	1	10	11	11	14	6
Salmonella Typhi	5	3	5	5	5	5	5	0	5
Salmonella Enteritidis	7	2	7	0	0	7	2	6	0
Other *Salmonella*	48	39	27	5	17	39	33	36	25
Total no. of MDR isolates	**104**	**86**	**77**	**11**	**40**	**68**	**78**	**82**	**42**

[1]Multi-drug resistance (MDR) defined as predicted genotypic resistance to 3 ≥ antibiotic categories. [2]Antibiotic category: STR: Streptomycin, AMP; Ampicillin, ESC; Extended Spectrum Cephalosporin, CHL; Chloramphenicol, CIP; Ciprofloxacin, SUL; Sulfonamide, TET; Tetracycline, TMP; Trimethoprim.

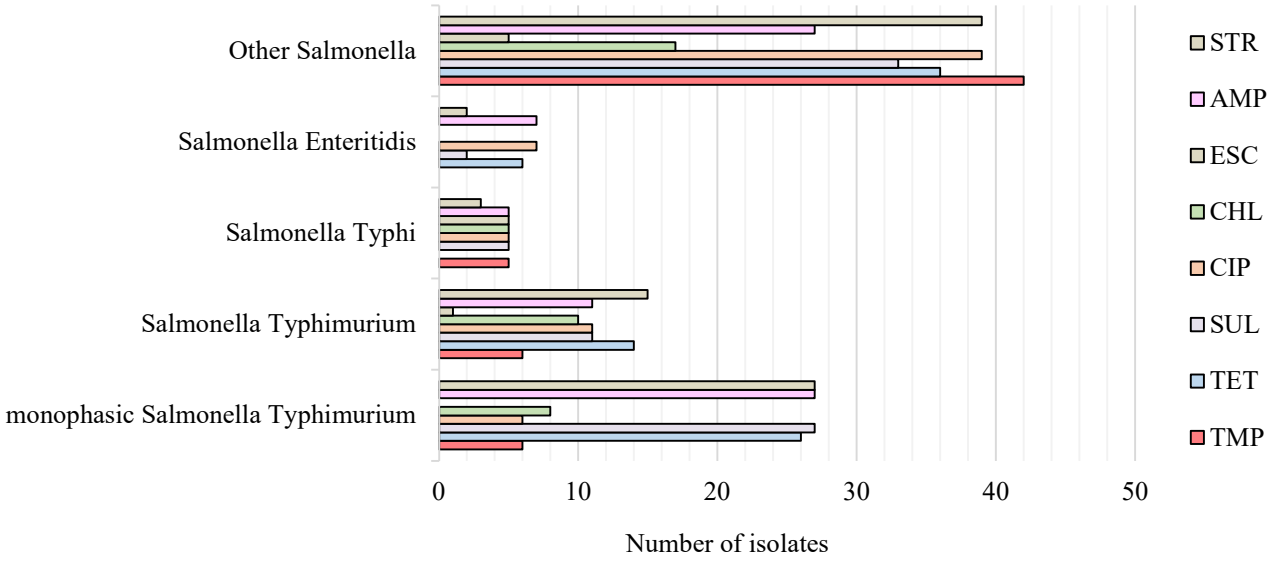


FIGURE 70. Number of predicted genotypic multi-drug resistant (MDR) *Salmonella* isolates (n=104) identified in Norway 2024, stratified according to serotype and resistance to different antibiotic categories; STR: Streptomycin, AMP; Ampicillin, ESC; Extended Spectrum Cephalosporin, CHL; Chloramphenicol, CIP; Ciprofloxacin, SUL; Sulfonamide, TET; Tetracycline, TMP; Trimethoprim.

CORRELATION BETWEEN PHENOTYPIC AND PREDICTED GENOTYPIC RESISTANCE IN SALMONELLA

TABLE 39. Concordance between phenotypic and predicted genotypic resistance to selected antibiotic categories in *Salmonella* isolates identified in Norway 2024.

Antibiotic categories	Tested	Phenotype WT[1]		Phenotype NWT[1]		Sensitivity (%)	Spesificity (%)
		Genotype R	Genotype S	Genotype R	Genotype S		
Penicillins	546	0	468	61	17	100.0	96.5
ESC[2]	546	1	534	11	0	91.7	100.0
Carbapenems	546	0	546	0	0	-	100.0
Fluoroquinolones	546	4	428	112	2	96.6	99.5
Tetracycline	546	7	473	58	8	89.2	98.3
Phenicols	546	2	511	29	4	93.5	99.2

[1]Wild type (WT) and non-wild type (NWT) categorisation according to EUCAST epidemiological cut-off values (ECOFF), and clinical breakpoints in abscense of ECOFF for *Salmonella enterica* (v.15.0). [2]Predicted genotypic resistance to cefotaxime and ceftazidime is combined as predicted genotypic resistance against extended spectrum cephalosporin (ESC).

RESULTS AND COMMENTS

The NRL annually performs antimicrobial susceptibility testing on a selection of the received *Salmonella* isolates. Selection criteria are set to ensure inclusion of the most important *Salmonella* serovars and important antibiotics for the monitoring of emergence and dissemination of antimicrobial resistance in Norway. Additionally, from 2020 onwards, the NRL has screened all *Salmonella* isolates for antimicrobial resistance determinants following whole genome sequencing to predict genotypic resistance. In 2020 and 2021, during the Covid-19 pandemic, the government enforced infection control measures which included travel restrictions that substantially reduced travel associated *Salmonella* infections. Analysis of trends in antimicrobial resistance must be interpreted accordingly.

In 2024 the NRL identified a total of 9 outbreak clusters, including four different clusters of *S.* Typhimurium (n=114, 14, 11, and 11), two *S.* Newport clusters (n=72 and 26), as well as one cluster each of *S.* Napoli (n=17), *S.* Muenster (n=17) and *S.* Hvittingfoss (n=11). The largests *S.* Typhimurium cluster along with the two *S.* Newport clusters were part of the largest outbreak of salmonellosis recorded in Norway since the 1980s. The outbreak was linked to imported alfalfa sprouts (Arthur Rakover et al. 2025. DOI: 10.1007/s15010-025-02556-2). Also, one of the smaller *S.* Typhimurium clusters and the *S.* Hvittingfoss cluster were suspected to be associated with consumption of alfalfa sprouts from an earlier batch. Antimicrobial resistance results from only a single strain from each of these clusters are included in this report.

The overall resistance in *S.* Typhimurium was higher in strains associated with travel compared to strains from domestically acquired infections. We observed a stable trend in resistance to most tested antibiotics in strains from domestically acquired infections. We observed an increase in ciprofloxacin resistance for strains from infections associated with travel. Two ESBL producers were identified ($bla_{\text{CTX-M-15}}$ and $bla_{\text{CMY-2}}$). Variants of the plasmid-mediated quinolone resistance gene *qnr* were identified as probable mediator for the observed ciprofloxacin resistance in 8 of 13 strains. An MDR

genotype was assigned to 17.2 % of the strains, largely attributed to resistance against streptomycin, sulfonamide, and tetracycline.

The overall resistance level in the monophasic variant of *S.* Typhimurium was higher than for *S.* Typhimurium. We observed a stable trend in resistance over the last five years for all the tested antibiotics. High levels of resistance were seen for ampicillin and tetracycline in strains from both domestically acquired and travel associated infections. No ESBL-producing strains were identified. An MDR genotype was identified in 71.8% of the strains, largely attributed to resistance against streptomycin, ampicillin, chloramphenicol, sulfonamide, and tetracycline.

Antibiotic resistance in *S.* Enteritidis is generally low. An apparent sudden emergence of ciprofloxacin resistance in 2016 was linked to the change in antibiotic used for testing fluoroquinolone resistance (from ciprofloxacin to pefloxacin). When screening for genotypic resistance determinants, the presence of various mutations in the quinolone resistance-determining regions (QRDRs) of *gyrA* as well as the presence of *qnr* was confirmed. Five ESBL-producing strains were identified by genotypic resistance, four encoding $bla_{\text{TEM-52}}$ and one bla_{DHA}. Only one of the $bla_{\text{TEM-52}}$ strains also conferred phenotypic resistance to extended spectrum cephalosporins. An MDR genotype was identified for 2.7% of the strains, attributed to resistance against ampicillin, ciprofloxacin, and tetracycline.

The overall level of antibiotic resistance in *S.* Typhi is high. Two ESBL-producing strains were identified, both encoding $bla_{\text{CTX-M-15}}$. An MDR genotype was identified in 28.6% of the strains, largely attributed to resistance against streptomycin, ampicillin, chloramphenicol, ciprofloxacin, sulfonamide, and trimethoprim.

Among other *Salmonella* serotypes (n=363), the most common serotypes identified were *S.* Newport (n=122), *S.* Stanley (n=31), *S.* Paratyphi B variant Java (n=25), *S.* Muenster (n=24, *S.* Chester (n=17), *S.* Napoli (n=21), *S.* Hvittingfoss (n=17), *S.* Agona (n=16) and *S.* Infantis (n=11). Overall predicted genotypic resistance was low (<12%) across all screened antibiotics, except for quinolones (19%) and tetracycline (12.9%). Five ESBL-producing strains were identified, encoding $bla_{\text{CTX-M-55}}$ (n=3), $bla_{\text{CTX-M-3}}$ (n=1) and $bla_{\text{CMY-2}}$ (n=1). In addition, one strain encoding $bla_{\text{CTX-M-55}}$ also encoded $bla_{\text{CTX-M-14}}$. Presence of various mutations in the QRDRs of *gyrA* and variants of *qnr* were predicted as conferring resistance to quinolones. An MDR genotype was identified in 13.2% of the *Salmonella* strains of other serotypes. The MDR genotype was largely attributed to resistance towards streptomycin, ampicillin, ciprofloxacin, sulfonamide, tetracycline, and trimethoprim.

In total, 18 strains were predicted as genotypically resistant to extended spectrum cephalosporin: *S.* Typhi (n=5), *S.* Enteritidis (n=5), *S.* Typhimurium (n=2), *S.* Kentucky (n=2), *S.* Paratyphi B variant Java (n=1), *S.* Bredeney (n=1), *S.* Dublin (n=1), and *S.* Infantis (n=1). Resistance was mediated by different variants of $bla_{\text{CTX-M}}$ (n=11), $bla_{\text{TEM-52}}$ (n=4), $bla_{\text{CMY-2}}$ (n=2) and $bla_{\text{DHA-1}}$ (n=1) genes. The overall correlation between phenotypic resistance and predicted genotypic resistance was high, both sensitivity and specificity were generally above 90% for all tested and screened antibiotics.

CAMPYLOBACTER SPP.

Campylobacter jejuni from broilers

Caecal samples from 56 broiler flocks were examined. These were flocks identified as *Campylobacter* positive in the surveillance programme for *Campylobacter* spp. in broiler flocks in Norway in 2024, or flocks that for some reasons had not been tested in the *Campylobacter* surveillance programme. The *Campylobacter* surveillance programme examined 2,071 flocks from 495 producers (Pettersen *et al.* 2024). *C. jejuni* isolates were obtained from 56 of these flocks, and all of these were susceptibility tested. The results are presented in Table 40, Figures 71-72, and in the text.

TABLE 40. Antimicrobial resistance in *Campylobacter jejuni* from broiler (n=56) in 2024.

Substance	Resistance (%) [95% CI]		Distribution (%) of MIC values (mg/L)*														
			0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	512	≥1024
Tetracycline	1.8	[0.1 – 9.6]				96.4	1.8						1.8				
Chloramphenicol	0.0	[0.0 – 6.4]						98.2		1.8							
Ertapenem	3.6	[0.4 – 12.3]		96.4			1.8	1.8									
Erythromycin	1.8	[0.1 – 9.6]					98.2										1.8
Gentamicin	0.0	[0.0 – 6.4]			5.4	94.6											
Ciprofloxacin	8.9	[3.0 – 9.6]		80.4	10.7				1.8	3.6	3.6						

*Bold vertical lines denote epidemiological cut-off values. CI=confidence interval. White fields show range of dilutions tested for each antimicrobial agent. MIC values higher than the highest concentration tested are given as the lowest MIC value above the range. MIC values equal to or lower than the lowest concentration tested are given as the lowest concentration tested.

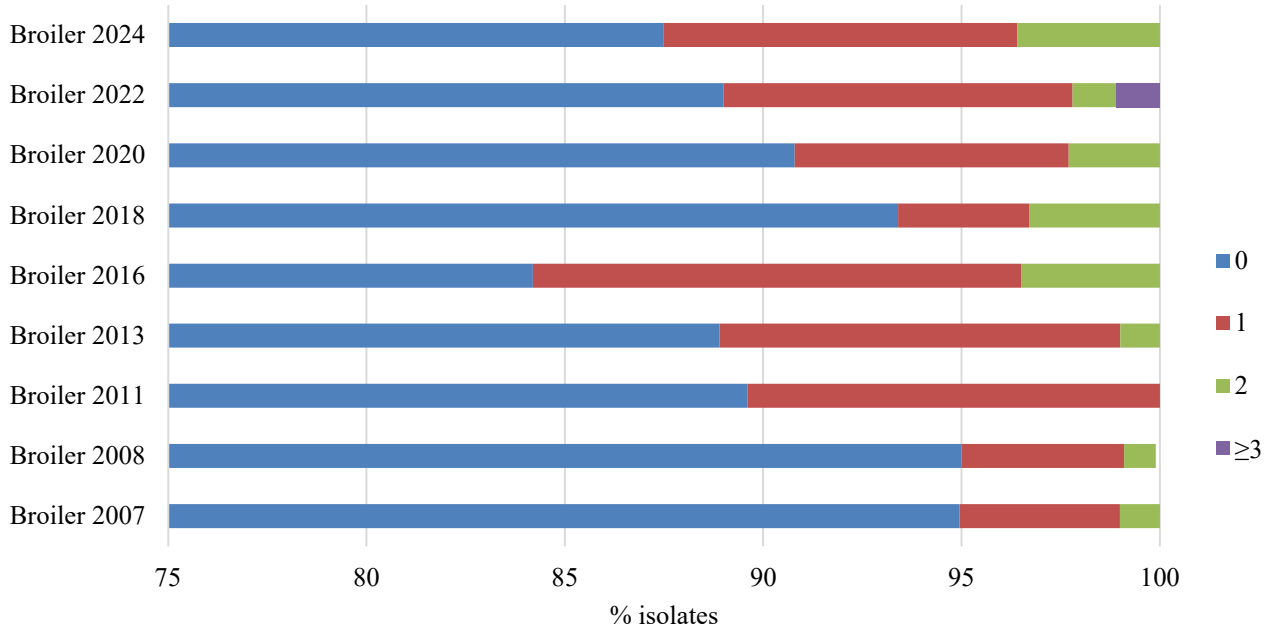


FIGURE 71. Antimicrobial resistance profiles for *Campylobacter jejuni* isolates from broilers in 2007-2024. Proportions of isolates susceptible to all (blue), or resistant to one (red), two (green) or three and more (purple) antimicrobial classes are illustrated. The epidemiological cut-off values used in NORM-VET 2024 were applied.

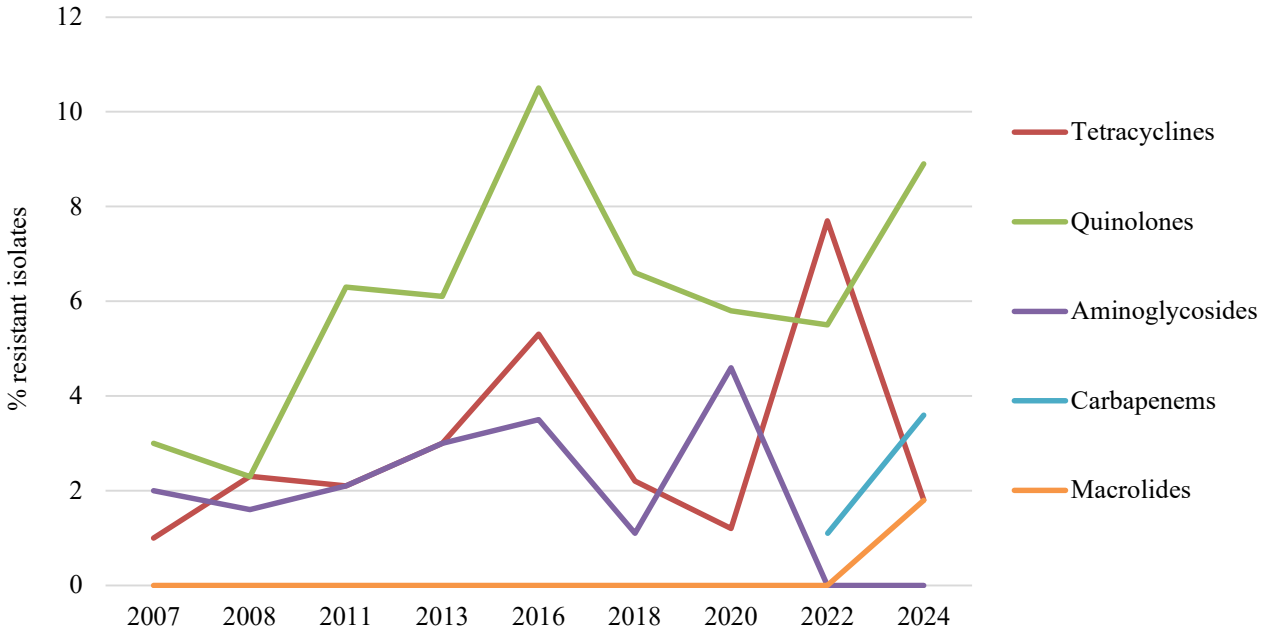


FIGURE 72. Prevalence of resistance to various antimicrobials in *Campylobacter jejuni* from Norwegian broilers in 2007-2024. The epidemiological cut-off values used in NORM-VET 2024 were applied.

RESULTS AND COMMENTS

BROILER

A total of 87.5% of the *C. jejuni* isolates were susceptible to all antimicrobial agents included in the test panel. Resistance to one antimicrobial class was detected in 8.9% of the isolates, while resistance to two antimicrobial classes was detected in 3.6% of the isolates (Figure 71). According to the EFSA classification described in Appendix 6, this corresponds to a moderate occurrence of antimicrobial resistance among *C. jejuni* isolates from broilers. Resistance to the quinolone ciprofloxacin was the most frequently identified resistance determinant.

The antimicrobial agents included in the panel for susceptibility testing of *C. jejuni* changed between 2020 and 2022. Streptomycin and the quinolone nalidixic acid were replaced by chloramphenicol and the carbapenem ertapenem. This has to be taken into account when evaluating the trends in Figures 71-72. Aminoglycoside resistance has previously been due to reduced susceptibility to streptomycin, thereby dropping to zero in 2022 when streptomycin was no longer included.

As Figure 72 shows, there has been an increase in quinolone resistance since 2007. An increase in resistance to quinolones in *C. jejuni* from broilers has also been observed in several of the countries reporting to EFSA (EFSA and ECDC European Union Summary Report 2022-2023). Resistance to the quinolone ciprofloxacin was also the most frequently identified resistance determinant in cattle isolates in 2023, and in the domestically acquired human clinical isolates (NORM/NORM-VET 2023).

Two isolates showed decreased susceptibility to the carbapenem ertapenem. Resistance to ertapenem was also detected in one isolate in 2022. Whole genome sequencing of both the 2022 and the 2024 isolates was not able to determine the resistance mechanisms. There is currently an ongoing project initiated by EFSA, to further investigate carbapenem resistance in *Campylobacter* spp..

In a European perspective, the occurrence of resistance in *C. jejuni* (including quinolone resistance) from Norwegian broilers is quite low, although the occurrence varies between countries reporting to EFSA with the Nordic countries having the lowest resistance rates (EFSA and ECDC European Union Summary Report 2022-2023). Further monitoring is needed to follow the situation in Norway in the years to come.

Campylobacter spp. from human clinical cases

In 2024, 3,091 human campylobacteriosis cases were notified to MSIS. Most cases with known place of acquisition were infected abroad (53%). Surveillance data suggested that most cases were sporadic, and no outbreak clusters were reported. The first ten *Campylobacter* isolates each month from two and first five from two sentinel regional laboratories were submitted to the NRL for Enteropathogenic Bacteria at the NIPH. In addition, isolates recovered from blood cultures were submitted to the NRL for surveillance purposes. A total of 396 isolates were received at NRL, antimicrobial susceptibility testing was performed on 376 unique *Campylobacter jejuni* and 20 *Campylobacter coli* isolates (Table 41) against four different antibiotic groups: macrolides (erythromycin), aminoglycosides (gentamicin), fluoroquinolones (ciprofloxacin), and tetracycline. The results from the antimicrobial susceptibility testing are presented in Tables 42-44, Figures 73-75, and in the related text.

TABLE 41. Number of antimicrobial susceptibility tested *Campylobacter* spp. isolates recovered from human clinical specimens in Norway 2024, by species and place of acquisition.

Campylobacter spp.	No. of isolates tested in 2024	Place of acquisition		
		Norway	Abroad	Unknown
Campylobacter jejuni	376	156	152	68
Campylobacter coli	20	3	13	4
Total	**396**	**159**	**165**	**72**

ANTIMICROBIAL RESISTANCE IN CAMPYLOBACTER JEJUNI

TABLE 42. Percentage distributions of antimicrobial susceptibility categories in domestically acquired *Campylobacter jejuni* (n=156) from human clinical specimens in Norway 2024.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	Susceptible	Resistant	S	I	R
Tetracycline	≤ 2	> 2	82.7	-	17.3
Erythromycin	≤ 4	> 4	100.0	-	0.0
Gentamicin[1]	≤ 2	> 2	100.0	-	0.0
Ciprofloxacin[2]	≤ 0.001	> 0.5	0.0	74.4	25.6

[1]Breakpoints according to ECOFF. [2]Breakpoints for ciprofloxacin adjusted according to EUCAST in keeping with the new I-definition and current dosing practice for infections (v.15.0)

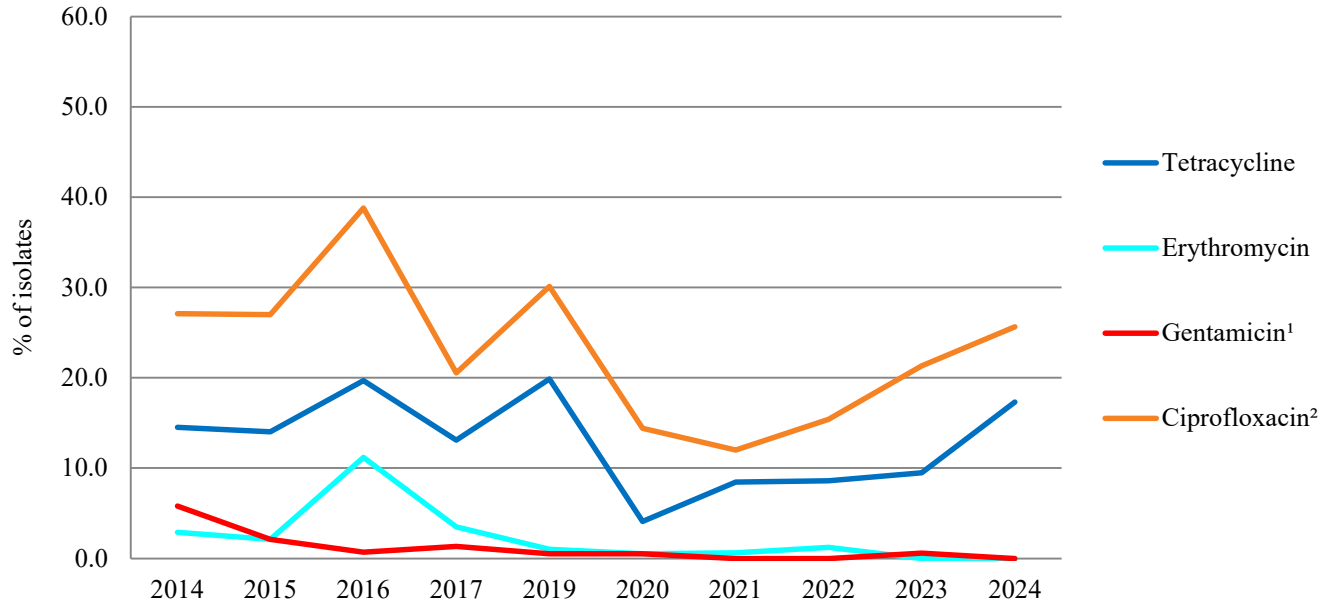


FIGURE 73. Trend 2014-2024. Percentage of domestically acquired *Campylobacter jejuni* resistant to selected antimicrobial agents in Norway. [1]Breakpoints according to ECOFF. [2]Breakpoints for ciprofloxacin adjusted 2020 onwards, according to EUCAST in keeping with the new I-definition and current dosing practice for infections (v.15.0).

TABLE 43. Percentage distributions of antimicrobial susceptibility categories in travel associated *Campylobacter jejuni* (n=152) from human clinical specimens in Norway 2024.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	Susceptible	Resistant	S	I	R
Tetracycline	≤ 2	> 2	37.5	-	62.5
Erythromycin	≤ 4	> 4	98.7	-	1.3
Gentamicin[1]	≤ 2	> 2	99.3	-	0.7
Ciprofloxacin[2]	≤ 0.001	> 0.5	0.0	19.1	80.9

[1]Breakpoints according to ECOFF. [2]Breakpoints for ciprofloxacin adjusted according to EUCAST in keeping with the new I-definition and current dosing practice for infections (v.15.0).

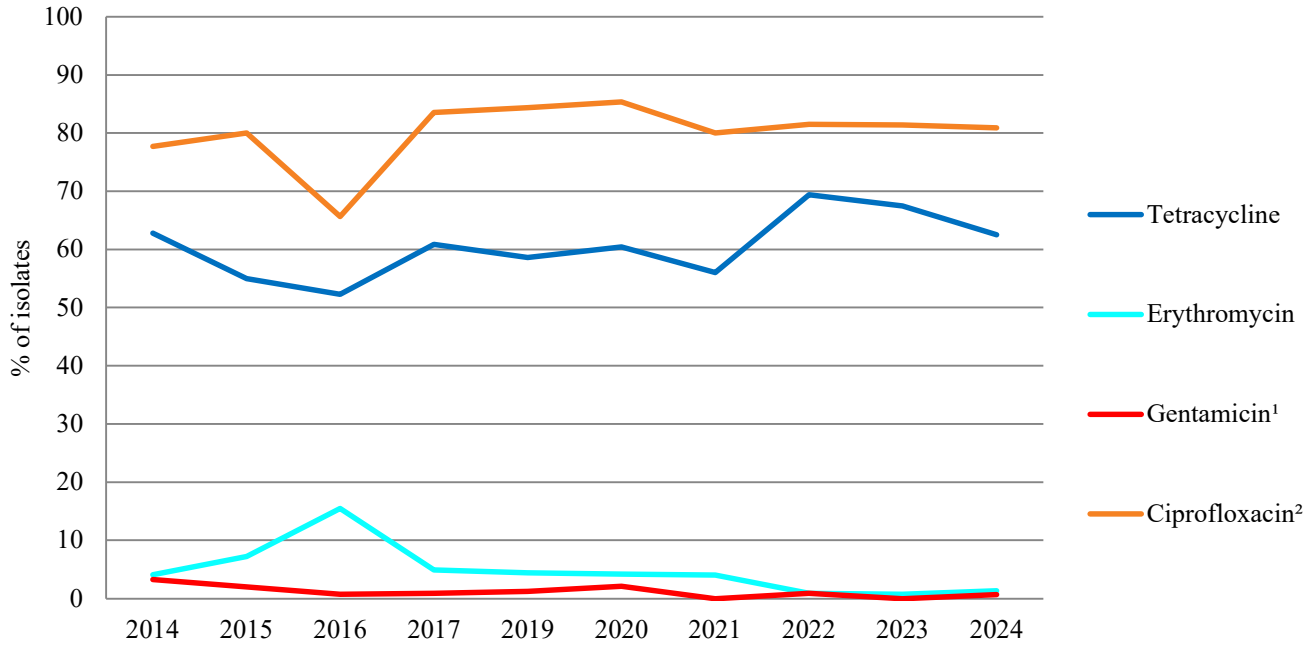


FIGURE 74. Trend 2014-2024. Percentage of travel associated *Campylobacter jejuni* resistant to selected antimicrobial agents in Norway. [1]Breakpoints according to ECOFF. [2]Breakpoints for ciprofloxacin adjusted 2020 onwards, according to EUCAST in keeping with the new I-definition and current dosing practice for infections (v.15.0).

ANTIMICROBIAL RESISTANCE IN CAMPYLOBACTER COLI

TABLE 44. Percentage distributions of antimicrobial susceptibility categories in *Campylobacter coli* (n=20) from human clinical specimens irrespective of place of acquisition, in Norway 2024.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	Susceptible	Resistant	S	I	R
Tetracycline	≤ 2	> 2	35.0	-	65.0
Erythromycin	≤ 8	> 8	85.0	-	15.0
Gentamicin[1]	≤ 2	> 2	90.0	-	10.0
Ciprofloxacin[2]	≤ 0.001	> 0.5	0.0	15.0	85.0

[1]Breakpoints according to ECOFF. [2]Breakpoints for ciprofloxacin adjusted according to EUCAST in keeping with the new I-definition and current dosing practice for infections (v.15.0).

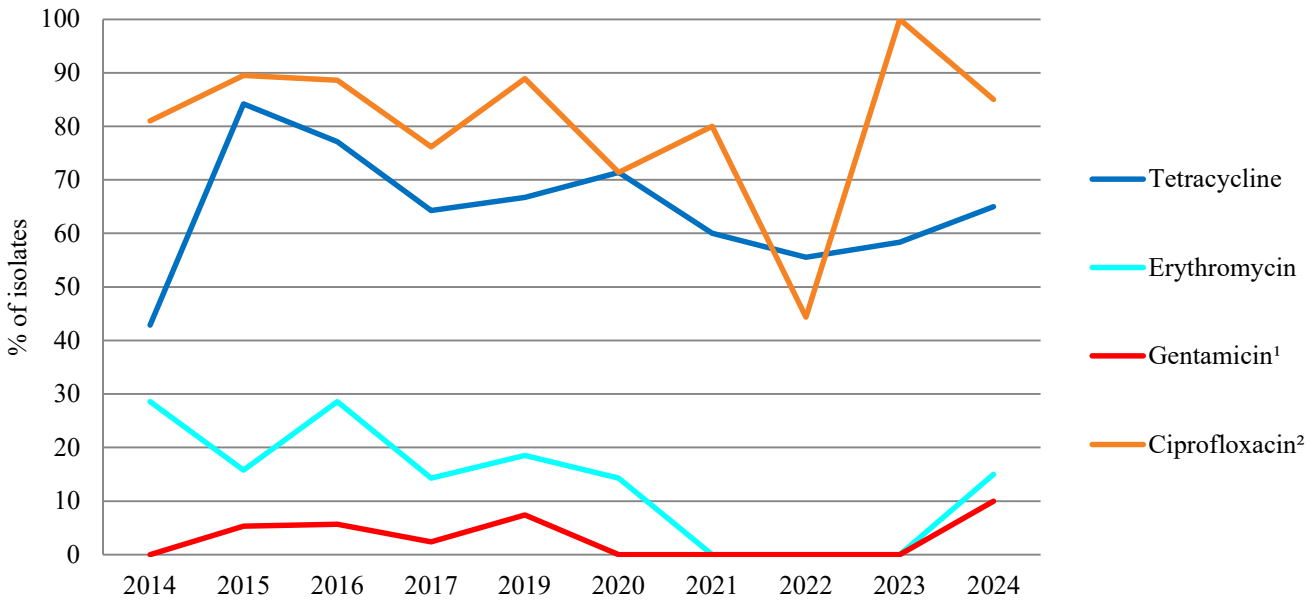


FIGURE 75. Trend 2014-2024. Percentage of *Campylobacter coli* resistant to selected antimicrobial agents irrespective of place of acquisition in Norway. [1]Breakpoints according to ECOFF. [2]Breakpoints for ciprofloxacin adjusted according to EUCAST in keeping with the new I-definition and current dosing practice for infections (v.15.0).

RESULTS AND COMMENTS

The NRL annually performs antimicrobial susceptibility testing on all *C. jeuni* and *C. coli* isolates received at NRL as part of the sentinel surveillance system. As of 31 October 2020, the EUCAST Scientific Committee adjusted the breakpoints for fluroquinolone sensitive isolates of both *C. jejuni* and *C. coli* from ≤0.5 mg/L to ≤0.001mg/L, thus introducing a new I-definition between the sensitive and resistant isolates. Data in this report have retrospectively been adjusted from 2020 onwards, to re-assign resistant isolates within this new definition as intermediate.

For *C. jejuni*, we observed a stable trend in resistance to all tested antibiotics. Resistance levels against tetracycline and ciprofloxacin were higher in strains from travel associated infections compared to domestically acquired infections.

For *C. coli,* we observed a stable trend in resistance to all tested antibiotics. All strains were resistant to ciprofloxacin irrespective of place of acquisition.

We identified an MDR phenotype in two travel associated *C. jejuni* strains, displaying resistance to ciprofloxacin, tetracycline, and erythromycin.

YERSINIA ENTEROCOLITICA

Yersinia enterocolitica from human clinical specimens

In 2024, 89 human yersiniosis cases were notified to MSIS. Most cases with known place of acquisition were domestically acquired (71.2%). The National Reference Laboratory (NRL) for Enteropathogenic Bacteria at the Norwegian Institute of Public Health (NIPH) received 87 isolates of human pathogenic *Yersinia* from the primary diagnostic laboratories. No outbreak clusters were identified, and 87 unique isolates were screened for antimicrobial resistance determinants following whole genome sequencing. Antimicrobial susceptibility testing was performed on 84 isolates (Table 45) against four different antibiotic groups: beta-lactams (ampicillin, cefotaxime, ceftazidime and meropenem), fluoroquinolone (ciprofloxacin), tetracycline and chloramphenicol. The results are presented in Tables 46-48 and Figures 76-77, and in the related text.

TABLE 45. Number of *Yersinia enterocolitica* isolates tested for phenotypic antimicrobial susceptibility (AST) and predicted genotypic resistance (GR) recovered from human clinical specimens in Norway 2024, by serotype and place of acquisition.

Yersinia enterocolitica	No. of isolates tested in 2024		Place of acquisition					
			Norway		Abroad		Unknown	
	Phenotypic AST	Predicted GR	Phenotypic AST	Predicted GR	Phenotypic AST	Predicted GR	Phenotypic AST	Predicted GR
Y. enterocolitica O:3	70	72	43	44	17	17	10	11
Y. enterocolitica O:9	13	13	4	4	4	4	5	5
Y. enterocolitica (other serotypes)	1	2	1	1	-	-	-	1
Total	**84**	**87**	**48**	**49**	**21**	**21**	**15**	**17**

ANTIMICROBIAL RESISTANCE IN YERSINIA ENTEROCOLITICA SEROTYPE O:3 AND O:9

TABLE 46. Percentage distributions of antimicrobial susceptibility categories in *Yersinia enterocolitica* O:3 and O:9 (n=83) from human clinical specimens irrespective of place of acquisition, in Norway 2024.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Ampicillin	≤ 8	> 8	0.0	-	100.0
Cefotaxime	≤ 1	> 2	100.0	0.0	0.0
Ceftazidime	≤ 1	> 4	100.0	0.0	0.0
Meropenem	≤ 2	> 8	100.0	0.0	0.0
Ciprofloxacin	≤ 0.25	> 0.5	95.2	4.8	0.0
Tetracycline[1]	≥ 17 mm	< 17 mm	98.8	-	1.2
Chloramphenicol	≤ 8	> 8	84.3	-	15.7

[1]Breakpoints according to national zone distributions.

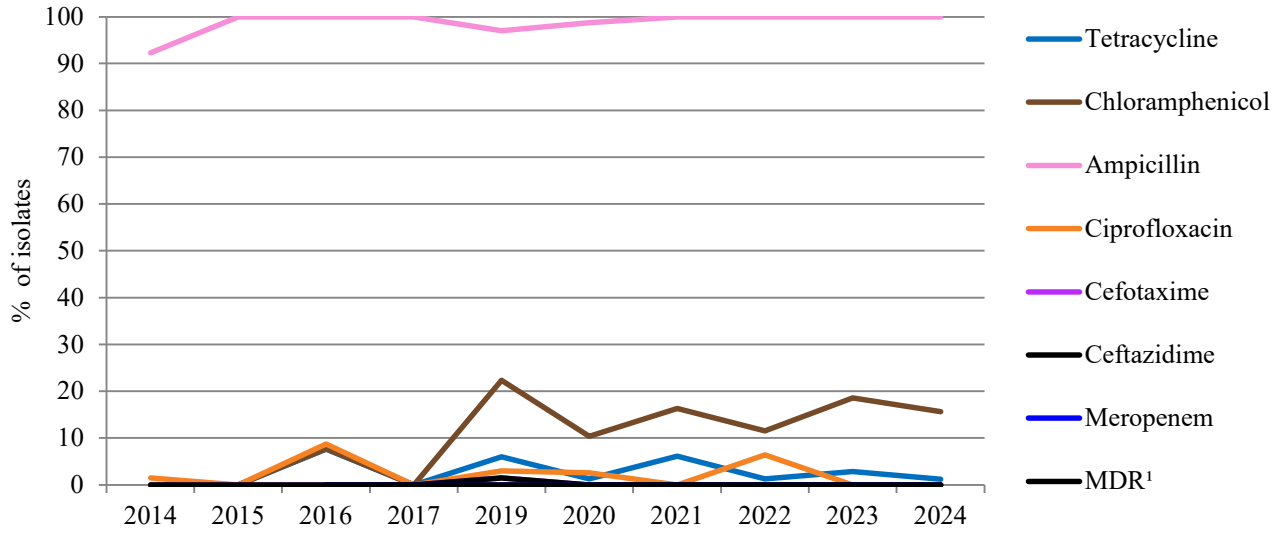


FIGURE 76. Trend 2014-2024. Percentage of *Yersinia enterocolitica* O:3 and O:9 resistant to selected antimicrobial agents irrespective of place of acquisition, in Norway.

TABLE 47. Percentage distributions of genotypic resistance in *Yersinia enterocolitica* O:3 and O:9 (n=85) compared to phenotypic wild type/non-wild type distribution (n=83) from human clinical specimens in Norway 2024.

	Phenotype[1] (%)		Predicted genotype[2] (%)	
Antibiotic	Wild type	Non-wild type	S	R
Gentamicin	-	-	100.0	0.0
Streptomycin	-	-	84.7	15.3
Ampicillin	100.0	0.0	0.0	100.0
Meropenem	100.0	0.0	100.0	0.0
Cefotaxime[3]	100.0	0.0	100.0	0.0
Ceftazidime[3]	100.0	0.0		
Colistin	-	-	100.0	0.0
Chloramphenicol	84.3	15.7	85.9	14.1
Ciprofloxacin	95.2	4.8	100.0	0.0
Sulfonamide	-	-	84.7	15.3
Tetracycline	98.8	1.2	98.8	1.2
Trimethoprim	-	-	98.8	1.2

[1]Wild type (WT) and non-wild type (NWT) categorisation according to EUCAST epidemiological cut-off values (ECOFF), and clinical breakpoints in absence of ECOFF for *Yersinia enterocolitica* (v.15.0). [2]R and S categorisation based on presence or absence of resistance determinants. [3]Predicted genotypic resistance to cefotaxime and ceftazidime is combined to predict genotypic resistance against extended spectrum cephalosporins.

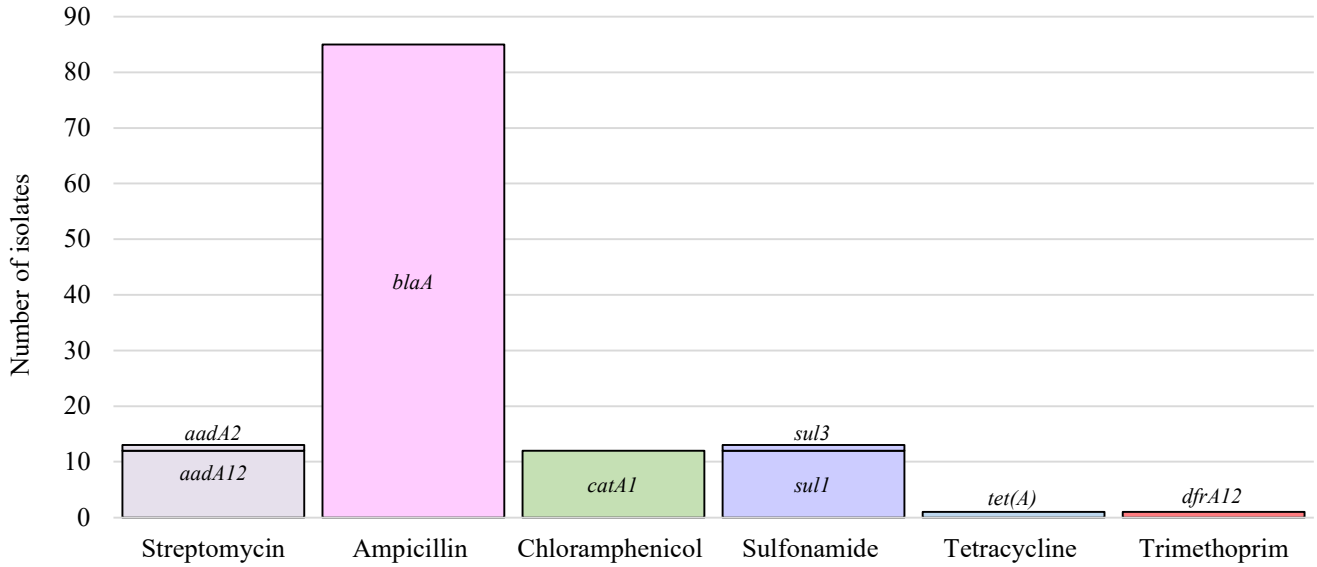


FIGURE 77. Identified resistance determinants in *Yersinia enterocolitica* O:3 and O:9 (n=85) to selected antimicrobial agents in Norway 2024.

CORRELATION BETWEEN PHENOTYPIC AND PREDICTED GENOTYPIC RESISTANCE IN YERSINIA

TABLE 48. Concordance between phenotypic and predicted genotypic resistance to selected antibiotic categories in *Yersinia enterocolitica* O:3 and O:9 isolates identified in Norway 2024.

Antibiotic categories	Tested	Phenotype WT[1]		Phenotype NWT[1]		Sensitivity (%)	Specificity (%)
		Genotype R	Genotype S	Genotype R	Genotype S		
Penicillins	83	83	0	0	0	-	-
ESC[2]	83	0	83	0	0	-	100.0
Carbapenems	83	0	83	0	0	-	100.0
Fluoroquinolones	83	0	79	0	4	-	95.2
Tetracycline	83	0	82	1	0	100.0	100.0
Phenicols	83	0	70	12	1	100.0	98.6

[1]Wild type (WT) and non-wild type (NWT) categorisation according to EUCAST epidemiological cut-off values (ECOFF), and clinical breakpoints in absence of ECOFF for *Yersinia enterocolitica* (v.15.0). [2]Predicted genotypic resistance to cefotaxime and ceftazidime is combined as predicted genotypic resistance against extended spectrum cephalosporins (ESC).

RESULTS AND COMMENTS

The NRL annually performs antimicrobial susceptibility testing on all pathogenic *Yersinia enterocolitica* isolates. Additionally, from 2020 onwards, the NRL has screened all isolates for antimicrobial resistance determinants following whole genome sequencing to predict genotypic resistance.

Antimicrobial resistance for *Yersinia enterocolitica* serotypes O:3 and O:9 has been combined and presented without distinction of place of acquisition. We observed a stable trend in resistance to all tested antibiotics. All isolates expressed intrinsic resistance to ampicillin, attributed to the *blaA* gene. In addition, resistance to chloramphenicol was identified in 15.7% of the strains, attributed to the *catA1* gene.

The overall correlation between phenotypic and predicted genotypic resistance was high, both sensitivity and specificity were above 95% for the tested and screened antibiotics.

SHIGELLA SPP.

Shigella spp. from human clinical specimens

In 2024, 96 human cases of shigellosis were notified to MSIS. Most cases with known place of acquisition were infected abroad (73.5%). The National Reference Laboratory (NRL) for Enteropathogenic Bacteria at the Norwegian Institute of Public Health (NIPH) received 96 *Shigella* spp. isolates from primary diagnostic laboratories. 96 unique isolates were screened for antimicrobial resistance determinants following whole genome sequencing. Antimicrobial susceptibility testing was performed on 94 *Shigella* isolates (Table 49). Isolates were susceptibility tested against four different antibiotic groups: beta-lactams (ampicillin, cefotaxime, ceftazidime and meropenem), fluoroquinolone (ciprofloxacin), tetracycline and chloramphenicol. The results are presented in Tables 50-55, Figures 78-82, and in the text.

TABLE 49. Number of *Shigella* spp. isolates tested for phenotypic antimicrobial susceptibility (AST) and predicted genotypic resistance (GR) recovered from human clinical specimens in Norway 2024, by species and place of acquisition.

Shigella spp.	No. of isolates tested in 2024		Place of acquisition					
			Norway		Abroad		Unknown	
	Phenotypic AST	Predicted GR	Phenotypic AST	Predicted GR	Phenotypic AST	Predicted GR	Phenotypic AST	Predicted GR
S. sonnei	51	52	10	10	32	33	9	9
S. flexneri	36	37	11	11	19	19	6	7
S. boydii	6	6	-	-	6	6	-	-
S. dysenteriae	1	1	-	-	1	1	-	-
Total	**94**	**96**	**21**	**21**	**58**	**59**	**15**	**16**

ANTIMICROBIAL RESISTANCE IN SHIGELLA SONNEI

TABLE 50. Percentage distributions of antimicrobial susceptibility categories in *Shigella sonnei* (n=51) from human clinical specimens irrespective of place of acquisition, in Norway 2024.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Ampicillin	≤ 8	> 8	47.1	-	52.9
Cefotaxime	≤ 1	> 2	56.9	5.9	37.2
Ceftazidime	≤ 1	> 4	88.2	5.9	5.9
Meropenem	≤ 2	> 8	100.0	0.0	0.0
Pefloxacin[1]	≥ 24 mm	< 24 mm	25.5	0.0	74.5
Tetracycline[2]	≥ 17 mm	< 17 mm	23.5	-	76.5
Chloramphenicol	≤ 8	> 8	96.1	-	3.9

[1]Low-level resistance against ciprofloxacin is underestimated using breakpoints based on ciprofloxacin disk diffusion. Susceptibility to ciprofloxacin is inferred from pefloxacin disk diffusion according to EUCAST clinical breakpoints (v.15.0) [2]Breakpoints according to national zone distributions.

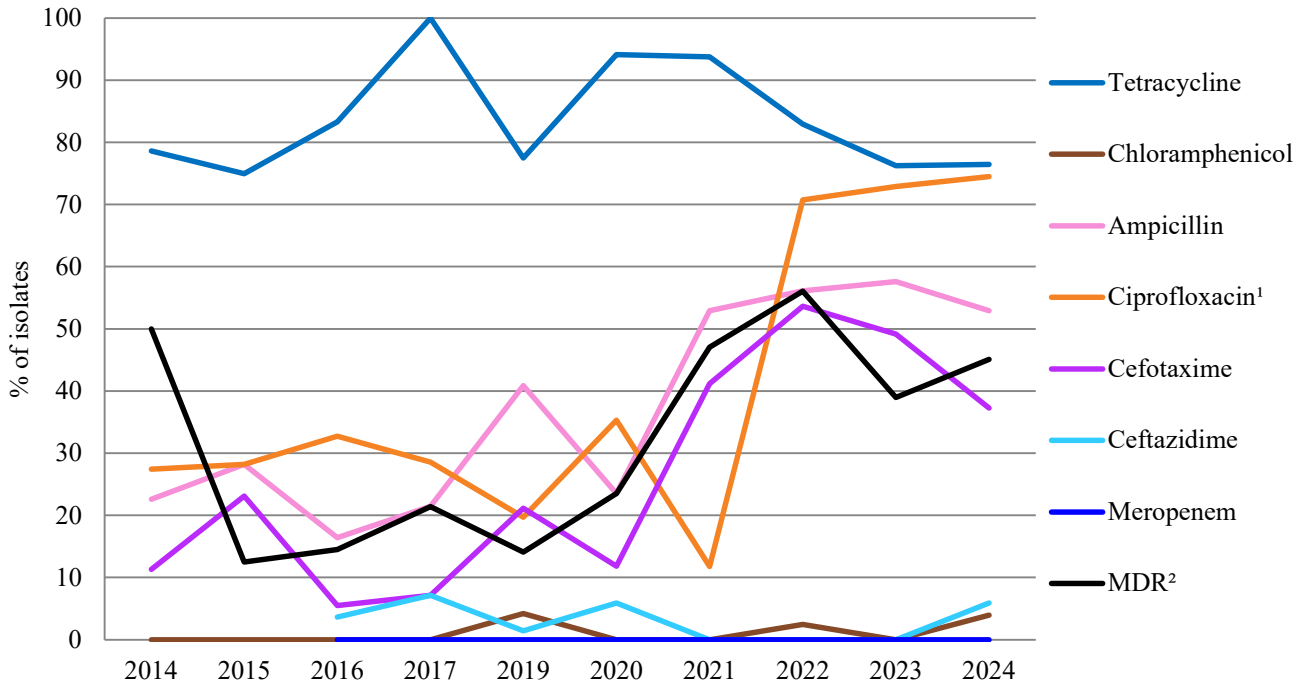


FIGURE 78. Trend 2014-2024. Percentage of *Shigella sonnei* resistant to selected antimicrobial agents irrespective of place of acquisition, in Norway. [1]Resistance to ciprofloxacin is inferred from pefloxacin disk diffusion 2022 onwards, to better align with observed genotypic resistance. [2]MDR is defined as acquired non-susceptibility to antimicrobials from three or more categories.

TABLE 51. Percentage distributions of genotypic resistant *Shigella sonnei* (n=52) compared to phenotypic wild type/non-wild type distribution (n=51) from human clinical specimens in Norway 2024.

	Phenotype[1] (%)		Predicted genotype[2] (%)	
Antibiotic	Wild type	Non-wild type	S	R
Gentamicin	-	-	96.2	3.8
Streptomycin	-	-	11.5	88.5
Ampicillin	47.1	52.9	51.9	48.1
Meropenem	100.0	0.0	100.0	0.0
Cefotaxime[3]	56.9	43.1	55.8	44.2
Ceftazidime[3]	88.2	11.8		
Colistin	-	-	100.0	0.0
Chloramphenicol	96.1	3.9	96.2	3.8
Ciprofloxacin	25.5	74.5	26.9	73.1
Sulfonamide	-	-	19.2	80.8
Tetracycline	23.5	76.5	28.8	71.2
Trimethoprim	-	-	1.9	98.1

[1]Wild type (WT) and non-wild type (NWT) categorisation according to EUCAST epidemiological cut-off values (ECOFF), and clinical breakpoints in absence of ECOFF for *Shigella sonnei* (v.15.0). [2]R and S categorisation based on presence or absence of resistance determinants. [3]Predicted genotypic resistance to cefotaxime and ceftazidime is combined to predict genotypic resistance against extended spectrum cephalosporins.

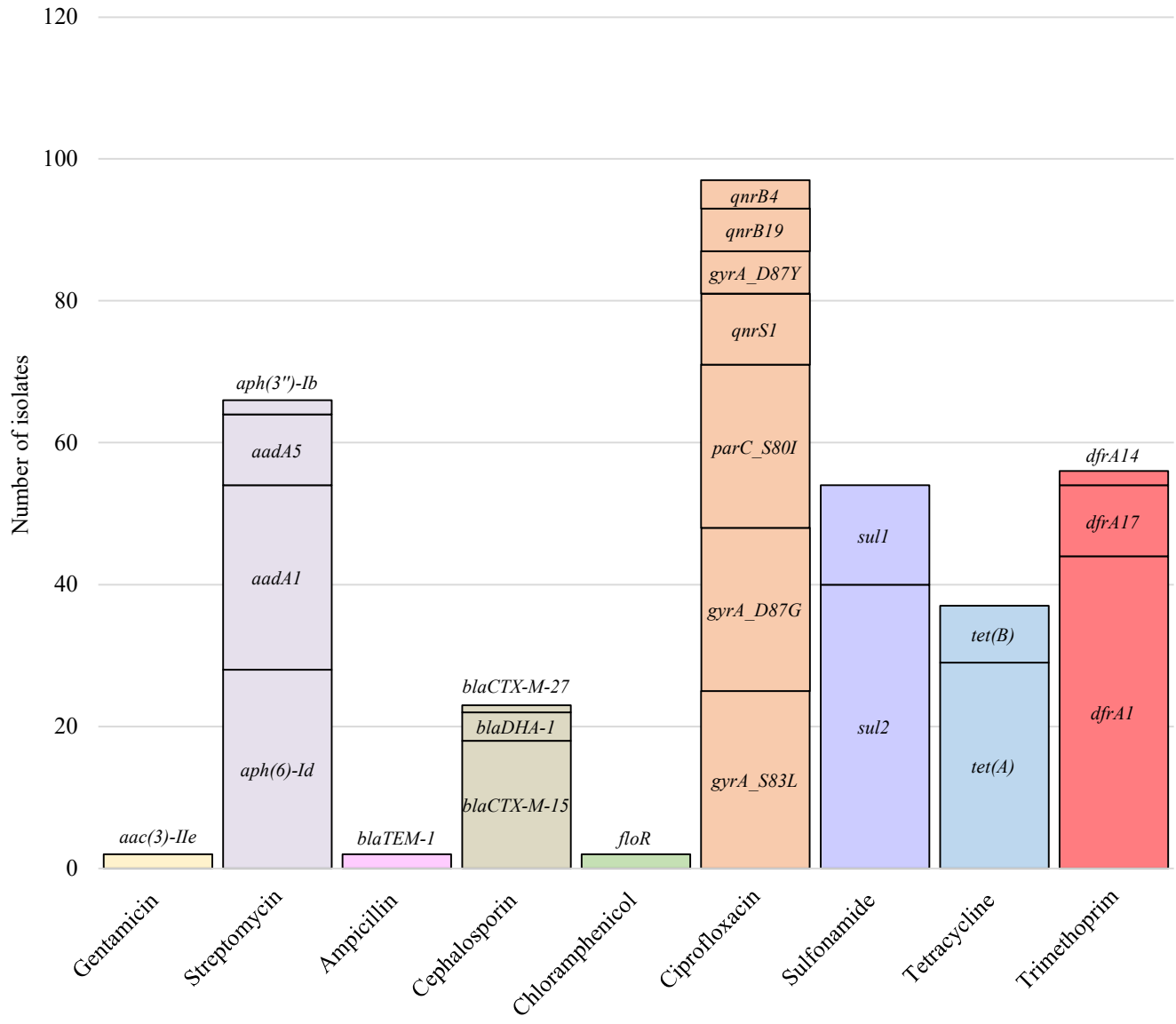


FIGURE 79. Identified resistance determinants in *Shigella sonnei* (n=52) to selected antimicrobial agents in Norway 2024.

ANTIMICROBIAL RESISTANCE IN SHIGELLA FLEXNERI

TABLE 52. Percentage distributions of antimicrobial susceptibility categories in *Shigella flexneri* (n=36) from human clinical specimens irrespective of place of acquisition in Norway 2024.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Ampicillin	≤ 8	> 8	5.6	-	94.4
Cefotaxime	≤ 1	> 2	86.1	0.0	13.9
Ceftazidime	≤ 1	> 4	91.7	2.8	5.5
Meropenem	≤ 2	> 8	100.0	0.0	0.0
Pefloxacin[1]	≥ 24 mm	< 24 mm	55.6	0.0	44.4
Tetracycline[2]	≥ 17 mm	< 17 mm	5.6	-	94.4
Chloramphenicol	≤ 8	> 8	36.1	-	63.9

[1]Low-level resistance against ciprofloxacin is underestimated using breakpoints based on ciprofloxacin disk diffusion. Susceptibility to ciprofloxacin is inferred from pefloxacin disk diffusion according to EUCAST clinical breakpoints (v.15.0). [2]Breakpoints according to national zone distributions.

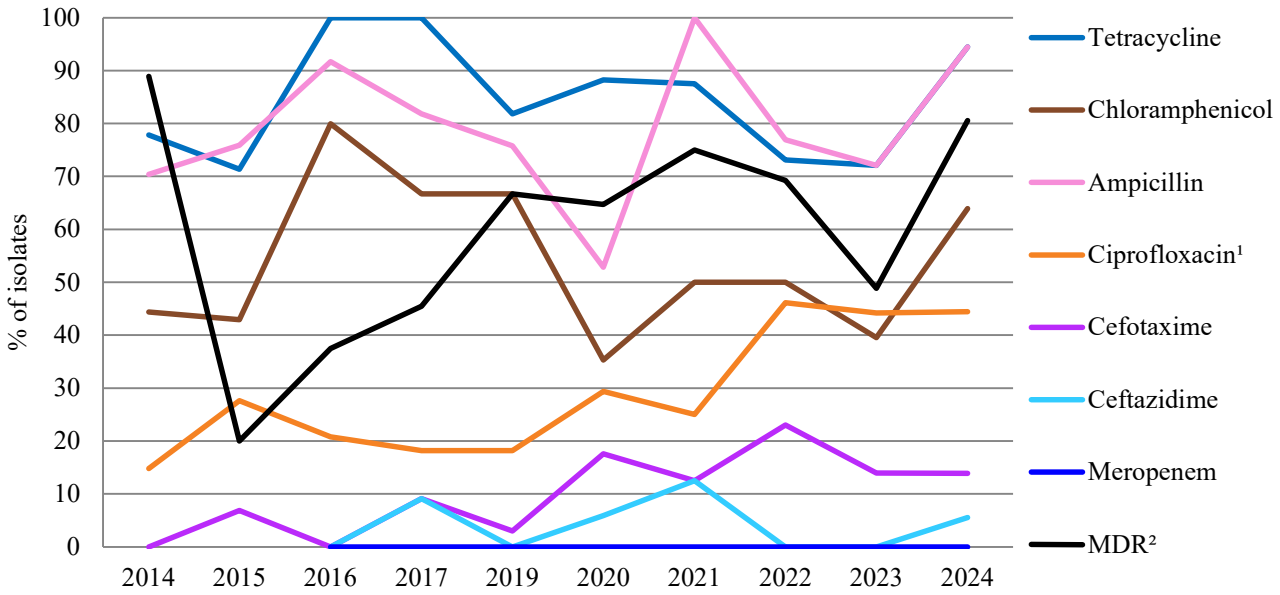


FIGURE 80. Percentage of *Shigella flexneri* resistant to selected antimicrobial agents irrespective of place of acquisition in Norway, trend 2014-2024. [1]Resistance to ciprofloxacin is inferred from pefloxacin disk diffusion 2022 onwards, to better align with observed genotypic resistance. [2]MDR is defined as acquired non-susceptibility to antimicrobials from three or more categories.

TABLE 53. Percentage distributions of genotypic resistance in *Shigella flexneri* (n=37) compared to phenotypic wild type/non-wild type distribution (n=36) from human clinical specimens in Norway 2024.

	Phenotype[1] (%)		Predicted genotype[2] (%)	
Antibiotic	Wild type	Non-wild type	S	R
Gentamicin	-	-	100.0	0.0
Streptomycin	-	-	43.2	56.8
Ampicillin	5.6	94.4	5.4	94.6
Meropenem	100.0	0.0	100.0	0.0
Cefotaxime[3]	86.1	13.9	83.8	16.2
Ceftazidime[3]	91.7	8.3		
Colistin	-	-	0.0	100.0
Chloramphenicol	33.3	66.7	35.1	64.9
Ciprofloxacin	55.6	44.4	54.1	45.9
Sulfonamide	-	-	56.8	43.2
Tetracycline	5.6	94.4	8.1	91.9
Trimethoprim	-	-	18.9	81.1

[1]Wild type (WT) and non-wild type (NWT) categorisation according to EUCAST epidemiological cut-off values (ECOFF), and clinical breakpoints in absence of ECOFF for *Shigella flexneri* (v.15.0). [2]R and S categorisation based on presence or absence of resistance determinants. [3]Predicted genotypic resistance to cefotaxime and ceftazidime is combined to predict genotypic resistance against extended spectrum cephalosporins.

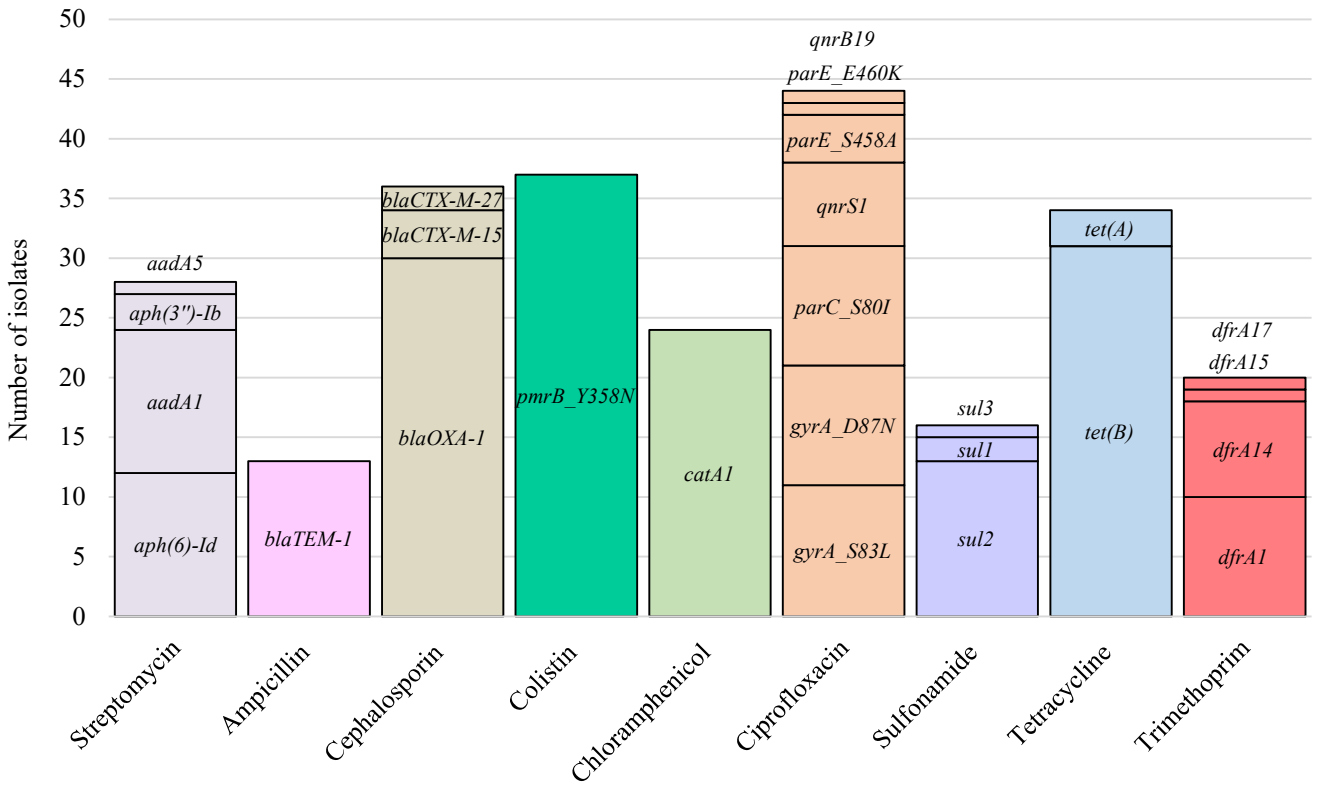


FIGURE 81. Identified resistance determinants in *Shigella flexneri* (n=37) to selected antimicrobial agents in Norway 2024.

MULTI-DRUG RESISTANCE IN SHIGELLA

TABLE 54. Number of predicted genotypic multi-drug resistance in (MDR) *Shigella* spp. isolates identified in Norway 2024, stratified according to species and resistance to different antibiotic categories.

Shigella spp.	MDR[1]	Antibiotic categories[2]							
		STR	AMP	ESC	CHL	CIP	SUL	TET	TMP
Shigella sonnei	48	44	25	23	2	37	42	37	47
Shigella flexneri	36	21	35	6	24	17	16	34	30
Shigella boydii	6	5	4	2	0	4	5	5	5
Shigella dysenteriae	1	0	1	1	0	1	0	1	1
Total no. of MDR isolates	**91**	**70**	**65**	**32**	**26**	**59**	**63**	**77**	**83**

[1]Multi-drug resistance (MDR) defined as predicted genotypic resistance to 3 ≥ antibiotic categories. [2]Antibiotic category: STR: Streptomycin, AMP; Ampicillin, ESC; Extended Spectrum Cephalosporin, CHL; Chloramphenicol, CIP; Ciprofloxacin, SUL; Sulfonamide, TET; Tetracycline, TMP; Trimethoprim.

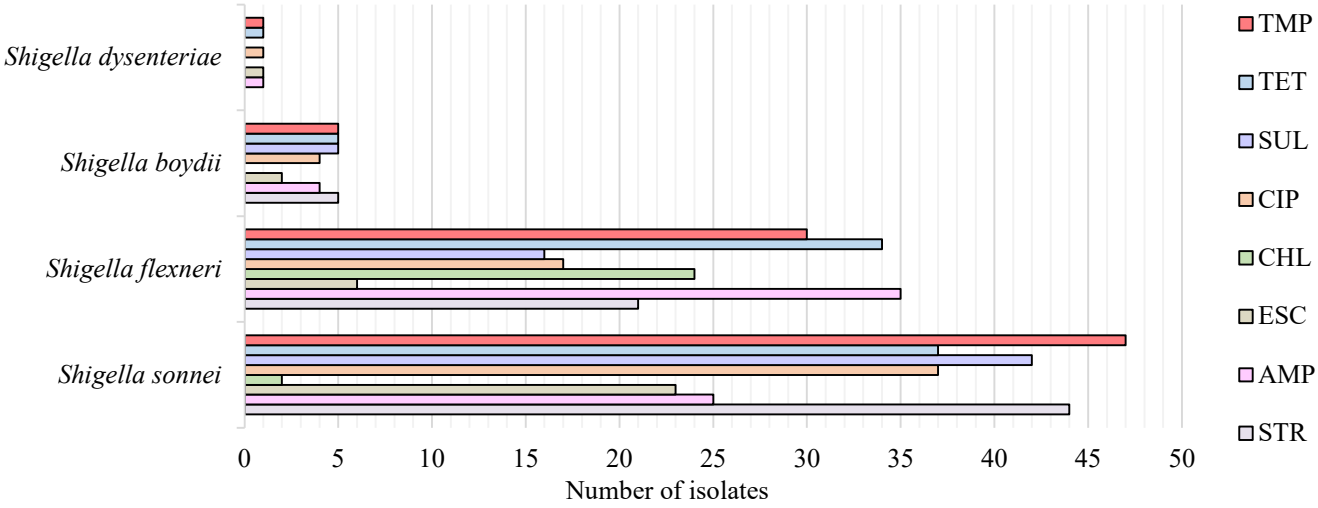


FIGURE 82. Number of predicted genotypically multi-drug resistant (MDR) *Shigella* spp. isolates (n=91) identified in Norway 2024, stratified according to species and resistance to different antibiotic categories; STR: Streptomycin, AMP; Ampicillin, ESC; Extended Spectrum Cephalosporin, CHL; Chloramphenicol, CIP; Ciprofloxacin, SUL; Sulfonamide, TET; Tetracycline, TMP; Trimethoprim.

CORRELATION BETWEEN PHENOTYPIC AND PREDICTED GENOTYPIC RESISTANCE IN SHIGELLA

TABLE 55. Concordance between phenotypic and predicted genotypic resistance to selected antibiotic categories in *Shigella spp*. (n=94) isolates identified in Norway 2024.

		Phenotype WT[1]		Phenotype NWT[1]			
Antibiotic categories	Tested	Genotype R	Genotype S	Genotype R	Genotype S	Sensitivity (%)	Specificity (%)
Penicillins	94	0	28	64	2	100.0	93.3
ESC[2]	94	0	63	31	0	100.0	100.0
Carbapenems	94	0	94	0	0	-	100.0
Fluoroquinolones	94	0	35	59	0	100.0	100.0
Tetracycline	94	0	15	76	3	100.0	83.3
Phenicols	94	0	68	25	1	100.0	98.6

[1]Wild type (WT) and non-wild type (NWT) categorisation according to EUCAST epidemiological cut-off values (ECOFF), and clinical breakpoints in abscense of ECOFF for *Shigella spp.* (v.15.0). [2]Predicted genotypic resistance to cefotaxime and ceftazidime is combined as predicted genotypic resistance against extended spectrum cephalosporins (ESC).

RESULTS AND COMMENTS

The NRL annually performs antimicrobial susceptibility testing on all *Shigella* spp. isolates. Since 2020, the NRL has screened all isolates for antimicrobial resistance determinants following whole genome sequencing to predict genotypic resistance. From 2022 onwards, ciprofloxacin resistance is inferred from susceptibility to pefloxacin, as low-level resistance against ciprofloxacin is underestimated using breakpoints based on ciprofloxacin disk diffusion, and to better align phenotypic resistance with predicted genotypic resistance.

A stable and large proportion of *S. sonnei* is recorded resistant to tetracycline over the last decade. In addition, since 2020 an increasing trend of resistance towards ciprofloxacin and extended spectrum cephalosporins is recorded. The observed increase in resistance to ciprofloxacin from 30% in 2020 to over 74.5% in 2024 is attributed in part to the change in antibiotic used for screening (ciprofloxacin vs. pefloxacin), and in part to an increase in identification of resistant strains. This is confirmed by the presence of resistance determinants against ciprofloxacin in 53% of the strains in 2020 and in 73% in 2024. When screening for genotypic resistance determinants, the presence of various mutations in the quinolone resistance-determining regions (QRDRs) of *gyrA* and *parC,* as well as the presence of different *qnr* variants was confirmed. A total of 23 ESBL-producing strains (44.2%) were identified, of which 18 encoded the $bla_{\text{CTX-M-15}}$ gene, one encoded the $bla_{\text{CTX-M-27}}$ gene, and four encoded $bla_{\text{DHA-1}}$. An MDR genotype was identified for 92.3% of the strains, largely attributed to resistance against streptomycin, ciprofloxacin, sulfonamide, tetracycline, and trimethoprim.

For *S. flexneri* a large proportion of strains were recorded resistant to tetracycline and ampicillin over the last decade. In addition, an increasing trend of resistance towards ciprofloxacin and extended spectrum cephalosporins was observed. The observed increase in resistance to ciprofloxacin from around 30% in 2020 to 44.4% in 2024 is largely attributed to the change in the antibiotic used for screening. When screening for genotypic resistance determinants, the presence of various mutations in the QRDRs of *gyrA* and *parC,* as well as the presence of *qnrS1* is detected. A total of six ESBL-producing strains (16.2%) were identified, four of which encoded the $bla_{\text{CTX-M-15}}$ gene and two the $bla_{\text{CTX-M-27}}$ gene. All *S. flexneri* strains (n=37) harboured the *pmrB*_Y358N mutation, which has been associated with colistin resistance. Mutations in the *pmrB* can lead to modifications in the lipopolysaccharides on the bacterial cell surface and thus reduce the accessibility of colistin to bacterial membranes. None of the strains were susceptibility tested for colistin. An MDR genotype was identified in 97.3% of the strains, largely attributed to resistance against streptomycin, ampicillin, tetracycline, and trimethoprim.

In addition to the *S. sonnei* and *S. flexneri* strains identified as ESBL producers, two of the six *S. boydii* strains and the single *S. dysenteriae* strain also encoded ESBL genes, $bla_{\text{CTX-M-15}}$ (n=2) and $bla_{\text{DHA-1}}$ (n=1). Overall correlation between phenotypic resistance and predicted genotypic resistance was high.

HUMAN CLINICAL ISOLATES

Gunnar Skov Simonsen, Jan Egil Afset, Cecilie Torp Andersen, Bente Børud, Caroline V. Knudsen, Anne Torunn Mengshoel and Karine Nordstrand

Distribution of bacterial species in blood cultures

Surveillance of antimicrobial resistance is usually based on prevalences of reduced susceptibility and resistance to certain combinations of antimicrobials and bacterial species in clinical samples. The NORM surveillance programme generally follows this approach. However, there is a serious limitation to the model because a transition in the distribution from susceptible bacterial species to inherently more resistant ones will represent de facto emergence of resistance which is not easily detected. In order to complement the surveillance of individual species, NORM collects data on all positive blood cultures from the laboratory information systems of the participating institutions. A patient with a given microbial isolate was excluded from registration with a new isolate of the same species within a month from the first entry. This rule was applied irrespective of changes in the organism´s susceptibility pattern. Isolates of a different species from the same patient were included in the surveillance. It proved difficult to systematically evaluate the clinical significance of species which are commonly part of the normal skin flora. In Table 56, proportions are therefore estimated for all isolates and for all isolates excluding species considered to be common skin contaminants such as coagulase negative staphylococci, *Micrococcus* spp., *Bacillus* spp., *Corynebacterium* spp. and *Cutibacterium* spp.. This does not imply that such isolates cannot cause infections, but only that it was not possible to enforce a standardised protocol for inclusion of the clinically significant isolates. Similarly, all isolates were registered as individual findings although polymicrobial bloodstream infections are regularly detected in some patients. Limitations in the data extraction procedure prohibited in-depth analysis of these parameters.

TABLE 56. Number of blood culture isolates in 2024, proportion of all isolates, and proportion of isolates excluding possible skin contaminants (coagulase negative staphylococci, *Micrococcus* spp., *Bacillus* spp., *Corynebacterium* spp. and *Cutibacterium* spp.) 2020-2024. The table is based on data from the information systems of all laboratories in Norway (n=19).

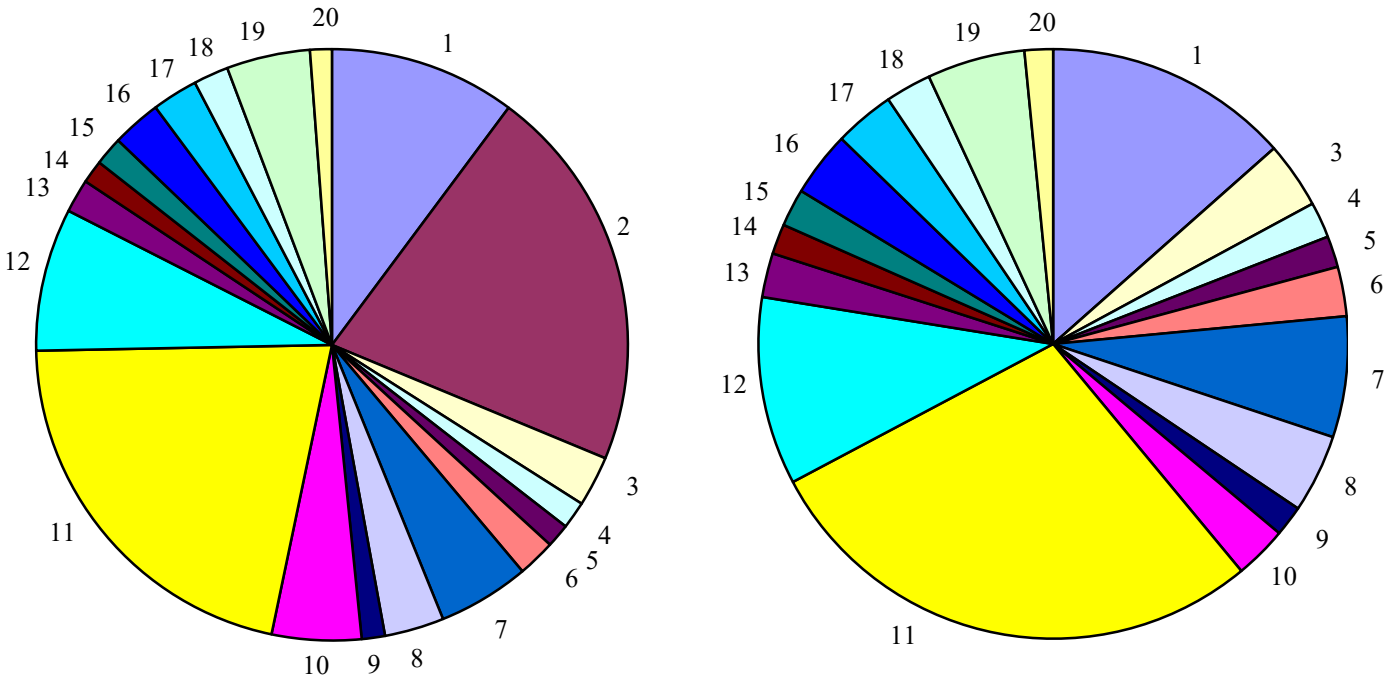
Species	No. of isolates 2024	% of all isolates					% of all isolates excluding skin flora				
		2020	2021	2022	2023	2024	2020	2021	2022	2023	2024
Staphylococcus aureus	2,312	10.6	10.5	10.7	10.2	10.1	13.7	13.8	14.1	13.4	13.4
Coagulase negative staphylococci	4,777	20.4	21.1	21.3	21.6	21.0	-	-	-	-	-
Streptococcus pneumoniae	627	1.6	1.6	2.5	2.6	2.8	2.1	2.1	3.4	3.5	3.7
Streptococcus pyogenes	339	0.8	0.4	0.6	1.8	1.5	1.0	0.5	0.8	2.3	2.0
Streptococcus agalactiae	294	1.7	1.6	1.5	1.2	1.3	2.1	2.0	2.0	1.6	1.7
Beta-haemolytic streptococci group C and G	465	2.3	2.4	2.0	2.1	2.1	2.9	3.1	2.6	2.8	2.7
Viridans- and non-haemolytic streptococci	1,137	5.4	5.1	5.8	5.2	5.0	7.0	6.7	7.7	6.8	6.6
Enterococcus faecalis	738	3.5	3.7	3.5	3.3	3.3	4.5	4.9	4.7	4.3	4.3
Enterococcus faecium	288	1.1	1.4	1.4	1.4	1.3	1.4	1.8	1.8	1.8	1.7
Other Gram-positive aerobic and facultative anaerobic bacteria	1,107	3.5	4.2	4.3	4.2	4.9	2.4	2.7	2.5	2.7	2.9
Escherichia coli	4,854	24.7	23.2	21.7	21.8	21.3	32.0	30.7	28.4	28.8	28.2
Klebsiella spp.	1,769	7.5	7.7	7.8	7.4	7.8	9.6	10.1	10.3	9.8	10.2
Enterobacter spp.	416	1.7	1.9	1.7	1.6	1.8	2.2	2.4	2.3	2.2	2.4
Proteus spp.	284	1.6	1.4	1.3	1.3	1.3	2.1	1.8	1.7	1.7	1.7
Other *Enterobacterales*	612	2.3	1.9	2.4	2.4	2.7	3.0	2.5	3.2	3.2	3.6
Pseudomonas spp.	354	1.9	1.9	1.9	1.7	1.6	2.4	2.5	2.5	2.3	2.1
Other Gram-negative aerobic and facultative anaerobic bacteria	569	1.8	2.0	2.1	2.4	2.5	2.3	2.6	2.8	3.2	3.3
Bacteroides spp.	432	2.2	2.3	2.0	2.1	1.9	2.9	3.0	2.6	2.8	2.5
Other anaerobic bacteria	1,035	4.2	4.6	4.3	4.5	4.6	4.9	5.4	5.0	5.3	5.4
Yeasts	270	1.2	1.1	1.2	1.2	1.2	1.5	1.4	1.6	1.5	1.6
Total	**22,679**	**100.0**	**100.0**	**100.0**	**100.0**	**100.0**	**100.0**	**100.0**	**100.0**	**100.0**	**100.0**

As seen in Table 56 and Figure 83, aerobic and facultative Gram-positive and Gram-negative bacteria represented 53.3% and 39.0% of all isolates, respectively. The predominance of Gram-positives among all isolates was at the same level as in previous years. The most common Gram-positive species were coagulase negative staphylococci, which constituted 21.0%. This is a slight decrease from 21.6% recorded in 2023. The difference between aerobic Gram-positives and Gram-negatives was reversed when species of the skin flora (coagulase negative staphylococci, *Micrococcus* spp., *Bacillus* spp., *Corynebacterium* spp. and *Cutibacterium* spp.) were excluded, with 39.0% aerobic Gram-positives and 51.5% aerobic Gram-negatives.

Among aerobic Gram-positives, the prevalence of *S. pneumoniae* steadily declined from 12.1% in 2005 to 4.0% in 2019 (skin contaminants excluded), following the introduction of the conjugate pneumococcal vaccine in the national childhood immunisation programme in June 2006. The prevalence was even lower in the pandemic years 2020-2021 (2.1%), but has now increased again to 3.7%. The occurrence of *Streptococcus pyogenes* has stabilised at approximately the same number (n=339) as in 2023 (n=380), which is significantly higher than in previous years (n=138 in 2022). Their proportion of invasive isolates now exceeds pre-pandemic levels. The rates for other aerobic Gram-positives have remained relatively stable over many years.

E. coli (28.2%) and other *Enterobacterales* (17.9%) accounted for the vast majority of aerobic Gram-negative isolates. The proportion of *E. coli* is apparently slowly decreasing, but further surveillance is needed to confirm this trend. *Pseudomonas* spp. remained stable at 2.1%, all figures excluding skin flora.

Anaerobic bacteria and yeasts were less prevalent. Anaerobes accounted for 6.5% (7.9% excluding skin flora). Yeasts accounted for 1.2% (1.6% excluding skin flora). The major pathogens among anaerobes were members of *Bacteroides* spp. (1.9%/2.5%) and among yeasts *Candida albicans* (0.6%/0.8%). However, a multitude of other species were also represented.



1. *Staphylococcus aureus*
2. Coagulase negative staphylococci
3. *Streptococcus pneumoniae*
4. *Streptococcus pyogenes*
5. *Streptococcus agalactiae*
6. Betahaemolytic streptococci group C and G
7. Non-haemolytic and viridans streptococci
8. *Enterococcus faecalis*
9. *Enterococcus faecium*
10. Other Gram-positive bacteria
11. *Escherichia coli*
12. *Klebsiella* spp.
13. *Enterobacter* spp.
14. *Proteus* spp.
15. Other *Enterobacterales*
16. *Pseudomonas* spp.
17. Other Gram-negative bacteria
18. *Bacteroides* spp.
19. Other anaerobic bacteria
20. Yeasts

FIGURE 83. Distribution of all blood culture isolates (left, n=22,679) and blood culture isolates excluding common skin contaminants (right, n=17,176) such as coagulase negative staphylococci, *Micrococcus* spp., *Bacillus* spp., *Corynebacterium* spp. and *Cutibacterium* spp. Data for 2024 were retrieved from the information systems of all Norwegian laboratories (n=19).

Escherichia coli in blood cultures

TABLE 57. *Escherichia coli* blood culture isolates in 2024 (n=2,297). Sampling, laboratory methods, and data handling are described in Appendix 5. Distributions of zone diameters are available at www.antibiotikaresistens.no.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Ampicillin	≤ 8	> 8	61.6	-	38.4
Amoxicillin-clavulanic acid*	≤ 8	> 8	79.5	-	20.5
Piperacillin-tazobactam	≤ 8	> 8	95.6	-	4.4
Cefotaxime**	≤ 1	> 2	92.7	0.8	6.5
Ceftazidime	≤ 1	> 4	92.9	1.0	6.1
Cefepime	≤ 1	> 4	92.7	1.4	5.9
Meropenem**	≤ 2	> 8	100.0	0.0	0.0
Aztreonam	≤ 1	> 4	92.4	2.4	5.2
Gentamicin***	≤ 2	> 2	94.3	-	5.7
Ciprofloxacin**	≤ 0.25	> 0.5	87.3	3.0	9.7
Tigecycline	≤ 0.5	> 0.5	99.8	-	0.2
Trimethoprim-sulfamethoxazole****	≤ 2	> 4	77.3	0.8	21.9
ESBL	Negative	Positive	93.3	-	6.7

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. ESBL=Extended spectrum beta-lactamase. *Breakpoints for intravenous administration. **Breakpoints for indications other than meningitis. ***Breakpoints for infections originating from the urinary tract. ****Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only.

RESULTS AND COMMENTS

NORM results are interpreted according to NordicAST/ EUCAST clinical breakpoints at the time of analysis and categorised as susceptible with standard exposure (S), susceptible with increased exposure (I), or resistant (R). The vast majority of isolates were fully susceptible (S) to broad-spectrum agents such as cefotaxime (92.7%), ceftazidime (92.9%), gentamicin (94.3%), cefepime (92.7%), piperacillin-tazobactam (95.6%), tigecycline (99.8%), aztreonam (92.4%) and meropenem (100.0%) (Table 57). There were no major changes in resistance rates from 2023-2024.

The prevalence of resistance to gentamicin at 5.7% was a small increase from 5.1% in 2022 and 5.4% in 2023 (Figure 84). Data were interpreted according to the breakpoints for bacteremia in urinary tract infections, although NordicAST/ EUCAST no longer consider aminoglycosides sufficient for monotherapy in infections originating from other sources. A high proportion of gentamicin resistant isolates (51/132, 38.6%) also produced extended spectrum beta-lactamase (ESBL) enzymes. The prevalence at individual laboratories varied due to relatively small numbers. When aggregated by region there were only minor geographical variations (South-East 5.5%, Middle 5.9%, West 6.1%, North 6.3%).

The prevalence of resistance to ciprofloxacin was 9.7% in 2023 compared to 10.0% in both 2022 and 2023. The breakpoint for ciprofloxacin resistance has been changed many times over the years, most recently in 2017 with a reduction from R > 1 mg/L to R > 0.5 mg/L and from S ≤ 0.5 mg/L to S ≤ 0.25 mg/L. The long-term trend for ciprofloxacin resistance cannot be precisely determined due to changes in susceptibility test methodology, but it appears that the increase seen during 2006-2017 has turned to a slowly decreasing trend over the last eight years. The temporal association between ciprofloxacin resistance and ciprofloxacin usage is depicted in Figure 85. A similar association between quinolone use and resistance in systemic *E. coli* isolates is also reported internationally. The resistance rates for ampicillin (36.6% in 2022, 37.9% in 2023 and 38.4% in 2024) and trimethoprim-sulfamethoxazole (20.2% in 2022, 21.9% in 2023 and 21.9% in 2024) remain essentially unchanged.

Detection of ESBL was based on reduced zone diameters for cefotaxime and/or ceftazidime. All isolates with reduced susceptibility were further characterised by combination disks or MIC gradient tests. A total of 155 isolates (6.7%) were reported as ESBL positive, which is a small increase from 2022 (6.0%) and 2023 (5.8%) (Figure 87). The isolates originated from laboratories across the country, and estimates at local level are uncertain due to small numbers. When aggregated at regional level there were geographical differences in the prevalence of ESBL production, but the results should be interpreted with caution; Middle (2.8%), North (6.3%), West (6.9%), and South-East (7.8%). Most of the ESBL isolates were phenotypically resistant to cefotaxime (n=146), ceftazidime (n=129), cefepime (n=123) and aztreonam (n=116), whereas many were susceptible to tigecycline (n=153), piperacillin-tazobactam (n=126) and/or gentamicin (n=104). Sixty-eight isolates were susceptible to amoxicillin-clavulanic acid using breakpoints for non-urinary tract infections, whereas 87 were resistant. The ESBL isolates thus displayed high rates of co-resistance to other antibiotic classes, and 32 (1.3% of all strains) were ESBL positive and concomitantly resistant to both ciprofloxacin and gentamicin. All isolates were clinically susceptible to meropenem, and no carbapenemase-producing strains were detected by the screening breakpoints.

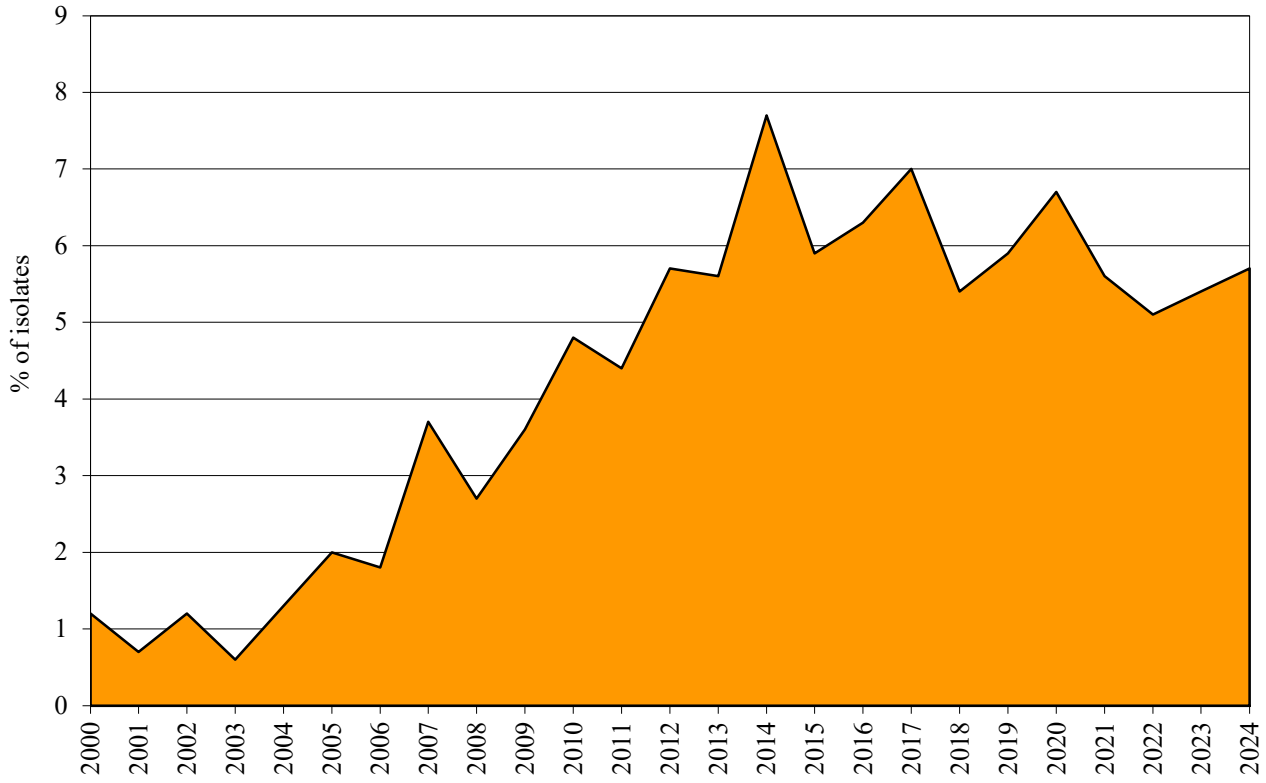


FIGURE 84. Prevalence of resistance to gentamicin in *Escherichia coli* blood culture isolates 2000-2024.

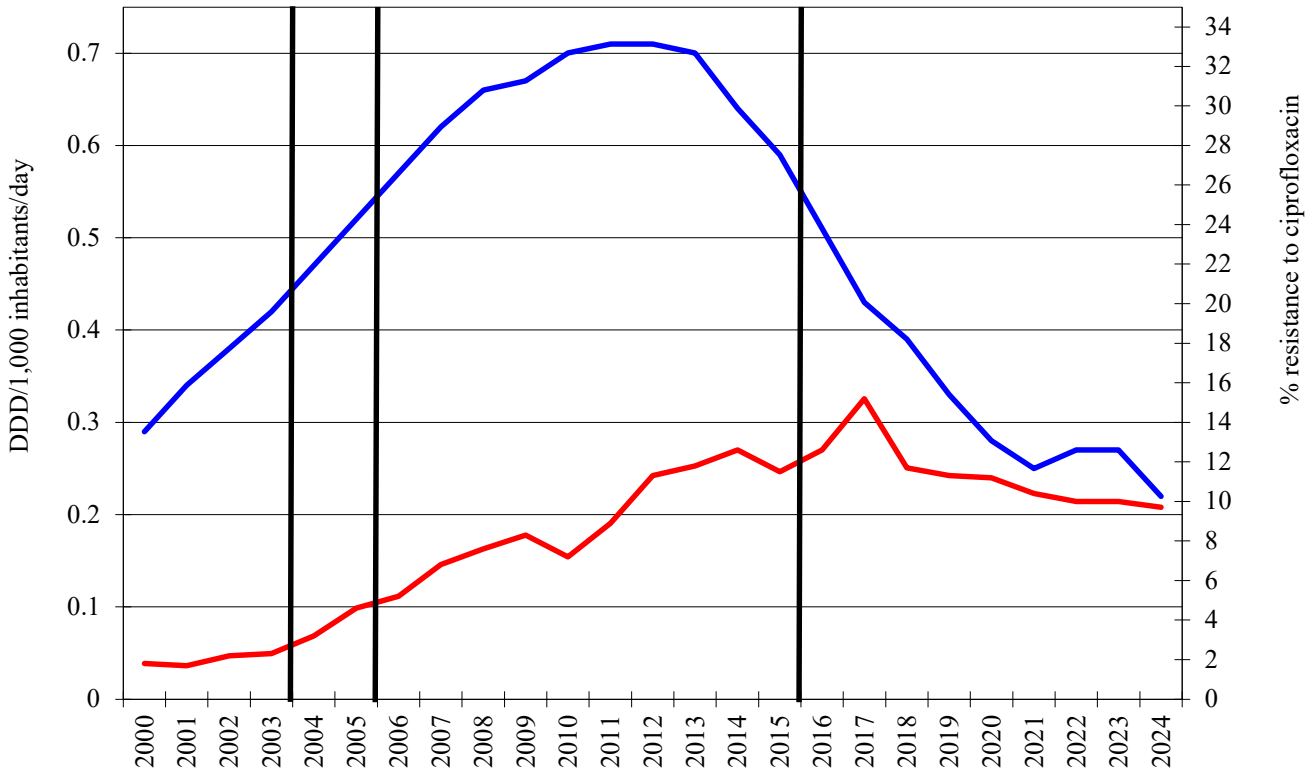


FIGURE 85. Usage of ciprofloxacin (blue) and prevalence of ciprofloxacin resistance in *Escherichia coli* blood culture isolates (red) as defined by MIC > 4 mg/L (2000-2003), MIC > 2 mg/L (2004-2005), MIC > 1 mg/L (2006-2015), and MIC > 0.5 mg/L (2016-2024). The breakpoints cannot be calibrated over the entire time period due to changes in susceptibility test methodology.

Escherichia coli in urine

TABLE 58. *Escherichia coli* urinary tract isolates in 2024 (n=1,317). Sampling, laboratory methods, and data handling are described in Appendix 5. Distributions of zone diameters are available at www.antibiotikaresistens.no.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Ampicillin	≤ 8	> 8	69.8	-	30.2
Mecillinam	≤ 8	> 8	95.2	-	4.8
Amoxicillin-clavulanic acid*	≤ 32	> 32	93.3	-	6.7
Piperacillin-tazobactam	≤ 8	> 8	96.4	-	3.6
Cefalexin	≤ 16	> 16	92.9	-	7.1
Cefotaxime**	≤ 1	> 2	95.5	0.6	3.9
Ceftazidime	≤ 1	> 4	95.7	1.4	2.9
Meropenem**	≤ 2	> 8	100.0	0.0	0.0
Aztreonam	≤ 1	> 4	95.2	2.1	2.7
Gentamicin***	≤ 2	> 2	95.2	-	4.8
Ciprofloxacin**	≤ 0.25	> 0.5	91.3	1.5	7.2
Nitrofurantoin	≤ 64	> 64	98.9	-	1.1
Fosfomycin*	≤ 8	> 8	97.4	-	2.6
Trimethoprim	≤ 4	> 4	81.0	-	19.0
Trimethoprim-sulfamethoxazole****	≤ 2	> 4	82.2	0.6	17.2
ESBL	Negative	Positive	96.1	-	3.9

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. ESBL=Extended spectrum beta-lactamase. *Breakpoints for oral administration in uncomplicated urinary tract infections. **Breakpoints for indications other than meningitis. ***Breakpoints for infections originating from the urinary tract. ****Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only.

RESULTS AND COMMENTS

Urinary tract isolates of *E. coli* have been included in the surveillance programme every year since NORM was established in 2000. The prevalence of resistance for 2024 is shown in Table 58 and the rates of resistance for 2000-2024 are shown in Figure 86. The footnotes indicate where EUCAST/NordicAST breakpoints specific for urinary tract infections have been applied.

The prevalence of resistance among urinary tract isolates has remained relatively stable over the last 25 years. The prevalence of resistance to ampicillin has gradually increased from approximately 25% to around 35% (30.2% in 2024). Resistance to trimethoprim and trimethoprim-sulfamethoxazole has remained stable around 20% and was determined to be 19.0% and 17.2%, respectively, in 2024. The prevalence of resistance to mecillinam was 4.8% in 2024 compared to 4.4% in 2023. Ciprofloxacin is used as a second-line agent for urinary tract infections in Norway. When adjusting for changes in breakpoint (see legend Figure 85), the prevalence of resistance has remained remarkably stable around 8-9% over the last five years. In 2024, 7.2% of the isolates were resistant to ciprofloxacin in addition to 1.5% that were only susceptible to increased exposure through adjustment of dosage or higher concentration at the site of infection. The corresponding rates for blood culture isolates were 9.7% resistance and 3.0% susceptibility to increased exposure. The persistent discrepancy between urinary tract isolates and isolates from bloodstream infections suggests that systemic infections are caused by selected pathogenic lineages with increased virulence and accumulation of mutations in gyrase and/or topoisomerase genes, whereas urinary tract isolates may be more representative of the wild type normal flora.

The prevalence of resistance to amoxicillin-clavulanic acid was 6.7% in 2024 compared to 7.6% in 2023, but this phenotype is technically challenging to determine and therefore prone to fluctuations. The breakpoint used (R > 32 mg/L) is only valid for uncomplicated urinary tract infections. Almost all isolates remained fully susceptible to nitrofurantoin (98.9%) and fosfomycin (97.4%).

Fifty-two isolates (3.9%) were reported as ESBL producers. This is at the same level as 3.8% in 2022 and 3.9% in 2023. As seen in Figure 87, the prevalence of *E. coli* ESBL is still lower in urine than in blood culture isolates (6.7%). ESBL positive strains were isolated in all parts of the country. Thirty-eight isolates were retrieved from samples submitted by general practitioners, while the others were found in hospitalised patients (n=7), or in patients from outpatient clinics (n=4), nursing homes (n=2) or unknown location (n=1). The ESBL isolates were all resistant to ampicillin, and the majority were also resistant to cefalexin (51/52), cefotaxime (48/52), ceftazidime (35/52) and aztreonam (34/52). Almost all ESBL isolates were *in vitro* susceptible to mecillinam (47/52). This agent may be a viable treatment option in uncomplicated UTI provided a dosage of 400 mg x 3. Many ESBL isolates were resistant to trimethoprim (35/52), trimethoprim-sulfamethoxazole (32/52) and ciprofloxacin (23/52), but remained susceptible to nitrofurantoin (52/52), fosfomycin (51/52) and gentamicin (42/52). All isolates were clinically susceptible to meropenem, and no zone diameters below the screening breakpoint for carbapenemase producers were detected.

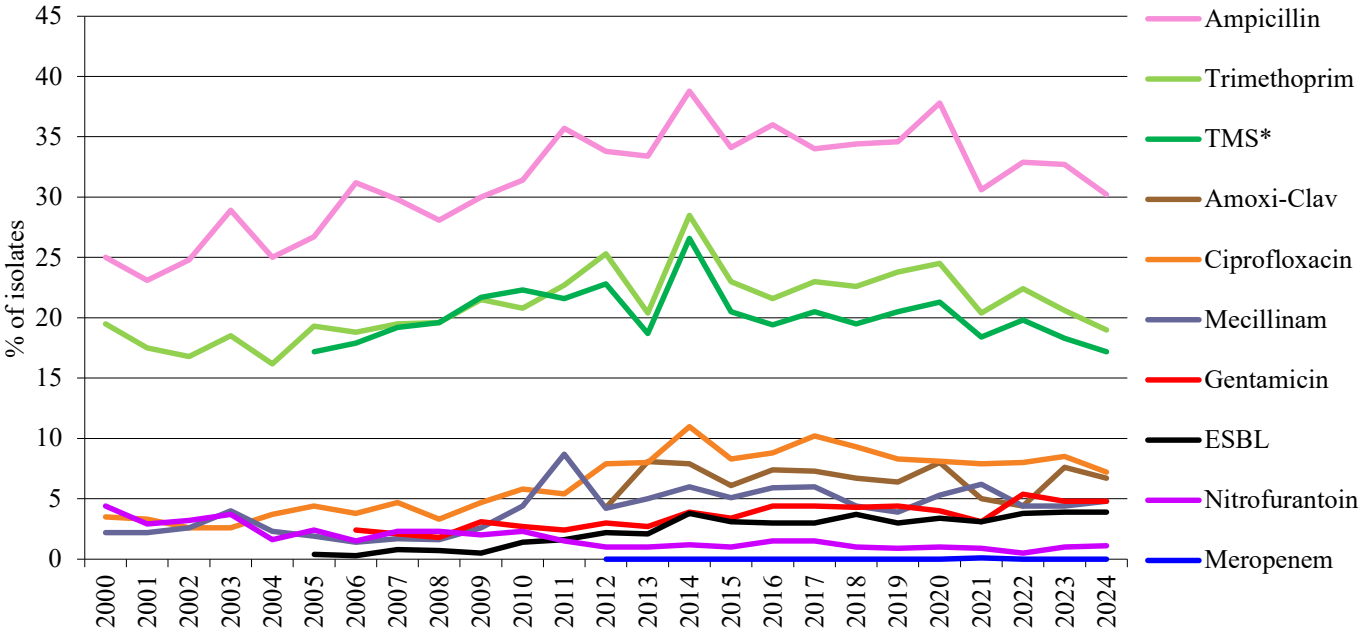


FIGURE 86. Prevalence of resistance to various antimicrobial agents in urinary tract *Escherichia coli* isolates 2000-2024. Isolates are categorised according to the breakpoints at the time of analysis for each year. *TMS=Trimethoprim-sulfamethoxazole.

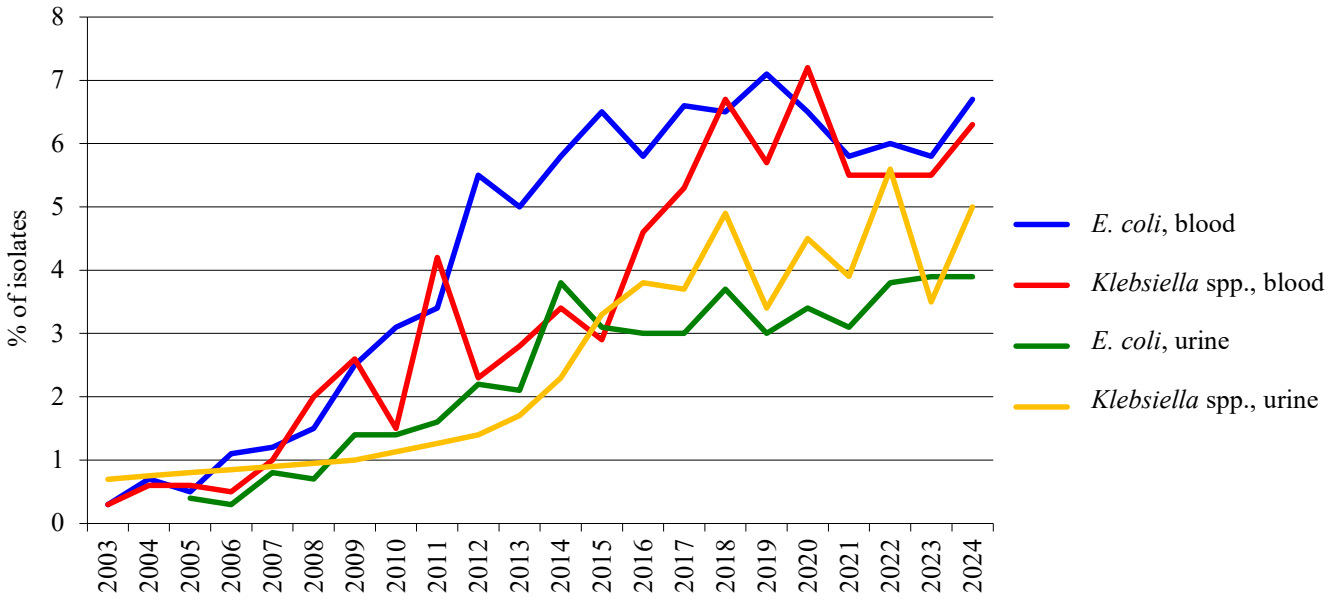


FIGURE 87. Prevalence of ESBL production among *Escherichia coli* and *Klebsiella* spp. isolates from blood and urine 2003-2024.

Klebsiella spp. in blood cultures

TABLE 59. *Klebsiella* spp. blood culture isolates in 2024 (n=1,230), except for amoxicillin-clavulanic acid (n=1,193) where 37 *K. aerogenes* isolates are excluded due to lack of breakpoints. Sampling, laboratory methods, and data handling are described in Appendix 5. Distributions of zone diameters are available at www.antibiotikaresistens.no.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Amoxicillin-clavulanic acid*	≤ 8	> 8	88.1	-	11.9
Piperacillin-tazobactam	≤ 8	> 8	88.8	-	11.2
Cefotaxime**	≤ 1	> 2	92.6	0.7	6.7
Ceftazidime	≤ 1	> 4	92.0	2.0	6.0
Cefepime	≤ 1	> 4	90.7	2.7	6.6
Meropenem**	≤ 2	> 8	99.6	0.0	0.4
Aztreonam	≤ 1	> 4	91.6	1.0	7.4
Gentamicin***	≤ 2	> 2	95.5	-	4.5
Ciprofloxacin**	≤ 0.25	> 0.5	87.4	3.7	8.9
Trimethoprim-sulfamethoxazole****	≤ 2	> 4	86.0	0.2	13.8
ESBL	Negative	Positive	93.7	-	6.3

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. ESBL=Extended spectrum beta-lactamase. *Breakpoints for intravenous administration. **Breakpoints for indications other than menigitis. ***Breakpoints for infections originating from the urinary tract. ****Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only.

TABLE 60. *Klebsiella pneumoniae* blood culture isolates in 2024 (n=883). Sampling, laboratory methods, and data handling are described in Appendix 5. Distributions of zone diameters are available at www.antibiotikaresistens.no.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Amoxicillin-clavulanic acid*	≤ 8	> 8	87.9	-	12.1
Piperacillin-tazobactam	≤ 8	> 8	88.4	-	11.6
Cefotaxime**	≤ 1	> 2	92.6	0.2	7.2
Ceftazidime	≤ 1	> 4	91.5	1.9	6.6
Cefepime	≤ 1	> 4	90.3	2.6	7.1
Meropenem**	≤ 2	> 8	99.4	0.0	0.6
Aztreonam	≤ 1	> 4	92.1	1.0	6.9
Gentamicin***	≤ 2	> 2	95.4	-	4.6
Ciprofloxacin**	≤ 0.25	> 0.5	84.6	4.4	11.0
Trimethoprim-sulfamethoxazole****	≤ 2	> 4	83.5	0.1	16.4
ESBL	Negative	Positive	92.6	-	7.4

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. ESBL=Extended spectrum beta-lactamase. *Breakpoints for intravenous administration. **Breakpoints for indications other than menigitis. ***Breakpoints for infections originating from the urinary tract. ****Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only.

TABLE 61. *Klebsiella oxytoca* blood culture isolates in 2024 (n=275). Sampling, laboratory methods, and data handling are described in Appendix 5. Distributions of zone diameters are available at www.antibiotikaresistens.no.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Amoxicillin-clavulanic acid*	≤ 8	> 8	89.1	-	10.9
Piperacillin-tazobactam	≤ 8	> 8	90.9	-	9.1
Cefotaxime**	≤ 1	> 2	92.7	2.2	5.1
Ceftazidime	≤ 1	> 4	94.5	1.5	4.0
Cefepime	≤ 1	> 4	91.3	2.9	5.8
Meropenem**	≤ 2	> 8	100.0	0.0	0.0
Aztreonam	≤ 1	> 4	90.6	0.7	8.7
Gentamicin***	≤ 2	> 2	95.6	-	4.4
Ciprofloxacin**	≤ 0.25	> 0.5	95.3	1.8	2.9
Trimethoprim-sulfamethoxazole****	≤ 2	> 4	92.7	0.4	6.9
ESBL	Negative	Positive	96.0	-	4.0

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. ESBL=Extended spectrum beta-lactamase. *Breakpoints for intravenous administration. **Breakpoints for indications other than menigitis. ***Breakpoints for infections originating from the urinary tract. ****Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only.

TABLE 62. *Klebsiella aerogenes* blood culture isolates in 2024 (n=37). Sampling, laboratory methods, and data handling are described in Appendix 5. Distributions of zone diameters are available at www.antibiotikaresistens.no.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Piperacillin-tazobactam	≤ 8	> 8	81.1	-	18.9
Cefotaxime*	≤ 1	> 2	86.5	2.7	10.8
Ceftazidime	≤ 1	> 4	83.8	5.4	10.8
Cefepime	≤ 1	> 4	91.9	5.4	2.7
Meropenem*	≤ 2	> 8	100.0	0.0	0.0
Aztreonam	≤ 1	> 4	86.5	2.7	10.8
Gentamicin**	≤ 2	> 2	97.3	-	2.7
Ciprofloxacin*	≤ 0.25	> 0.5	97.3	0.0	2.7
Trimethoprim-sulfamethoxazole***	≤ 2	> 4	97.3	0.0	2.7
ESBL	Negative	Positive	100.0	-	0.0

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. ESBL=Extended spectrum beta-lactamase. *Breakpoints for indications other than menigitis. **Breakpoints for infections originating from the urinary tract. ***Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only.

RESULTS AND COMMENTS

Klebsiella spp. isolates in blood cultures were speciated as follows: 883 (71.7%) *K. pneumoniae* (including *K. pneumoniae, K. quasipneumoniae, K. variicola, K. quasivariicola* and *K. africana*); 275 (22.4%) *K. oxytoca* (including *K. oxytoca, K. michiganensis, K. grimontii, K. pasteurii, K. huaxiensis* and *K. spallanzanii*): 37 (3.0%) *K. aerogens*; and 35 unspecified *Klebsiella* isolates (2.9%), giving a total of 1,230 *Klebsiella* spp. (Tables 59-62).

The majority of *Klebsiella* spp. isolates were susceptible to aminoglycosides, and the prevalence of gentamicin resistance remained stable at 4.5% in 2024 compared to 4.5% in 2022 and 4.3% in 2023. Gentamicin resistance was slightly more common in *K. pneumoniae* (4.6%) and *K. oxytoca* (4.4%) than in *K. aerogenes* (2.7%). Aminoglycoside resistance in common *Enterobacterales* species is a cause for great concern as these antimicrobials have traditionally been used in the empirical regimen for treatment of sepsis in Norway.

As for *E. coli*, the breakpoints for ciprofloxacin were reduced from R > 1 mg/L to R > 0.5 mg/L and from S ≤ 0.5 to S ≤ 0.25 in 2017. The prevalence of resistance to ciprofloxacin peaked at 11-12% in 2016-2017, but has now stabilised at 8.1% in 2023 and 8.9% in 2024. Resistance to ciprofloxacin was much more common in *K. pneumoniae* (11.0%) than in *K. oxytoca* (2.9%) and *K. aerogenes* (2.7%). Overall resistance to trimethoprim-sulfamethoxazole increased from 11.9% in 2023 to 13.8% in 2024. The prevalence of resistance to trimethoprim-sulfamethoxazole was significantly lower in *K. oxytoca* (6.9%) and *K. aerogenes* (2.7%) than in *K. pneumoniae* (16.4%).

Comparison of resistance to beta-lactam antibiotics between *Klebsiella* species is complicated by the chromosomal K1 beta-lactamase in *K. oxytoca* and chromosomal AmpC in *K. aerogenes*. Most *Klebsiella* spp. isolates were susceptible (S+I) to cefotaxime (93.3%), ceftazidime (94.0%), cefepime (93.4%) and the beta-lactam/beta-lactamase inhibitor combination piperacillin-tazobactam (88.8%), see Figure 88. The prevalence of resistance to 3rd generation cephalosporins has remained essentially unchanged 2018-2024. The rate of resistance to pipera-

cillin-tazobactam has not changed over the last three years (11.0% in 2022, 10.7% in 2023 and 11.2% in 2024).

As for *E. coli*, the detection of extended spectrum beta-lactamases (ESBL) was based on zone diameters of cefotaxime and ceftazidime disks. Isolates with reduced zone diameters were further characterised by combination disks or MIC gradient tests. The prevalence of phenotypically confirmed ESBL isolates increased slightly from 2023 (5.5% in *Klebsiella* spp.; 6.3% in *K. pneumoniae*) to 2024 (6.3% in *Klebsiella* spp.; 7.4% in *K. pneumoniae*), see Figure 87. The 77 ESBL isolates originated from 17 different laboratories and were identified as *K. pneumoniae* (n=65, 84%), *K. oxytoca* (n=11, 14%) and *Klebsiella* spp. (n=1). ESBL isolates were often resistant to cefotaxime (74/77), cefepime (72/77), ceftazidime (68/77) and aztreonam (69/77), and co-resistance was frequently seen for trimethoprim-sulfamethoxazole (70/77), ciprofloxacin (58/77) and gentamicin (43/77). Many isolates remained susceptible to piperacillin-tazobactam (32/77). A total of five meropenem resistant *K. pneumoniae* isolates (0.4%) were verified as carbapenemase producers (CPE) and contained OXA-48-like (n=2), OXA-48-like + NDM (n=2) or KPC (n=1) enzymes. Additional isolates were only susceptible to increased meropenem exposure (I) or had zone diameters below the screening breakpoint, but did not contain any known carbapenemase genes. Thirty-nine ESBL isolates (3.2% of all *Klebiella* isolates) were concomitantly resistant to gentamicin and ciprofloxacin, and three of these were also among the carbapenemase producers.

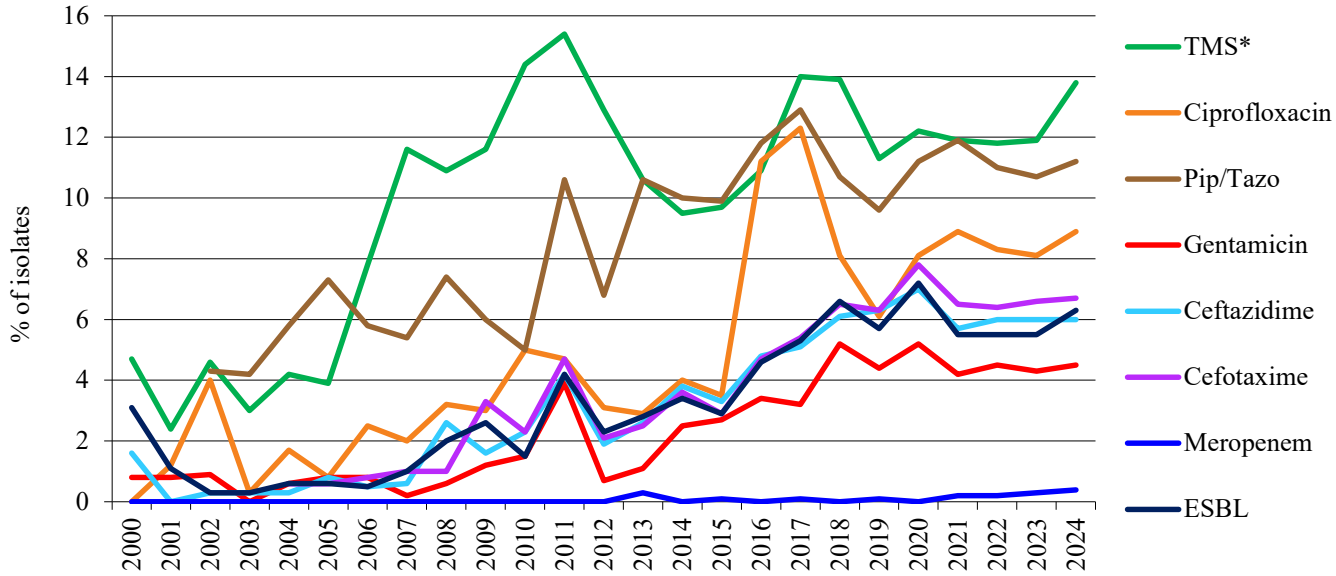


FIGURE 88. Prevalence of resistance to various antimicrobial agents in *Klebsiella* spp. blood culture isolates 2000-2024. Isolates are categorised according to the breakpoints at the time of analysis. *TMS=Trimethoprim-sulfamethoxazole.

Klebsiella spp. in urine

TABLE 63. *Klebsiella* spp. urinary tract isolates in 2024 (n=1,050), except for amoxicillin-clavulanic acid and cefalexin (n=996) where 54 *K. aerogenes* isolates are excluded due to lack of breakpoints. Sampling, laboratory methods, and data handling are described in Appendix 5. Distributions of zone diameters are available at www.antibiotikaresistens.no.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Mecillinam	≤ 8	> 8	91.1	-	8.9
Amoxicillin-clavulanic acid*	≤ 32	> 32	94.8	-	5.2
Piperacillin-tazobactam	≤ 8	> 8	91.2	-	8.8
Cefalexin	≤ 16	> 16	92.2	-	7.8
Cefotaxime**	≤ 1	> 2	94.0	0.1	5.9
Ceftazidime	≤ 1	> 4	93.8	1.2	5.0
Cefepime	≤ 1	> 4	93.7	1.2	5.1
Meropenem**	≤ 2	> 8	100.0	0.0	0.0
Aztreonam	≤ 1	> 4	92.6	1.3	6.1
Gentamicin***	≤ 2	> 2	96.3	-	3.7
Ciprofloxacin**	≤ 0.25	> 0.5	90.4	3.7	5.9
Trimethoprim	≤ 4	> 4	82.7	-	17.3
Trimethoprim-sulfamethoxazole****	≤ 2	> 4	85.6	1.0	13.4
ESBL	Negative	Positive	95.0	-	5.0

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. ESBL=Extended spectrum beta-lactamase. *Breakpoints for oral administration in uncomplicated urinary tract infections. **Breakpoints for indications other than meningitis. ***Breakpoints for infections originating from the urinary tract. ****Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only.

TABLE 64. *Klebsiella pneumoniae* urinary tract isolates in 2024 (n=773). Sampling, laboratory methods, and data handling are described in Appendix 5. Distributions of zone diameters are available at www.antibiotikaresistens.no.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Mecillinam	≤ 8	> 8	92.1	-	7.9
Amoxicillin-clavulanic acid*	≤ 32	> 32	96.0	-	4.0
Piperacillin-tazobactam	≤ 8	> 8	92.0	-	8.0
Cefalexin	≤ 16	> 16	92.9	-	7.1
Cefotaxime**	≤ 1	> 2	94.1	0.1	5.8
Ceftazidime	≤ 1	> 4	93.4	1.3	5.3
Cefepime	≤ 1	> 4	93.7	1.3	5.0
Meropenem**	≤ 2	> 8	100.0	0.0	0.0
Aztreonam	≤ 1	> 4	93.9	0.9	5.2
Gentamicin***	≤ 2	> 2	96.6	-	3.4
Ciprofloxacin**	≤ 0.25	> 0.5	87.8	4.8	7.4
Trimethoprim	≤ 4	> 4	79.6	-	20.4
Trimethoprim-sulfamethoxazole****	≤ 2	> 4	83.0	1.0	16.0
ESBL	Negative	Positive	94.3	-	5.7

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. ESBL=Extended spectrum beta-lactamase. *Breakpoints for oral administration in uncomplicated urinary tract infections. **Breakpoints for indications other than meningitis. ***Breakpoints for infections originating from the urinary tract. ****Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only.

TABLE 65. *Klebsiella oxytoca* urinary tract isolates in 2024 (n=206). Sampling, laboratory methods, and data handling are described in Appendix 5. Distributions of zone diameters are available at www.antibiotikaresistens.no.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Mecillinam	≤ 8	> 8	86.9	-	13.1
Amoxicillin-clavulanic acid*	≤ 32	> 32	90.8	-	9.2
Piperacillin-tazobactam	≤ 8	> 8	88.8	-	11.2
Cefalexin	≤ 16	> 16	89.8	-	10.2
Cefotaxime**	≤ 1	> 2	93.7	0.0	6.3
Ceftazidime	≤ 1	> 4	95.1	0.5	4.4
Cefepime	≤ 1	> 4	92.7	0.5	6.8
Meropenem**	≤ 2	> 8	100.0	0.0	0.0
Aztreonam	≤ 1	> 4	88.4	2.9	8.7
Gentamicin***	≤ 2	> 2	93.7	-	6.3
Ciprofloxacin**	≤ 0.25	> 0.5	96.6	1.0	2.4
Trimethoprim	≤ 4	> 4	91.3	-	8.7
Trimethoprim-sulfamethoxazole****	≤ 2	> 4	92.7	0.5	6.8
ESBL	Negative	Positive	96.1	-	3.9

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. ESBL=Extended spectrum beta-lactamase. *Breakpoints for oral administration in uncomplicated urinary tract infections. **Breakpoints for indications other than meningitis. ***Breakpoints for infections originating from the urinary tract. ****Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only.

TABLE 66. *Klebsiella aerogenes* urinary tract isolates in 2024 (n=54). Sampling, laboratory methods, and data handling are described in Appendix 5. Distributions of zone diameters are available at www.antibiotikaresistens.no.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Mecillinam	≤ 8	> 8	96.3	-	3.7
Piperacillin-tazobactam	≤ 8	> 8	90.7	-	9.3
Cefotaxime*	≤ 1	> 2	94.4	0.0	5.6
Ceftazidime	≤ 1	> 4	90.7	3.7	5.6
Cefepime	≤ 1	> 4	98.1	1.9	0.0
Meropenem*	≤ 2	> 8	100.0	0.0	0.0
Aztreonam	≤ 1	> 4	90.7	1.9	7.4
Gentamicin**	≤ 2	> 2	100.0	-	0.0
Ciprofloxacin*	≤ 0.25	> 0.5	100.0	0.0	0.0
Trimethoprim	≤ 4	> 4	88.9	-	11.1
Trimethoprim-sulfamethoxazole***	≤ 2	> 4	92.5	1.9	5.6
ESBL	Negative	Positive	100.0	-	0.0

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. ESBL=Extended spectrum beta-lactamase. *Breakpoints for indications other than meningitis. **Breakpoints for infections originating from the urinary tract. ***Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only.

RESULTS AND COMMENTS

Klebsiella spp. urinary tract isolates have previously been included in the NORM surveillance programme in 2001, 2003, 2009 and 2012-2023. Due to methodological changes it is not possible to directly compare the results from 2001 and 2003 with the ones from later surveys. There are no *Klebsiella* spp. disk diffusion breakpoints for fosfomycin or nitrofurantoin, and *K. aerogenes* is not included in the breakpoints for oral administration of cefalexin and amoxicillin-clavulanic acid. The urinary tract isolates in NORM 2024 were speciated as follows: 773 (73.7%) *K. pneumoniae* (including *K. pneumoniae, K. quasi-pneumoniae, K. variicola, K. quasivariicola* and *K. africana*); 206 (19.6%) *K. oxytoca* (including *K. oxytoca, K. michiganensis, K. grimontii, K. pasteurii, K. huaxiensis* and *K. spallanzanii*); 54 (5.1%) *K. aerogens*; and 17 isolates (1.6%) not identified to the species level, giving a total of 1,050 *Klebsiella* spp. isolates (Tables 63-66).

The prevalence of resistance to urinary tract antibiotics was slightly lower in *Klebsiella* spp. than in *E. coli* isolates (Table 58). The majority of isolates remained susceptible to gentamicin at 96.3% compared to 95.7% in 2022 and 97.4% in 2023. Among urinary tract *E. coli*, 95.2% were gentamicin susceptible in 2024. The rate of resistance to ciprofloxacin in *Klebsiella* spp. decreased from 6.4% in 2023 to 5.9% in 2024. The comparable rate for urinary tract *E. coli* in 2024 was 7.2%. Susceptibility to trimethoprim (87.7% in 2023; 82.7% in 2024) and trimethoprim-sulfamethoxazole (86.7% in 2023; 85.6% in 2024) was slightly higher than in *E. coli* (81.0% and 82.2%, respectively).

All *Klebsiella* isolates are inherently resistant to ampicillin due to the chromosomal SHV beta-lactamase. As for *Klebsiella* spp. blood culture isolates, ESBL detection in urinary tract isolates was based on resistance to cefotaxime and/or ceftazidime and subsequent confirmatory ESBL combination disk or MIC gradient tests. Fifty-two isolates (5.0%) were reported as ESBL producers, of which 44 were *K. pneumoniae* and eight were *K. oxytoca*. They were retrieved from 17 different laboratories and originated from hospital inpatients (n=22), outpatient clinics (n=6), general practices (n=21) and nursing homes (n=3). The 5.0% ESBL rate (5.7% in *K. pneumoniae*) was an increase from 2023 (3.5% for all *Klebsiella*, 3.7% for *K. pneumoniae*) but at the same level as in 2022 (5.6% for all *Klebsiella*, 6.0% in *K. pneumoniae*). As expected, the 52 ESBL isolates were generally resistant to broad-spectrum beta-lactam antibiotics (cefalexin, cefotaxime, ceftazidime, cefepime, aztreonam). There was also widespread co-resistance to trimethoprim (n=49), trimethoprim-sulfamethoxazole (n=49), ciprofloxacin (n=31) and gentamicin (n=26), but many isolates remained susceptible to mecillinam (n=44), amoxicillin-clavulanic acid (n=28) and/or piperacillin-tazobactam (n=22). Twenty-one ESBL isolates (2.0% of all *Klebsiella* isolates) were concomitantly resistant to gentamicin and ciprofloxacin. No isolates were clinically resistant to meropenem, and carbapenemase production was not detected by the screening procedure.

Carbapenemase-producing Gram-negative bacteria in Norway 2024

Carbapenem resistance in Gram-negative bacteria continues to increase globally and carbapenemase-producing organisms (CPO) is one of the most important bacteria associated with mortality and morbidity due to antibiotic resistance (1). In Norway, infection and colonisation with CPO is notifiable to the Norwegian Surveillance System for Communicable Diseases (MSIS) and confirmed at the Norwegian Centre for Detection of Antimicrobial Resistance (K-res). Here we summarise the 2024 data based on analysed cases and isolates at K-res.

Carbapenemase-producing *Enterobacterales* (CPE)

In 2024, 265 patients with CPE were identified (Figure 89). This is an increase from 237 in 2023, corresponding to an increased incidence from 4.3 to 4.7 per 100,000 person-years. The proportion of cases suspected to be imported decreased to 69% in 2024 from 77% in 2023. For 12%, there was no suspicion of import in 2024 compared to 11% in 2023. The proportion with missing information on import increased to 18% in 2024 from 12% in 2023. In total, suspected import was associated with 47 different countries plus "Abroad," which was specified for 2% of patients. Ukraine accounted for the largest proportion of patients with suspected import (15% of all cases and 21% of imported cases). This is a decrease from 2023 (29% of all cases and 38% of imported cases). After Ukraine, the proportion of suspected import among all cases was 6% for both Turkey and Egypt, and 5% for Iraq.

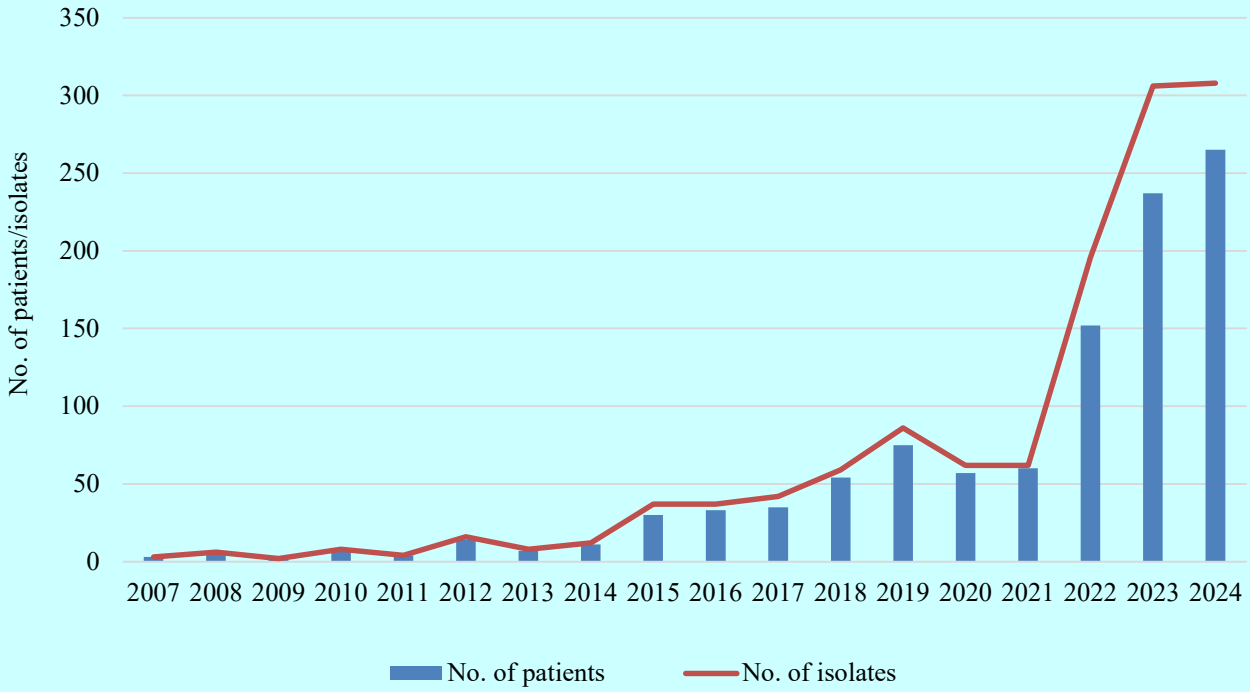


FIGURE 89. Number of patients with confirmed CPE and number of CPE isolates in Norway 2007-2024.

A total of 308 CPE isolates from 265 patients were detected in 2024, compared to 306 isolates from 237 patients in 2023 (Figure 89). In 35 patients, 2-4 CPE isolates were detected of different species/carbapenemase genes or the same species but different sequence types (STs). 67% of the isolates were reported as screening isolates (65% in 2023). 3.5% of the isolates were detected in blood cultures and 14% in urine. This is at the same level as in 2023 (3.0% in blood and 14% in urine).

As in previous years, the CPE population is dominated by *Escherichia coli* and *Klebsiella pneumoniae* species complex (Figure 90). Compared to 2023, the proportion of *E. coli* increased from 43% in 2023 to 54% in 2024, while the proportion of the *K. pneumoniae* species complex decreased from 40% to 36%. Thirty isolates of other *Enterobacterales* species were detected in 2024, accounting for 9.7% compared to 17% in 2023.

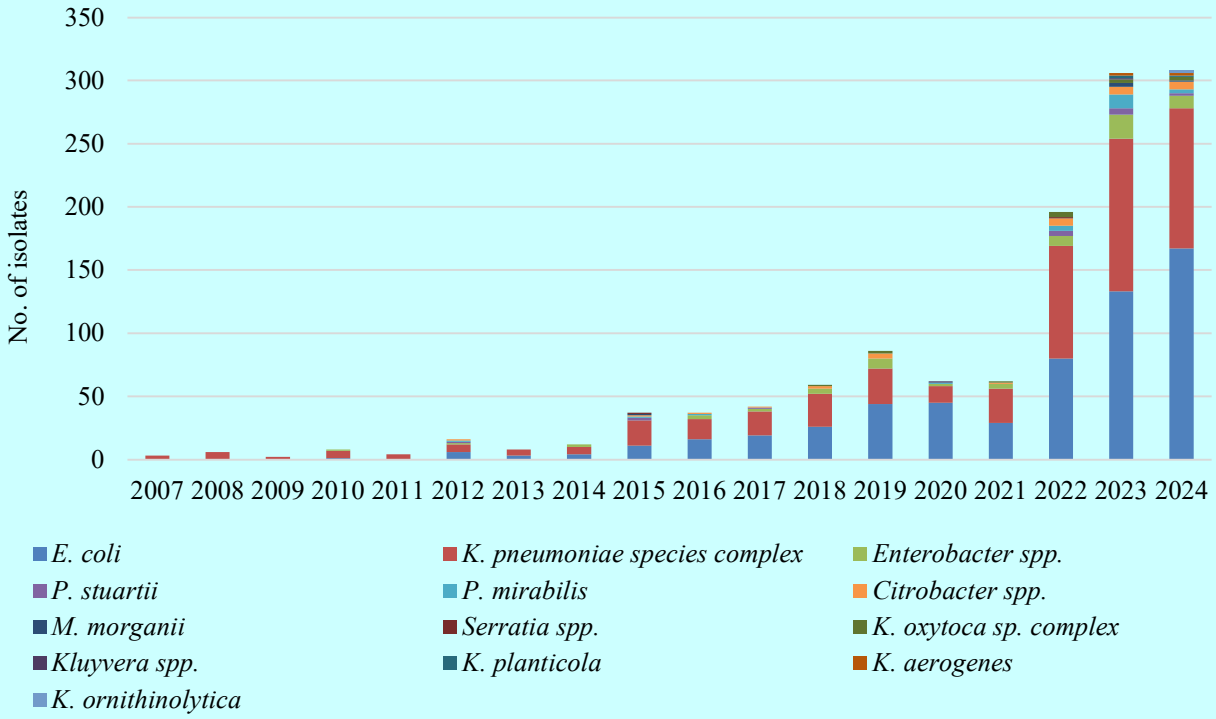


FIGURE 90. Species distribution of CPE isolates in Norway 2007-2024.

NDM and OXA-48-like remain the dominant carbapenemases as in previous years (Figure 91). The proportion of these increased from 2023 to 2024 (NDM: 42% in 2024 vs. 38% in 2023, OXA-48-like: 41% in 2024 vs. 37% in 2023). 9% of the isolates in 2024 had both NDM and OXA-48-like compared to 12% in 2023. 6% of the isolates had KPC, including three isolates with both KPC and NDM. One *E. coli* isolate had three carbapenemases: NDM, KPC, and OXA-48-like. IMI/NMC has been detected in one to five isolates over the past five years but was not detected in 2024.

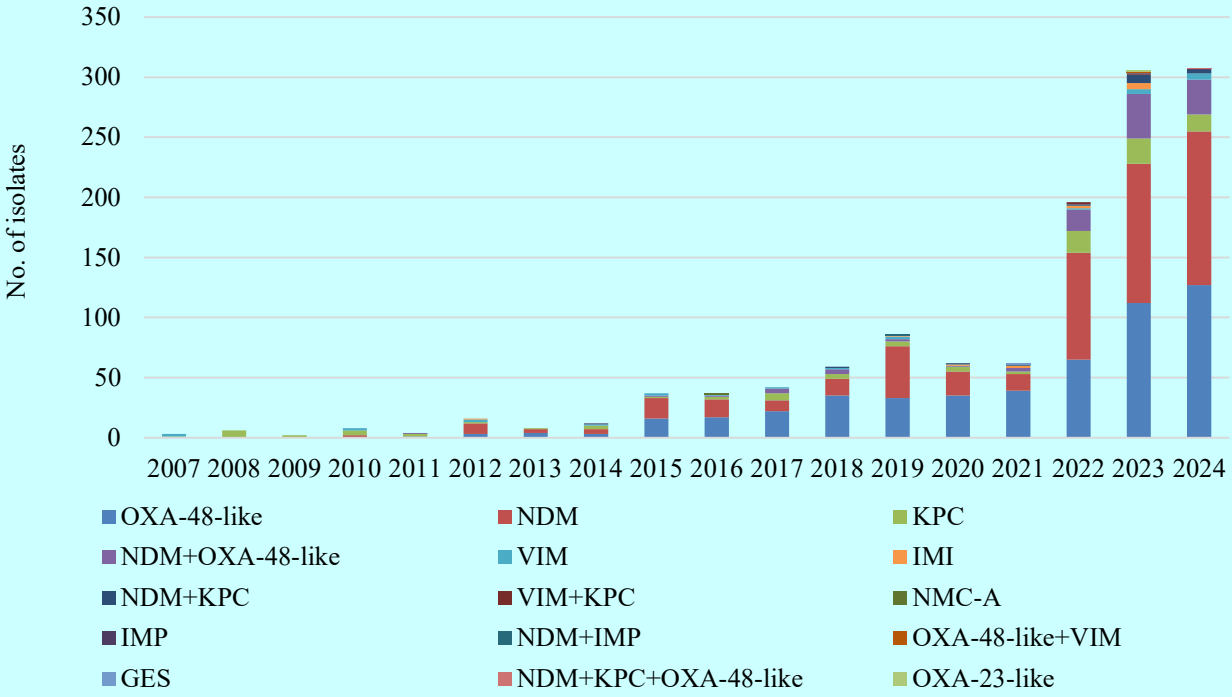


FIGURE 91. Carbapenemase variant distribution among CPE isolates in Norway 2007-2024.

The genotypic diversity of sequence types (STs) and carbapenemase genes continues to increase. In 2024, a minimum of 49 different *E. coli* STs were detected compared to 40 in 2023 (Figure 92). Five isolates belonged to a currently novel STs. The eight most prevalent STs (ST38, ST648, ST167, ST69, ST361, ST410, ST405, and ST131) accounted for 54% of *E. coli* isolates. These are known global high-risk clones with increasing prevalence in Europe (2-7). The most common ST-carbapenemase gene combination was ST648-NDM-5. NDM-5 (n=59), OXA-244 (n=44), OXA-48 (n=21), and OXA-181 (n=14) were the most frequently detected carbapenemase genes in *E. coli*. NDM-5 was also found in combination with other carbapenemase genes in seven isolates.

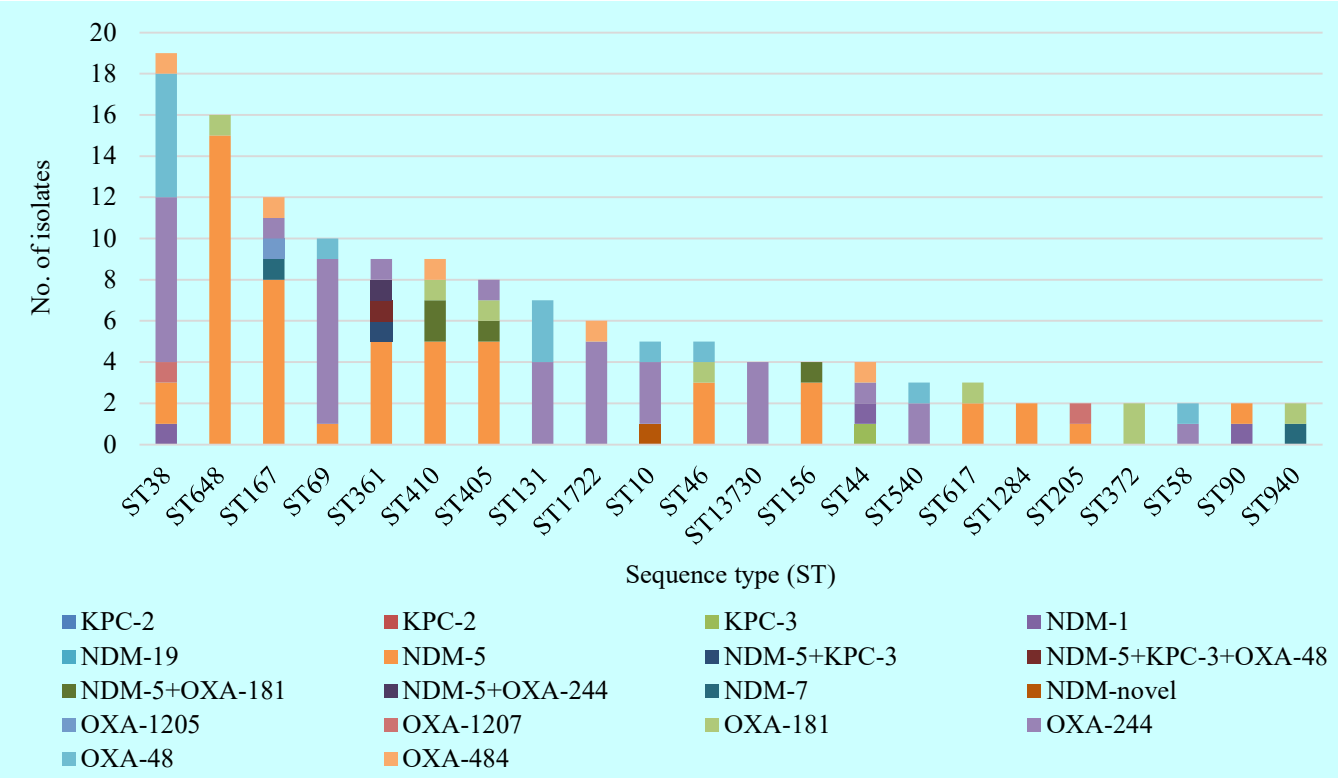


FIGURE 92. Carbapenemase variant distribution by STs among carbapenemase-producing *E. coli* identified in 2024. Only STs with ≥2 isolates are shown in the Figure. Thirty-one single ST isolates are not shown.

Phylogenetic analysis based on core genome multilocus sequence typing (cgMLST) revealed six clusters consisting of 2-5 related isolates (Figure 93). Two clusters (clusters 1 and 6) consisted exclusively of isolates associated with import. In both clusters, there was an association with import from both Pakistan and Iraq. For these clusters, it is assumed that transmission occurred before detection in Norway. The other four clusters (clusters 2, 3, 4, and 5) included isolates associated with import and isolates without import or where import data were missing. In all these clusters, isolates were detected at different laboratories and over a relatively long period (approx. 3-10 months). Further detailed relatedness analysis and epidemiological investigation of some clusters could not establish an epidemiological link.

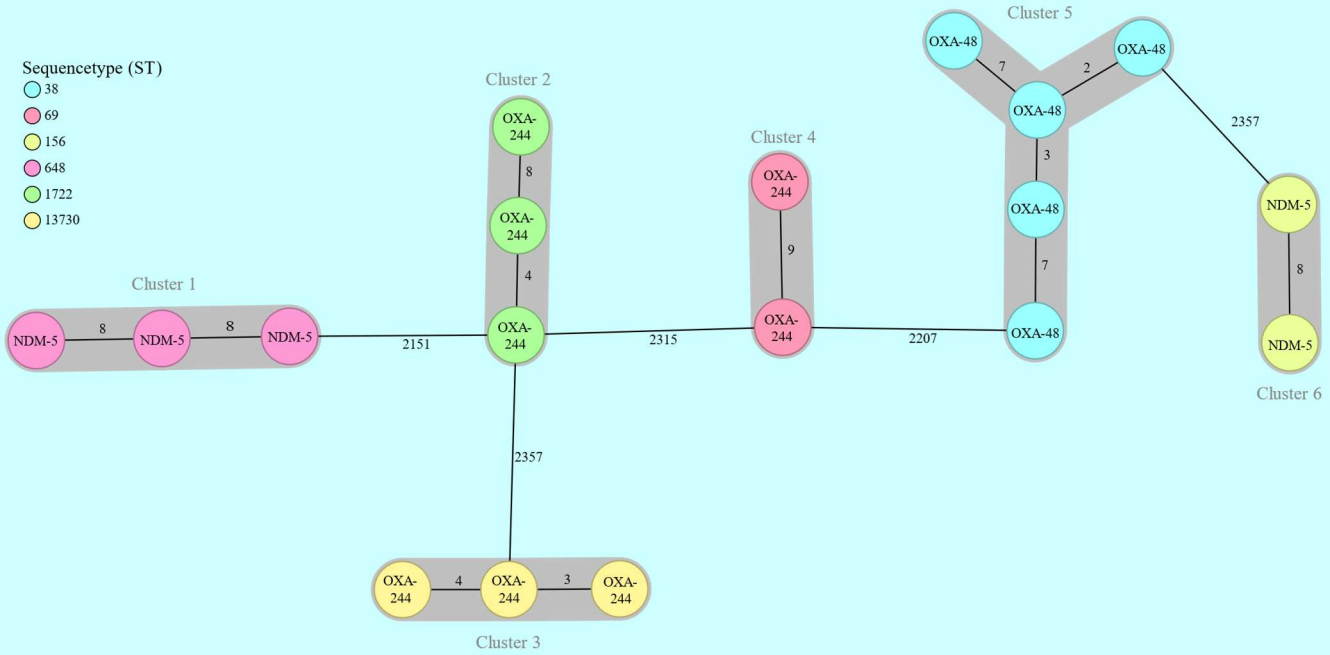


FIGURE 93. Minimum spanning network of closely related carbapenemase-producing *E. coli* identified in Norway in 2024. The analysis is based on 2,513 core genome alleles and created using SeqSphere+ software and *E. coli* K12 as reference genome. The isolates are represented by circles and coloured according to ST. Specific carbapenemase variants are indicated within each circle and number of allelic differences along the connecting lines. Grey shading between isolates indicates close relationship (≤10 allele differences).

A recently published risk assessment from the ECDC highlights an increased detection of *E. coli* high-risk clones (e.g. ST167, ST361, ST405, ST410, ST648 carrying bla_{NDM-5}, ST38 with $bla_{OXA-244}$ and ST131 with a variety of carbapenemases) in the EU/EEA, with a risk of community spread (7). In Norway, there are indications that community spread may be occurring. Among the four most common STs in 2024, there are differences in association with import: for ST69 and ST38, 30% and 42% of isolates were associated with import, respectively, while for ST167 and ST648, 83% and 81% were associated with import, respectively. ST69 and ST38 were also more frequently found in clinical samples, while ST167 and ST648 were linked to screening samples.

Among the 111 *K. pneumoniae* species complex isolates**,** 109 (98%) were *K. pneumoniae*. One *K. variicola* of a previously unknown ST with OXA-181 and one *K. quasipneumoniae* subsp. *quasipneumoniae* ST196 with NDM-1 were detected. The *K. pneumoniae* isolates belonged to at least 27 different STs (Figure 94). Two isolates belonged to a previously unknown ST. ST147 was the dominant ST, accounting for 28% of *K. pneumoniae* isolates, followed by ST307 (11%), ST395 (11%), and ST23 (7%). These four STs made up 57% of *K. pneumoniae* isolates. These STs and others detected, such as ST101, ST11, and ST15, are known global high-risk clones (8-9). NDM-1 (n=28) and OXA-48 (n=17) were the most common carbapenemase genes in *K. pneumoniae*. Additionally, NDM-1 and OXA-48 were detected together in 20 isolates. 48% of the isolates with NDM-1 or NDM-1+OXA-48 were ST147. OXA-48 alone was not associated with a specific ST but was found in 10 different STs. The most common ST-carbapenemase gene combinations were ST147-NDM-1 (n=14), ST147-NDM-1+OXA-48 (n=9), and ST395-NDM-1+OXA-48 (n=6).

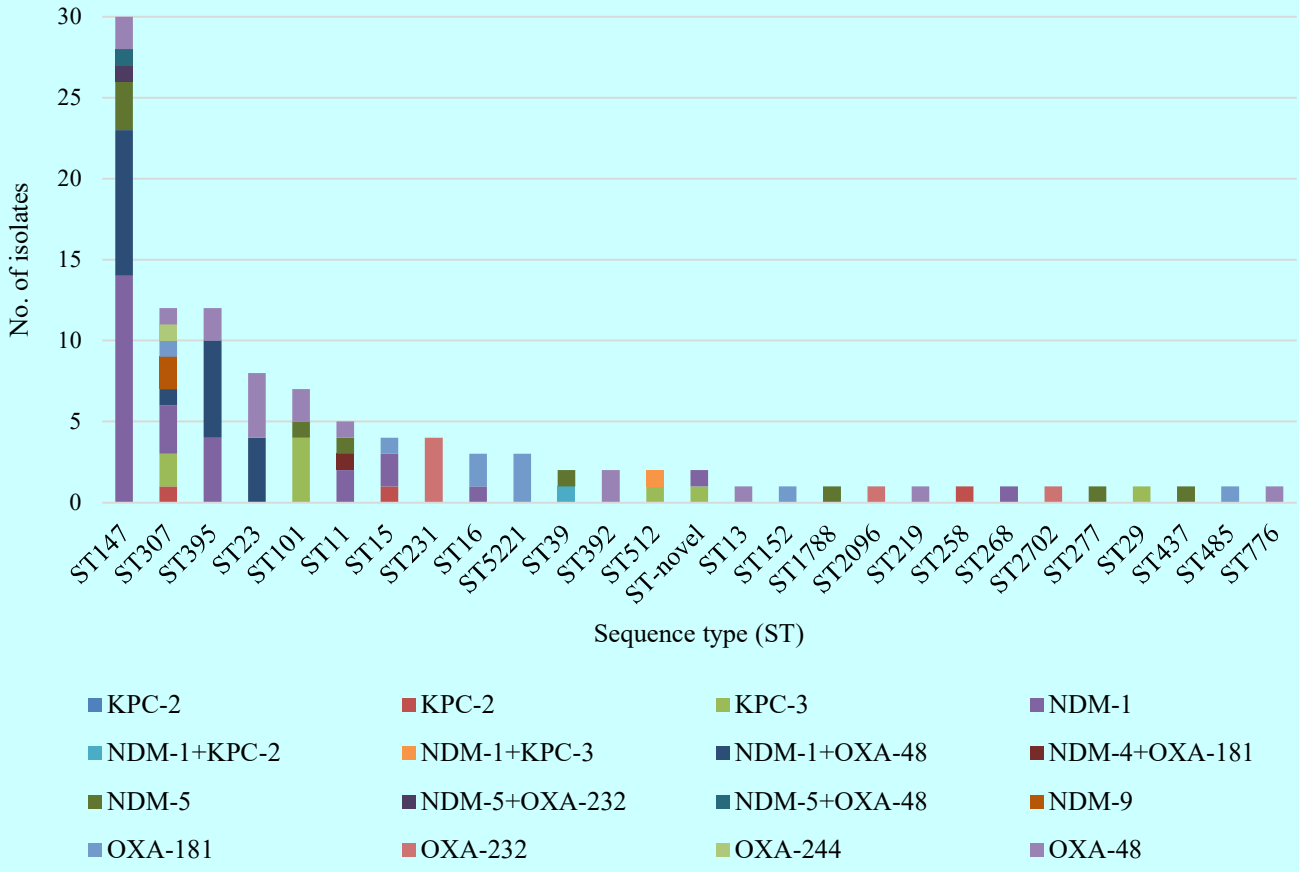


FIGURE 94. Carbapenemase variant distribution by STs among carbapenemase-producing *K. pneumoniae* identified in 2024.

No isolates were genotypically interpreted as hypervirulent *K. pneumoniae***.** ST23 with capsule type 1 (KL1) is known as a hypervirulent clone (8). We detected eight ST23 isolates in 2024, all with capsule type KL57 and associated with import from Ukraine. ST23-KL57 represents a different genetic lineage than ST23-KL1, and it is unclear whether ST23-KL57 results in a 'hypervirulent' clinical picture (10,11).

Phylogenetic analysis of carbapenemase-producing *K. pneumoniae* isolates based on core-genome MLST (Figure 95) showed 12 clusters consisting of 2-8 related isolates. Five clusters (clusters 1, 2, 5, 6, and 7) consisted exclusively of isolates associated with import. In four of these, the isolates were only associated with import from Ukraine. Six clusters (clusters 3, 4, 8, 10, 11, and 12) included isolates with both suspected import and those without suspected import or where import data were not provided. Epidemiological investigations indicated probable transmission within Norway in two of the clusters. For one cluster, no epidemiological link was found, and for the others, epidemiological data were lacking. Cluster 9, consisting of two *K. pneumoniae* ST307–NDM-9 isolates, belonged to an outbreak that began in 2023.

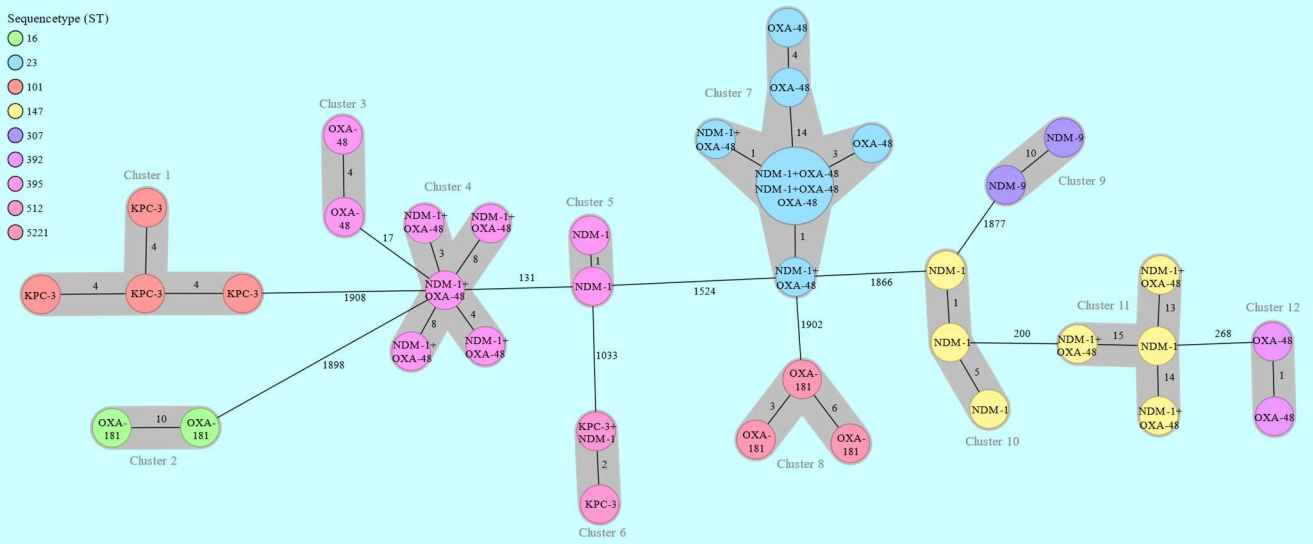


FIGURE 95. Minimum spanning network of closely related carbapenemase-producing *K. pneumoniae* identified in Norway in 2024. The analysis is based on 2,358 core genome alleles and created using SeqSphere+ software and *K. pneumoniae* NTUH-K2044 as reference genome. The isolates are represented by circles and coloured according to ST. Specific carbapenemase variants of each isolate are indicated within each circle and number of allelic differences along the connecting lines. The size of the circles is proportional to the number of isolates. Grey shading between isolates indicates close relationship (≤15 allele differences).

In 2024, 30 non-*E. coli*/*K. pneumoniae* species complex isolates were detected (Table 67), compared to 52 in 2023. The isolates were found in 28 patients, of whom 23 (82%) were associated with import from 12 different countries plus "Abroad." There is no suspicion of domestic transmission within Norway. Two carbapenemase-producing *Klebsiella ornithinolytica* (formerly *Raoultella ornithinolytica*) were detected for the first time in Norway in 2024. Both isolates carried NDM-1 and were identified at two different laboratories. One of the isolates was associated with import.

TABLE 67. ST-carbapenemase variant combinations detected in 2024 among *Enterobacterales* species other than *E. coli* and the *K. pneumoniae* species complex.

Species	ST-carbapenemase variant combination
C. freundii (n=4)	ST22-NDM-1 (n=1), ST22-NDM-7 (n=1), ST98-NDM-1 (n=1), ST1180-VIM-1 (n=1)
C. portucalensis (n=2)	ST506-NDM-1 (n=1), ST-novel-VIM-1 (n=1)
E. hormaechei (n=10)	ST50-NDM-5 (n=1), ST78-NDM-1 (n=1), ST90-OXA-48 (n=1), ST93-IMP-1 (n=1), ST144-VIM-4 (n=1), ST148-NDM-1 (n=1), ST171-NDM-1 (n=1), ST231-NDM-1 (n=2), ST419-VIM-1 (n=1)
K. aerogenes (n=2)	ST4-OXA-48 (n=1), ST4-OXA-181 (n=1)
K. michiganensis (n=2)	ST-novel-OXA-181 (n=1), ST135-NDM-1+OXA-48 (n=1)
K. oxytoca (n=1)	ST-novel-NDM-1 (n=1)
M. morganii (n=1)[1]	NDM-5 (n=1)
P. mirabilis (n=3)[1]	NDM-1 (n=2), OXA-48 (n=1)
P. stuartii (n=2)[1]	NDM-1 (n=1), NDM-5 (n=1)
K. ornithinolytica (n=2)[1]	NDM-1 (n=2)
K. planticola (n=1)[1]	VIM-1 (n=1)

[1] MLST scheme not established.

Susceptibility testing of the CPE isolates showed no significant changes in resistance patterns compared to 2023 (Figure 96). As expected, a high proportion of isolates were resistant to non-beta-lactam antibiotics such as aminoglycosides (30–57%), fluoroquinolones (78%), and trimethoprim-sulfamethoxazole (66%). The proportion resistant to colistin was 5% in 2024, down from 14% in 2023.

Resistance to newer beta-lactam/beta-lactamase inhibitor combinations remain high: ceftazidime-avibactam (54%), imipenem-relebactam (42%), and meropenem-vaborbactam (26%). The activity of these combinations depends on the inhibitor's profile and which carbapenemases they are active against (12,13). All isolates with metallo-beta-lactamases (MBLs) were resistant to ceftazidime-avibactam, while all isolates with KPC or OXA-48-like carbapenemases were susceptible. Resistance to meropenem (33%) and imipenem (34%) alone is roughly at the same level as resistance to meropenem-vaborbactam (26%) and imipenem-relebactam (42%). This is due to the relatively low proportion of CPE isolates with class A carbapenemases (e.g. KPC) in Norway. All isolates with only KPC were susceptible to meropenem-vaborbactam and imipenem-relebactam.

The activity of cefiderocol also depends on the carbapenemase variant (14); 90% of isolates with MBL (including those with both MBL and other carbapenemases) were resistant to cefiderocol, while 34% of isolates with only class A or class D carbapenemases were resistant. For cefiderocol, 37% of the isolates had a zone diameter within the Area of Technical Uncertainty (ATU) and were here interpreted as resistant. This has limited impact since the ATU (21-23 mm) mainly falls within the resistant range (R < 23 mm).

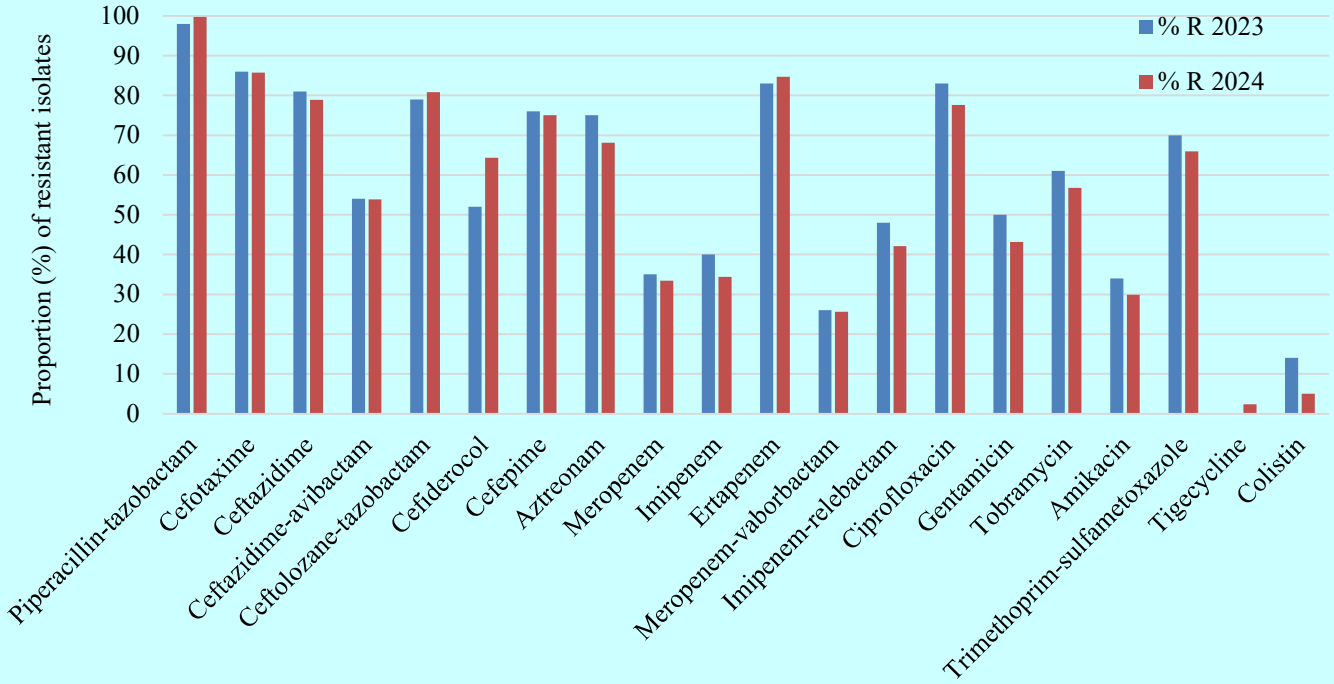


FIGURE 96. Proportion (%) of resistant isolates for CPE in 2023 and 2024. Categorisation according to the NordicAST breakpoint table v.15. Susceptibility testing was performed using broth microdilution, except for cefiderocol (disc diffusion). Results within the Area of Technical Uncertainty (ATU) for cefiderocol, piperacillin-tazobactam, and ciprofloxacin were conservatively interpreted as resistant. Imipenem and imipenem-relebactam apply to *Enterobacterales* excluding *Morganellaceae*. Colistin applies to *Enterobacterales* excluding *M. morganii*, *P. mirabilis*, and *P. stuartii* (expected resistance according to EUCAST Expected Resistant Phenotypes v.1.2). Tigecycline applies only to *E. coli*.

Carbapenemase-producing *Pseudomonas* spp.

Twenty-four patients with carbapenemase-producing *Pseudomonas* spp. were identified in 2024, compared to 27 patients in 2023 (Figure 97). The majority of cases were linked to imports (83%) from six different countries, with Ukraine accounting for 70%, a proportion similar to that in 2023. For two patients, there was no suspicion of import, and for another two, the status of import was unclear. In two patients, two different carbapenemase-producing *P. aeruginosa* strains were isolated, resulting in a total of 26 isolates overall. Nine of these were detected through screening, five from rectal swabs and four from other or unknown sample materials. The remaining isolates were from clinical samples, including one from a blood culture, one from the respiratory tract, two from urine, and 13 from other specimen types.

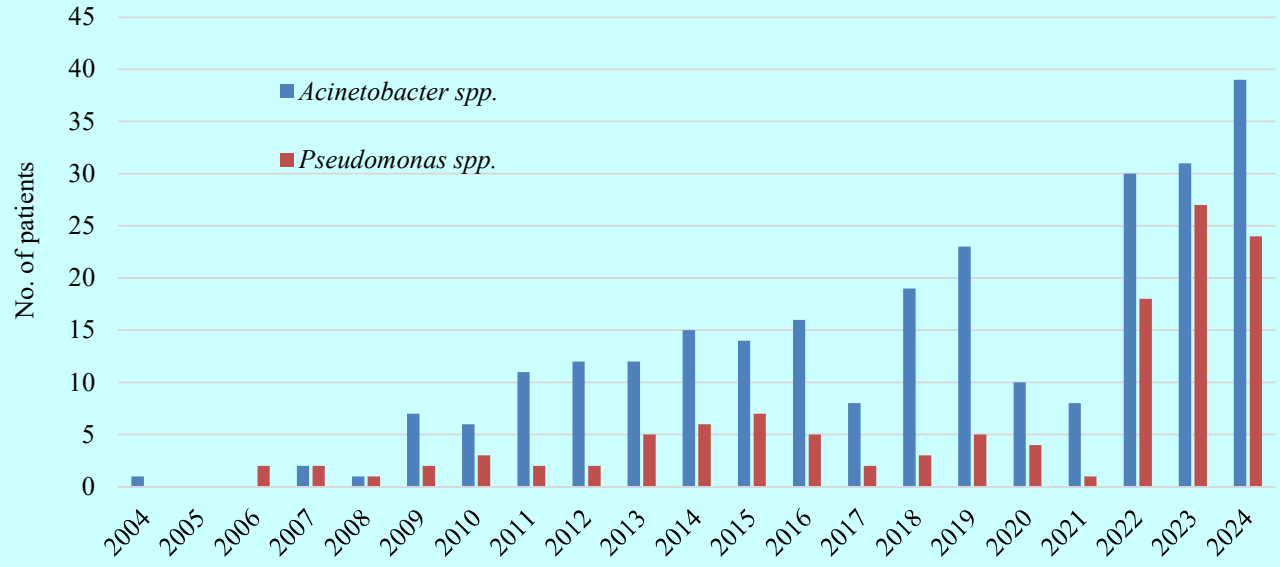


FIGURE 97. Number of patients with confirmed carbapenemase-producing *Pseudomonas* spp. and *Acinetobacter* spp. in Norway, 2004-2024.

Whole genome sequencing revealed that 25 of the isolates were *Pseudomonas aeruginosa*, while one was *Pseudomonas paraeruginosa* (ST1978; VIM-28). One of the isolates encoded two carbapenemases (ST773; NDM-1 and VIM-2). Eleven different STs of *P. aeruginosa* were detected, including one novel ST. The dominant clone was ST1047–IMP-1 (n=9) (Figure 98). The most prevalent carbapenemase variant was NDM-1, found in ten different isolates across five sequence types. As in previous years, ST1047 and ST773 were primarily associated with imports from Ukraine. Other known global clones included high-risk clones ST111 (n=1), ST235 (n=2), ST357 (n=3), and ST654 (n=1) (15).

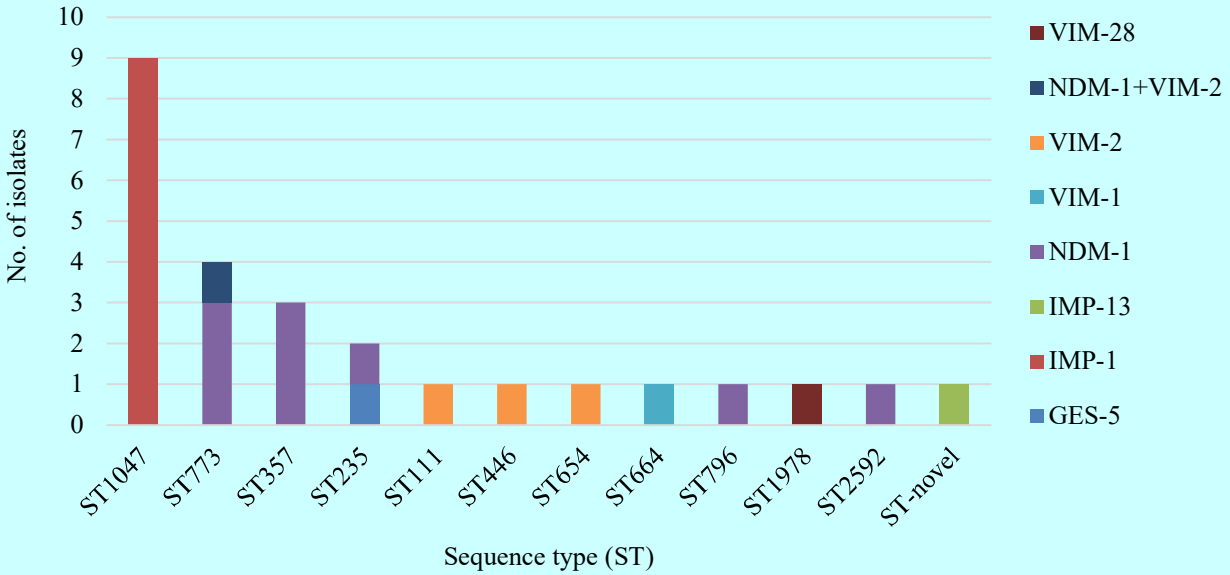


FIGURE 98. Distribution of STs and carbapenemase variants among carbapenemase-producing *Pseudomonas* spp. (n=26) isolated in Norway in 2024.

Phylogenetic analysis of the *P. aeruginosa* isolates (Figure 99) revealed a cluster of closely related ST1047 isolates (4–5 allele differences). For the first isolate in the cluster, the import status remains unknown. The subsequent isolates were identified 1, 6, and 8 months later at a different hospital and were associated with imports from Ukraine. Based on epidemiological data, it is presumed that the isolates were not linked to transmission within Norway.

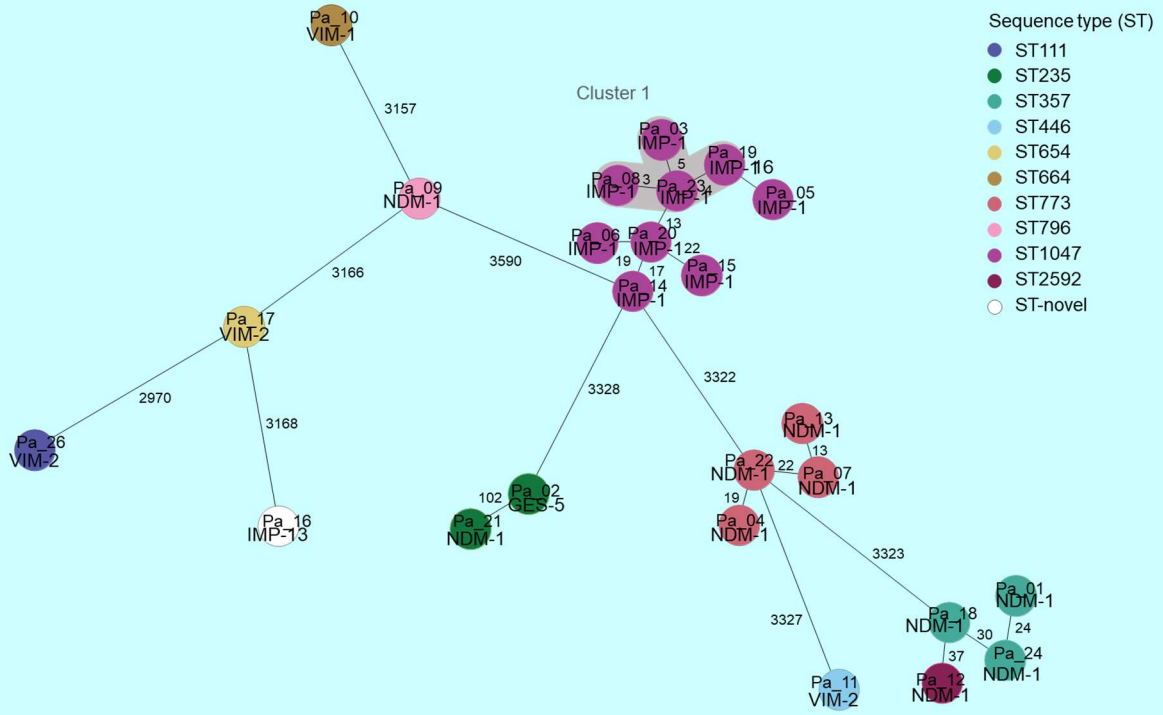


FIGURE 99. Minimum spanning tree of carbapenemase-producing *P. aeruginosa* isolated in Norway in 2024 (n=25). The tree is based on 3,867 core genome alleles and was created using SeqSphere+ software, with *P. aeruginosa* PAO1 as the reference genome. The isolates are represented by circles and are coloured according to their STs. Specific carbapenemase variants of each isolate are indicated within each circle along with the number of allelic differences shown by the connecting lines. Cluster 1, comprising closely related isolates (≤12 allele differences), is highlighted in grey.

Most isolates were resistant to meropenem (100%) and imipenem (96%), as well as to most other anti-pseudomonal agents (Table 68). The percentage of isolates resistant to aztreonam, cefiderocol, and amikacin was somewhat higher than reported for the overall period (2006-2022) (16). Among the isolates categorised as cefiderocol resistant, four out of six had a zone diameter within the ATU range (20-21 mm) and were interpreted as resistant (R < 22 mm). No colistin resistance was observed.

TABLE 68. Proportion (%) of resistance among carbapenemase-producing *Pseudomonas* spp. (n=26) in 2024[1].

Antibiotic	Resistant isolates (%)
Meropenem	100
Meropenem-vaborbactam	92
Imipenem	96
Imipenem-relebactam	100
Aztreonam	46
Ceftazidime	96
Ceftazidime-avibactam	96
Cefepime	96
Ceftolozane-tazobactam	100
Piperacillin-tazobactam	96
Cefiderocol	23
Amikacin	81
Tobramycin	96
Ciprofloxacin	96
Colistin	0

[1]Categorisation according to the NordicAST breakpoint table v.15. Susceptibility testing was performed using broth microdilution, except for cefiderocol (disc diffusion). Results within the Area of Technical Uncertainty (ATU) for cefiderocol were conservatively interpreted as resistant.

Carbapenemase-producing *Acinetobacter* spp.

In 2024, 39 patients with carbapenemase-producing *Acinetobacter* spp. were detected, compared to 31 patients in 2023 (Figure 97). Thirty-three (85%) of the cases were associated with import from 13 different countries. The proportion of imported cases in 2023 was 94%. Among the imported cases, the proportion linked to Ukraine fell from 55% in 2023 to 36% in 2024. Thirty percent of imported cases were linked to Thailand. For three patients, there was no suspicion of import, and for another three, the import status was unclear.

In four patients, two different carbapenemase-producing isolates were detected, resulting in a total of 43 isolates in 2024. One isolate was detected in a blood culture. Twenty-six (60%) of the isolates were reported as screening isolates, including 11 from rectal screening and 15 from other specimen types.

Whole genome sequencing showed that 41 isolates were *Acinetobacter baumannii*, one was *Acinetobacter seifertii*, and one was *Acinetobacter johnsonii*. As in previous years, *A. baumannii* ST2 (n=20) was the dominant clone, followed by ST19 (n=6), ST78 (n=5), and ST164 (n=4) (Table 69). All of these are known global high-risk clones (17-19). OXA-23 was the dominant carbapenemase variant, detected in a total of 30 isolates, including in combination with NDM-1/-5 in eight isolates (Table 69). OXA-72 was detected in ten isolates, and NDM-1 in three isolates.

TABLE 69. Species/ST–carbapenemase variant combinations detected among *Acinetobacter* spp. (n=43) in 2024.

ST	Carbapenemase variant
ST2 (n=20)	OXA-23 (n=12), NDM-5+OXA-23 (n=6), NDM-5+OXA-23-lik (n=1), OXA-72 (n=1)
ST19 (n=6)	OXA-23 (n=5), OXA-72 (n=1)
ST78 (n=5)	OXA-72 (n=5)
ST164 (n=4)	OXA-23 (n=2), NDM-1+OXA-23 (n=1), OXA-72 (n=1)
ST1 (n=1)	OXA-72 (n=1)
ST15 (n=1)	NDM-1 (n=1)
ST158 (n=1)	OXA-23 (n=1)
ST29 (n=1)	NDM-1 (n=1)
ST-novel (n=2)	OXA-23 (n=2)
A. seifertii (n=1)[1]	OXA-72 (n=1)
A. johnsonii (n=1)[1]	NDM-1 (n=1)

[1]MLST scheme not established.

Phylogenetic analysis of the *A. baumannii* isolates revealed five clusters of closely related isolates (≤9 allele differences) (Figure 100). Three of the clusters (clusters 1, 2, and 5) consisted exclusively of isolates associated with import; cluster 1: two ST164–OXA-23 isolates detected at two different laboratories, associated with import from Thailand, cluster 2: three ST19–OXA-23 isolates detected at two laboratories, associated with import from Ukraine and cluster 5: two ST2–NDM-5+OXA-23

isolates detected at two laboratories, associated with import from Thailand. For these clusters, it is considered that the isolates were acquired outside Norway and are not linked to domestic transmission. Cluster 3 consisted of two ST2–OXA-23 isolates with the same sample date and from the same laboratory. Import information was missing for both isolates, and a possible epidemiological link is unknown. Cluster 4 consisted of two ST2–OXA-23 isolates from the same laboratory, detected 117 days apart. The first isolate was associated with import from Greece, and epidemiological investigation confirmed transmission within Norway.

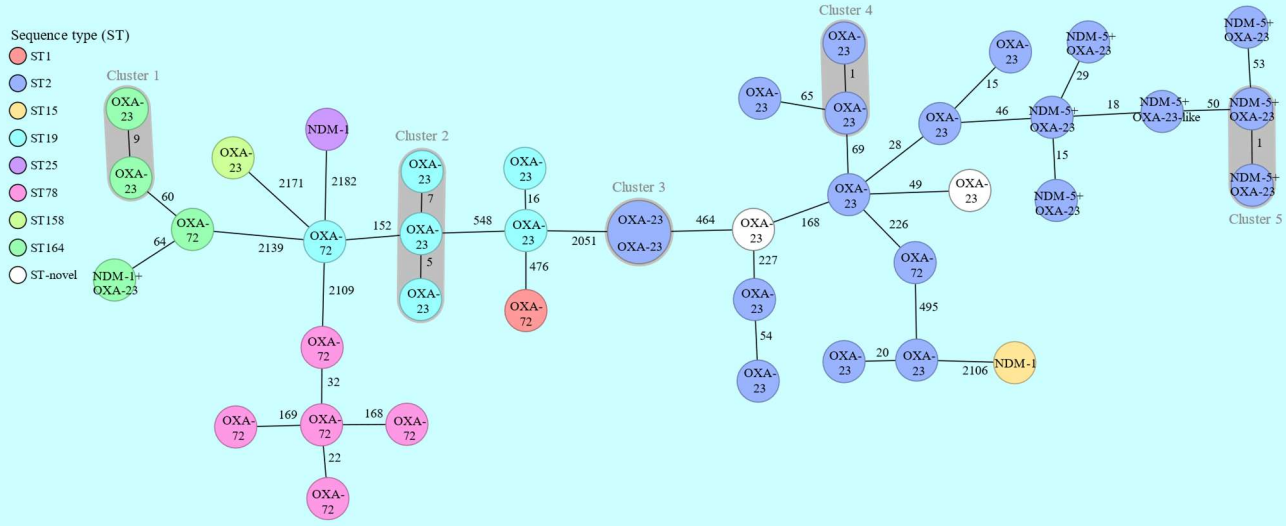


FIGURE 100. Minimum spanning network of carbapenemase-producing *A. baumannii* identified in Norway in 2024. The analysis is based on 2,390 core genome alleles and created using SeqShere+ software and *A. baumannii* ACICU as the reference genome. The isolates are represented by circles and colour-coded according to ST. Specific carbapenemase variants of each isolate are indicated within each circle and number of allelic differences along the connecting lines. Circle sizes represent the number of isolates. Shading between isolates indicates close relationship (≤9 allele differences).

All isolates were resistant to meropenem and imipenem, and co-resistance was prevalent (Table 70). The high proportion of resistance to aminoglycosides can be explained by the fact that 51% of isolates were positive for the 16S rRNA methylase gene *armA*, particularly associated with ST2 and ST78. The two ST2-OXA-23 isolates in cluster 4 were pan-resistant, including resistance to carbapenems, ciprofloxacin, aminoglycosides, and colistin. These isolates were also resistant to, among others, ampicillin-sulbactam and minocycline. The isolates tested intermediate (I) using CLSI breakpoints and interpreted as resistant based on tentative EUCAST breakpoints for sulbactam-durlobactam, a new beta-lactam/beta-lactamase inhibitor combination approved in the USA. Sulbactam-durlobactam has been developed specifically for OXA-carbapenemase-producing *A. baumannii* (20).

TABLE 70. Proportion (%) of resistance among carbapenemase-producing *Acinetobacter* spp. (n=43) in 2024[1].

Antibiotic	Resistant isolates (%)
Meropenem	100
Imipenem	100
Ciprofloxacin	98
Amikacin	84
Gentamicin	74
Tobramycin	65
Trimethoprim-sulfamethoxazole	77
Colistin	5

[1]Categorisation according to the NordicAST breakpoint table v.15. Susceptibility testing was performed using broth microdilution.

Conclusion

The occurrence of carbapenemase-producing Gram-negative bacteria continues to rise in Norway, although the increase from 2023 to 2024 (11%) was lower than the increase from 2022 to 2023 (48%). This corresponds to an increase in incidence from 3.7 in 2022 to 5.9 in 2024 per 100,000 person-years. Although most cases in 2024 were associated with import (72%), this proportion decreased from 80% in 2023. However, for 16% data on import is missing.

Whole genome sequencing showed a continued increase in the genetic diversity of isolates and carbapenemase genes, but with a dominance of known global high-risk clones associated with an increased potential for further spread. Phylogenetic analyses revealed a few clusters of related isolates and single cases of domestic spread. Worryingly, the increased proportion of global high-risk clones of *E. coli* (e.g. ST38 and ST69) not associated with import may indicate ongoing community spread.

The high level of co-resistance, including to the new beta-lactam/beta-lactamase inhibitor combinations and cefiderocol, illustrates the significant treatment challenges posed by infections with carbapenemase-producing Gram-negative bacteria.

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Haemophilus influenzae in blood cultures and cerebrospinal fluids

TABLE 71. *Haemophilus influenzae* in blood cultures and cerebrospinal fluids in 2024 (n=93). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Ampicillin*	≤ 1	> 1	83.9	-	16.1
Amoxicillin-clavulanic acid**	≤ 2	> 2	95.7	-	4.3
Cefuroxime**	≤ 1	> 2	85.0	3.2	11.8
Cefotaxime	≤ 0.125	> 0.125	97.8	-	2.2
Ceftriaxone	≤ 0.125	> 0.125	100.0	-	0.0
Meropenem***	≤ 2	> 2	100.0	-	0.0
Ciprofloxacin	≤ 0.03	> 0.03	98.9	-	1.1
Chloramphenicol	≤ 2	> 2	100.0	-	0.0
Tetracycline	≤ 2	> 2	100.0	-	0.0
Trimethoprim-sulfamethoxazole****	≤ 0.5	> 1	89.2	0.0	10.8
Beta-lactamase	Negative	Positive	88.2	-	11.8

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. *Breakpoints for indications other than endocarditis and meningitis. **Breakpoints for intravenous administration. ***Breakpoints for indications other than meningitis. ****Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only.

TABLE 72. *Haemophilus influenzae* in blood cultures and cerebrospinal fluids in 2024 (n=93). Distribution (%) of MICs (mg/L).

	≤0.004	0.008	0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	≥ 128
Ampicillin*					1.1	10.8	41.9	23.7	6.5	5.4		2.2	2.2	1.1		5.4
Amoxi-clav**				2.2	5.4	8.6	39.8	28.0	7.5	4.3	4.3					
Cefuroxime**							3.2	20.4	61.3	3.2	5.4	2.2	2.2	2.2		
Cefotaxime		7.5	31.2	44.1	9.7	5.4	2.2									
Ceftriaxone			91.4	5.4	2.2	1.1										
Meropenem***			2.2	18.3	47.3	25.8	5.4	1.1								
Ciprofloxacin	20.5	54.8	23.7											1.1		
Chloramp.			1.1			1.1	1.1	35.5	60.2	1.1						
Tetracycline						1.1	11.8	82.8	4.3							
TMS****	1.1	7.5	38.7	26.9	4.3	4.3	2.2	4.3		1.1	1.1	2.2	2.2	4.3		

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. *Breakpoints for indications other than endocarditis and meningitis. **Breakpoints for intravenous administration. ***Breakpoints for indications other than meningitis. ****Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only.

RESULTS AND COMMENTS

Systemic *H. influenzae* isolates were first included in the NORM surveillance programme in 2013. Resistance data are provided on an annual basis by the Reference Laboratory at the Norwegian Institute of Public Health. The number of isolates in 2024 (n=93) was a slight decline from 2022 (n=130) and 2023 (n=121). Five isolates were retrieved from cerebrospinal fluids, and one of these patients also had a blood culture isolate. Apart from this, all isolates represented unique patients (Tables 71-72). The breakpoint for resistance to ciprofloxacin was reduced from R > 0.06 mg/L to R > 0.03 mg/L in 2024. All other EUCAST/NordicAST breakpoints remained unchanged.

The rate of ampicillin resistance decreased from 21.5% in 2023 to 16.1% in 2024, but this is in line with 14.6% in 2022. Beta-lactamase production was detected in 11/93 isolates (11.8%). This is a decrease from 2023 (15.7%), but at the same level as in 2021 (12.7%) and 2022 (10.8%). Different substrates have been suggested for screening of beta-lactam resistance in *H. influenzae*. The penicillin G 1U disk (PCG1) successfully identified all ampicillin (15/15) and cefuroxime (11/11) resistant isolates. Fifteen out of 82 (18.3%) beta-lactamase negative isolates were resistant to PCG1, thus indicating chromosomal alterations in penicillin-binding proteins (PBPs). In addition, one PCG1 resistant and beta-lactamase positive isolate was resistant to amoxicillin-clavulanic acid with the 2-1 µg disk, suggesting concomitant beta-lactamase production and chromosomal resistance. In total, PBP-mediated resistance was detected in 16/93 (17.2%) isolates.

Two isolates were resistant to cefotaxime (MIC 0.25 mg/L), and they were both also resistant to amoxicillin-clavulanic acid and cefuroxime. However, all isolates remained fully susceptible to ceftriaxone and meropenem. As observed in previous surveys of systemic *H. influenzae* isolates, resistance rates to ciprofloxacin (1.1%), tetracycline (0.0%) and chloramphenicol (0.0%) were very low. The 10.8% resistance rate to trimethoprim-sulfamethoxazole was at the same level as in 2022 (13.1%) and 2023 (9.9%).

Neisseria meningitidis in blood cultures and cerebrospinal fluids

TABLE 73. *Neisseria meningitidis* in blood cultures and cerebrospinal fluids in 2024 (n=12). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	Susceptible	Resistant	Susceptible	Intermediately susceptible	Resistant
Penicillin G*	≤ 0.25	> 0.25	100.0	-	0.0
Ceftriaxone	≤ 0.125	> 0.125	100.0	-	0.0
Ciprofloxacin	≤ 0.016	> 0.016	100.0	-	0.0
Chloramphenicol	≤ 2	> 2	100.0	-	0.0
Rifampicin	≤ 0.25	> 0.25	100.0	-	0.0
Tetracycline	≤ 2	> 2	100.0	-	0.0

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. *Penicillin G=Benzylpenicillin.

TABLE 74. *Neisseria meningitidis* in blood cultures and cerebrospinal fluids in 2024 (n=12). Distribution (n) of MICs (mg/L).*

	≤0.004	0.008	0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	≥ 128
Penicillin G*					4	6	2									
Ceftriaxone			12													
Ciprofloxacin	12															
Chloramph.								2	9	1						
Rifampicin	4	4	1	1	2											
Tetracycline						4	1	7								
Azithromycin						2		2	6	2						

Shaded areas in each row indicate susceptibility with standard exposure (light), susceptibility with increased exposure (medium) and resistance (dark). Non-shaded cells represent MIC values that are not covered by the standard test method. *Penicillin G=Benzylpenicillin.

RESULTS AND COMMENTS

N. meningitidis from blood cultures and cerebrospinal fluids were first included in NORM in 2013. The Reference Laboratory at the Norwegian Institute of Public Health provides data for *N. meningitidis* on an annual basis. The EUCAST/NordicAST breakpoint remained unchanged from the previous year. Results are presented in Tables 73-74.

Twelve isolates were received from the 14 reported cases of systemic infections caused by *N. meningitidis* in 2024. Six isolates were recovered from cerebrospinal fluids (CSF) and six from blood cultures. There were no known associations between the cases. The number of isolates is a slight increase from four, five and nine isolates in the pandemic years 2020-2022, respectively, but at the same level as in 2023 (n=13). The isolates belonged to serogroups B (n=6) and Y (n=6). The six serogroup B isolates belonged to five different sequence types (STs) while the six serogroup Y isolates were all ST-23.

No resistance according to clinical breakpoints was detected for any of the antimicrobials tested. EUCAST/ NordicAST has not established breakpoints for azithromycin, but the MIC distribution does not indicate the presence of acquired macrolide resistance (Table 74).

Neisseria gonorrhoeae

TABLE 75. *Neisseria gonorrhoeae* from all specimen types in 2024 (n=1,471). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Penicillin G*	≤ 0.06	> 1	4.8	74.0	21.2
Ceftriaxone	≤ 0.125	> 0.125	99.7	-	0.3
Cefixime	≤ 0.125	> 0.125	99.6	-	0.4
Ciprofloxacin	≤ 0.03	> 0.06	42.5	0.5	57.0
Tetracycline	≤ 0.5	> 0.5	60.1	-	39.9
Spectinomycin	≤ 64	> 64	100.0	-	0.0
Beta-lactamase	Negative	Positive	79.5	-	20.5

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. *Penicillin G=Benzylpenicillin.

TABLE 76. *Neisseria gonorrhoeae* from all specimen types in 2024 (n=1,471) Distribution (%) of MICs (mg/L).

	≤0.004	0.008	0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	≥ 128
Penicillin G*	0.2	0.3	1.4	0.7	2.1	19.6	31.0	17.4	6.0	8.6	5.2	2.8	1.8	2.9		
Ceftriaxone	35.0	10.2	51.7	2.3	0.3	0.2	0.1	0.2								
Cefixime			73.9	15.8	9.2	0.6	0.1	0.1	0.1	0.1						
Ciprofloxacin	34.3	6.9	1.0	0.3	0.5	0.3	0.4	1.1	9.0	22.8	15.8	5.1	0.8	1.6		
Tetracycline			0.2	0.2	1.2	6.5	21.8	30.2	15.3	1.6	1.3	6.5	10.9	3.6	0.5	0.2
Spectinomycin					0.1			0.1	0.1	0.1	0.9	14.2	57.2	27.1	0.3	
Azithromycin			0.1	2.4	8.0	13.9	21.3	14.3	18.9	16.5	1.8	0.7	0.3	0.3	0.2	1.2

Shaded areas in each row indicate susceptibility with standard exposure (light), susceptibility with increased exposure (medium) and resistance (dark). Non-shaded cells represent MIC values that are not covered by the standard test method. *Penicillin G=Benzylpenicillin.

RESULTS AND COMMENTS

Neisseria gonorrhoeae was surveyed in NORM in 2003 and 2010, and then yearly since 2013 by the Reference Laboratory at the Norwegian Institute of Public Health in collaboration with Oslo University Hospital. In 2024, a total of 1,471 gonococcal isolates were available for further analyses. This is a dramatic increase from earlier years (n=220 in 2021, n=827 in 2022), but at the same level as in 2023 (n=1,500). The proportion of cases with positive culture among all reported cases (including PCR-only positives) was 45.0% (1,417/3,150) in 2024 compared to 44.5% (827/1,857) in 2022 and 50.3% (1,500/2,985) in 2023. This may suggest a true epidemiological change in the population over the last years.

From some patients several isolates were collected from different clinical sites at the same point of time. Thus, the Reference Laboratory in 2024 received isolates from 1,390 unique episodes of infection. The isolates in 2024 were recovered from urethra (n=603), anus (n=310), throat (n=193), cervix uteri/vagina (n=172), eye (n=6) or "others/unknown" (n=187). A total of 1,084 (73.7%) isolates were from men and 387 (26.3%) from women. This corresponds well with the figures from 2022 (75.9% men and 24.1% women) and earlier years, but differs from 2023 when the predominance of men (62.1%) over women (37.9%) was less marked. From MSIS it has been reported that gonococcal infections often are acquired abroad, but with increasing secondary transmission in sexual networks within Norway. The most frequent sequence type (ST), ST-1580, decreased from 28% in 2023 to 16% in 2024, while ST-9362 increased from 8% to 13%.

The results from susceptibility testing are presented in Tables 75-76. A majority of isolates were either susceptible only to increased exposure (74.0%) or resistant (21.2%) to penicillin G. The corresponding figures for 2023 were 80.1% and 15.7%, respectively. A total of 302 isolates (20.6%) produced beta-lactamase, which is an increase from 2022 (16.4%) and 2023 (13.7%). Most beta-lactamase positive isolates (252/302, 83.4%) were also resistant to ciprofloxacin. Forty-two isolates (3.6%) were resistant and 1,084 (90.5%) were only susceptible to increased exposure to penicillin G in spite of being beta-lactamase negative. This illustrates the complex mechanisms for penicillin resistance in this species.

Six isolates were resistant to cefixime (MIC 0.25-2 mg/L) and four of them were also resistant to ceftriaxone (MIC 0.25-0.5 mg/L). These four were all ST-16406, the most extensively resistant sequence type of *N. gonorrhoeae* to date. The first case was reported in 2022, with subsequent cases in Cambodia, Australia, the United Kingdom, Austria, France, and now Norway. The oral cephalosporin cefixime is no longer recommended for empirical treatment in Europe. Ceftriaxone resistant isolates from Norway have previously been linked to treatment failure. The results confirm the emergence of cephalosporin resistant gonococci in Norway. The standard treatment for gonorrhoeae is now ceftriaxone alone. Azithromycin was previously used in combination with ceftriaxone, but 20.9% of the isolates displayed azithromycin MIC values above the EUCAST screening breakpoint for acquired resistance of 1 mg/L. The corresponding figure for 2023 was 24.4%. The prevalence of ciprofloxacin resistance persisted at a high level (57.0%) in 2024. Ciprofloxacin is consequently not a viable alterna-tive except in cases where susceptibility has been docu-mented. All strains were susceptible to spectinomycin.

Staphylococcus aureus in blood cultures

TABLE 77. *Staphylococcus aureus* blood culture isolates in 2024 (n=1,614). Sampling, laboratory methods, and data handling are described in Appendix 5. Distributions of zone diameters are available at www.antibiotikaresistens.no.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Erythromycin	≤ 1	> 1	93.2	-	6.8
Clindamycin	≤ 0.25	> 0.25	98.8	-	1.2
Fusidic acid	≤ 1	> 1	96.5	-	3.5
Ciprofloxacin	≤ 0.001	> 2	0.0	98.3	1.7
Gentamicin	≤ 2	> 2	99.2	-	0.8
Linezolid	≤ 4	> 4	100.0	-	0.0
Rifampicin	≤ 0.06	> 0.06	99.2	-	0.8
Tetracycline	≤ 1	> 1	97.5	-	2.5
Tigecycline	≤ 0.5	> 0.5	99.2	-	0.8
Trimethoprim-sulfamethoxazole*	≤ 2	> 4	99.8	0.1	0.1
Beta-lactamase	Negative	Positive	37.1	-	62.9
Cefoxitin screen	≥ 22	< 22	98.9	-	1.1
MRSA** (*mecA*)	Negative	Positive	98.9	-	1.1

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. *Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only. **MRSA=Methicillin resistant *Staphylococcus aureus*.

RESULTS AND COMMENTS

S. aureus blood culture isolates have been included in the NORM surveillance programme since it was initiated in 2000. For the 2024 data, the most recent EUCAST/ NordicAST breakpoint protocol was applied. The breakpoints for resistance to erythromycin and tetracycline have both been reduced from R > 2 mg/L to R > 1 mg/L, thus eliminating the I category of susceptible to increased exposure. For historical comparison, the present R categories correspond to the combined I+R categories in previous years. The breakpoint for resistance to ciprofloxacin was increased from R > 1 mg/L to R > 2 mg/L from 2024 onwards.

Eighteen methicillin resistant *S. aureus* (MRSA) isolates were detected in the NORM surveillance system in 2024, corresponding to a prevalence of 1.1% (Table 77). This is a slight decrease from 1.8% in 2023, but at the same level as in 2022 (1.0%). The isolates originated from 11 different hospitals, and there was no significant clustering among institutions. Laboratory screening for MRSA in NORM is performed using cefoxitin disks and there was full concordance between cefoxitin and *mecA* PCR results. Some MRSA isolates were concomitantly resistant to erythromycin (8/18), ciprofloxacin (7/18), gentamicin (5/18), tetracycline (4/18), fusidic acid (3/18), clindamycin (1/18) and/or rifampicin (1/18). All MRSA isolates were susceptible to tigecycline, rifampicin, linezolid and trimethoprim-sulfamethoxazole. The results from susceptibility testing of all Norwegian MRSA isolates are presented in Table 80 on page 131. The NORM findings are slightly lower than the 49/2,313 *S. aureus* blood culture isolates (2.1%) reported from the databases of the participating laboratories. One of the eight *S. aureus* isolates recovered from cerebrospinal fluids were methicillin resistant, thus bringing the total number of systemic MRSA isolates to 50/2,321 (2.2%). This is an increase from 1.8% in 2023.

One hundred nine *S. aureus* isolates (6.8%) were resistant to erythromycin. This is at the same level as in 2023 (6.8%). The macrolide resistance phenotypes of erythromycin resistant isolates were determined by the double disk diffusion (DDD) test. Seven isolates (6.5%) were constitutively MLS_B resistant, 82 (75.2%) were inducibly MLS_B resistant, and 20 (18.3%) displayed efflux mediated M-type resistance. These figures represent 0.4%, 5.1% and 1.2% of all *S. aureus* isolates from blood cultures, respectively. The distribution of MLS_B resistance phenotypes was essentially the same as in 2023.

The prevalence of resistance to fusidic acid (3.5%) was at the same level as 4.4% in 2022 and 3.7% in 2023. The 1.7% prevalence of ciprofloxacin resistance is a further decline from 4.9% in 2022 and 3.1% in 2023, but this may in part be explained by an adjustment of the resistance breakpoint (see above). It should be noted that the wild type population of *S. aureus* is defined as susceptible only to increased exposure to this agent. There were no significant changes for gentamicin, rifampicin, tigecycline or trimethoprim-sulfamethoxazole. All isolates were fully susceptible to linezolid. The general test panel for *S. aureus* did not include vancomycin in 2024.

Figure 101 shows the prevalence of resistance to various antimicrobials. A total of 62.9% of the isolates were beta-lactamase positive, which is a significant decrease from 68.5% in 2022 and 68.0% in 2023. Resistance to ciprofloxacin and tetracycline was more common among beta-lactamase positive isolates (2.4% and 3.3%, respectively) than in beta-lactamase negative ones (0.7% and 1.3%, respectively). There were no significant differences in the prevalence of resistance to other non-beta-lactam antibiotics between beta-lactamase positive and negative isolates.

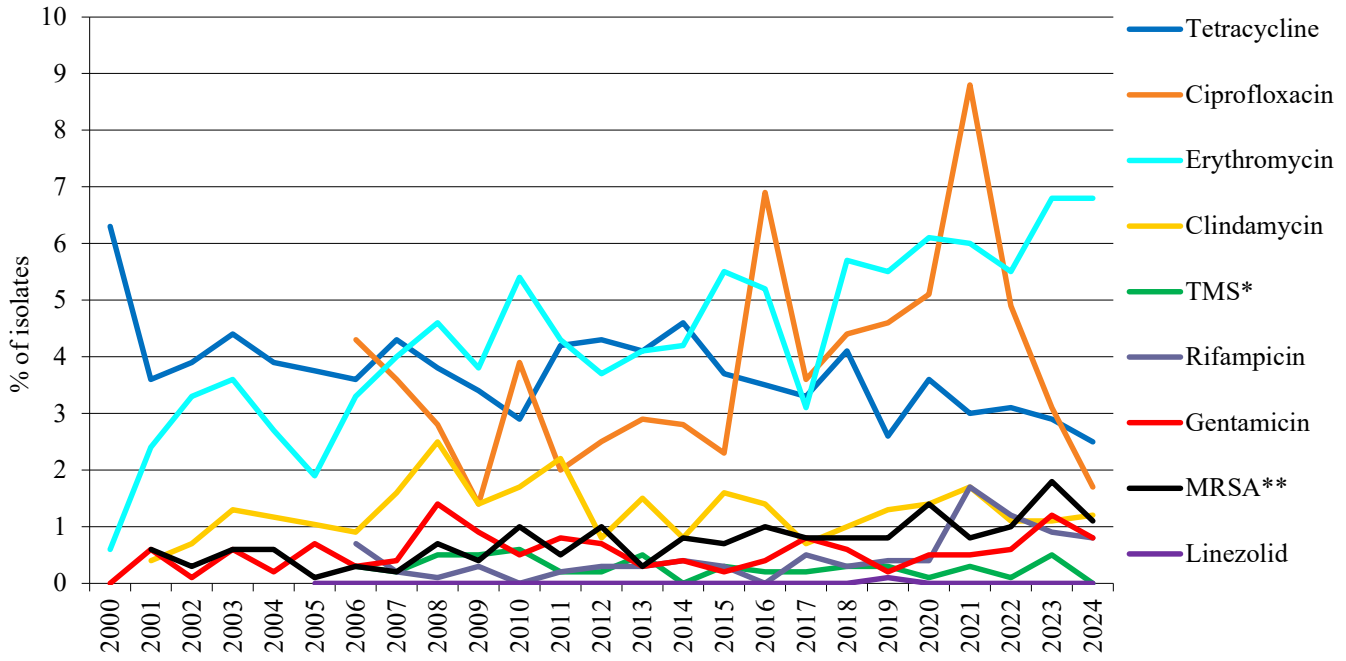

FIGURE 101. Prevalences of antimicrobial resistance among *Staphylococcus aureus* blood culture isolates 2000-2024. Doxycycline was replaced by tetracycline in 2006. Isolates are categorised according to the breakpoints at the time of analysis. *TMS=Trimethoprim-sulfamethoxazole. **MRSA=Methicillin resistant *Staphylococcus aureus*.

Staphylococcus aureus in wound specimens

TABLE 78. *Staphylococcus aureus* isolates in wound specimens in 2023 (n=841). Sampling, laboratory methods, and data handling are described in Appendix 5. Distributions of zone diameters are available at www.antibiotikaresistens.no.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Erythromycin	≤ 1	> 1	91.7	-	8.3
Clindamycin	≤ 0.25	> 0.25	98.6	-	1.4
Fusidic acid	≤ 1	> 1	95.6	-	4.4
Ciprofloxacin	≤ 0.001	> 2	0.0	98.2	1.8
Gentamicin	≤ 2	> 2	99.5	-	0.5
Linezolid	≤ 4	> 4	100.0	-	0.0
Rifampicin	≤ 0.06	> 0.06	99.8	-	0.2
Tetracycline	≤ 1	> 1	96.9	-	3.1
Tigecycline	≤ 0.5	> 0.5	99.9	-	0.1
Trimethoprim-sulfamethoxazole*	≤ 2	> 4	99.8	0.0	0.2
Beta-lactamase	Negative	Positive	27.5	-	72.5
Cefoxitin screen	≥ 22	< 22	98.1	-	1.9
MRSA** (*mecA*)	Negative	Positive	98.1	-	1.9

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. *Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only. **MRSA=Methicillin resistant *Staphylococcus aureus*.

RESULTS AND COMMENTS

S. aureus from wound specimens were screened for methicillin resistance by the cefoxitin disk method in the same way as blood culture isolates. Sixteen out of 841 (1.9%) isolates were confirmed as MRSA by *mecA* PCR. The prevalence was at the same level as in 2022 (1.6%) and 2023 (1.3%). The MRSA isolates originated from patients visiting general practitioners (n=12), hospital wards (n=3) and a nursing home (n=1) in different parts of the country. Many MRSA isolates (8/16) were co-resistant to erythromycin (6/16), clindamycin (3/16), tetracycline (3/16), fusidic acid (2/16), gentamicin (2/16) and/or ciprofloxacin (1/16) in different combinations. All MRSA isolates were susceptible to tigecycline, rifampicin, trimethoprim-sulfamethoxazole and linezolid. No isolates were reported with zone diameters below the cefoxitin screening breakpoint without being confirmed as MRSA by *mecA* PCR. This confirms high specificity of the cefoxitin screen as well as a low prevalence of *mecC* MRSA (see page 131).

The prevalence of resistance to fusidic acid in *S. aureus* wound isolates decreased from 5.9% in 2023 to 4.4% in 2024 (Table 78 and Figure 102). The prevalence of this phenotype has thus stabilised after the previous epidemic which peaked at 25.0% in 2004. The prevalence of resistance to fusidic acid is still lower in blood culture isolates (3.5%) than in wound isolates (4.4%). For other antimicrobial agents such as gentamicin, rifampicin, trimethoprim-sulfamethoxazole and tetracycline there were only minor changes from 2023-2024, and the prevalence of resistance was in general similar for blood culture isolates and isolates from wound specimens. All isolates were phenotypically susceptible to linezolid.

Seventy (8.3%) isolates were resistant to erythromycin. This is a further increase from 5.8% in 2022 and 7.2% in 2023, but at the same level as 8.5% in 2021. The rates include the former I category due to a change of the breakpoint for resistance (see above). All erythromycin resistant isolates were further examined to determine the macrolide resistance phenotype. The majority were either inducibly (52/70; 74% of erythromycin resistant isolates) or constitutively (7/70; 10% of erythromycin resistant isolates) resistant to clindamycin, thus representing the $iMLS_B$ and $cMLS_B$ phenotypes, respectively. A minor proportion of the isolates displayed low-level resistance to erythromycin only (11/70; 16% of erythromycin resistant isolates) which is compatible with efflux mediated M-type resistance. The findings are in accordance with the results from previous years.

A total of 72.5% of the isolates were beta-lactamase positive in 2024 compared to 69.8% in 2022 and 69.0% in 2023. There were no significant differences in non-beta-lactam resistance rates between beta-lactamase negative and positive isolates.

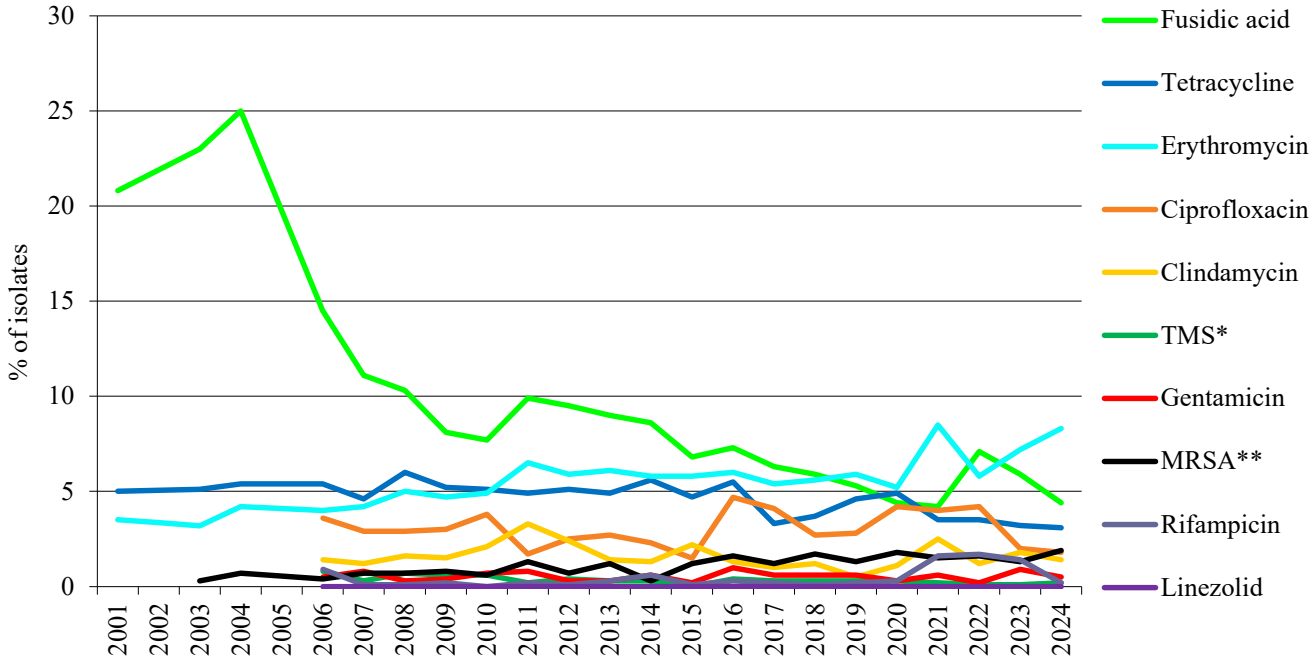

FIGURE 102. Prevalence of antimicrobial resistance among *Staphylococcus aureus* wound isolates 2001-2024. Doxycycline was replaced by tetracycline in 2006. Isolates are categorised according to the breakpoints at the time of analysis. *TMS=Trimethoprim-sulfamethoxazole. **MRSA=Methicillin resistant *Staphylococcus aureus*.

Methicillin resistant *Staphylococcus aureus* (MRSA) infections in Norway 2024

The number of persons reported with MRSA to the Norwegian Surveillance System for Communicable Diseases (MSIS) in Norway was 2,942 in 2024, a 15% increase compared to 2023 (2,548 persons). A total of 1,222 (42%) persons were reported with MRSA infection and 1,689 (57%) persons with colonisation (1% unknown). The incidence rate in the form of all MRSA cases per 100,000 person-years was 53, and 22 and 31 for infections and colonisations, respectively (Figure 103). The incidence of MRSA was relatively stable for a period before the corona pandemic, during which it decreased, probably as a result of strict infection prevention and control measures to curb the spread of Covid-19. In 2024 the incidence rate was higher than it was in the peak year of 2017. The reasons for the increase are unclear and will be followed up.

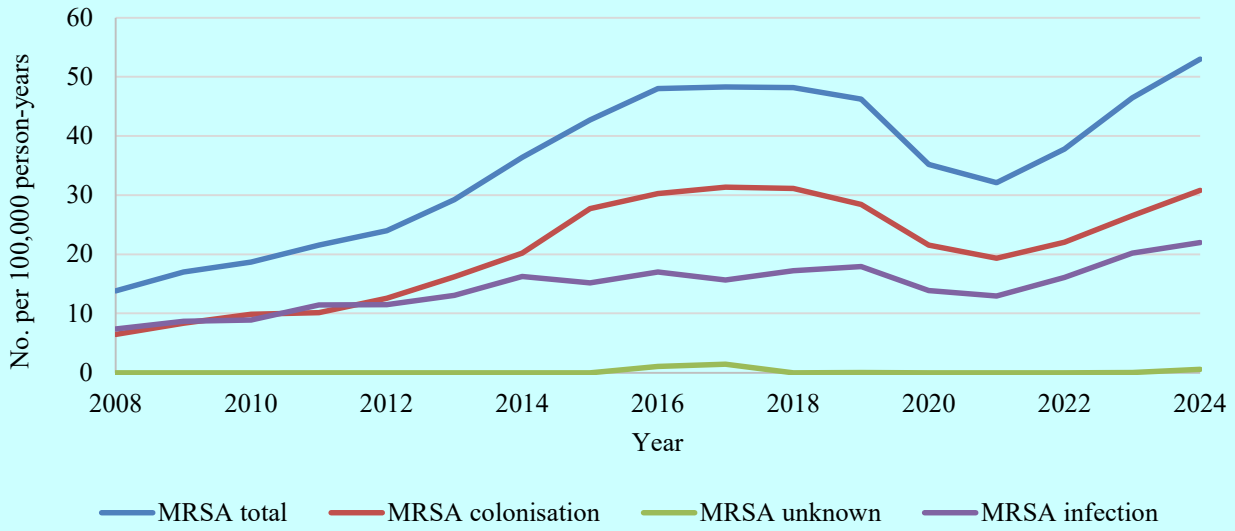

FIGURE 103. Number of persons notified with MRSA per 100,000 person-years in Norway 2008-2024, in total, and by infection and colonisation.

In 2024, 578 (20%) persons were reported to have acquired MRSA abroad, while 755 (26%) persons were reported to have acquired MRSA in Norway. Of note, however, is that information regarding a possible place of infection is lacking in 55% of all reported cases (Figure 104). Persons notified with genetically different MRSA during a year may be included more than once in the categorisation of place of acquisition.

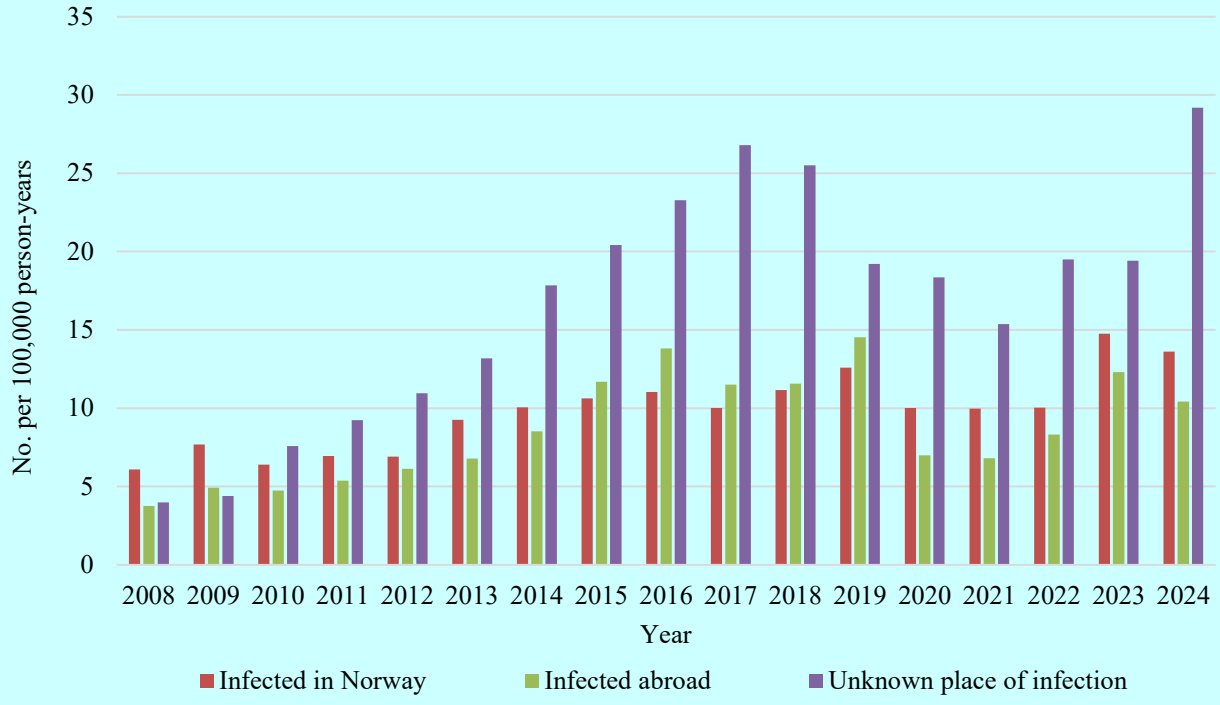

FIGURE 104. Number of persons notified with MRSA per 100,000 person-years in Norway 2008-2024, by assumed place of infection.

The Norwegian Reference Laboratory for Methicillin resistant *Staphylococcus aureus* (MRSA) at St. Olavs Hospital, Trondheim University Hospital, received 3,375 MRSA isolates from 2,931 persons in 2024, including both MRSA carriage and infections. Staphylococcal protein A (*spa*)-typing was the main genotyping method used on all isolates, while whole genome sequencing was performed on selected isolates. In 2024, 463 different *spa*-types were identified, of which 382 (82.5%) were reported less than five times. This high proportion of rarely observed *spa*-types reflects the considerable genotypic diversity of MRSA seen in Norway and other Nordic countries. Table 79 shows the 10 most common MRSA *spa*-types in Norway in 2024 with associated clonal complexes (CC).

Livestock-associated MRSA (LA-MRSA), defined as PVL-negative MRSA of clonal complex (CC) 398, still has a low incidence with 25 human isolates identified in 2024, the same number as in 2023. PVL-positive MRSA CC398 is increasing, with 67 human isolates in 2024 versus 46 in 2023. Two isolates were *mecC*-positive. The laboratory received 41 *mecA*-positive *Staphylococcus argenteus* (MRSArg) (39 in 2023) and 54 *mecA*-positive *Staphylococcus lugdunensis* (34 in 2023).

TABLE 79. The ten most common MRSA *spa*-types in Norway in 2024.

spa-type	CC	No. of isolates	% of isolates
t304	CC6	353	10.8 %
t127	CC1	217	6.6 %
t355	CC152	185	5.7 %
t223	CC22	149	4.6 %
t008	CC8	140	4.3 %
t002	CC5	122	3.7 %
t3841	CC672	118	3.6 %
t1476	CC8	84	2.6 %
t021	CC30	78	2.4 %
t005	CC22	72	2.2 %

Antimicrobial susceptibility testing was performed with the EUCAST disc diffusion method by the referring laboratories and interpreted according to the 2024 NordicAST breakpoints (Table 80). The highest proportion of co-resistance was found for erythromycin (40.3%), followed by tetracycline (29.2%), ciprofloxacin (27.6%) and clindamycin (22.8%). More moderate levels of resistance were observed for fusidic acid (17.6%) and gentamicin (17.5%). Low prevalence of resistance was found for trimethoprim-sulfamethoxazole (2.3%), rifampicin (1.5%) and mupirocin (0.2%). No isolates showed decreased susceptibility to linezolid or vancomycin. Ceftaroline was excluded from the table because of very limited data.

TABLE 80. Antibiotic susceptibility results from all human MRSA and MRSArg in 2024.

	Breakpoints (mg/L)		Proportion of isolates (%)			Isolates (n)
	S	R	S	I	R	
Erytromycin	≤ 1	> 1	59.7	-	40.3	3,417
Clindamycin*	≤ 0.25	> 0.25	77.2	-	22.8	3,414
Fusidic acid	≤ 1	> 1	82.4	-	17.6	3,413
TMS**	≤ 2	> 4	96.4	1.4	2.3	3,405
Tetracycline	≤ 1	> 1	70.8	-	29.2	3,412
Gentamicin	≤ 2	> 2	82.5	-	17.5	3,415
Ciprofloxacin	≤ 0.001	> 2	-	72.4	27.6	3,358
Mupirocin	≤ 1	> 1	99.8	-	0.2	3,371
Rifamipicin	≤ 0.06	> 0.06	98.5	-	1.5	3,415
Linezolid	≤ 4	> 4	100.0	-	-	3,416
Vancomycin	≤ 2	> 2	100.0	-	-	3,410

TMS=Trimethoprim-sulfamethoxazole. *Total clindamycin resistance including inducible resistant MRSA cases (16.1%). **Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only. S=Susceptible with standard exposure. I=Susceptible with increased exposure. R=Resistant.

The prevalence of resistance for erythromycin, tetracycline and ciprofloxacin has increased the last few years, but this trend seemed to stabilise in 2024 (Figure 105). The fusidic acid and gentamicin resistance rates continued to increase slightly. The changes in susceptibility profiles may be attributable to shifts in the epidemiological distribution of the most prevalent *spa*-types, but some technical difficulties are also relevant, especially for ciprofloxacin and clindamycin. For ciprofloxacin, there were many isolates with zone diameter close to the breakpoint, which may have contributed to different interpretation of the result by different laboratories. For clindamycin, the variation in susceptibility results over the years has not necessarily been caused by actual changing resistance rates, but also by differences in interpretation or lack of reporting of inducible clindamycin resistance.

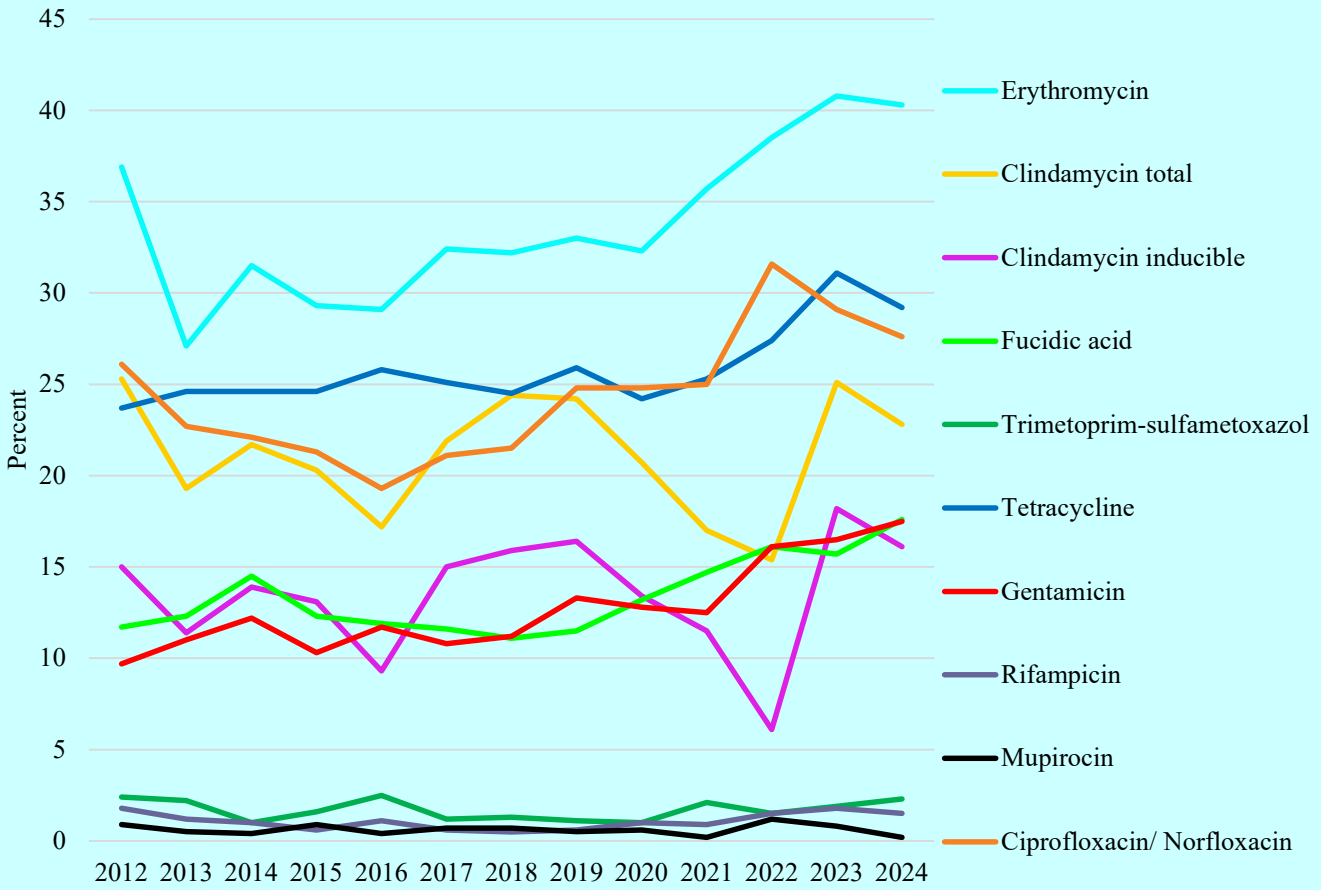

FIGURE 105. Prevalence of antimicrobial resistance in all MRSA and MRSArg isolates from 2012-2024. Isolates are categorised according to the breakpoints at the time of testing. Results for cefoxitin are not shown.

Figure 106 shows the most common combinations of resistance to the tested antibiotics for MRSA isolates in 2024. Cefoxitin resistance alone was by far the most common profile for Norwegian MRSA isolates (30.8%), followed by resistance to cefoxitin, erythromycin, tetracycline and clindamycin (6.9%) and the combination of resistance to cefoxitin, erythromycin and tetracycline (6.3%).

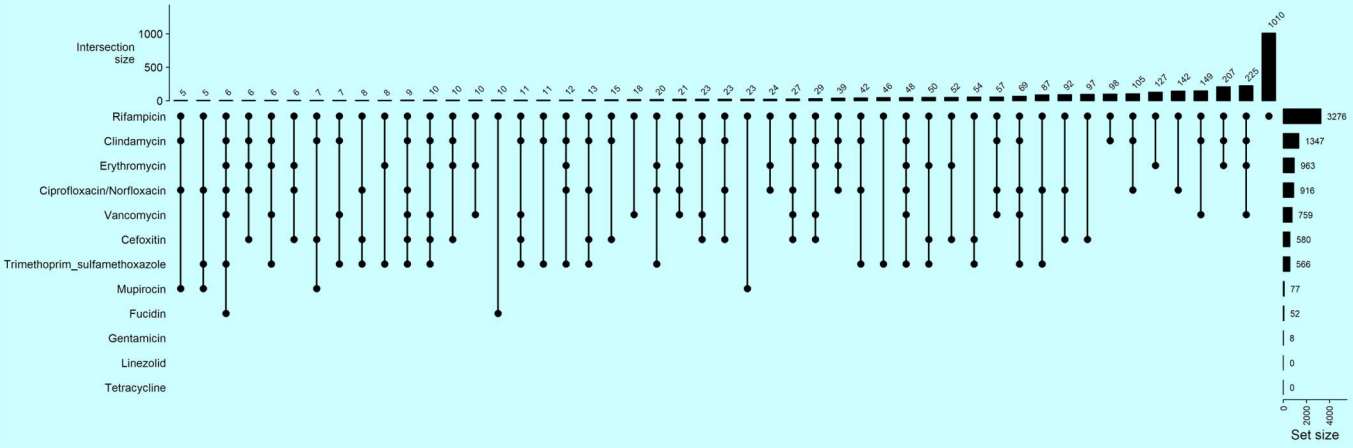

FIGURE 106. The most common combinations of antimicrobial resistance in Norwegian MRSA isolates in 2024. Clindamycin resistance is given as total resistance including inducible resistant isolates.

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Outbreaks of resistant microbes in Norway 2024

In Norway, it is mandatory to report outbreaks of infectious diseases to the Norwegian Institute of Public Health (NIPH). According to the Norwegian Surveillance System for Communicable Diseases (MSIS) regulation (1), the following outbreaks must be reported: 1) outbreaks of diseases that are notifiable to MSIS, 2) suspected food- and waterborne outbreaks, 3) outbreaks of particularly severe diseases (e.g. those with high mortality, complication rates, or serious clinical manifestations) 4) particularly extensive outbreaks and 5) outbreaks in healthcare institutions.

The aims of outbreak reporting include alerting and sharing information with relevant authorities and asking for assistance if needed. Reported local outbreaks can be seen in connection and reveal larger national outbreaks. The reporting contributes to an overview of the epidemiological situation at both local and national levels. Additionally, the data is a basis for infection control recommendations, outbreak management strategies, and national and international reporting.

Outbreaks are reported by municipal medical officers, hospitals, and food safety authorities through a web-based system called Vesuv. Data collected in Vesuv include information on the time and place of the outbreak, number of cases, main symptoms, suspected or confirmed pathogen, transmission route, and more. No individual patient data are registered in Vesuv. Although mandatory, some underreporting is suspected. This may be because outbreaks are not detected or because detected outbreaks are not reported. Because outbreaks should be reported as soon as they are suspected, some data in Vesuv – such as the number of cases – may be incomplete or not updated as the situation evolves.

Definition of an outbreak

An outbreak can be defined as two or more cases of the same infectious disease where a common source is suspected, or a number of cases that exceeds the expected level within a given area and time (2).

Reported outbreaks in 2024

The following data are obtained from Vesuv and the annual report of infectious disease outbreaks (3). In 2024, a total of 389 outbreaks were reported to Vesuv. Of those, 81% were reported from healthcare institutions. Of the 316 nosocomial outbreaks, 39 were caused by antimicrobial resistant microbes, with a total of 168 cases. One community outbreak of antimicrobial resistant microbes was reported in 2024, caused by methicillin resistant *Staphylococcus aureus* (MRSA), with four cases. Table 81 shows the outbreaks of resistant microbes in healthcare institutions from 2020 to 2024. Table 82 shows the outbreaks in 2024 by type of healthcare institution.

TABLE 81. Outbreaks of antimicrobial resistant microbes in healthcare institutions, Vesuv 2020-2024.

Pathogen	2024		2020	2021	2022	2023
	Outbreaks (n)	Cases (n)	Outbreaks (n)			
Methicillin resistant *Staphylococcus aureus* (MRSA)	12	40	8	3	2	5
Vancomycin resistant enterococci (VRE)	10	81	5		1	5
Carbapenemase-producing *Enterobacterales*	9	20			2	8
Carbapenemase-producing *Acinetobacter baumannii*	3	6				
E. coli (ESBL-producing)	2	6	2			2
Linezolid resistant enterococci (LRE)	2	10		1	1	2
Klebsiella spp. (ESBL-producing)	1	5			1	1
Total	39	168	15	4	7	23

TABLE 82. Outbreaks of antimicrobial resistant microbes by type of healthcare institution, Vesuv 2024.

Pathogen	Long-term care facility	Hospital
Methicillin resistant *Staphylococcus aureus* (MRSA)	4	8
Vancomycin resistant enterococci (VRE)	5	5
Carbapenemase-producing *Enterobacterales*	1	8
Carbapenemase-producing *Acinetobacter baumannii*		3
E. coli (ESBL-producing)	1	1
Linezolid resistant enterococci (LRE)		2
Klebsiella spp. (ESBL-producing)	1	
Total	12	27

There were 2-3 cases in each of the 12 carbapenamase-producing organism (CPO) outbreaks. Of the nine outbreaks of carbapenemase-producing *Enterobacterales*, eight were caused by *Klebsiella pneumoniae* and one by *E. coli*. The rise in CPO outbreaks in recent years is partly due to an increase in hospital-reported cases, but also driven by a routine implemented in 2023, whereby NIPH is notified by the National Centre for Detection of Antimicrobial Resistance about genetically linked CPO clusters. NIPH subsequently reports these outbreaks in Vesuv.

Seven of the ten vancomycin resistant enterococci (VRE) outbreaks are linked to a larger, ongoing outbreak involving several hospitals and long-term care facilities. This outbreak was detected in 2023 and continues into 2025. Additionally, two outbreaks of linezolid resistant enterococci (LRE) were reported from two different hospitals. Outbreaks of methicillin resistant *Staphylococcus aureus* (MRSA) are affecting both hospitals and long-term care facilities, and the number of reported outbreaks was higher in 2024 than in the previous years. The number of cases in the outbreaks varied between 2 and 7. No outbreak of *Candida auris* has ever been reported in Norway.

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Enterococcus spp. in blood cultures

TABLE 83. *Enterococcus* spp. blood culture isolates in 2024 (n=735), except for imipenem (n=503) where 232 enterococcal isolates not identified as *E. faecalis* are excluded due to lack of breakpoints. Sampling, laboratory methods, and data handling are described in Appendix 5. Distributions of zone diameters are available at www.antibiotikaresistens.no.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Ampicillin	≤ 4	> 4	78.8	-	21.2
Imipenem	≤ 0.001	> 4	0.0	99.2	0.8
Gentamicin HLR*	≤ 128	> 128	84.1	-	15.9
Linezolid	≤ 4	> 4	99.7	-	0.3
Tigecycline	≤ 0.5	> 0.5	98.6	-	1.4
Vancomycin	≤ 4	> 4	98.1	-	1.9
Vancomycin (*vanA* or *vanB*)	Negative	Positive	99.7	-	0.3

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. *HLR=High Level Resistance.

TABLE 84. *Enterococcus faecalis* blood culture isolates in 2024 (n=503). Sampling, laboratory methods, and data handling are described in Appendix 5. Distributions of zone diameters are available at www.antibiotikaresistens.no.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Ampicillin	≤ 4	> 4	100.0	-	0.0
Imipenem	≤ 0.001	> 4	0.0	99.2	0.8
Gentamicin HLR*	≤ 128	> 128	93.8	-	6.2
Linezolid	≤ 4	> 4	100.0	-	0.0
Tigecycline	≤ 0.5	> 0.5	98.2	-	1.8
Vancomycin	≤ 4	> 4	100.0	-	0.0
Vancomycin (*vanA* or *vanB*)	Negative	Positive	100.0	-	0.0

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. *HLR=High Level Resistance.

TABLE 85. *Enterococcus faecium* blood culture isolates in 2024 (n=196). Sampling, laboratory methods, and data handling are described in Appendix 5. Distributions of zone diameters are available at www.antibiotikaresistens.no.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Ampicillin	≤ 4	> 4	23.0	-	77.0
Gentamicin HLR*	≤ 128	> 128	56.6	-	43.4
Linezolid	≤ 4	> 4	99.0	-	1.0
Tigecycline	≤ 0.5	> 0.5	99.5	-	0.5
Vancomycin	≤ 4	> 4	99.0	-	1.0
Vancomycin (*vanA* or *vanB*)	Negative	Positive	99.0	-	1.0

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. *HLR=High Level Resistance.

RESULTS AND COMMENTS

As in previous years, enterococci were analysed both as a genus and separately for *E. faecalis* and *E. faecium*. The results for each species are microbiologically more valid as resistance rates differ significantly between *E. faecalis* and *E. faecium*. However, overall rates of resistance are of interest when formulating empirical treatment strategies because they include the probability of systemic infections with each enterococcal species. The overall results for enterococci are presented in Table 83. The surveillance in NORM 2024 included 503 (68.4) *E. faecalis* isolates (70.6% in 2022), 196 (26.7%) *E. faecium* isolates (26.0% in 2022), and 36 (4.9%) unspeciated or belonging to other species (3.3% in 2022). The ratio of *E. faecalis* to *E. faecium* isolates has declined in many countries, but has in Norway remained stable around 2.5 over the last four years (2.6 in 2024). The panel of antimicrobial agents examined was unchanged from 2023-2024, but the EUCAST/ NordicAST breakpoints for imipenem are now only valid for *E. faecalis*.

E. faecalis was universally susceptible to ampicillin (Table 84). The prevalence of resistance to ampicillin in *E. faecium* was 77.0% in 2024 compared to 76.5% in 2023 (Table 85). The results for imipenem closely mirrored those of ampicillin, but this agent should be restricted to *E. faecalis* infections and the wild type is only susceptible to increased exposure. The prevalence of high-level gentamicin resistance (HLGR) in *E. faecalis* was 6.2%, which is at the same level as 6.9% in 2022 and 6.4% in 2023 (Figure 107). The prevalence of HLGR in *E. faecium* decreased from 50.7% in 2023 to 43.4% in 2024. Practically all HLGR *E. faecium* isolates (84/85) were also resistant to ampicillin and imipenem. Conversely, 84/151 (55.6%) ampicillin resistant *E. faecium* displayed HLGR. High-level gentamicin resistance in enterococci is of great concern as it abolishes the bactericidal synergy between amino-glycosides and beta-lactams often used for treatment of severe enterococcal infections.

Transferrable vancomycin resistance has not yet become endemically established in clinical enterococcal isolates in Norway, but recent outbreaks have occurred in different parts of the country. Two *E. faecium* blood culture isolates (1.0%) were reported as vancomycin resistant in NORM in 2024 and both were confirmed by PCR to harbour transferrable vancomycin resistance (1 *vanA* and 1 *vanB*). Two other *E. faecium* isolates (1.0%) were phenotypically resistant to linezolid, and relevant genetic features were detected in both (*poxtA* and a chromosomal G2576T mutation, respectively).

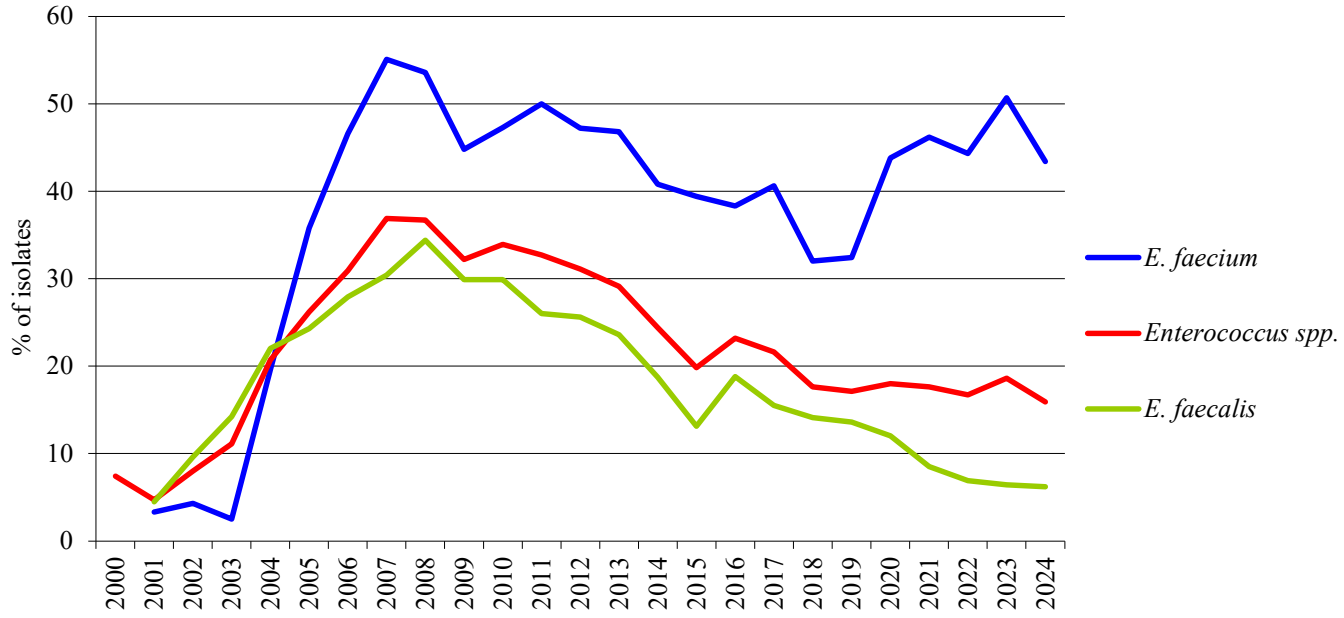

FIGURE 107. Prevalence of high-level resistance to gentamicin in blood culture isolates of *Enterococcus faecalis*, *E. faecium* and all enterococci combined during 2000-2024. The breakpoint was decreased from R ≥ 1,024 mg/L to R > 128 mg/L in 2004.

Vancomycin resistant enterococci and linezolid resistant enterococci in Norway 2024

Vancomycin resistant enterococci

Vancomycin resistance in enterococci is due to changes in the peptide sidechain that prevent vancomycin from inhibiting crosslinking in the peptidoglycan cell wall (1). So far 10 gene clusters known to encode vancomycin resistance (*vanA*, *vanB*, *vanC*, *vanD*, *vanE*, *vanG*, *vanL*, *vanM, vanN* and *vanP*) have been reported in enterococci, including the intrinsic *vanC* operon in *Enterococcus casseliflavus* and *Enterococcus gallinarum.* The other gene clusters are mostly associated with mobile genetic elements in *Enterococcus faecium* and/or *Enterococcus faecalis* and disseminated by horizontal gene transfer involving plasmids and integrative conjugative elements (2).

A worrying increase in invasive vancomycin resistant *E. faecium* has been reported in Europe from 2016-2020 (3). In Norway, the incidence rate of VRE infection/colonisation has increased the last years from 0.6 per 100,000 person-years in 2021 to 4.4 in 2024, but the number of invasive VRE infections is still low. In 2024, 239 persons with VRE (including linezolid resistant VRE (LVRE)) were registered in the Norwegian Surveillance System for Communicable Diseases (MSIS), a 169% increase compared to 2023. This increase can largely be attributed to one large outbreak (see below). The total number of VRE isolates is larger than the number of persons with VRE as four persons had two different VRE isolates. The overview of the molecular epidemiology of VRE in Norway in 2024 is not complete but the Norwegian Centre for Detection of Antimicrobial Resistance (K-res) has received isolates and/or whole genome sequence (WGS) data on the majority (225/243; 93%) of the VRE from 2024 including twelve LVRE.

Among the 225 WGS VRE isolates from 2024, we mainly identified *E. faecium* with *vanA* (n=190) or *vanB* (n=20), but also *vanA* (n=4) or *vanB* (n=4) *E. faecalis* as well as *vanA E. avium* (n=4), *vanA E. raffinosus* (n=2) and *E. gallinarum* (n=1) with both *vanA* and intrinsic *vanC* (Figure 108). Global prevalence of vancomycin resistance is also dominant in *E. faecium*, and *vanA* is more frequent than *vanB* (2).

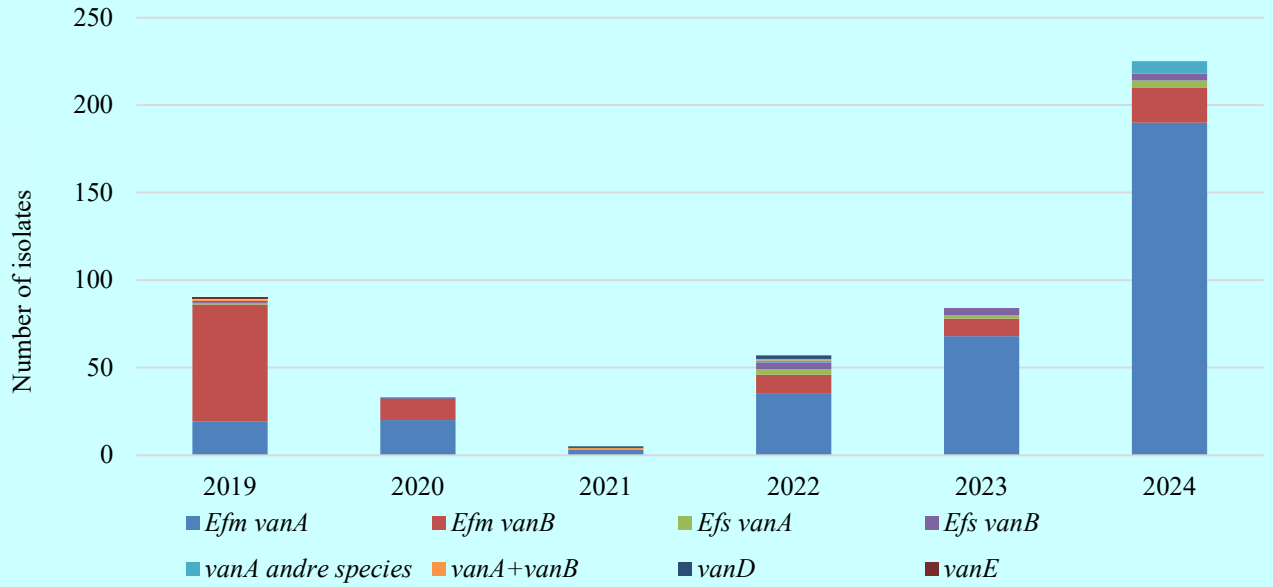

FIGURE 108. Species and genotype distribution of Norwegian VRE isolates that K-res has WGS data on for 2019-2024, including LVRE. *Efm = E. faecium*, *Efs = E. faecalis.*

Seventeen different sequence types (STs) of *E. faecium* were registered in 2024 (Figure 109). The majority (n=201/210; 96%) belong to known pandemic hospital adapted STs (ST17, ST18, ST78, ST80, ST117, ST203, ST787, ST792, ST1299, ST1421 and ST1478). All *E. faecalis* VRE were ST6 (n=8) (Figure 110) which is often linked to clinical isolates and hospitals (4).

In 2024, the majority of the WGS VRE (n=198/225; 88%) were obtained as screening samples collected during the management of hospital- and nursing home-associated outbreaks. Thirteen clusters with two to 124 isolates of ST17, ST80 and ST117 *E. faecium* (Figure 109) and one cluster with three ST6 isolates of *E. faecalis* (Figure 110) were identified. Nine of the clusters contained isolates with epidemiological connection and were considered outbreaks: *E. faecium vanA* ST117 cluster 1 (n=121), *vanB* ST117 cluster 1 (n=3), *vanA* ST80 cluster 2 (n=13), *vanB* ST117 cluster 3 (n=8), *vanA* ST80 cluster 4 (n=3), *vanA* ST80 cluster 5 (n=3), *vanB* ST117 cluster 8 (n=2), *vanA* ST80 cluster 9 (n=2) and *vanA+poxtA* ST80 cluster 13 (n=2) in Figure 109 as well as *E. faecalis vanB* ST6 cluster 1 (n=3) in Figure 110. Seven of these clusters were connected to hospitals in the South-Eastern health region, while the *vanB E. faecium* cluster 8 (n=2) and the *vanB E. faecalis* ST6 cluster (also detected in 2023) contained isolates from the Western health region and both the South-Eastern and the Western, respectively. *E. faecium* cluster 1 belongs to the same cluster that was associated with import mainly from Ukraine in 2022. Four of the *E. faecium* clusters contained 2-3 isolates that were not closely related in time and/or place and/or the isolates were associated with import and thus not considered outbreaks. Hospital associated clones of *E. faecium* can typically survive for a long time in the hospital environment which can make it difficult to identify true epidemiological links. K-res has used a three-month sliding window for genomic outbreak analyses of *E. faecium,* which is supported by studies from the Public Health Laboratory in Victoria, Melbourne, Australia (5).

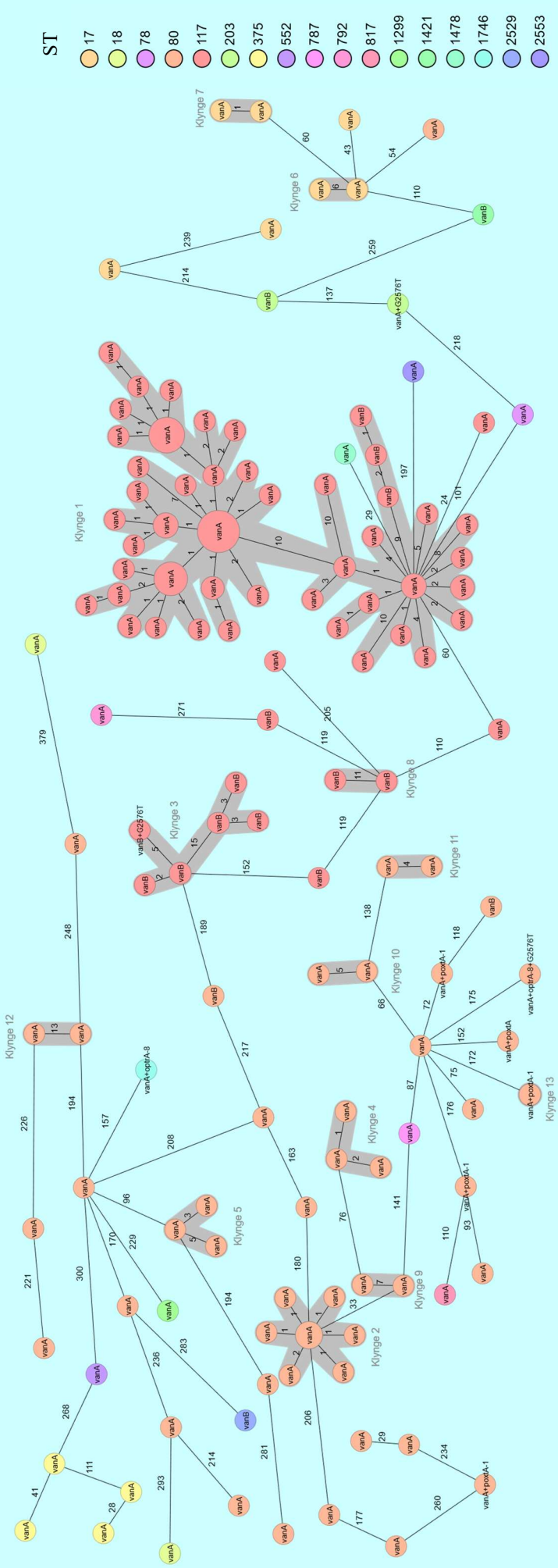

FIGURE 109. Minimum spanning network built from core genome allelic profile of 210 Norwegian VRE *E. faecium* 2024 isolates using Ridom-SeqSphere+ software with integrated core genome (cg) MLST scheme with *E. faecium* Aus0004 as reference strain. The isolates are colour coded according to sequence type (ST). VRE and LRE mechanisms are indicated in the circles. Isolates with zero allelic differences end up in the same circle. The number of allelic differences between the isolates is indicated on the lines between the circles. Clusters (≤20 allelic differences) are highlighted with grey markings.

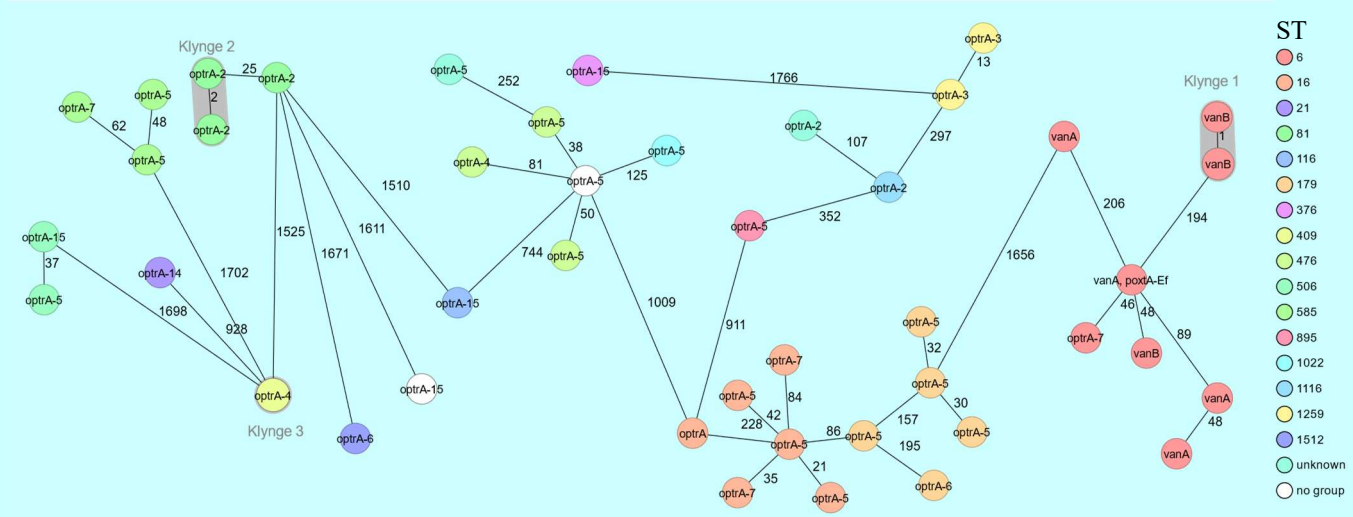

FIGURE 110. Minimum spanning network built from core genome allelic profile of 47 Norwegian *E. faecalis* isolates (VRE (n=7), LVRE (n=1) and LRE (n=39)) from 2024 using Ridom-SeqSphere+ software with integrated cgMLST scheme with *E. faecalis* OG1RF as reference strain. The isolates are colour coded according to ST. VRE and LRE genotypes are indicated in the circle, and number of allelic differences between the isolates is indicated on the lines between the circles. Isolates with zero allelic differences end up in the same circle. Clusters (≤7 allelic differences) are highlighted with grey marking.

Conclusion

In 2024, 239 persons with VRE (including 12 LVRE) were reported to MSIS, a 169% increase from 2023. There has been a continual increase in annual incidence rate of VRE from 0.6 per 100,000 person-years in 2021 to 4.4 in 2024. In this report, we present WGS data for 225 VRE from 2024, dominated by *E. faecium* (n=210) with *vanA* (n=190) or *vanB* (n=20). The majority of the VRE *E. faecium* (96%) belonged to widespread hospital adapted clones reported worldwide. The VRE are mainly from screening samples (88%) and linked to clusters of variable sizes in the South-Eastern health region. Nine outbreaks were registered, five of which were caused by two to 121 *vanA E. faecium* (ST80 and ST117), two by *vanB E. faecium* (ST117), one by *vanA+poxtA E. faecium* (ST80) and one by *vanB E. faecalis* (ST6). Thus, the majority of VRE (63%) were related to domestic spread and in particular a large outbreak of *vanA E. faecium* ST117 in the South-Eastern health region. Spread of *vanB E. faecalis* ST6 from the South-Eastern to the Western health region was suspected in one case.

Linezolid resistant enterococci

Linezolid binds to the ribosome and inhibits bacterial protein synthesis. Acquired resistance to linezolid may be due to structural changes in the ribosome based on mutations in the ribosomal RNA and/or ribosomal proteins or ribosomal protection proteins encoded by *optrA* and *poxtA/poxtA-Ef* inhibiting binding of linezolid. The *optrA* and *poxtA/poxtA-Ef* genes can be localised on mobile genetic elements (6-8). Mutation-based resistance is associated with treatment with oxazolidinones. The most common chromosomal mutation that causes linezolid resistance is the G2576T mutation in the 23S rDNA. Most species have more than one copy of the 23S rDNA in their genome and the resistance level correlates with the number of mutated copies (9). In the NORM 2022 and 2023 reports 0.5% of the invasive *Enterococcus* isolates were categorised as linezolid resistant, contrasting 0% in previous years. Globally there is also a small increase of reported LRE. In 2024, 64 persons with LRE (including LVRE) were detected in Norway representing an annual incidence rate of 1.1 per 100,000 person-years. This is comparable to 2023 (Figure 111). Approximately half of the LRE (n=34/64; 53%) in 2024 were clinical isolates. The majority (n=40/64; 63%) were *E. faecalis*.

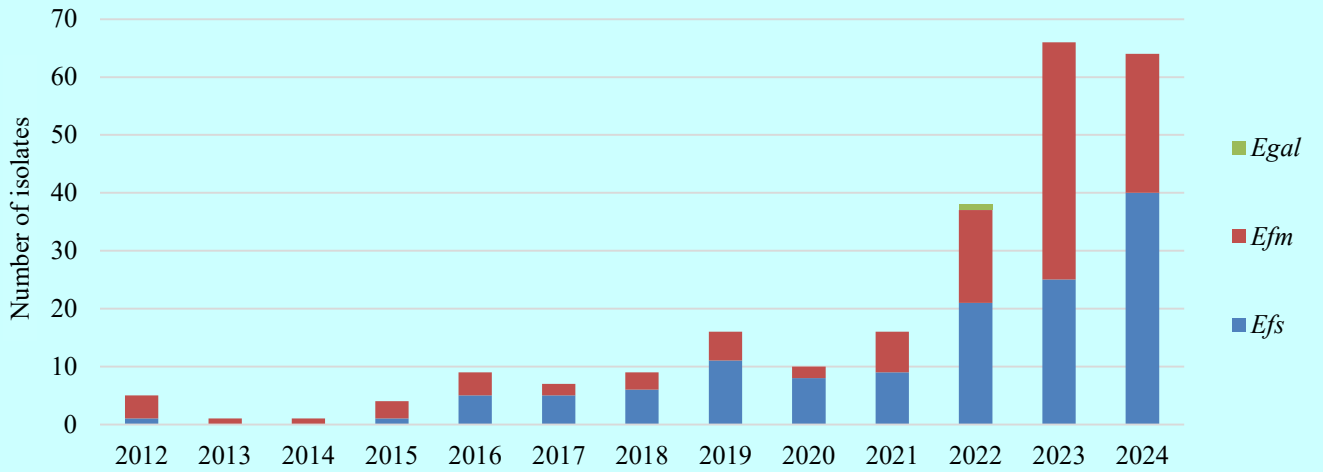

FIGURE 111. The number of linezolid resistant *E. faecium* (*Efm*), *E. faecalis* (*Efs*) and *E. gallinarum* (*Egal*) in Norway 2012-2024, including LVRE.

Linezolid resistance in enterococci was previously mostly mediated by point mutations in the chromosomal 23S rDNA regions, mainly the G2576T mutation, which is known to occur during linezolid exposure. However, in 2024, 24 LRE were *E. faecium*, of which only 13 had the mutational based linezolid resistance, while seven had *poxtA/poxtA-Ef*, three *optrA* and one both *optrA* and a G2576T mutation. In the *E. faecalis* isolates (n=40), 39 had *optrA* and one had *poxtA-Ef* (Figure 112). Of the clinical LRE isolates from 2024 (n=34), 21 were *optrA E. faecalis*, nine *E. faecium* with mutational based resistance, one *poxtA-Ef E. faecalis*, one *poxtA E. faecium*, one *optrA E. faecium* and one *E. faecium* with both *optrA* and the G2576T mutation. The 30 carrier isolates were dominated by *E. faecalis* with *optrA* (n=17) and *E. faecium* with *poxtA* (n=6) or mutation-based resistance (n=4). Twenty of the LRE isolates were associated with import, but information about import is lacking for 34 isolates. Most of the *E. faecium* isolates (n=22) belonged to well-known pandemic hospital associated sequence types (ST17, ST80, ST117, ST202 and ST203). The *E. faecalis* isolates (n=40) belonged to 16 different STs of which ST16, ST81, ST179, ST409, ST476 and ST585 were found in three or more isolates (Table 86).

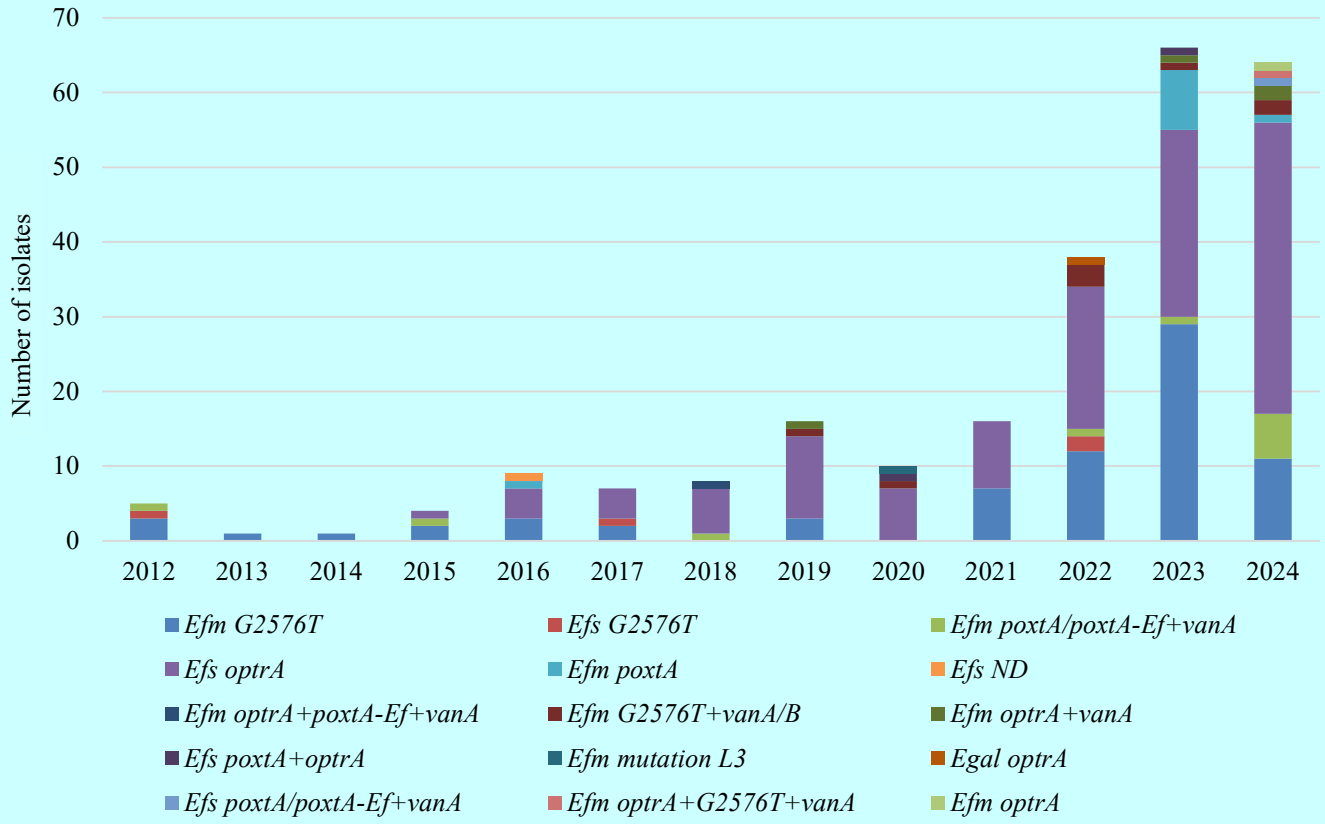

FIGURE 112. Number of LRE according to resistance mechanisms per year. *Efm = E. faecium. Efs = E. faecalis*. *Egal = E. gallinarum.* ND = not determined genotype. This isolate was not sent to K-res or archived at the primary laboratory.

TABLE 86. Species, resistance mechanism and sequence type among LRE in Norway 2024.

Species	Resistance mechanism	ST
E. faecalis (n=40)	*optrA* (n=39)	ST16 (n=5); ST179 (n=5); ST81 (n=3); ST409 (n=3); ST476 (n=3); ST585 (n=3); ST6 (n=2); ST506 (n=2); ST1259 (n=2); ST21 (n=1); ST116 (n=1); ST376 (n=1); ST895 (n=1); ST1022 (n=1); ST1116 (n=1); ST1512 (n=1); unknown ST (n=4)
	poxtA-Ef (n=1)	ST16 (n=1)
E. faecium (n=24)	23S rDNA G2576T mutation (n=13)	ST17 (n=8); ST80 (n=2); ST117 (n=2); ST203 (n=1)
	poxtA/poxA-Ef (n=7)	ST80 (n=6); ST184 (n=1)
	optrA (n=3)	ST80 (n=1); ST202 (n=1); ST1746 (n=1)
	optrA+G2576T (n=1)	ST80 (n=1)

In 2024, several clusters/outbreaks with LRE were observed. Whole genome analyses showed that three ST409 and two ST81 *optrA E. faecalis* from 2024, respectively, belonged to the same clusters (Figure 110, clusters 3 and 2). An epidemiological link was found for the ST409 *optrA E. faecalis* from the South-Eastern health region, while no epidemiological link was detected for ST81 *optrA E. faecalis*. Phylogenetic analyses also showed two clusters of *E. faecium* with the G2576T mutation in the 23S rDNA (ST17 n=10 cluster 1 and ST80 n=2 cluster 2) as well as a cluster of *E. faecium* with *poxtA+vanA* (ST80 n=2 cluster 3) (Figure 113). An epidemiological link was also demonstrated for these three *E. faecium* clusters from the South-Eastern health region. Thus, they were considered outbreaks including the first outbreak with *poxtA+vanA* LRE registered in Norway.

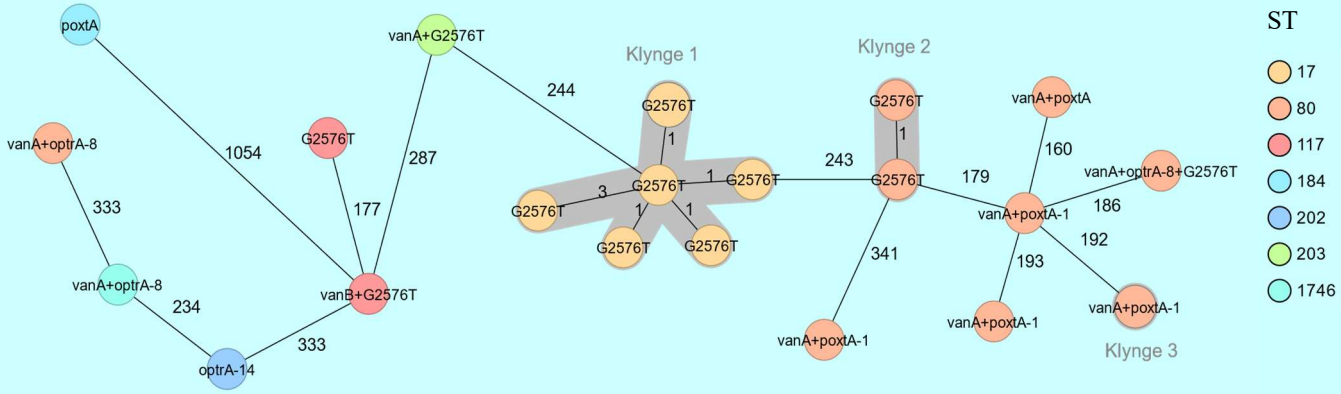

FIGURE 113. Minimum spanning network built from core genome allelic profile of the 24 Norwegian LRE *E. faecium* 2024 isolates using Ridom-SeqSphere+ software with integrated cgMLST scheme with *E. faecium* Aus0004 as reference strain. The isolates are colour coded according to ST. VRE and LRE mechanisms are indicated in the circle. Isolates with zero allelic differences end up in the same circle. Number of allelic distances between the isolates is given at the lines between the circles. Clusters with ≤20 allelic distances are highlighted with grey marking.

Conclusion

In 2024, 64 persons were reported in Norway with LRE (including 12 VLRE) representing an annual incidence rate of 1.1 per 100,000 person-years, comparable to 2023 data. Half of the LRE (n=34/64; 53%) in 2024 were clinical isolates. *E. faecalis* with transferable resistance (*optrA* n=39) and *E. faecium* with 23S rRNA mutations (n=13) were dominant. Phylogenetic and epidemiological analyses confirmed five clusters of LRE in 2024 and four of these were outbreaks in the South-Eastern health region. Less than a fourth of the LRE (23%) were related to domestic spread. Notably, the first outbreak in Norway with the *poxtA+vanA* gene combination was detected.

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Streptococcus pneumoniae in blood cultures and cerebrospinal fluids

TABLE 87. *Streptococcus pneumoniae* in blood cultures and cerebrospinal fluids in 2024 (n=630). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Penicillin G*	≤ 0.06	> 1	93.3	5.6	1.1
Cefotaxime*	≤ 0.5	> 2	98.9	1.1	0.0
Ceftriaxone*	≤ 0.5	> 2	98.7	1.3	0.0
Erythromycin	≤ 0.25	> 0.25	94.0	-	6.0
Clindamycin	≤ 0.5	> 0.5	95.9	-	4.1
Tetracycline	≤ 1	> 1	92.7	-	7.3
Trimethoprim-sulfamethoxazole**	≤ 1	> 2	92.1	2.2	5.7

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. *Breakpoints for indications other than endocarditis and meningitis. **Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only.

TABLE 88. *Streptococcus pneumoniae* in blood cultures and cerebrospinal fluids in 2024 (n=630). Distribution (%) of MICs (mg/L).

	≤0.008	0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	≥ 128
Penicillin G*	5.1	45.9	38.7	3.7	0.5	2.4	2.5	0.2	0.3	0.6	0.2				
Cefotaxime*	0.6	36.8	54.1	3.2	1.9	1.7	0.5	0.8	0.3						
Ceftriaxone*	0.2	9.4	77.6	6	2.9	1.9	0.8	0.8	0.5						
Erythromycin	0.2		15.4	77.1	1.3				0.2	0.3	1.1	0.3	0.2		4.0
Clindamycin		0.3	3.2	81.7	10.5	0.2						0.2	0.2	0.2	3.7
Tetracycline					18.6	67.3	6.8			0.8	0.5	0.5	4.1	1.4	
TMS**				0.2	21	61.4	5.2	4.3	2.2	1.6	4.0	0.2			
Chloramph.									42.2	56.5		1.3			
Norfloxacin									0.6	10.5	61.9	26.0	0.9		

Shaded areas in each row indicate susceptibility with standard exposure (light), susceptibility with increased exposure (medium) and resistance (dark). Non-shaded cells represent MIC values that are not covered by the standard test method and antibiotics without defined breakpoints. S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. *Breakpoints for indications other than endocarditis and meningitis, see text. **Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only.

RESULTS AND COMMENTS

All systemic *S. pneumoniae* isolates in Norway are submitted to the National Reference Laboratory for Pneumococci at the Norwegian Institute of Public Health. The EUCAST/NordicAST penicllin G resistance break-point for infections other than endocarditis and meningitis was reduced from R > 2 mg/L to R > 1 mg/L in 2024, and all comparisons with previous results have been adjusted accordingly. Breakpoints for chloramphenicol are no longer valid, and norfloxacin screening for quinolone resistance is only validated using disk diffusion. The oxacillin screening disk was not applied in the NORM 2024 protocol. The number of pneumococcal isolates was significantly reduced during the pandemic years 2020-2021, but has now returned to pre-pandemic levels.

The results are summarised in Tables 87-88 and Figures 114-115. Thirty strains were isolated from cerebrospinal fluids and 17/30 were concomitantly retrieved from blood cultures. Both blood culture isolates and isolates from cerebrospinal fluids were included from patients with positive cultures from both specimen type. The results for penicillin G, cefotaxime and ceftriaxone were interpreted according to the general breakpoints for pneumococci. The isolates from cerebrospinal fluids were in addition categorised according to the breakpoints for endocarditis and meningitis (penicillin G R > 0.06 mg/L, cefotaxime and ceftriaxone both R > 0.5 mg/L).

A total of 5.6% (35/630) of *S. pneumoniae* isolates were only susceptible to increased penicillin G exposure (MIC 0.125-1 mg/L), and seven isolates (1.1%) were classified as resistant (MIC > 1 mg/L). The rates of susceptibility only to increased penicillin G exposure (I) have fluctuated over the years, and this may in part be due to technical issues. The 5.6% prevalence recorded in 2024 is a decrease from 9.3% in 2022 and 7.4% in 2023. One cerebrospinal fluid isolate was resistant to penicillin G (MIC 2 mg/L) as well as cefotaxime and ceftriaxone (both 1 mg/L) according to meningitis breakpoints. Two additional cerebrospinal iosolates were resistant to penicillin G (MIC 0.25 mg/L), but remained susceptible to cephalosporins. The six penicillin resistant blood culture isolates (MIC 2-8 mg/L) were only susceptible to increased cefotaxime and ceftriaxone exposure (MIC 1-2 mg/L), but none of them were classified as cephalosporin resistant. Thirty-three blood culture isolates were susceptible only to increased penicillin G exposure (0.125-1 mg/L), and one of them was also susceptible only to increased ceftriaxone exposure (MIC 1 mg/L).

The prevalence of erythromycin resistance decreased from 6.5% in 2023 to 6.0% in 2024 (Figure 114). Most of these isolates (26/38) were resistant to both erythromycin and clindamycin, which is compatible with a constitutive MLS_B

phenotype. The remaining 12 isolates displayed low-level resistance to erythromycin and were susceptible to clindamycin, as seen in efflux-mediated M-type resistance. Double disk diffusion tests were not performed. The distribution of MLS phenotypes was not significantly altered from previous years. The results may suggest a continuing predominance of *erm*-encoded macrolide resistance as opposed to the *mef*-dominated peak 2002-2009 (Figure 115).

The 5.7% resistance rate to trimethoprim-sulfamethoxazole was lower than 7.4% recorded in 2023. The prevalence of tetracycline resistance remained essentially unchanged at 7.3% compared to 7.7% in 2023 (Figure 114). The vast majority of isolates (98.7%) apparently belonged to the wild type distribution for chloramphenicol, but clinical breakpoints for this antibiotic are no longer available. The low prevalence of high-level norfloxacin resistance (Table 88) may reflect the limited use of levofloxacin and moxifloxacin for respiratory tract infections in Norway.

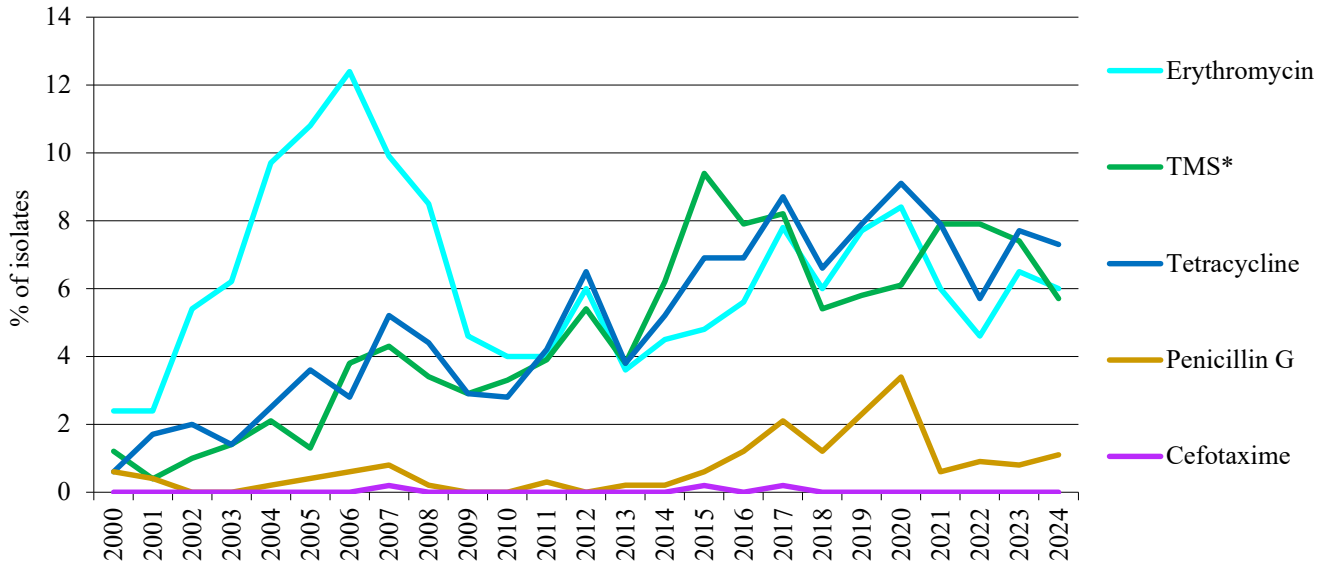

FIGURE 114. Prevalence (%) of resistance to antimicrobial agents in *Streptococcus pneumoniae* blood culture and cerebrospinal fluid isolates during 2000-2024. Doxycycline was substituted by tetracycline in 2005. *TMS=Trimethoprim-sulfamethoxazole.

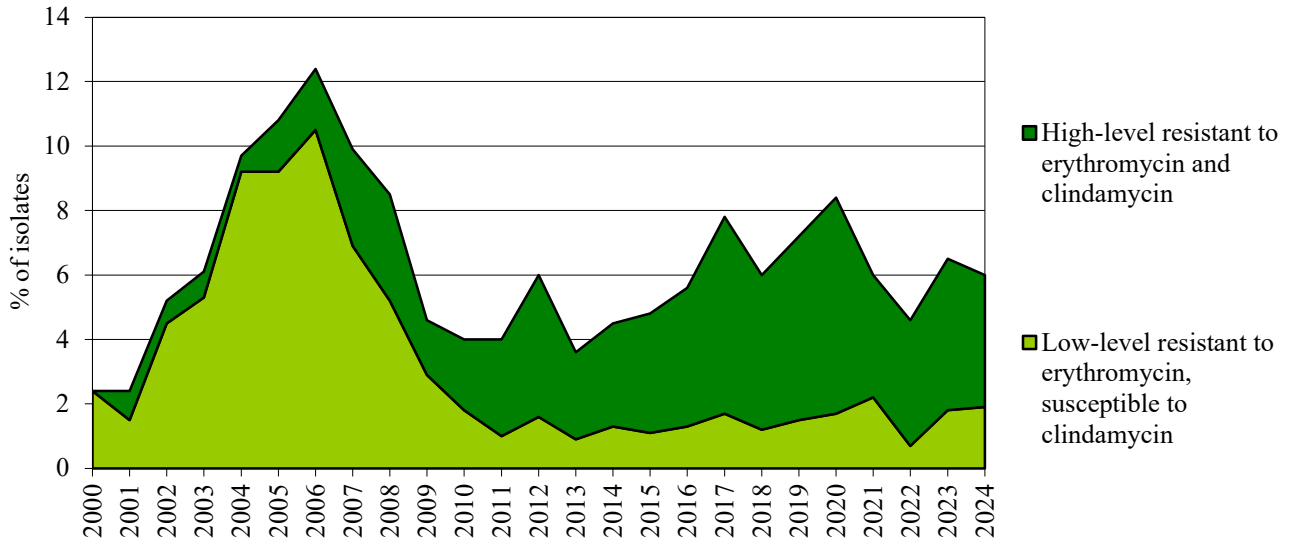

FIGURE 115. Prevalence of resistance (%) to erythromycin and clindamycin in *Streptococcus pneumoniae* blood culture isolates during 2000-2024.

Streptococcus pyogenes in blood cultures

TABLE 89. *Streptococcus pyogenes* in blood cultures in 2024 (n=354). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Penicillin G	≤ 0.03	> 0.03	100.0	-	0.0
Erythromycin	≤ 0.25	> 0.25	93.2	-	6.8
Clindamycin	≤ 0.5	> 0.5	95.5	-	4.5
Tetracycline	≤ 1	> 1	85.6	-	14.4
Trimethoprim-sulfamethoxazole*	≤ 1	> 2	98.0	0.0	2.0

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. *Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only.

TABLE 90. *Streptococcus pyogenes* in blood cultures in 2024 (n=354). Distribution (%) of MICs (mg/L) and zone diameters for oxacillin (mm).

	≤0.004	0.008	0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	≥ 128
Penicillin G		12.4	86.2	1.4												
Erythromycin	0.3			5.6	46.9	40.1	0.3		0.6	0.8	0.3	0.3	0.6	0.3		4.0
Clindamycin			2.0	31.1	56.2	5.6	0.3	0.3		0.6	0.3				0.3	3.4
Tetracycline				0.3	9.6	63.6	11.8	0.3			0.6	2.0	3.7	4.8	2.0	1.4
TMS*		0.3	5.6	34.5	50.8	6.5		0.3			0.3	0.6	0.3	0.8		

Shaded areas in each row indicate susceptibility with standard exposure (light), susceptibility with increased exposure (medium) and resistance (dark). Non-shaded cells represent MIC values that are not covered by the standard test method. *TMS=Trimethoprim-sulfamethoxazole. Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only.

RESULTS AND COMMENTS

The Reference Laboratory at the Norwegian Institute of Public Health provides resistance data for systemic *S. pyogenes* (beta-haemolytic group A streptococci - GAS) isolates on an annual basis. The number of isolates was reduced during the pandemic years 2020-2022, but a sharp increase was seen in 2023 (n=382) and 2024 (n=354). The results were categorised according to the most recent EUCAST/ NordicAST clinical breakpoint protocol. The breakpoint for resistance to penicillin G was reduced from R > 0.25 mg/L to R > 0.03 mg/L in 2024.

As expected, all isolates were fully susceptible to penicillin G (Tables 89-90). The rate of resistance to erythromycin remained unchanged at 6.8% in 2024 compared to 6.5% in 2023. The prevalence of clindamycin resistance increased from 2.9% in 2023 to 4.5% in 2024, but this is at the same level as 4.2% in 2022. High-level resistance to erythromycin was in most cases (12/14) linked to clindamycin resistance, presumably due to *erm*-encoded constitutive expression of MLS_B resistance. The remaining 10 erythromycin resistant isolates were either resistant (4/10) or susceptible (6/10) to clindamycin, thus representing either inducible MLS_B resistance or *mef*-encoded effluxs. Phenotypic MLS testing was not performed.

The prevalence of tetracycline resistance increased from 10.2% in 2023 to 14.4% in 2024. One may suspect that the changing rate of tetracycline resistance is linked to shifts in the distribution of *S. pyogenes* clones in the population. The prevalence of resistance to trimethoprim-sulfamethoxazole has been stable at very low levels (0.0% in 2022, 0.3% in 2023), and only seven isolates (2.0%) with this phenotype was detected in 2024.

Streptococcus pyogenes in specimens from the respiratory tract and wounds

TABLE 91. *Streptococcus pyogenes* in respiratory tract specimens in 2024 (n=484). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Penicillin G	≤ 0.03	> 0.03	100.0	-	0.0
Erythromycin	≤ 0.25	> 0.25	95.9	-	4.1
Clindamycin	≤ 0.5	> 0.5	98.8	-	1.2
Tetracycline	≤ 1	> 1	92.4	-	7.6
Trimethoprim-sulfamethoxazole*	≤ 1	> 2	98.1	1.2	0.6

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. *Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only.

TABLE 92. *Streptococcus pyogenes* in wound specimens in 2024 (n=458). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Penicillin G	≤ 0.03	> 0.03	100.0	-	0.0
Erythromycin	≤ 0.25	> 0.25	96.1	-	3.9
Clindamycin	≤ 0.5	> 0.5	96.5	-	3.5
Tetracycline	≤ 1	> 1	88.9	-	11.1
Trimethoprim-sulfamethoxazole*	≤ 1	> 2	99.1	0.2	0.7

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. *Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only.

RESULTS AND COMMENTS

Streptococcus pyogenes (beta-haemolytic group A streptococci - GAS) from wounds and respiratory tract specimens have previously been surveyed in NORM in 2002, 2004, 2006, 2008, 2013 and 2019. The results from 2024 are presented in Tables 91-92 and trends for selected antibiotics 2002-2024 in Figure 116. As for systemic isolates, the breakpoint for resistance to penicillin G was reduced from R > 0.25 mg/L to R > 0.03 mg/L in 2024. Wound and respiratory tract isolates were examined by disk diffusion, in contrast to MIC gradient tests for systemic isolates.

Penicillin G resistance has never been detected in group A streptococci, and no such isolates were found in the present survey. Macrolide resistant group A streptococci have been a problem in many European countries. In NORM, the prevalence of erythromycin resistance remained relatively stable in 2024 with 4.1% resistance in respiratory tract samples (5.1% in 2019 when adjusting the breakpoint for resistance to R > 0.25) and 3.9% in wound samples (6.1% in 2019 after adjustment), respectively. The prevalence of resistance to clindamycin was also essentially unchanged at 1.2% in 2024 compared to 2.7% in 2019, and at 3.5% in 2024 compared to 2.2% in 2019 for respiratory tract and wound isolates, respectively. In total, 38 non-systemic isolates were erythromycin resistant and were classified as either constitutively (14/38, 1.5% of all isolates) or inducibly (10/14, 1.1% of all isolates) MLS_B resistant. In addition, 14 isolates displayed a phenotype compatible with *mef*-encoded efflux (1.5% of all isolates). Clindamycin resistance was not detected among erythromycin susceptible isolates.

As seen in Figur 116, the prevalence of resistance to tertacycline in isolates from wound specimens was 11.1%. This is significantly higher than in respiratory tract isolates (7.6%) and consistent with previous findings in NORM. Similar differences in resistance rates by sample source were not seen for trimethoprim-sulfamethoxazole or erythromycin. One may speculate that differences in resistance rates between isolates from different clinical conditions are caused by clonal variation, but further studies are needed to support this hypothesis.

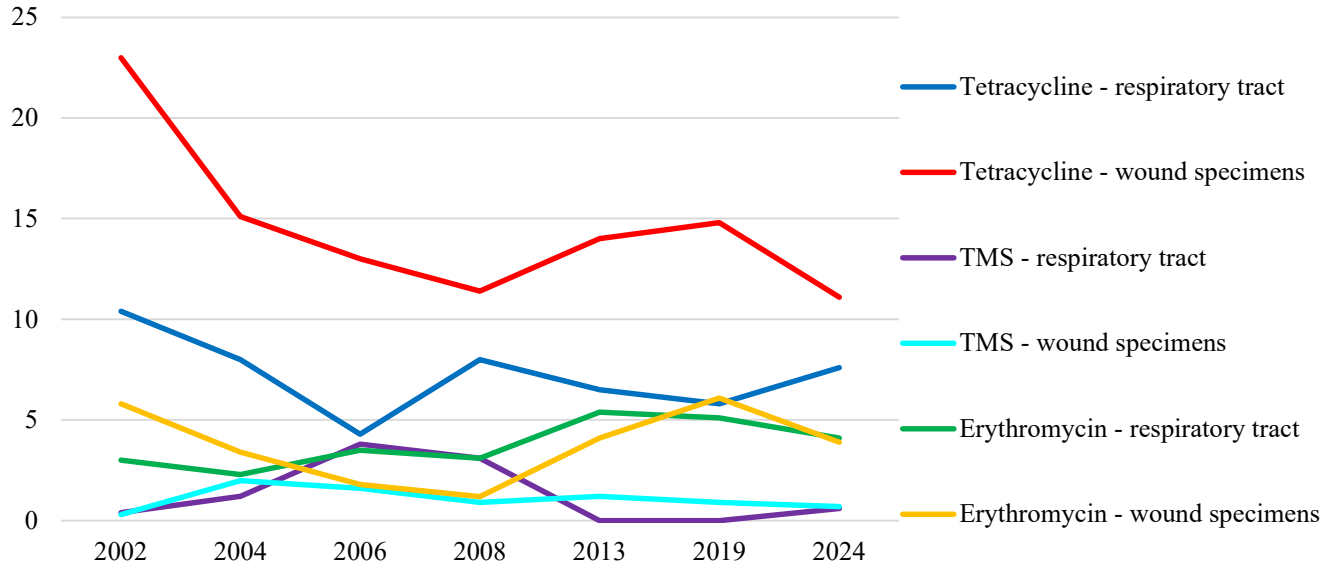

FIGURE 116. Prevalences of resistance to various antimicrobial agents in *Streptococcus pyogenes* in specimens from the respiratory tract and wounds 2002-2024. Doxycycline used in 2002-2006 was replaced by tetracycline in 2008. All data are categorised according to the 2024 NordicAST/EUCAST breakpoint protocol. Please note that the x-axis is not to scale. TMS=Trimethoprim-sulfamethoxazole.

Streptococcus agalactiae in blood cultures and cerebrospinal fluids

TABLE 93. *Streptococcus agalactiae* isolates in blood cultures and cerebrospinal fluids in 2024 (n=279). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Penicillin G	≤ 0.125	> 0.125	100.0	-	0.0
Erythromycin	≤ 0.25	> 0.25	76.0	-	24.0
Clindamycin	≤ 0.5	> 0.5	86.4	-	13.6
Tetracycline	≤ 1	> 1	28.7	-	71.3
Vancomycin	≤ 2	> 2	100.0	-	0.0

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant.

TABLE 94. *Streptococcus agalactiae* isolates in blood cultures and cerebrospinal fluids in 2024 (n=279). Distribution (%) of MICs (mg/L).

	≤0.004	0.008	0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	≥ 128
Penicillin G			1.4	18.6	75.3	4.7										
Erythromycin					1.1	27.2	47.7	0.7		1.4	3.6	5.4	4.3		0.4	8.2
Clindamycin				0.7	4.3	55.2	25.8	0.4	1.8	1.1	0.4	0.7		0.4		9.4
Tetracycline				0.7	17.9	7.5	0.7		1.8		0.4	4.7	33.0	30.1	3.2	
Vancomycin					0.4	5.7	78.5	15.4								
Gentamicin													2.5	18.6	59.9	19.0

Shaded areas in each row indicate susceptibility with standard exposure (light), susceptibility with increased exposure (medium) and resistance (dark). Non-shaded cells represent MIC values that are not covered by the standard test method or antibiotics without defined breakpoints.

RESULTS AND COMMENTS

All systemic isolates of *Streptococcus agalactiae* (beta-haemolytic group B streptococci) in Norway are referred to the National Reference Laboratory at St. Olavs Hospital, Trondheim University Hospital, where confirmatory identification and susceptibility testing is performed. Since 2014, the Reference Laboratory has provided resistance data for invasive *S. agalactiae* isolates to NORM on a yearly basis. The EUCAST/NordicAST breakpoints for penicillin G were reduced from S ≤ 0.25 and R > 0.25, to S ≤ 0.125 and R > 0.125 in 2024. The other breakpoints in this report remained unchanged.

A total of 279 isolates were retrieved from invasive infections in 2024 compared to 282 in 2023. Twenty-three isolates (8.2%) originated from neonates and small children < 1 year of age. Almost all isolates (277/279; 99.3%) were recovered from blood cultures, but there were also two isolates from cerebrospinal fluids. No patients had isolates from both specimen types, and the 279 included isolates thus represented unique infection episodes.

As seen in Tables 93-94 there were no isolates with reduced susceptibility to penicillin G or vancomycin. A total of 67 isolates (24.0%) were resistant to erythromycin compared to 22.7% in 2023. All were analysed by double disk diffusion for MLS_B resistance phenotype. Constitutive MLS_B resistance was found in 33/67 isolates (49.2%), while inducible MLS_B resistance was detected in 17/67 isolates (25.4%). The remaining 17/67 isolates (25.4%) had results in accordance with the efflux-mediated M phenotype encoded by *mef* genes. All erythromycin susceptible isolates were concomitantly susceptible to clindamycin.

There are no clinical breakpoints for aminoglycosides in *S. agalactiae*, but combination therapy with a beta-lactam is often used in clinical practice for treatment of sepsis of unknown origin. High-level resistance to gentamicin (MIC ≥ 128 mg/L) was detected in 19.0% of the isolates compared to 12.4% in 2023. The prevalence of resistance to tetracycline (71.3%) was at the same level as in 2023 (72.0%) with a majority of isolates displaying MIC values of 16-32 mg/L (Table 94).

Streptococcus dysgalactiae in blood cultures

TABLE 95. *Streptococcus dysgalactiae* in blood cultures in 2024 (n=276). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Penicillin G	≤ 0.03	> 0.03	100.0	-	0.0
Erythromycin	≤ 0.25	> 0.25	87.3	-	12.7
Clindamycin	≤ 0.5	> 0.5	97.1	-	2.9
Tetracycline	≤ 1	> 1	73.2	-	26.8
Trimethoprim-sulfamethoxazole*	≤ 1	> 2	100.0	0.0	0.0

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. *Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only.

RESULTS AND COMMENTS

Streptococcus dysgalactiae (group C and G streptococci) from blood and wounds were included in the NORM surveillance programme in 2018. Respiratory tract isolates have never been surveyed before in Norway. In 2018, susceptibility testing was performed using MIC gradient tests whereas the 2024 isolates were analysed by agar diffusion. Breakpoints for penicillin G, erythromycin and tetracycline have been changed since 2018, see below. The figures in the tables of the present report are therefore not directly comparable to the results from 2018.

All isolates were still susceptible to penicillin G in spite of the reduction of breakpoints from S ≤ 0.25 mg/L and R > 0.25 mg/L to S ≤ 0.03 mg/L and R > 0.03 mg/L. As in 2018, there was no resistance to trimethoprim-sulfamethoxazole. Similar to *S. pyogenes* and *S. agalactiae*, a considerable proportion of *S. dysgalactiae* isolates were resistant (26.8%) to tetracycline. The comparable number for 2018 was 34.3% (I + R with the breakpoint for resistance at R > 1 mg/L). Erythromycin resistance was detected in 35 isolates (12.7%) compared to 10.9% in 2018, and these were further analysed by double disk diffusion. Four isolates (11%) displayed constitutive MLS_B resistance, 23 (66%) were inducibly resistant to clindamycin, whereas eight (23%) were categorised as M-type resistant.

Streptococcus dysgalactiae in specimens from the respiratory tract and wounds

TABLE 96. *Streptococcus dysgalactiae* in respiratory tract specimens in 2024 (n=87). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Penicillin G	≤ 0.03	> 0.03	100.0	-	0.0
Erythromycin	≤ 0.25	> 0.25	85.1	-	14.9
Clindamycin	≤ 0.5	> 0.5	92.0	-	8.0
Tetracycline	≤ 1	> 1	71.3	-	28.7
Trimethoprim-sulfamethoxazole*	≤ 1	> 2	100.0	0.0	0.0

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. *Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only.

TABLE 97. *Streptococcus dysgalactiae* in wound specimens in 2024 (n=233). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Penicillin G	≤ 0.03	> 0.03	100.0	-	0.0
Erythromycin	≤ 0.25	> 0.25	89.3	-	10.7
Clindamycin	≤ 0.5	> 0.5	97.4	-	2.6
Tetracycline	≤ 1	> 1	76.8	-	23.2
Trimethoprim-sulfamethoxazole*	≤ 1	> 2	100.0	0.0	0.0

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. *Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only.

RESULTS AND COMMENTS

Streptococcus dysgalactiae (group C and G streptococci) were also surveyed in specimens from the respiratory tract and wound samples. As for blood cultures, the isolates were identified on the basis of colony morphology, group antigens, biochemical tests and MALDI-TOF analysis. Further details are given in appendix 5.

All isolates were susceptible to penicillin G and trimethoprim-sulfamethoxazole. The rates of tetracycline resistance (28.7% and 23.2% in respiratory tract and wound samples, respectively) were at the same level as in blood culture isolates (26.8%). For comparison, tetracycline resistance was 26.9% in wound isolates in 2018 after adjustment for revision of breakpoints (see above). The 38 erythromycin resistant isolates (11.9%) were most often constitutively (n=10; 26%) or inducibly (n=22; 58%) resistant to clindamycin. In addition, six isolates (16%) displayed low-level erythromycin resistance compatible with *mef*-encoded M-type resistance. The genetic basis for macrolide resistance was not further explored. Both the overall macrolide resistance rates and the distribution of MLS resistance phenotypes were approximately the same as in 2018.

How war and conflict drive antibiotic resistance

A significant number of people injured during war and conflict develop infections. As health services become overwhelmed, hygiene measures become compromised. This leads to high levels of antibiotic resistance (ABR) in conflict areas. In Ukraine war casualties are often first treated close to the frontlines in basic health structures and reception centers. These are simple setups meant for basic care and stabilisation. Antibiotic treatments are often started already at this point to save lives. Broad-spectrum antibiotics are being used and there are often no infrastructure or equipment for microbiological sampling. Patients are then transferred from the initial stabilisation center to a larger intermediate facility, and eventually to a local hospital. The most complicated cases end up at tertiary or university hospitals. By the time a patient reaches a hospital capable of conducting microbiological testing, they may have passed through three or four different facilities. All of these are often operating beyond capacity, with severely compromised infection prevention and control. All along the patient may receive broad-spectrum antibiotics, which drive the selection of resistant bacteria, and each patient has ample opportunity to transmit these to fellow patients, staff, and the environment in each facility (1).

Healthcare structures in war zones quickly become incubators for ABR

High levels of ABR are also reported in Iraq. Iraq has experienced a sequence of conflicts since the 1980s with a progressive deterioration of its national healthcare system. Lack of trained staff, inadequate hygiene and infection control measures, lack of microbial testing, as well as difficult access to appropriate antibiotics have become the situation in every hospital. The health workers struggle with the debridement of highly contaminated wounds from explosives or burns, with inappropriate diagnostics and drug regimens. All are potential contributors to the rising rates of ABR in Iraq (2). In addition, resistance co-selection from heavy metal contamination from weapons may be a contributing factor to rising levels of ABR in health facilities. Emergence of *Acinetobacter baumannii* in Iraq is associated with war injuries that are heavily contaminated with shrapnel from weapons which contain toxic metals such as lead, copper, mercury and others that select for antimicrobial resistance (3).

What is most striking is the overall lack of data from conflict areas

There are many more individual reports on ABR from conflict areas. But these are individual reports. On the WHO's global map over antibiotic resistance, the large areas with no data are the most telling (4). These areas are among the world's poorest, and many of them are affected by war and conflict. In places where the situation may be the worst, we have no overview. Conducting surveillance and research in conflict zones is not easy. It is unsafe, resources are scarce, and those available prioritise direct life-saving emergency care. Even in countries that do report data, the overview is often incomplete, as only samples from larger central hospitals are registered and reported. In rural districts and conflict-ridden areas, sample collection and resistance testing may be entirely absent.

The collapse of healthcare services creates fear and resistant bacteria in the community

War and conflict also spread ABR in the community outside the health facilities, and even to a greater extent. Widespread ABR is observed in refugee camps, especially in regions that once had reasonably functioning healthcare systems, but where these systems and infrastructures collapsed. This is not only because they are overwhelmed by war-related injuries and flight of healthcare personnel. Patients with "everyday illnesses" are left without care, and people turn to pharmacies and unskilled vendors for advice. Unstable supply chains and the fear of shortages lead to hoarding. This, in turn, leads to widespread misuse as people believe that antibiotics are useful also for non-infectious conditions.

Patients with diabetes and other chronic conditions are especially affected. They are left without their regular medications and may be living in miserable conditions, becoming more vulnerable to infections. ABR has risen rapidly among Syrian refugees in Lebanon, who can confirm this dynamic (5). The same dynamic is reported from healthcare workers in Gaza, and high levels of antibiotic consumption are also reported from Afghanistan (6).

Dire living conditions increase vulnerability to infections

When people live in extreme conditions without access to clean water and adequate sanitation, in overcrowded spaces, with little and poor-quality food, they become more vulnerable to diseases. Basic health services are lacking, and vaccination programmes are disrupted. This is the case in Sudan, the world's worst ongoing humanitarian crisis, measured by the number of refugees (14.5 million) and people affected by hunger (25 million) (7). Such conditions are vulnerable to epidemic outbreaks. Malaria cases are rising in Sudan, measles is spreading, and uncontrolled cholera outbreaks have been reported both in South-Sudan and in Sudanese refugee camps in Ethiopia (8).

In these situations, people collect rainwater in buckets, mosquitoes flourish, and parasitic and viral diseases spread. That antibiotics do not work against these diseases is not necessarily known to the population. With no functioning healthcare system, people buy pills from market vendors, and the little antibiotics that are available, are inadequately used, and may also be of poor quality. Also, in the eastern regions of the Democratic Republic of Congo, where the population is less exposed to antibiotics, reports demonstrate high levels of ABR (9).

What can be done

There *are* ways to reverse this trend. The UK health system proved that this is possible also on a large scale when it managed to control and reverse alarmingly high levels of MRSA (10). The most important measures are prevention of infections, particularly by focusing on infection control measures in health facilities in war zones, but also access to accurate diagnostics that enable appropriate treatment and thereby avoiding both overuse and misuse of antibiotics. Strengthening primary healthcare in crisis-hit areas is vital, along with improving diagnostics in unstable, conflict-ridden zones. Examples include the use of ultrasound in emergency diagnostics (11) and Mini labs for blood culture testing in field hospitals (12). Norway has a strong voice in various international fora on ABR. However, many of these fora lack a truly global perspective, and conflict-ridden areas are easily forgotten.

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Impact of the war in Ukraine on AMR in Norway

Armed conflicts are well-recognised drivers of antimicrobial resistance (AMR), both within conflict zones and internationally (1). War disrupts healthcare systems, compromises infection prevention, and leads to increased and often unregulated use of antibiotics, particularly in the treatment of traumatic injuries. These conditions foster the emergence and spread of AMR. High rates of carbapenemase-producing *Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Acinetobacter baumannii*, have been documented in war-related injuries, including in the current conflict in Ukraine (2). The large-scale displacement of people and medical evacuation of patients from conflict zones to hospitals abroad can contribute to cross-border transmission of resistant pathogens.

Norwegian surveillance data show increase in patients with CPO

In 2024, 305 patients with carbapenemase-producing organisms (CPO) were notified to the Norwegian Surveillance System for Communicable Diseases (MSIS) - a 21% increase from 2023 (3). The incidence rate reached 5.5 per 100,000 person-years. The majority, 64% of the cases, were likely acquired abroad. Ukraine accounted for 19% of all CPO isolates, making it the most frequently reported foreign source (Figure 117). Many Ukrainian patients treated in Norwegian hospitals arrive through the EU Civil Protection Mechanism (UCPM), coordinated nationally by Oslo University Hospital. The MedEvac system ensures transfer from specialist care in Ukraine (or neighboring countries) directly to specialist care in Norway. However, the majority of Ukrainian patients arrive independently, outside of official MedEvac programs, and are managed like other asylum seekers.

The situation in Ukraine represents a high-risk AMR environment, exacerbated by long-standing challenges predating the 2022 invasion. In 2021, 64.4% of invasive *Klebsiella pneumoniae* isolates in Ukraine were resistant to carbapenems, as reported by ECDC (4). The rise in CPO cases in Norway cannot be attributed to MedEvac patients alone. The increase is primarily driven by international travel and migration from countries with a high prevalence of CPO. The prevalence of CPO has risen substantially across Europe over the past years, contributing to the growing number of imported cases in Norway. The estimated total EU incidence of carbapenem resistant *Klebsiella pneumoniae* bloodstream infections was 57.5% higher in 2023 than in 2019 (5).

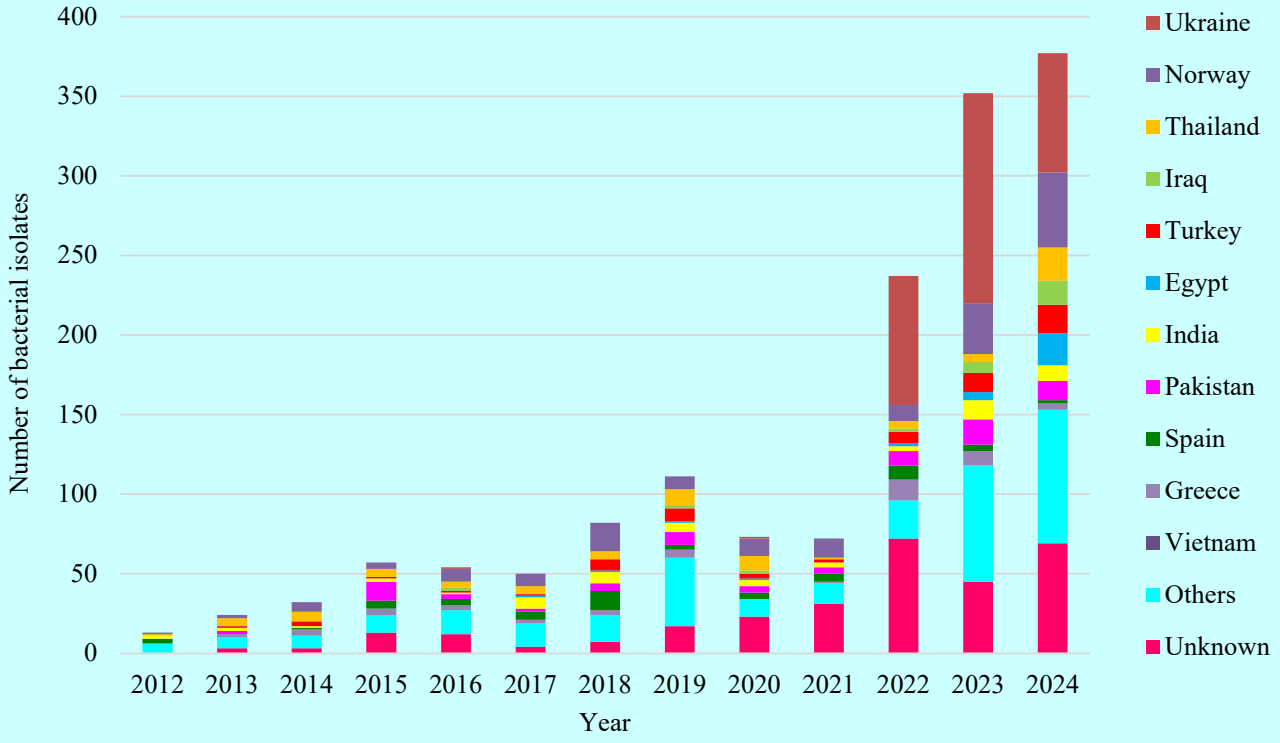

FIGURE 117. Number of bacterial isolates of CPO reported to MSIS in the period 2012-2024 distributed by presumed place of infection. Source: MSIS, FHI.

Robust infection prevention is crucial in preventing spread of CPO

For Norwegian healthcare providers, these developments underline the importance of robust infection control, targeted screening of patients with recent healthcare exposure abroad, and awareness of the AMR risk associated with conflict-affected regions. The Norwegian Institute of Public Health (NIPH) recommends pre-emptive isolation and screening of patients transferred from hospitals abroad, including those in Ukraine (6). Although the number of CPO outbreaks in Norway remains relatively low, with 12 small-scale outbreaks reported to NIPH in 2024, the existence of these highlights the persistent threat of AMR (7).

Treatment of CPO in Norway

Treatment of infections caused by multi-drug resistant (MDR) and extensively drug resistant (XDR) bacteria poses significant challenges and is often associated with a high risk of poor clinical outcomes. Effective antibiotic treatment relies on access to comprehensive microbiological diagnostics. The choice of antibiotics for empirical treatment is influenced by factors such as the risk of resistance, availability of antibiotics, severity of the infection, and the presence of comorbidities (e.g., kidney failure). Ukrainian war victims transferred to Norwegian hospitals through the MedEvac system have a particularly high risk of CPOs due to complex war injuries with multiple surgical interventions, extended courses of broad-spectrum antibiotics, and inadequate microbiological diagnostics in war zones. In such cases, the initiation of last-resort antibiotics, classified as Reserve antibiotics by the World Health Organization's AWaRE categorisation (8,9), is warranted. Norwegian recommendations (10) for the management of CPOs largely align with European guidelines for treating infections caused by MDR Gram-negative bacteria (11). When a CPO infection is suspected, it is advisable to commence empirical treatment with a combination of ceftazidime-avibactam and aztreonam. This combination creates a synergistic effect, as aztreonam effectively targets CPO strains that produce extended spectrum metallo-beta-lactamases (MBLs) (12). However, many MBL-producing strains also possess co-enzymes that can hydrolyse aztreonam (e.g., AmpC, ESBL), though this challenge can be mitigated by the inclusion of the beta-lactamase inhibitor avibactam. Recently, the availability of the new drug combination aztreonam-avibactam in Norway presents an opportunity to replace the more complex administration of ceftazidime-avibactam in conjunction with aztreonam (13).

Despite a higher threshold for the use of antibiotics such as colistin and tigecycline due to concerns over side effects and variable clinical efficacy, these agents have been employed as alternatives, particularly when there is a threat of carbapenem resistant *Acinetobacter baumannii*. Furthermore, early experiences with the new antibiotic cefiderocol have indicated a somewhat higher resistance rate than anticipated, leading to the recommendation that it should not be used as monotherapy until a definitive resistance profile is established (10).

Over the past three years, the rise in patients with CPO infections in Norway has led to an increased use of antibiotics targeting carbapenemase-producing Gram-negative bacteria in Norwegian hospitals (Figure 118).

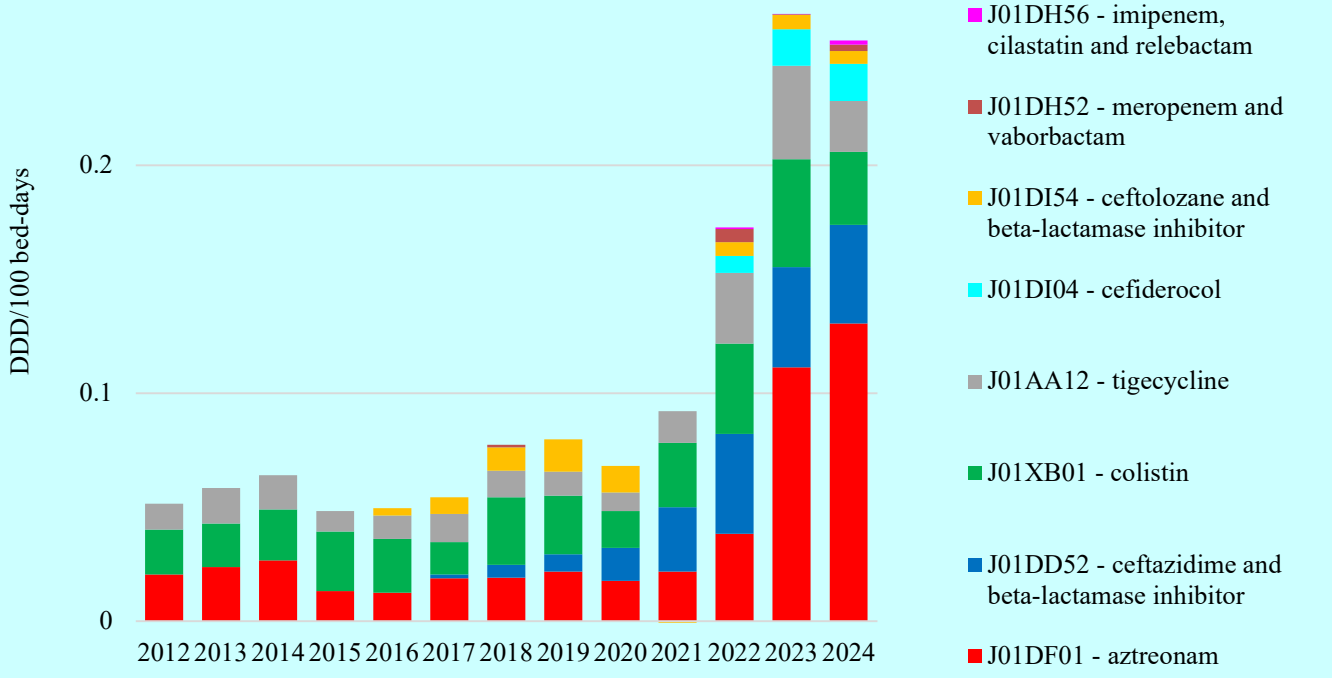

FIGURE 118. Antibiotics utilised to treat carbapenemase resistant Gram-negative bacteria in Norwegian hospitals (somatic) 2012-2024, measured in DDD/100 bed-days. Source: Hospital pharmacies drug statistics database.

Access to last resort antibiotics for patients with CPO

Treating MedEvac patients requires the availability of last resort antibiotics. Ideally, these would be newly approved antibiotics shown to treat carbapenem resistant infections. Unfortunately, though, these rarely exist. Of the 16 antibiotics approved globally since 2017, seven have some activity against carbapenem resistant infections (14). Two of the seven have not yet been approved by the European Medicines Agency, and only three are marketed in Norway. Yet the Norwegian Hospital Procurement Trust has been proactive to secure stocks of the unregistered antibiotics approved in Europe. Maintaining reliable access to older, last resort antibiotics like colistin, aztreonam, and tigecycline, is also critical. Another potential tool that may be explored is the use of bacteriophages, which has been shown to effectively treat some difficult-to-treat infections (15).

Microbiological challenges and adaptation during the MedEvac response at Oslo University Hospital

The MedEvac patients have challenged the Department of Microbiology to expand the service and increase knowledge concerning extensive screening procedures, identification of polymicrobial infections with multiple MDRs and complicated susceptibility testing.

Most of the patients transferred from Ukrainian war hospitals are colonised with multiple MDR or XDR organisms, and well-functioning infection prevention and control measurements are required to prevent transmission. However, it has been logistically challenging to obtain samples from all locations as is advised in national guidelines (6). Close communication with the nursing staff and simplification of the sampling process has proven helpful and necessary. For the Department of Microbiology, an effective and accurate handling of the increasing number of samples is labor intensive. Nevertheless, isolation, identification, susceptibility testing, and finally, sequencing of isolates by the Norwegian National Advisory Unit on Detection of Antimicrobial Resistance, is pivotal for surveillance, and must be a prioritised task for the laboratory.

Most patients in the MedEvac cohort are diagnosed with bone and/or soft tissue infection. The majority of these are caused by multiple MDR Gram-negative bacteria, often in combination with Gram-positive bacteria such as *Enterococcus* spp. and coagulase-negative staphylococci. The complexity of the samples, often comprising numerous samples from several locations, and the detection of multiple microbes with different resistance mechanisms within the same sample, is challenging and time consuming for the laboratory. Close cooperation with the infectious disease specialists and surgeons about what and how to treat is necessary throughout the treatment course. Finally, in order to give effective treatment identification of genotypic resistance mechanisms in addition to phenotypic susceptibility testing of reserve antibiotics such as ceftazidim/avibactam, ceftolozane/tazobactam, cefiderocol and colistin should be available to the clinician within reasonable time.

The first three years of Ukrainian patients has, although it has been labour intensive, provided us with valuable experience regarding diagnosis and treatment of MDR infections and has ensured that we have updated our knowledge and diagnostic tools to face the expected increase of these infections in the coming years.

Resistensbestemmelse			
Mikrobe:	**KLPNEU**	**ESCOLI 2**	**ACBAUM**
Amikacin	R (>32)	S (4)	R (>32)
Us-Ampicillin	R	R	
Aztreonam	R (>32)	R (16)	
Us-Cefiderocol	R	S	
Ceftazidim/avibactam	R (>16)	S (0.5)	
Ciprofloksacin	R (>2)	R (>2)	R (>2)
Colistin	(0.5)	(0.5)	(1)
Ertapenem	R (>2)	S (0.125)	
Gentamicin	R (>8)	R (>8)	
Imipenem	R (8)	S (0.5)	R (>16)
Meropenem	R (16)	S (0.125)	R (>16)
Piperacillin/tazobactam	R (>32)	S (4)	
Tigesyklin	(1)	S (0.25)	(1)
Tobramycin	R (>8)	R (>8)	S (2)
Trimetoprim-Sulfa	R (>8)	S (2)	R (8)
Ceftolozane/Tazobactam	R (>32)	S (0.5)	

FIGURE 119. Susceptibility profiles of a clinical sample with *K. pneumoniae* (blaNDM + blaOXA-48-like), *E. coli* (ESBL-A) and *A. baumannii* (blaOXA 23). Department of Medical Microbiology, Oslo University Hospital.

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Resistance to empiric antibiotic combinations used to treat bloodstream infections – Holding the line?

The resistance to empiric antibiotic combinations among significant bloodstream infection (BSI) pathogens (Table 98) has remained largely unchanged since 2023 (1). The recent surge of invasive *Streptococcus pyogenes* and reemergence of invasive *Streptococcus pneumoniae* over the last two years (Table 56) has not been complicated by increased levels of antimicrobial resistance. Methicillin resistant *Staphylococcus aureus (*MRSA) remained uncommon, accounting for only 1.1 % of *S. aureus* BSI cases. Overall, the resistance rates among significant Gram-positives have remained stable for more than a decade, providing no immediate cause for concern.

ESBL rates and gentamicin resistance in the principal Gram-negative pathogens *E. coli* and *Klebsiella* spp., have held steady at 5-6 % for the third consecutive year, maintaining a favourable trend. Nonetheless, even at these relatively low rates, ESBL-producing strains continue to account for more than 300 bloodstream infection episodes annually, placing a substantial clinical and operational burden on hospitals. Fortunately, despite the overall rise in carbapenemase-producing strains (pages 114-123), these remain rare in BSIs.

Given the current epidemiological landscape of AMR, beta-lactam/gentamicin combinations perform at least as well as cefotaxime and piperacillin-tazobactam, thus continuing to justify their position as first-line empirical therapies for most serious infections (2). The line holds for another year.

TABLE 98. Resistance (%) to broad-spectrum antibiotics and antibiotic combinations in key bloodstream infection pathogens.

Antibiotic drug combinations[1]		Proportion of invasive isolates resistant (%)										
		E. coli (n=2,297)	*Klebsiella* spp. (n=1,230)	ESBL *Enterobacterales** (n=336)	*H. influenzae* (n=93)	*Enterococcus* spp. (n=735)	*Streptococcus pneumoniae* (n=630)	*Streptococcus pyogenes* (n=354)	*Streptococcus agalactiae* (n=279)	*Streptococcus dysgalactiae* (n=276)	*Staphylococcus aureus* (n=1,614)	MRSA** (n=3,415)
PEN	GEN	5.7	4.5	38.7	28.0[2]	-	1.1	0.0	0.0	0.0	0.8	17.5
PEN	CIP	9.7	8.9	58.9	0.0	-	1.1	0.0	0.0	0.0	1.7	27.6
CLI	GEN	5.7	4.5	38.7	100.0	100.0	4.1	4.5	13.6	2.9	0.1	5.6
AMP	GEN	5.3	4.5	38.7	16.1	21.2[4]	X	0.0[5]	0.0[5]	0.0[5]	0.8	17.5
PTZ	GEN	0.5	2.9	19.3	4.3[3]	21.2[4]	X	0.0[5]	0.0[5]	0.0[5]	0.3[6]	17.5
CTX		6.5	6.7	94.9	2.2	100.0	0.0	0.0[5]	0.0[5]	0.0[5]	1.1[7]	100.0
PTZ		4.4	11.2	32.7	4.3[3]	21.2[4]	X	0.0[5]	0.0[5]	0.0[5]	1.1[7]	100.0
MER		0.0	0.4	1.5	0.0	100.0	X	0.0[5]	0.0[5]	0.0[5]	1.1[7]	100.0

[1]Antibiotic abbreviations: PEN=penicillin G, GEN=gentamicin, CIP=ciprofloxacin, CLI=clindamycin, AMP=ampicillin, PTZ=piperacillin-tazobactam, CTX=cefotaxime, MER=meropenem. [2]Inferred from benzylpenicillin 1 unit (PCG1). [3]Inferred from amoxicillin-clavulanate. [4]Inferred from ampicillin only. [5]Inferred from penicillin only. [6]Piperacillin-tazobactam inferred from cefoxitin. [7]Inferred from cefoxitin. X: No data available. -: No breakpoint/susceptibility testing not recommended. **Escherichia coli* and *Klebsiella* spp. **Includes MRSA from all specimen types.

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Mycobacterium tuberculosis

In 2024 (2023 in parenthesis), 181 (153) persons were reported with tuberculosis disease (TB) to MSIS. Of these, 12 (18) were born in Norway. In addition to these 181 persons in 2024, six came to Norway under TB treatment.

154 (124) cases were confirmed with *M. tuberculosis* complex (MTBC) by culture and 15 (10) cases were confirmed by genotypic tests only (culture negative). Of the culture positive cases, 1 (3) were identified as *M. bovis, M. africanum* or *M. orygis*, the rest were *M. tuberculosis*. Resistance results reported to MSIS are shown in Table 99. Results from testing of both isolates and direct samples are included. There were 15 (16) rifampicin resistant (RR-) TB cases including 13 (15) multi-drug resistant (MDR-) TB cases resistant to both rifampicin and isoniazid. All the RR-TB cases in 2023 and 2024 were culture positive. 6 (4) of the MDR-TB cases had resistance to fluoro-quinolones, so-called pre-XDR (extensively drug resistant) TB. All RR-TB cases had TB for the first time, except six MDR-TB cases who had received chemotherapy in the past (including four cases of pre-XDR). None of the RR-TB cases had previously received preventive treatment.

In addition to the MDR-TB cases, 13 (14) TB cases had strains resistant to isoniazid (sensitive to rifampicin), 6 (4) of them only with low-level resistance.

TABLE 99. Antimicrobial resistance for MTBC reported to MSIS (not *M. bovis* BCG) in 2024 from isolates or direct samples. Figures from 2023 in parentheses.

Origin of birth	No. of cases	Resistance to antimicrobial agents				
		Isoniazid	Rifampicin	Ethambutol	Pyrazinamide	MDR-TB
		157 (125)	162 (131)	145 (122)	139 (120)	157 (129)
Norway	12 (18)	1 (1)	1 (0)	0 (0)	1 (1)	0 (0)
Europe excluding Norway	52 (59)	16 (20)	11 (13)	8 (12)	7 (7)	11 (12)
Asia	76 (40)	4 (6)	0 (2)	0 (1)	4 (4)	0 (2)
Africa	39 (35)	5 (2)	3 (1)	0 (0)	1 (0)	2 (1)
America	2 (1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Total	181 (153)	26 (29)	15 (16)	8 (13)	13 (12)	13 (15)
Proportion resistant isolates (%)		16.6 (23.2)	9.3 (12.2)	5.5 (10.7)	9.4 (10.0)	8.3 (12.0)

MDR-TB: Multi-drug resistant tuberculosis, resistant to at least rifampicin and isoniazid.

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Candida spp. in blood cultures

TABLE 100. Antimicrobial susceptibility of *Candida albicans* blood culture isolates in 2024 (n=134). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Amphotericin B	≤ 1	> 1	100.0	-	0.0
Fluconazole	≤ 2	> 4	100.0	0.0	0.0
Voriconazole	≤ 0.06	> 0.25	100.0	0.0	0.0
Anidulafungin	≤ 0.016	> 0.016	98.6	-	1.4
Micafungin	≤ 0.03	> 0.03	98.6	-	1.4

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant.

TABLE 101. *Candida albicans* blood culture isolates in 2024 (n=134). Distribution (%) of MICs (mg/L).

	≤0.004	0.008	0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥ 256
Ampho. B				3.0	18.7	55.2	20.9	2.2									
Fluconazole					1.5	9.7	59.7	29.1									
Voriconazole	7.5	56.0	35.8	0.7													
Anidulafungin	35.8	48.5	14.2		0.7		0.7										
Micafungin	0.7	40.3	55.2	2.2		0.7		0.7									
Caspofungin			1.5	11.9	44.0	34.3	6.0	1.5	0.7								

Shaded areas in each row indicate susceptibility with standard exposure (light), susceptibility with increased exposure (medium) and resistance (dark). Non-shaded rows indicate that breakpoints have not been defined.

TABLE 102. Antimicrobial susceptibility of *Candida glabrata* blood culture isolates in 2024 (n=37). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Amphotericin B	≤ 1	> 1	100.0	-	0.0
Fluconazole	≤ 0.001	> 16	0.0	94.6	5.4
Anidulafungin	≤ 0.06	> 0.06	97.3	-	2.7
Micafungin	≤ 0.03	> 0.03	97.3	-	2.7

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant.

TABLE 103. *Candida glabrata* blood culture isolates in 2024 (n=37). Distribution (%) of MICs (mg/L).

	≤0.004	0.008	0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥256
Ampho. B		2.7		2.7	2.7	13.5	45.9	32.4									
Fluconazole								2.7	2.7	2.7	29.7	27.0	29.7	2.7			2.7
Voriconazole			2.7		8.1	24.3	29.7	16.2	10.8	5.4	2.7						
Anidulafungin		2.7	73.0	18.9	2.7	2.7											
Micafungin		13.5	81.1	2.7	2.7												
Caspofungin					10.8	35.1	48.6	5.4									

Shaded areas in each row indicate susceptibility with standard exposure (light), susceptibility with increased exposure (medium) and resistance (dark). Non-shaded rows indicate that breakpoints have not been defined.

TABLE 104. Antimicrobial susceptibility of *Candida tropicalis* blood culture isolates in 2024 (n=25). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Amphotericin B	≤ 1	> 1	100.0	-	0.0
Fluconazole	≤ 2	> 4	88.0	4.0	8.0
Voriconazole	≤ 0.125	> 0.25	92.0	0.0	8.0
Anidulafungin	≤ 0.06	> 0.06	96.0	-	4.0
Micafungin	≤ 0.06	> 0.06	96.0	-	4.0

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant.

TABLE 105. *Candida tropicalis* blood culture isolates in 2024 (n=25). Distribution (%) of MICs (mg/L).

	≤0.004	0.008	0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥ 256
Ampho. B						24.0	36.0	32.0	8.0								
Fluconazole							8.0	36.0	32.0	12.0	4.0				4.0		4.0
Voriconazole			8.0	24.0	24.0	36.0				4.0				4.0			
Anidulafungin			60.0	20.0	16.0				4.0								
Micafungin			20.0	68.0	8.0			4.0									
Caspofungin				4.0	20.0	44.0	24.0	4.0			4.0						

Shaded areas in each row indicate susceptibility with standard exposure (light), susceptibility with increased exposure (medium) and resistance (dark). Non-shaded rows indicate that breakpoints have not been defined.

TABLE 106. Antimicrobial susceptibility of *Candida parapsilosis* blood culture isolates in 2024 (n=17). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Amphotericin B	≤ 1	> 1	100.0	-	0.0
Fluconazole	≤ 2	> 4	88.2	11.8	0.0
Voriconazole	≤ 0.125	> 0.25	94.4	5.6	0.0
Anidulafungin	≤ 4	> 4	100.0	-	0.0
Micafungin	≤ 4	> 4	100.0	-	0.0

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant.

TABLE 107. *Candida parapsilosis* blood culture isolates in 2024 (n=17). Distribution (%) of MICs (mg/l).

	≤0.004	0.008	0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥ 256
Ampho. B					17.6	17.6	23.5	41.2									
Fluconazole						5.9	5.9	29.4	41.2	5.9	11.8						
Voriconazole		11.8	5.9	35.3	29.4	11.8	5.9										
Anidulafungin								11.8	11.8	35.3	41.2						
Micafungin						4.0		20.0	56.0	20.0							
Caspofungin								70.6	29.4								

Shaded areas in each row indicate susceptibility with standard exposure (light), susceptibility with increased exposure (medium) and resistance (dark). Non-shaded rows indicate that breakpoints have not been defined.

TABLE 108. Antimicrobial susceptibility of *Candida dubliniensis* blood culture isolates in 2024 (n=14). Sampling, laboratory methods, and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Amphotericin B	≤ 1	> 1	100.0	-	0.0
Fluconazole	≤ 2	> 4	100.0	0.0	0.0
Voriconazole	≤ 0.06	> 0.25	100.0	0.0	0.0
Anidulafungin	≤ 0.03	> 0.03	100.0	-	0.0
Micafungin	≤ 0.06	> 0.06	100.0	-	0.0

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant.

TABLE 109. *Candida dubliniensis* blood culture isolates in 2024 (n=14). Distribution (%) of MICs (mg/L).

	≤0.004	0.008	0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥256
Ampho. B			28.6	35.7	14.3	21.4											
Fluconazole					7.1	50.0	28.6	14.3									
Voriconazole	14.2	42.9	42.9														
Anidulafungin		28.6	71.4														
Micafungin		21.4	71.4	7.1													
Caspofungin				21.4	28.6	50.0											

Shaded areas in each row indicate susceptibility with standard exposure (light), susceptibility with increased exposure (medium) and resistance (dark). Non-shaded rows indicate that breakpoints have not been defined.

RESULTS AND COMMENTS

All *Candida* isolates from blood culture from Norwegian patients are included in the NORM surveillance. The National Reference Laboratory for Medical Mycology at Oslo University Hospital performs confirmatory identification and susceptibility testing of all isolates from fungemia. Identical isolates from the same episode, defined as cultures less than four weeks apart without changes in the susceptibility pattern, are counted as one in this survey. Fungemia with other species than *Candida* (n=7) are not included, and new nomenclature of fungi with renaming of many previous *Candida* spp. into new species is not implemented to prevent confusion and awaiting changes of names by EUCAST and even broader acceptance in the entire medical mycology community.

During 2024, we registered 255 isolates from blood culture. The number of unique candidemia isolates was 238 in 223 different patients, compared to 250 isolates in 226 patients in 2023. There were eight mixed infections with more than one *Candida* spp., three reinfections more than 4 weeks apart and six new infections with another species in 14 patients.

The species distribution of the two most frequent species, *C. albicans* (n=134; 56.3%) and *C. glabrata* (n=37; 15. 5%), was unchanged compared to 134 and 39 last year. The number of other species is low. The proportion of *C. tropicalis* increased from 5.6% to 10.5% (n=14 to n=25) and *C. dubliniensis* from 4.4% to 5.9% (n=11 to n=14). The number of *C. parapsilosis* declined from 25 (10.0%) to 17 (7.1%). In 2024 the number of more infrequent species was only 11 (4.6%) compared to 27 (10.8%) last year. *C. auris,* the only notifiable fungal pathogen, was not detected in blood cultures in Norway in 2024.

All isolates were susceptibility tested to amphotericin B, fluconazole, voriconazole, caspofungin, anidulafungin and micafungin. All but voriconazole are tested by E-test according to the manufacturer's instructions (AB bioMérieux), whereas voriconazole was tested by MTS (Liofilchem). All results were interpreted according to the updated EUCAST clinical breakpoint protocol version 11.0 (revised and valid from 02.12.2024). Unexpected susceptibility patterns were confirmed by EUCAST standardised broth microdilution method and for some isolates by *fks* sequencing at Statens Serum Institut in Copenhagen. The results are presented in Tables 100-109.

In 2024, EUCAST lowered the anidulafungin breakpoint for *C. albicans* and established breakpoints for *C. dubliniensis*. The micafungin breakpoint for *C. albicans* was increased and the ATU removed. Additionally, micafungin breakpoints were established for *C. dubliniensis* and *C. tropicalis*. The EUCAST guidance document "What to do when there are no breakpoints - guidance for rare yeasts" published in 2024 offers pragmatic treatment recommendations depending on species and MIC values for *C. guilliermondii*, *C. lusitaniae*, *C. kefyr* and other rare yeasts, and is available online.

The majority of *C. albicans* isolates (98.6%) were susceptible to all antifungal agents. There were only two echinocandin resistant strains and in one of them, mutations in the hot spot region of the *fks* gene were detected (R1361C).

Acquired fluconazole resistance was observed in two *C. glabrata* isolates (MIC 32-256 mg/L), and one *C. glabrata* isolate was echinocandin resistant. There were two azole resistant *C. tropicalis* isolates and one isolate with reduced sensitivity to fluconazole. Given the new breakpoint for micafungin, one isolate was regarded as resistant to both anidulafungin and micafungin. Two *C. parapsilosis* isolates showed reduced sensitivity to fluconazole of which one displayed reduced voriconazole sensitivity as well. Otherwise, all *C. parapsilosis* isolates were susceptible to all agents.

Acquired voriconazole resistance occurred in two fluconazole resistant *C. tropicalis* and reduced sensitivity to voriconazole in one C. *parapsilosis*, otherwise all isolates with defined breakpoints to voriconazole were susceptible. There is still insufficient evidence that *Candida* spp. is a good target for therapy with isavuconazole and breakpoints have not been set. All *C. dubliniensis* isolates were susceptible to all antifungal agents.

Of the 11 isolates not shown in the tables, there were two fluconazole resistant *C. krusei* and one fluconazole resistant *C. lipolytica*. *C. pelliculosa* (n=1), and *C. guillermondii* (n=1) are both regarded to have reduced sensitivity to fluconazole as well. *C. lusitaniae* (n=3) is regarded amphotericin B resistant. Two *C. kefyr* displayed low MIC values to all agents, which allows all agents to be considered suitable for therapy.

In conclusion, over the last 25 years the species distribution in candidemia in Norway slowly mirrors international data with a decline in the proportion of *C. albicans* from 75.0 % to 56.3%. The proportion of *C. glabrata* and other strains with reduced fluconazole susceptibility is still low and acquired resistance in *Candida* spp. is rare. The Norwegian treatment guidelines for candidemia with echinocandins as first-line treatment due to fungicidal effect, and de-escalation to fluconazole in stable patients infected with susceptible *Candida* spp., are still appropriate.

Antifungal resistance in dermatophytes and the consequences for diagnostics and treatment

Dermatophytes are a group of keratinophilic fungi responsible for common superficial infections involving the skin, hair, and nails, collectively termed dermatophytoses. These fungi are phylogenetically classified into seven genera: *Trichophyton, Epidermophyton, Microsporum, Nannizzia, Arthroderma, Paraphyton,* and *Lophophyton,* with *Trichophyton* species causing the majority of human infections globally. Within this genus, *Trichophyton rubrum* is the most prevalent species worldwide, frequently implicated in clinical manifestations such as tinea pedis, tinea corporis, and onychomycosis (1).

Terbinafine has excellent activity against most dermatophytes and is regarded first-line therapy, followed by less effective griseofulvin and azols. Most superficial infections are treated topically, whereas extensive infections and infections of nails and hair need long-term peroral treatment. Treatment used to be empirical, and relapses related to patient therapy interruptions or abandonment (1,2). Terbinafine resistance was first described in 2003.

Over the past decade we have witnessed an increasing number of severe, atypical cases of dermatophytoses worldwide. *T. indotineae*, a newly recognised species closely related to the *T. mentagrophytes*/*interdigitale* species complex, is a hypervirulent and often terbinafine resistant dermatophyte responsible for most of these infections. It was first detected in India and the Indian subcontinent, with subsequent spread internationally via travel and local transmission (1,2). Terbinafine resistance also occurs in *T. rubrum*, but without the same hypervirulence. Not all emerging dermatophytes are resistant to antifungals, like the often sexually transmitted *T. mentagrophytes* genotype VII (3).

Antifungal resistance in dermatophytes and treatment

Terbinafine inhibits ergosterol synthesis by inhibiting squalene epoxidase (SQLE), an enzyme that catalyses the conversion of squalene to lanosterol. Terbinafine resistance is primarily associated with a single variation at one of the four positions (Leu393, Phe397, Phe415, His440) in the *SQLE* gene. Other point mutations in the *SQLE* gene are responsible for azole resistance in various *Trichophyton* species, but resistance to azoles is also linked to target-site modifications or efflux mechanisms (4,5). Systemic azoles are the cornerstone of therapy of terbinafine resistant dermatophytes, with oral itraconazole (≥ 200 mg/day) recommended as a first-line option. Fluconazole and griseofulvin are not recommended for *T. indotineae* due to reported high-level resistance (6, 7).

Diagnostics

The growing prevalence of antifungal resistant dermatophytes poses several challenges to diagnostics and treatment. Conventional culture-based diagnostics are often slow and may not reliably detect resistant strains or distinguish among closely related species, such as differentiating *T. indotineae* from other *T. mentagrophytes/interdigitale* species complex members. The online reference library (MSI-2) by Normand et al. enables identification of dermatophythes by MALDI-TOF MS. Internal transcribed spacer (ITS) sequencing is the reference method for confirmation of *T. indotineae* and other dermatophytes from culture.

Point-of-care direct microscopy can confirm fungal infection, but species identification is recommended to guide treatment options and elucidate the origin of infection and managing possible outbreaks as different species are regarded zoonotic, anthropophilic, or geophilic. PCR-based diagnostics has replaced culture in most Norwegian laboratories and offer many advantages compared to culture with rapid turnaround time and better sensitivity. Detecting *T. indotineae* directly in DNA extracts from clinical samples is challenging as identification of different species within the *T. mentagrophytes/T. interdigitale* complex often fails. Culture is recommended in severe or extensive infections, in infections refractory to initial treatment and in unexpected PCR-negative samples. Depending on the PCR assay used, species identification and susceptibility testing normally requires fungal culture.

Species identification alone is not adequate to predict response to treatment. Detection of *SQLE* gene mutations directly in the specimen or on culture with an in-house or commercial assay is rapid and reliable, if detected. Antifungal susceptibility testing (AFST) is time consuming. Clinical breakpoints for antifungal agents and dermatophyte species are not established,

but tentative ECOFFs for terbinafine, voriconazole, itraconazole and amorolfine against *T. interdigitale* and *T. rubrum* are available and AFST is crucial for surveillance (8). AFST is not available in Norway and until 2025 all suspected terbinafine resistant isolates from the national mycology reference laboratory at OUS were referred to Statens Serum Institut (SSI), Copenhagen, Denmark for susceptibility testing by the EUCAST broth microdilution method and *SQLE* sequencing.

Terbinafine resistance in Norway

There has been a rapid increase in isolates submitted for AFST from only four isolates in 2020, to 29 in 2023 and 53 isolates sent from OUS to SSI in 2024. Among 85 dermatophyte isolates detected by culture in 2024, 53 isolates were referred for AFST. Forty-one of 85 dermatophytes were terbinafine resistant. Twenty-six of 28 *T. indotineae* and 15 of 19 *T. rubrum* isolates were confirmed terbinafine resistant. None of the isolates displayed itraconazole resistance. (Table 110). In 2025 the number of terbinafine resistant dermatophytes has increased further and due to capacity reasons only suspected terbinafine resistant isolates without *SQLE* gene mutations detected in our reference laboratory or suspected azole resistant isolates are routinely referred to SSI for susceptibility testing.

TABLE 110. Number of dermatophyte isolates detected at the Norwegian Reference Laboratory and sent to SSI for AFST 2024.

	T. indotineae	*T. rubrum*	Others	Total
Number of isolates at the reference laboratory	28	30	37	85
Number of isolates sent SSI for AFST	28	19	6*	53
Terbinafine susceptible isolates	2	4	6	12
Terbinafine resistant isolates	26	15	0	41
Itraconazole susceptible isolates	28	19	6	53
Itraconazole resistant isolates	0	0	0	0

SSI=Statens Serum Institut. AFST=Antifungal suscepotibility testing. **T. interdigitale* (n=2), *T. vialoceum* (n=2), *T. tonsurans* (n=1) and *Microsporum audouinii* (n=1).

Closing remarks

The emergence of the hypervirulent terbinafine resistant *T. indotineae* and spread of antimicrobial resistant dermatophytosis is suspected to be fueled by the use of topical antifungal-corticosteroid combination products, inappropriate prescription of antifungal drugs, misuse of over-the-counter topical antifungal drugs and inadequate adherence to prescribed courses of antifungal medication. All lessons known from AMR in bacteriology. The combination of unusual hypervirulence and resistance to the main antifungals used has resulted in a worldwide epidemic (4,9).

Although not severe, the clinical implications of difficult-to-treat dermatophytosis should not be underestimated. Extended infections or antifungal resistant dermatophytoses have become a global public health concern and challenge diagnostics and treatment of these infections (9). Clinicians and laboratories must be aware of and consider the possibility of *T. indotineae* infection and other difficult-to-treat dermatophytosis in patients with relevant anamnesis. Rapid diagnosis and prevention of inappropriate use of medications like steroids and ineffective antifungal agents is possible and necessary to stop further transmission.

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Appendix 1:
Material and methods for sales and use of antibacterial agents in animals

General information

In Norway, all medicinal products containing antibacterial agents are prescription-only medicines – this includes both veterinary medicinal products (VMPs) and human medicinal products (HMPs). The latter can be prescribed to animals according to the so-called cascade (Regulation (EU) 2019/6, Article 112-114) – i.e. if there is no VMP authorised for the condition, an HMP is allowed to be used. For food-producing species it requires that a maximum residue level (MRL) has been assigned for the active substance in question or that it is shown that an MRL is not necessary. Veterinarians in Norway are not allowed to dispense VMPs or HMPs, except for treatments until a pharmacy can provide the VMPs. In such cases the medicinal products must be sold at cost price.

Both VMPs and HMPs have to be dispensed through pharmacies that are supplied by wholesalers. Medicated feed (manufactured from premix VMPs) is supplied to the end user by feed mills and is currently only used for farmed fish; this is due to the small size of livestock herds in Norway and the low use of group/flock treatments. Group treatment of livestock (terrestrial animals) with antibacterial agents is administered through drinking water or as top-dressing on the feed.

Data sources

Sales data – terrestrial animals

Wholesalers and feed mills in Norway are mandated to provide sales statistics for all veterinary medicinal products, including when supplied as medicated feed, to the Norwegian Institute of Public Health (NIPH). Data on sales of each product presentation (name, form, strength and pack size) for terrestrial animals of the included VMPs (see table below) were obtained from the NIPH.

Use data – farmed fish and terrestrial animals

The Norwegian Food Safety Authority established the Veterinary Prescription Register (VetReg) for farmed fish 1 January 2011 and for terrestrial animals 1 January 2012. The veterinarians are mandated to report any administration and dispensings of VMPs and HMPs to VetReg for all terrestrial food-producing animals and horses while it is voluntary for all other animal species such as companion animals. Pharmacies and feed mills must report all dispensings, i.e. for all terrestrial animals and farmed fish, to veterinarians or animal owners, including medicines prescribed for companion animals and HMPs.

For farmed fish the reporting of use (kg active substance) of antibacterials, calculated from prescription data reported to VetReg, was shown to be in the same magnitude as the sales of the same VMPs reported by NIPH for the years 2013-2018 (1) and this is also the case for the years 2019-2024 (unpublished data). For the period 2013-2024, VetReg data are used for reporting of use of antibacterials for farmed fish.

For terrestrial food-producing animals the annual reporting of use (kg active substance) calculated from prescription data reported to VetReg was considerably lower by form and antibacterial substance when compared to the sales data from NIPH for the corresponding year (unpublished data). This is thought to be partly due to underreporting by pharmacies and veterinarians, but also due to several data-quality issues (2). Therefore, use data for terrestrial animals are not presented in this report in terms of kg used. It could not be verified whether the VetReg data are representative for the prescribing of VMPs by animal species, but as the prescribing patterns were relatively stable across this period and the data are believed to give a rough picture of the prescription patterns of antibacterial classes by animal species. VetReg data have therefore been used as an additional source to report use of antibacterial VMPs for the same food-producing terrestrial animal species for which use is mandatory to report to the European Medicines Agency (EMA) according to Regulation (EU) 2019/6, Article 57 (cattle, pigs, chicken and turkey). The use of VMPs and HMPs for cattle, pigs, chickens and turkeys was estimated by use of the following data reported to VetReg:

- Delivery to animal owners from pharmacies of antibacterial VMPs and HMPs for use in these species plus
- Veterinarians' use/delivery of antibacterial VMPs or HMPs for these species. Note that due to underreporting by veterinarians the data represents an underestimate.

The use of HMPs for companion animals was estimated by use of the following data reported to VetReg:

- Delivery to animal owners from pharmacies of antibacterial HMPs for use in companion animals.

Antibacterials included in the data set

The Anatomical Therapeutic Chemical classification system for veterinary medicinal products (ATCvet) classification system was used to identify the VMPs to be included in the data. Sales and use of VMPs belonging to the ATCvet codes shown in the table below were collected from the NIPH and from VetReg, respectively, for terrestrial animals. For farmed fish data were collected from VetReg. This is identical to the inclusion criteria by the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) (3). This also follows the inclusion criteria for sales data mandatory to report to the EMA from the reporting year 2023 according to Annex 1 of Commission Delegated Regulation (EU) 2021/578, except for an addition of three ATCvet codes: QA07AX03, QA07AX04 and QJ54. There were however no sales or use of VMPs belonging to any of these three ATCvet codes in 2023 or 2024. For the estimation of prescription of HMP antibacterials belonging to the ATC codes found in Annex 3 of Commission Delegated Regulation (EU) 2021/578 are included (extracted from VetReg data).

ATCvet codes/Antibacterial veterinary medicinal products included in the data.

Categories	ATCvet codes
Intestinal use	QA07AA; QA07AB
Intrauterine use	QG01AA; QG01AE, QG01BA; QG01BE; QG51AA; QG51AG
Systemic use	QJ01
Intramammary use	QJ51
Antiparasitic agents[1]	QP51AG

[1] Only sulfonamides

Antibacterial veterinary medicinal products belonging to the ATCvet categories shown in the table above and sold on special exemption from market authorisation are included in the sales data and prescription data. Dermatological preparations (QD) and preparations for sensory organs (QS) are not included in the data which is in accordance with the ESVAC protocol (4) and Annex 1 and 3 of (EU) 2021/578.

Data source animal population data. Denominator.

A method for calculating animal biomass was established to serve as a denominator for the reporting of ESVAC sales data (3). A new calculation of the biomass denominator was introduced for the reporting of European Sales and Use of Antimicrobials for Veterinary Medicine (ESUAvet) data (4). In the current report, biomass calculated according to ESVAC (in Figure 4, in text and in text box on ESUAvet page 25) and ESUAvet (text box on ESUAvet) has been used as denominator for sales of antibacterial VMPs. It is emphasised that the calculated biomass is purely a surrogate for the animal population at risk.

The biomass for each terrestrial animal category is calculated by multiplying numbers of livestock animals (cows, sows, sheep and horses) and slaughtered animals (cattle, pigs, sheep, goats, poultry and rabbits) by a theoretical weight at the most likely time for treatment (ESVAC) or at slaughter (ESUAvet). Both the animal categories included and the standard weights used differ somewhat between ESVAC and ESUAvet (3, 4)

The biomass is calculated for each species, weight class and/or production type, as follows:

- Number of animals slaughtered × standardised weight
- Number of livestock × standardised weight

The total biomass is calculated by summarising the above data. For farmed fish, biomass slaughtered fish is used in ESVAC and ESUAvet reports.

Data on animal population used to calculate biomass were obtained from Statistics Norway (https://www.ssb.no/jord[1]skog-jakt-og-fiskeri/jordbruk) and from a report (https:// ruralis.brage.unit.no/ruralis-xmlui/handle/11250/2367791) for horses; for the reporting year 2024 the national register of horses is used for horse population data. Living cows and sows are as reported pr October 1st, living sheep are as reported pr March 1st. From 2023 reporting pr March 1st is used for all species.

For farmed fish data on slaughtered biomass was obtained from the Norwegian Directorate of Fisheries (https://www.fiskeridir.no/Akvakultur/Tall-og-analyse/Akvakultur-statistikk-tidsserier). From 2023 data and onwards, the delivery registry for carcasses, available to the Norwegian Veterinary Institute, was additionaly used to obtain number of slaughtered animals per species of poultry and for lambs. The exact figures and references used for 2023 and 2024 are presented in Table 1 in the chapter Population statistics of the current report.

Analysis of the overall sales and use data

The sales and use data for each antibacterial VMP and HMP presentation were calculated to express weight of active substance. To comply with the ESVAC protocol (3), sales of derivatives (in previous report referred to as prodrugs) – e.g. procaine benzylpenicillin and penethamate hydriodide – have been calculated to the corresponding values for the active ingredient, here benzylpenicillin by use of standardised conversion factors (3). For VMPs where the strength is given in international units (IU), the weight of active substance has been calculated by use of ESVAC conversion factors for IUs (3). For data from 2023 and onwards, the conversion factors used in the ESUAvet report have been applied for sales data (5). ESVAC kept its own database with metadata on the VMPs (e.g on strength and active substance) while ESUAvet uses Union Product Database to obtain this information. Union Product Database's HMP counterpart is not fully functional yet and the Figures 5-7 therefore do not cover HMPs. For the estimations of use of HMPs, metadata were obtained from the Norwegian electronic prescription and support system, called FEST.

Stratification of sales data

The sales data of antibacterial VMPs for terrestrial animals have been split into sales for food-producing animals (including horses) and companion animals. Sales of antibacterial VMPs for companion animals refer to sales of tablets, injectables, oral solution and oral paste that are approved solely for companion animals; in addition, dihydrostreptomycin tablets of pack size 10 pieces have been included in the data on sales for companion animals (no sales after 2004). The other antibacterial VMPs are assumed sold for use only in food-producing animals (including horses). From the reporting year 2023 and onwards, the same stratification is done according to which species the VMPs are approved for: food-producing species if they are approved for any food-producing species, companion animals if not. This is in accordance with the ESUAvet methodology (4). There is some use in companion animals of VMPs marketed for food-producing animals. The sales are therefore slightly underestimated for companion animals and slightly overestimated for food-producing animals.

Sales data of VMPs for food-producing animals have been further stratified into VMPs for treatment of individual food-producing animals – i.e. bolus, oral paste, injectables, intramammary preparations, intrauterine preparations and tablets – and for group treatment – i.e. oral solution, including oral powder intended for solution, and oral powder.

Because cattle, pigs, sheep, and poultry accounted for more than 99% of the meat production in 2024 in Norway (https://www.ssb.no/slakt) these species as well as goats were included in a separate analysis of sales data. The sales data for 2013-2024 have been refined to obtain estimates on sales for the food-producing terrestrial species, exluding horses. Data on prescribtions per animal species obtained from the Veterinary Prescription Register (VetReg) have been used as supportive information for this refinement of the sales data. VetReg data show that for the years 2016-2023, more than 95% of the number of prescriptions of antibacterial oral paste VMPs were for horses. For 2024 this figure was 88%. Oral paste (numerator) and biomass for horses (denominator) have therefore been excluded from the analysis of data for the estimation of sales of antibacterial VMPs for cattle, pigs, sheep, goats and poultry.

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Appendix 2:
Collection and analysis of data on usage of antimicrobial agents in humans

Data sources
In Norway, antimicrobials are prescription only medicines, and only allowed sold through pharmacies. These data are collected from three databases: the Norwegian drug wholesales statistics database, the hospital pharmacies drug statistics database and the Norwegian Prescribed Drug Registry (NorPD).

The Norwegian Institute of Public Health collects data on drug use from wholesalers. The wholesales database covers total sales of antimicrobials to humans and animals in Norway and is based on sales of medicaments from drug wholesalers to pharmacies and healthcare institutions in Norway. The figures presented should be regarded as maximum figures based on the assumption that all medicaments sold are actually consumed. The actual drug consumption will probably be somewhat lower. Data are available since the beginning of the seventies.

Data on antibacterial use in hospitals are retrieved from *Sykehusapotekenes Legemiddelstatistikk* (the hospital pharmacies´ drug statistics database) which is a cooperation of the four regional pharmaceutical health trusts operating the hospital pharmacies in Norway. *Sykehusapotekenes Legemiddelstatistikk* collects sales data from each pharmacy delivering drugs to hospitals. Data are collected as sales from the pharmacy to hospital wards. Data have been available since 2006. Norwegian Centre for Antibiotic use in Hospitals (*Nasjonal kompetansetjeneste for antibiotikabruk i spesialisthelsetjenesten*) has analysed the data according to activity (bed-days).

Population statistics per 1 January are collected from Statistics Norway. Information on bed-days and admissions are collected from the Norwegian Patient Register. The definition of bed-days is: "*the number of whole days an admitted patient disposes a bed*". An admission is defined as: "*admission of patient where the medical interventions usually are complex and require hospitalisation for one or more days*" (1).

Data from nursing home setting is not available. However, the data is included in total sales data from the Norwegian drug wholesales statistics database and volume of use can be estimated. Antibiotics can be purchased through pharmacies or directly from wholesalers and the shares of the two may vary from one year to another. Due to this it is difficult to get exact sales and it hampers the ability to provide aggregated statistics in Norwegian nursing homes.

Data on the use in ambulatory care are retrieved from NorPD, a nation-wide prescription database situated at the Norwegian Institute of Public Health. This database includes all prescriptions being prescribed to out-patients in Norway. For analyses on prescriptions and DDDs, all prescriptions and DDDs to outpatients are included. For the results on annual prevalence (number of individuals per population group being prescribed antibiotics within a year) only prescriptions to individuals with national ID numbers are included. The data give us the exact population prevalence of antibacterial use in the total population in ambulatory care. More information is available at www.fhi.no. Data are available from 2004.

Drug Classification
The data are categorised according to the ATC classification system (2). Defined Daily Doses (DDDs) are employed as units of measurement. The ATC/DDD index of 2025 is used for all years.

Unit of measurement
The ATC/DDD system is recommended by the WHO to serve as a tool for drug utilisation research in order to improve quality of drug use. One component of this is the presentation and comparison of drug consumption statistics at international and other levels.

The use of defined daily dose (DDD) as a unit of measurement, simplifies and improves the evaluation of drug consumption over time, nationally and internationally. The DDD is a theoretical unit of measurement, and does not necessarily reflect the recommended or Prescribed Daily Dose.

The basic definition of the unit is:

The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults.

The DDDs for antibacterials are as a main rule based on the use in infections of moderate severity. Some antibacterials are only used in severe infections and their DDDs are assigned accordingly. The DDDs assigned are based on daily treatment.

Inclusion criteria
The antibacterials for human use included in this report belong to ATC group J01 *antibacterials for systemic use*. Oral vancomycin (A07AA09), fidaxomycin (A07AA12) and oral and rectal metronidazole (P01AB01) are also included in some figures. Antibacterials used in dermatological preparations (ATC group D) and preparations intended for sensory organs (ATC group S) are not included in the material.

References
1. Definitions Norwegian Patient Register https://www.fhi.no/he/npr/Ord-og-uttrykk-Norsk-pasientregister/
2. WHO Collaborating Centre for Drug Statistics Methodology. ATC index with DDDs 2025. WHO Collaborating Centre, Oslo

Appendix 3:
Sampling, microbiological methods and data processing in NORM-VET

Sampling strategy
The clinical isolates included in NORM-VET 2024 were *Campylobacter upsaliensis* (n=75) and *Streptococcus canis* from dogs (n=80 from ear infections and n=61 from infections in skin, urine, inner organs, etc.), and *Escherichia coli* from broilers (n=225) and turkey (n=47). Some of the *E. coli* isolates originated from the same flock, either from different animals or from different organs within an animal. All isolates were retrieved through clinical submissions to the Norwegian Veterinary Institute through the years 2020-2024 (*C. upsaliensis* from 2018-2024).

A total of 336 pooled samples from broilers were collected at slaughter for isolation of the indicator bacteria *Escherichia coli*, *Enterococcus faecalis* and *Enterococcus faecium*. From each poultry flock ten caecal samples were collected. Sampling was conducted by the Norwegian Food Safety Authority (NFSA) following the specifications set by EFSA (EFSA Journal 2019;17(6):5709).

In total, 326 broiler meat (one not analysed), 117 turkey meat (three not analysed), 318 sugar peas (three not analysed) and 345 dried fruit samples were collected at retail in all regions of Norway. Sampling was conducted by NFSA following the specifications set by EFSA (EFSA Journal 2019;17(6):5709). Samples were to be taken without taking place of origin into consideration, though only one sample per lot.

All the caecal and meat samples, and the samples of sugar peas and dried fruit, were used for selective isolation of *E. coli* resistant to extended spectrum cephalosporins (ESC) and carbapenem resistant *Enterobacterales* (CRE). In addition, selective isolation for vancomycin resistant *Enterococcus* spp. (VRE) was performed on the caecal samples. The meat samples were used for selective isolation of methicillin resistant *Staphylococcus aureus* (MRSA). The sugar peas and dried fruit samples were also used for isolation of the indicator bacteria *E. coli*, and selective isolation for colistin resistant *E. coli*.

Faecal and nasal swabs from 251 horses were collected by veterinarians. The horses sampled were from all over the country, and were between two months and 34 years old. A total of 18 horses were reported to have been abroad, the majority to Sweden or Denmark. Clinical symptoms from respiratory organs and the intestines were reported for eight and two horses, respectively. Antibiotic treatment had been given to 17 horses during the last year. With the exception of one horse, these were not the same horses reported to have clinical symptoms. The faecal samples were used for retrieving indicator *E. coli*, and for selective isolation of *E. coli* resistant to ESC and CRE. The nasal swabs were used for selective isolation of MRSA.

Indicator isolates of *E. coli*
Sample material, i.e. faecal content from horse and caecal content from ten broilers per flock were pooled and plated directly onto MacConkey agar (Difco). For sugar peas and dried fruit samples, aliquots of 10 µL from the overnight BPW-ISO broth was plated onto MacConkey agar (Difco). MacConkey agar plates were incubated at 44±0.5°C for 20±2h. Typical colonies were subcultured on blood agar and incubated at 37±1°C for 20±2h. Colonies were identified as *E. coli* by typical colony appearance and MALDI-TOF MS.

Indicator isolates of *E. faecalis* and *E. faecium*
Sample material, i.e. caecal content from ten broilers flocks were pooled and plated directly onto Slanetz and Bartley agar (Oxoid) and incubated at 44±0.5°C for 24-48h. Typical colonies were subcultured on blood agar incubated at 37±1°C for 20±2h. Colonies were identified as *E. faecalis* or *E. faecium* using MALDI-TOF MS.

Vancomycin resistant *Enterococcus* spp. (VRE)
Sample material, i.e. caecal content from ten broilers per flock were pooled and plated directly onto Slanetz and Bartley agar containing 4 mg/L vancomycin (Oxoid) and incubated at 44±0.5°C for 24-48h. Typical colonies were subcultured on Slanetz and Bartley agar containing 4 mg/L vancomycin and blood agar containing 5% bovine blood which were incubated at 37±1°C for 20±2h. Presumptive colonies were identified as *E. faecalis* or *E. faecium* by typical colony appearance and verified using MALDI-TOF MS.

Enrichment of samples before selective isolation
All samples were enriched prior to plating onto selective media. A total of 1±0.1 g caecal sample material was homogenised with 9 mL of BPW-ISO. Faecal swab samples from horses were inoculated in 5 mL of BPW-ISO. A total of 25±0.5 g sample material of broiler and turkey meat, sugar peas and dried fruit, was homogenised with 225 mL of BPW-ISO. Samples were incubated at 37±1°C for 20±2h according to the protocol from EURL-AR (https://www.eurl-ar.eu/protocols.aspx). After incubation, aliquots of the enrichment broth were plated onto selective media as described in the sections below.

***E. coli* resistant to extended spectrum cephalosporins (ESC)**
Aliquots from the overnight BPW-ISO broth from all faecal, caecal, meat, sugar peas, and dried fruit samples were plated onto MacConkey agar containing 1 mg/L cefotaxime and MacConkey agar containing 2 mg/L ceftazidime. The agar plates were incubated at 44±0.5°C for 18-24h. Presumptive ESC resistant *E. coli* were subcultured on MacConkey agar containing 1 mg/L cefotaxime and blood agar and confirmed as *E. coli* using MALDI-TOF MS before further phenotypical testing.

Carbapenem resistant *Enterobacterales* (CRE)
Aliquots from the overnight BPW-ISO broth from all faecal, caecal, meat, sugar peas, and dried fruit samples were plated onto CHROMID® CARBA and CHROMID® OXA-48 agar (bioMérieux, Marcy l'Etoile, France). The plates were incubated at 35±2°C for 18-22h. Presumptive CRE were subcultured on respective CHROMID® agar and blood agar, and species confirmed using MALDI-TOF MS before further phenotypical testing.

Colistin resistant *E. coli* (COL-R)
Before enriching the BPW-ISO broth containing sugar peas or dried fruit, 9 mL were transferred to a new tube and a 10 µg colistin disc was added. The tubes were incubated for 4-5h at 35±2°C. From the 9 mL tube, an aliquot of 50 µL was plated onto CHROMID® Colistin R agar (bioMérieux, Marcy l'Etoile, France) and the plates were incubated at 35±2°C for 18-24h. Presumptive COL-R were subcultured on CHROMID® agar and blood agar, and species confirmed using MALDI-TOF MS before further phenotypical testing.

Methicillin resistant *Staphylococcus aureus* (MRSA)
Nasal swabs from horses, as well as broiler and turkey meat samples, were analysed for methicillin resistant *Staphylococcus aureus* (MRSA). The nasal swabs were inoculated in 5 mL of Mueller-Hinton broth containing 6.5% NaCl and sample material from meat (25±0.5g) was chopped in pieces and incubated in Mueller-Hinton broth containing 6.5% NaCl at 37±1°C for 18-24 hours. A loopful of the overnight broth (10 µL) was plated onto Brilliance™ MRSA2 agar plate (Oxoid). Suspected colonies were subjected to species identification using MALDI-TOF MS before further phenotypical testing.

Genotyping
For genotyping of presumptive resistant isolates, whole genome sequencing (WGS) was performed at the NVI on an illumina® MiSeq or Illumina® NextSeq (Illumina, San Diego, California, USA). Paired end reads were subjected to analysis for both acquired genes and chromosomal point mutations using the ResPointFinder pipeline (commit 0cff411016d17acda1f76a88b5cdb5786e83973e) which the NVI has implemented on the IRIDA platform (www.irida.ca).

Susceptibility testing
Isolates were tested for antimicrobial susceptibility using a broth microdilution method at the NVI. Minimum inhibitory concentration (MIC) values were obtained using plates from Sensititre® (TREK Diagnostic LTD) with different panels depending on the bacteria to be tested as recommended by Decision 2020/1729/EU. Epidemiological cut-off values (ECOFF) recommended by the European Committee on Antimicrobial Susceptibility Testing (EUCAST, accessed 24.01.2024) were used with some exceptions as explained further in Appendix 7. See Appendix 6 for definitions of cut-off values. The table below gives an overview of which panel was used for which clinical isolate.

Overview of which Sensititre® TREK panel was used for which clinical isolate:

Clinical isolate tested	Sensititre® TREK panel
Campylobacter upsaliensis	EUCAMP3
Streptococcus canis	CLIN strep/staph* and/or CLIN lokal*
Escherichia coli	CLIN GN*

*Clinical panels designed at and purchased through Statens Veterinärmedicinska Anstalt.

Quality assurance systems
The following susceptible bacteria were included as quality control on a regular basis: *E. coli* ATCC 25922, *E. faecalis* ATCC 29212, *C. jejuni* ATCC 33560, and *S. pneumoniae* CCUG 33638/ATCC 49619 (CLIN strep/staph and/or CLIN lokal). In addition to the regular susceptible bacteria, the following bacteria received from EURL-AR were included: *Acinetobacter baumannii* 2012-70-100-69 (EUVSEC3 and EUVSEC2 panel), *C. coli* 2015-QC-ETP (EUCAMP3 panel), and *E. faecium* 2012-70-76-8 and *E. faecalis* 2012-70-103-3 (EUVENC panel). The results were approved according to reference values given by EUCAST when available. Additional control strains were included when necessary. The laboratories at the NVI are accredited according to the requirements of NS-EN ISO/IEC 17025 and participate in quality assurance programmes for veterinary pathogens (Veterinary Laboratories Agency Quality Assurance Unit, Loughborough, UK) and for resistance monitoring (EURL for Antimicrobial Resistance in Denmark).

Data processing
Susceptibility data were recorded and stored in the sample registration system at the NVI as discrete values (MIC). Data management was performed using SAS-PC System® v 9.4 for Windows (SAS Institute Inc. Cary. NC. USA) and R version 4.4.1 Copyright (C) 2024 (The R Foundation for Statistical Computing Platform), while the statistical analysis was performed in R. A chi-square test was used for assessing possible differences of occurrences. All differences yielding a p-value <0.05 were considered as statistically significant. However, because isolates from clinical submissions can have the same origin, the chi-square test is not the most appropriate test for such comparisons, thus any significant results need to be considered with care. For most comparisons the partial overlap will not have an impact. The 95% confidence intervals were calculated using the exact binomial test.

Appendix 4:
Sampling, microbiological methods and data processing of zoonotic and non-zoonotic enteropathogenic bacteria in NORM and NORM-VET

NORM-VET enteropathogenic bacteria
Sampling strategy – animals and food

Salmonella spp.

Isolates of *Salmonella* spp. were retrieved from the Norwegian *Salmonella* control programme for live animals, and from the surveillance of wild boar. Additional isolates were obtained from submissions to the National Reference Laboratory for Salmonella, and from clinical submissions or necropsies at the Norwegian Veterinary Institute (NVI). One isolate of each serovar per incident was included for susceptibility testing.

Campylobacter jejuni

Caecal samples were collected by the Norwegian Food Safety Authority at slaughter. Ten caecal samples from broilers were collected from each flock identified as *Campylobacter* positive in the surveillance programme for *Campylobacter* spp. in broiler flocks, and from flocks with unknown *Campylobacter* status. Caecal contents from ten broilers per flock were pooled and plated directly onto mCCDA agar (Oxoid) and incubated under microaerobic conditions at 41.5±1°C for 44±4h. Typical colonies were subcultured on blood agar and confirmed as *Campylobacter jejuni* using Matrix Assisted Laser Desorption/Ionization - Time of Flight Mass Spectrometry (MALDI-TOF MS) (Bruker Daltonics GmbH).

Susceptibility testing animal isolates

Isolates were tested for antimicrobial susceptibility at the NVI. MIC values were obtained using plates from Sensititre® (TREK Diagnostic LTD) with different panels depending on the bacteria to be tested as recommended by Decision 2020/1729/EU, see table below. For animal isolates, epidemiological cut-off (ECOFF) values recommended by the European Committee on Antimicrobial Susceptibility Testing (EUCAST, accessed 24.01.2024) were used, with some exceptions as further explained in Appendix 7.

Overview of Sensititre® TREK panels used:

Bacteria tested	Sensititre® TREK panel
Salmonella spp.	EUVSEC3
Camplylobacter jejuni/coli	EUCAMP3

Quality assurance systems NORM-VET

The following susceptible bacteria were included as quality controls on a regular basis: *E. coli* ATCC 25922 and *C. jejuni* ATCC 33560. In addition to the regular susceptible bacteria, the following bacteria received from EURL-AR were included: *C. coli* 2015-QC-ETP (EUCAMP3 panel) and *Acinetobacter baumannii* 2012-70-100-69 (EUVSEC3). The NVI laboratories are accredited according to the requirements of NS/EN ISO/IEC 17025 and participate in external quality assurance programmes for veterinary pathogens (Veterinary Laboratories Agency Quality Assurance Unit Loughborough, UK) and for resistance monitoring (EURL for Antimicrobial Resistance, Denmark).

Data processing animal isolates

Susceptibility data were recorded and stored in the sample registration system at NVI as discrete values (MIC). Data management was performed using SAS-PC System® v 9.4 for Windows (SAS Institute Inc. Cary. NC. USA) and R version 4.4.1 Copyright (C) 2024 (The R Foundation for Statistical Computing Platform), while the statistical analysis was performed in R. All changes and differences yielding a p-value <0.05 were considered as statistically significant. The 95% confidence intervals were calculated using the exact binomial test.

NORM - enteropathogenic bacteria
Sampling strategy - humans

All human isolates of *Salmonella, Yersinia enterocolitica* and *Shigella* were obtained from clinical cases. One isolate per patient or one isolate per recognised outbreak was included for susceptibility testing. *Campylobacter* isolates from a selection of a little less than 10% of campylo-bacteriosis cases registered were submitted in the following way: Two regional laboratories submitted the first ten and two submitted the first five isolates each month to the NRL for Enteropathogenic Bacteria at the Norwegian Institute of Public Health.

Identification of bacteria – human isolates

The reference analyses on human clinical isolates of enteropathogenic bacteria were performed according to conventional methods described in standard reference literature (e.g. Murray PR & al.: Manual of Clinical Microbiology, 8th edition ASM-Press, Washington 2003 and Ewing WH: Edwards and Ewing's Identification of *Enterobacteriaceae*, 4. edition, Elsevier, New York 1986).

Susceptibility testing – human isolates

Salmonella spp., *Yersinia* spp. and *Shigella* spp. isolates from humans were susceptibility tested at the NRL for Enteropathogenic Bacteria at the NIPH by agar disk diffusion tests according to the EUCAST standardised method for AMR testing of non-fastidious bacteria. *Campylobacter* isolates from humans were tested for antimicrobial susceptibility using MIC Test Strips.

For human isolates EUCAST clinical breakpoints for *Enterobacteriaceae*, v.15.0 2025 were used if defined. In absence of clinical breakpoints, ECOFFs or national zone distributions were used (e.g. tetracycline). Pefloxacin was used to infer ciprofloxacin resistance in *Salmonella* and *Shigella*.

Isolates with reduced susceptibility to cefotaxime or ceftazidime were tested for the presence of $ESBL_A$ by a double disk approximation test, and for the presence of $ESBL_M$ by an AmpC detection test. Isolates with reduced susceptibility to meropenem were forwarded to Norwegian Centre for Detection of Antimicrobial Resistance (K-Res) for further analyses.

Genotyping – human isolates

All *Enterobacterales* isolates received at NRL from primary diagnostic laboratories in Norway were screened

for antimicrobial resistance determinants using NCBI AMRFinderPlus (v.3.11.26) following whole genome sequencing (paired end, Illumina) and *de novo* assembly (SKESA 2.4.0) in Ridom SeqSphere+ (v.10.0.0).

Quality assurance systems – human isolates

The NRL for Enteropathogenic Bacteria at the NIPH is accredited according to the requirements of NS-EN ISO/IEC 17025. *E. coli* ATCC 25922 was used as quality control strain for AMR testing of non-fastidious *Enterobacteriaceae.* The NRL participated in the external quality assessment programme of ECDC for *Salmonella* spp. and *Campylobacter* for antimicrobial susceptibility testing.

Data processing – human isolates

The NRL at the NIPH stores susceptibility data of human isolates as either millimeter zone diameters or MIC values. The results were further analysed by WHONET 5.6 with the aid of the BacLink programme, both developed by Dr. John Stelling.

Appendix 5: Sampling, microbiological methods and data processing in NORM

General considerations and sampling

NORM is based on a combination of periodic sampling and testing in primary diagnostic laboratories, and annual results from national reference laboratories for specific microoganisms. Isolates are included from defined clinical conditions such as respiratory tract infections, wound infections, urinary tract infections, and sepsis. Surveillance schemes 2000-2024 are presented in the table below, for enteric infections see Appendix 4. In 2024, all 21 diagnostic laboratories in Norway participated in the surveillance system in addition to eleven reference laboratories. All diagnostic laboratories followed the same sampling strategy and used identical criteria for the inclusion of microbial strains. Only one isolate per patient and infectious episode was included unless otherwise stated. All microbes were identified using conventional methods as described in the ASM Manual of Clinical Microbiology. The surveillance period started in the beginning of January, and consecutive isolates were included for defined time periods for each surveillance category. The surveillance categories and sampling periods in 2024 were as follows: *E. coli* from blood cultures (6 months); *Klebsiella* spp., *Enterococcus* spp., *Staphylococcus aureus* and *Streptococcus dysgalactiae* from blood cultures (9 months); *Candida* spp. from blood cultures (12 months); *Streptococcus pneumoniae*, *Streptococcus pyogenes, Streptococcus agalactiae, Haemophilus influenzae* and *Neisseria meningitidis* from blood cultures and cerebrospinal fluids (12 months); *S. aureus* (1 week), *S. pyogenes* (3 weeks) and *S. dysgalactiae* (3 weeks) from wound specimens; *S. pyogenes* and *S. dysgalactiae* from respiratory tract specimens (3 weeks); *E. coli* (3 days) and *Klebsiella* spp. (3 weeks) from urinary tract infections; and *Mycobacterium tuberculosis* and *Neisseria gonorrhoeae* from all specimen types (12 months). *S. pneumoniae*, *S. pyogenes*, *N. meningitidis* and *H. influenzae* from blood cultures and cerebrospinal fluids were analysed at the the Norwegian Institute of Public Health (NIPH) in Oslo. *N. gonorrhoeae* was analysed at NIPH and Oslo University Hospital (OUS)/Ullevål. *Candida* spp. isolates were analysed at OUS/ Rikshospitalet. MRSA and *S. agalactiae* isolates were analysed at St. Olav University Hospital in Trondheim. *M. tuberculosis* isolates were analysed at NIPH, OUS/Ullevål and Rikshospitalet.

Susceptibility testing

E. coli, *Klebsiella* spp., *Enterococcus* spp., *S. aureus, S. dysgalactiae* and *S. pyogenes* (wound and respiratory tract) isolates were examined according to the EUCAST disk diffusion method using antibiotic disks and Mueller Hinton II agar from either Oxoid or Beckton Dickinson. Suitable antibiotics were selected for each bacterial species, and the results were interpreted according to the most recent breakpoints from NordicAST, which are harmonised with EUCAST. Beta-lactamase production in *S. aureus* and *N. gonorrhoeae* was examined by nitrocefin disks, acidometric agar plates (3.6 mg/L penicillin G and phenol red) or clover leaf test. *Enterococcus* strains were screened for glycopeptide resistance using vancomycin 6 mg/L BHI agar. *H. influenzae*, *S. pyogenes* (blood and cerebrospinal fluids), *S. agalactiae*, *N. meningitidis* and *N. gonorrhoeae* were susceptibility tested using MIC gradient tests (bioMerieux or Liofilchem) on MH II agar supplemented with 5% lysed horse blood or GC agar with 1% haemoglobin and Isovitalex (*N. gonorrhoeae*), whereas *S. pneumoniae* isolates were examined using Sensititre microdilution plates from Thermo Fisher Scientific. Susceptibility testing of *Candida* spp. isolates was performed by MIC gradient tests using RPMI agar containing 2% glucose and MOPS. Resistance values were recorded as inhibition zone sizes or MIC values in order to monitor trends in the occurrence of resistance. *M. tuberculosis* isolates were tested using the BACTEC MGIT 960 systems. All three test laboratories for *M. tuberculosis* participate in the WHO external DST quality control programme. They were also tested for mutations in the *rpoB* gene to detect rifampicin resistance.

Confirmation of resistance phenotypes

E. coli and *Klebsiella* spp. with reduced susceptibility to 3rd generation cephalosporins were examined for ESBL production using ESBL combination MIC gradient tests (Liofilchem), disks (BD) or tablets (Rosco) according to the instructions of the manufacturer. *S. aureus* isolates with reduced susceptibility to cefoxitin were examined by *mecA* PCR for confirmation of methicillin resistance (MRSA). *Enterococcus faealis* and *E. faecium* isolates displaying growth on the vancomycin screening agar were examined by *van* PCRs. The MLS phenotype of erythromycin resistant *S. aureus, S. pyogenes, S. agalactiae, S. dysgalactiae,* and *S. pneumoniae* isolates were analysed using the double disk diffusion (DDD) synergy assay with erythromycin and clindamycin disks.

Molecular typing and characterisation of isolates

The NORM report includes specific molecular analyses of carbapenemase-producing Gram-negatives, vancomycin resistant enterococci (VRE) and linezolid resistant enterococci (LRE). These microbes are notifiable to the Norwegian Surveillance System for Communicable Diseases (MSIS) and characterised by the Norwegian Centre for Detection of Antimicrobial Resistance (K-res). The analyses include whole genome sequencing of the isolates followed by analysis for resistance genes/mutations and molecular typing. Presence of resistance genes/ mutations was analysed using AMR-FinderPlus combined with the Bacterial Antimicrobial Resistance Reference Gene Database (1) plus LRE-Finder specifically for linezolid resistance markers (2). Molecular typing of the isolates was performed at two hierarchal levels using species-specific multilocus sequence typing (MLST) schemes, standard MLST and core genome MLST (cgMLST). Standard MLST includes comparison of the sequence of seven defined species-specific house-keeping genes (alleles) where each allele is assigned an arbitrary number. The standard MLST scheme enables definition of a specific sequence type (ST) (see e.g. https://pubmlst.org/). In contrast, cgMLST includes a defined set of ~1400-3800 alleles depending on the species allowing for analysis at a higher resolution (see e.g. references 3 and 4). For each cgMLST scheme a defined reference genome is applied and the analysis includes an allele-by-allele comparison with

defined thresholds for cluster analysis (https://www.cgmlst.org/ncs). A comparison table is used for distance calculation and enables creation of a minimum spanning tree (MST) (5). In the MST, isolates are visualised as circles and lines are created between the closest related isolates. This creates a network of the population. The length of the line is not proportional to the evolutionary distance. However, the number of allele differences between samples are indicated in the MST. Using species-specific defined cut-offs of allele differences for cluster determination, clusters of closely related isolates can be determined and visualised.

References

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Quality control

The following strains were used for quality control: *E. coli* ATCC 25922, *K. pneumoniae* ATCC 700603 (ESBL positive), *E. faecalis* ATCC 29212, *E. faecalis* ATCC 51299 (*vanB* positive), *S. pneumoniae* ATCC 49619, *S. pneumoniae* TIGR4, *S. aureus* ATCC 29213, *S. aureus* ATCC 25923, *S. aureus* ATCC 43300 (heterogeneous MRSA), *S. aureus* CCUG 35600 (homogeneous MRSA), *H. influenzae* ATCC 49766, *N. gonorrhoeae* CCUG 26213/ ATCC 49266, *N. gonorrhoeae* WHO L, *C. albicans* ATCC 90028, *C. krusei* ATCC 6258 and *C. parapsillosis* ATCC 22019.

Data processing

The specially designed web-based eNORM computer programme was used for registration and storage of patient data, sample data and resistance data. The results were further analysed by WHONET 5.6 with the aid of the BacLink programme, both developed by Dr. John Stelling. The distribution of microbial species in blood culture was based on extraction of routine data from the laboratory information systems of the participants. Additional isolates of the same species from the same patient recovered within one month after the initial finding were considered duplicates and omitted from the survey. No attempts were made to evaluate the clinical significance of each finding.

	Microbe	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Respiratory tract	*S. pneumoniae*	50	50		50		50		3 w		3 u			3 w		3 w		3 w		3 w		3 w			3 w	
	H. influenzae	50	50			25			3 w				3 w			3 w			3 w					3 w		
	S. pyogenes			50		25		25		2 w					3 w						3 w					3 w
	GCS/GGS																									3 w
	M. catarrhalis				50					4 w																
Urine	*E. coli*	50	50	50	50	50	50	50	1 w	2 d	2 d	2 d	2 w	2 d	2 d	3 d	3 d	3 d	3 d	3 d	3 d	1 w	3 d	3 d	3 d	3 d
	Klebsiella spp.	50	50		50						3 u			3 w	3 w	3 w	3 w	3 w	3 w	3 w	3 w	3 w	3 w	3 w	3 w	3 w
	Enterococcus spp.	50	50									2 w					3 w			3 w						
	Enterobacter spp.						50											3 w						3 w		
	Citrobacter spp.																							3 w		
	Serratia spp.																							3 w		
	Proteus spp.							25											3 w							
	P. aeruginosa																				3 w					
Wounds	*S. aureus*		50		50	50		50	2 w	2 w	2 u	1 w	1 w	1 w	1 w	1 w	1 w	1 w	1 w	1 w	1 w	1 w	1 w	1 w	1 w	1 w
	S. lugdunensis			50		25		25		4 w					3 w						3 w				3 m	
	S. pyogenes			50		25		25		4 w					3 w						3 w					3 w
	GCS/GGS																			4 w						3 w
Blood	*E. coli*	50	50	50	50	50	50	50	6 m	6 m	6 m	6 m	6 m	6 m	6 m	6 m	6 m	6 m	6 m	6 m	6 m	6 m	6 m	6 m	6 m	6 m
	Klebsiella spp.	25	25	25	25	25	25	25	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m
	Enterobacter spp.							12 m	12 m	9 m								9 m						9 m		
	Citrobacter spp.																							9 m		
	Serratia spp.																							9 m		
	Proteus spp.																		9 m							
	P. aeruginosa			12 m	12 m				12 m			12 m					9 m				9 m				12 m	
	Acinetobacter spp.								12 m	12 m															12 m	
	*H. influenzae**														12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m
	*N. menigitidis**														12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m
	S. aureus	50	50	50	50	50	50	50	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m
	S. lugdunensis																								12 m	
	Enterococcus spp.	20	20	20	20	20	20	20	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m	9 m
	*S. pneumoniae**	50	50	50	50	50	50	50	9 m	9 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m
	S. pyogenes (GAS)*						12 m	12 m							12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m
	S. agalactiae (GBS)*							50		12 m			12 m			12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m
	GCS/GGS																			12 m						9 m
	Obligate anaerober			12 m	12 m	12 m				12 m	12 m	12 m				12 m						12 m				
	Candida spp.							12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m
All locations	*N. gonorrhoeae*											12 m			12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m
	M. tuberculosis	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m	12 m

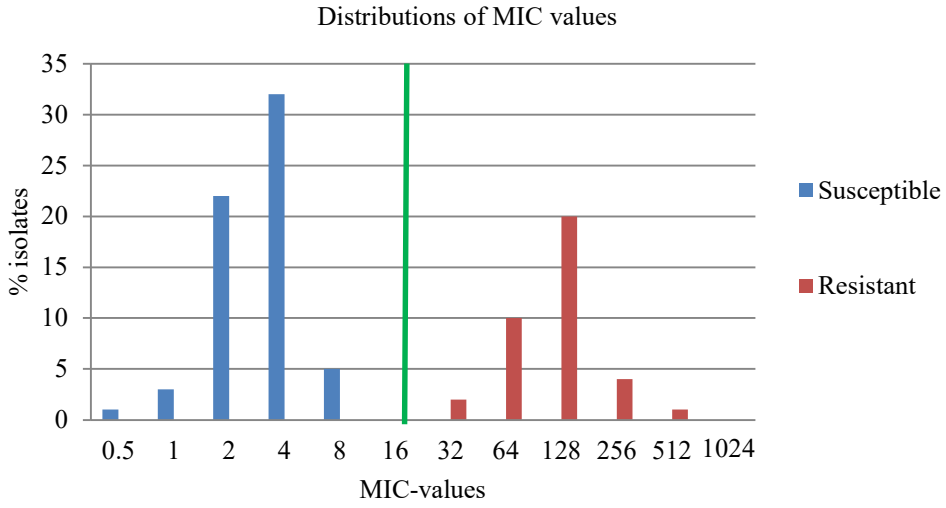
Surveillance at reference laboratories in red. d=days; w=weeks; m=months. *Also included isolates from cerebrospinal fluids.

Appendix 6:
Definitions and classification of resistances used in this report

General guidelines for the reader of this report

The results presented in the NORM and NORM-VET programmes are not directly comparable. This is because the sampling and also the classification of resistance differ between the programmes. Clinical breakpoints are used for the classification within NORM, while epidemiological cut-off values (ECOFF) are used for the classification of resistance within NORM-VET.

The terms and usage of these two ways of classification of resistance are further explained below. The ECOFF would normally be lower for minimum inhibitory concentration (MIC) values and higher for disk diameters than the clinical breakpoints. However, this is not always the case.



Epidemiological cut-off values

Based on the distribution of the MIC values, or the inhibition zone diameter distribution, each bacterial population could (in an ideal case) be divided into two sub-populations by a biphasic curve as shown in the example above. The curve to the left (blue) shows the susceptible or wild type distribution, whereas the curve to the right (red) shows the resistant or non-wild type distribution. In NORM-VET we have chosen to define the non-wild type distribution as resistant. The green line indicates a possible ECOFF value applicable to the distributions in the example. ECOFF may be used to detect emerging resistance in the bacterial populations.

However, for several bacterial populations and corresponding tested antimicrobial substances these distributions may be overlapping. A part of the population within the overlapping area may carry resistance mechanisms and others not. In the area with the non-wild type distribution, new resistance mechanisms are responsible for the resistance either alone or in addition to the resistance mechanisms present at lower MIC values. In order to establish MIC values for each specific bacterial population and antimicrobial agent, large amounts of data are collected and assessed. In the NORM-VET part of this report, we have mainly used the ECOFF values recommended by EUCAST.

Clinical breakpoints

Clinical breakpoints are defined in order to indicate if treatment of a specific pathogen is likely to succeed or not. Other factors like dosage and formulations also affect the clinical result. The MIC values are ideally obtained for the pathogen *in vitro*, and this is compared with the pre-determined clinical breakpoint to determine whether the organism is likely to respond *in vivo*.

Term used to describe antimicrobial resistance levels

In this report the levels of resistance (i.e. the percentage of resistant isolates among the tested isolates) in the NORM-VET programme have been classified according to the levels presented in the EFSA and ECDC Summary Report from 2021 and 2022, as follows:

Rare:	< 0.1%
Very Low:	0.1% to 1%
Low:	> 1% to 10%
Moderate:	> 10% to 20%
High:	> 20% to 50%
Very high:	> 50% to 70%
Extremely high:	> 70%

Appendix 7: Cut-off values NORM-VET

Epidemiological cut-off (ECOFF) values recommended by the European Committee on Antimicrobial Susceptibility Testing (EUCAST, accessed 24.01.2025) were used. For additional antimicrobial agents not defined in the EUCAST recommendations, EFSA recommended cut-off values were used, and some clinical breakpoints for clinical isolates.

In the NORM-VET figures; the penicillins are grouped together in the class Beta-lactams/penicillins; trimethoprim and sulfonamides are grouped together in the class Sulfonamides and trimethoprim; macrolides, lincosamides and streptogramins are grouped together in the class Macrolides/lincosamides/streptogramins, and the streptomycins are grouped together with other aminoglycosides in the class Aminoglycosides.

Overview of the antimicrobial classes and agents tested for with corresponding epidemiological cut-off values (mg/L) used in NORM-VET 2024:

Antimicrobial class	Antimicrobial agents	*Escherichia coli* (indicators)	*Salmonella enterica*	*Campylobacter coli* / *C. jejuni*	*Enterococcus faecalis* / *E. faecium*	*Escherichia coli* (clinical isolates)	*Streptococcus canis* (systemic infections/local ear infections)	*Campylobacter upsaliensis***
Tetracyclines	Tetracycline	>8	>8	>2 / >1	>4	>8	>2*	>2
	Tigecycline	>0.5	ND		>0.25			
Amphenicols	Chloramphenicol	>16	>16	>16	>32		>8**	>16
	Florfenicol						>4	
Penicillins with extended spectrum	Ampicillin	>8	>4		>4	>8		
	Temocillin	(>16)						
Beta-lactamase sensitive penicillins	Benzylpenicillin						>0.03*	
Combinations of penicillins, incl. beta-lactamase inhibitors	Amoxicillin-clavulanate					>8		
1st generation cephalosporins	Cefalexin					>32	ND	
2nd generation cephalosporins	Cefoxitin	(>16)						
3rd generation cephalosporins	Cefotaxime	>0.25	>0.5			>0.25		
	Ceftazidime	>1	>2					
Combinations of 3rd generation cephalosporins and clavulanic acid	Cefotaxime/clavulanate	(>0.25)						
	Ceftazidime/clavulanate	(>1)						
4th generation cephalosporins	Cefepime	(>0.125)						
Carbapenems	Meropenem	>0.06	ND			>0.06		
	Ertapenem	(>0.03)		ND/>0.125				>0.125
	Imipenem	(ND)						
Trimethoprim and derivatives	Trimethoprim	>2	>2					
Sulfonamides	Sulfamethoxazole	>64#	ND					
Combinations of sulfonamides and trimethoprim, incl. derivates	Sulfamethoxazole and trimethoprim					>0.5	>0.125	
Macrolides	Erythromycin			>8 / >4	>4		>0.25	>4
	Azithromycin	>16	>16					
Lincosamides	Clindamycin						>0.5*	

Antimicrobial class	Antimicrobial agents	*Escherichia coli* (indicators)	*Salmonella enterica*	*Campylobacter coli* / *C. jejuni*	*Enterococcus faecalis* / *E. faecium*	*Escherichia coli* (clinical isolates)	*Streptococcus canis* (systemic infections/local ear infections)	*Campylobacter upsaliensis***
Streptogramins	Quinupristin and dalfopristin				>32 / >2			
Other aminoglycosides	Gentamicin	>2	>2	>2	>64 / >32	>2		>2
	Amikacin	>8	>4					
	Neomycin					>8		
Fluoroquinolones	Ciprofloxacin	>0.064	>0.064	>0.5	>4 / >8			>0.5
	Enrofloxacin					>0.125	>2**	
Other quinolones	Nalidixic acid	>8	>8					
Glycopeptid antibacterials	Vancomycin				>4			
	Teicoplanin				>2			
Polymyxins	Colistin	>2	ND			>2		
Nitrofuran derivates	Nitrofurantoin					>64	>64**	
Other antibacterials	Linezolid				>4			
	Daptomycin				>4 / >8			

ND = not defined, ( ) = only ESBL/AmpC suspected isolates tested as described in Commission Implementing Decision of 17. Nov 2020 on the monitoring and reporting of antimicrobial resistance in zoonotic and commensal bacteria (2020/1729/EU), data not shown in the report tables. #Cut-offs defined by EFSA. *Cut-offs defined by Streptococcus Group G. **Cut-offs defined by clinical breakpoints. For nitrofurantoin, breakpoint for *Streptococcus agalactia* was used.

Appendix 8: Breakpoints NORM

NORM data are categorised according to the breakpoints of the Nordic Committee on Antimicrobial Susceptibility Testing (NordicAST) which are harmonised with EUCAST breakpoints. NordicAST breakpoints are available at www.nordicast.org.

Zoonotic and non-zoonotic enteropathogenic bacteria are also categorised based on EUCAST epidemiological cut-off values (ECOFF) as specified below.

Antimicrobials	MIC (mg/L)		*Escherichia coli*	*Klebsiella* spp.	*Haemophilus influenzae*	*Neisseria meningitidis*	*Neisseria gonorrhoeae*	*Salmonella* spp.	*Shigella* spp.	*Yersinia enterocolitica*	*Campylobacter jejuni*	*Campylobacter coli*	*Staphylococcus aureus*	*Enterococcus* spp.	*Streptococcus pneumoniae*	*Streptococcus pyogenes*	*Streptococcus agalactiae*	*Streptococcus dysgalactiae*	*Candida albicans*	*Candida glabrata*	*Candida tropicalis*	*Candida parapsilosis*	*Candida dubliniensis*
	S	R																					
Amphotericin B	≤ 1	> 1																	■	■	■	■	■
Ampicillin	≤ 1	> 1			■																		
	≤ 4	> 4						■[1]						■									
	≤ 8	> 8	■					■	■[2]	■[2]													
Amoxi-Clav*	≤ 2	> 2			■																		
	≤ 8	> 8	■	■[4]																			
	≤ 32	> 32	■	■[4]																			
Anidulafungin	≤ 0.016	> 0.016																	■				
	≤ 0.03	> 0.03																					■
	≤ 0.06	> 0.06																		■	■		
	≤ 4	> 4																				■	
Aztreonam	≤ 1	> 4	■	■																			
Cefalexin	≤ 16	> 16	■	■[4]																			
Cefepim	≤ 1	> 4	■	■																			
Cefixime	≤ 0.125	> 0.125					■																
Cefotaxime	≤ 0.125	> 0.125			■																		
	≤ 0.25	> 0.25								■[1]													
	≤ 0.5	> 0.5						■[1]															
	≤ 0.5	> 2													■								
	≤ 1	> 2	■	■				■	■[2]	■													
Cefoxitin	≥ 22 mm	< 22 mm											■										
Ceftaroline	≤ 1	> 2											■										
Ceftazidime	≤ 1	> 4	■	■				■	■[2]	■[2]													
	≤ 2	> 2						■[1]															
Ceftriaxone	≤ 0.125	> 0.125			■	■	■																
	≤ 0.5	> 2													■								
Cefuroxime	≤ 1	> 2			■																		
Chloramphenicol	≤ 2	> 2			■	■																	
	≤ 8	> 8						■[2]	■[2]	■[2]													

Antimicrobials	MIC (ml/L) S	MIC (ml/L) R	*Escherichia coli*	*Klebsiella* spp.	*Haemophilus influenzae*	*Neisseria meningitidis*	*Neisseria gonorrhoeae*	*Salmonella* spp.	*Shigella* spp.	*Yersinia enterocolitica*	*Campylobacter jejuni*	*Campylobacter coli*	*Staphylococcus aureus*	*Enterococcus* spp.	*Streptococcus pneumoniae*	*Streptococcus pyogenes*	*Streptococcus agalactiae*	*Streptococcus dysgalactiae*	*Candida albicans*	*Candida glabrata*	*Candida tropicalis*	*Candida parapsilosis*	*Candida dubliniensis*
Ciprofloxacin	≤ 0.001	> 0.5									■[2]	■[2]											
	≤ 0.001	> 2											■										
	≤ 0.016	> 0.016				■																	
	≤ 0.03	> 0.03			■																		
	≤ 0.03	> 0.06					■																
	≤ 0.06	> 0.06						■[2]	■[2]														
	≤ 0.125	> 0.125								■[1]													
	≤ 0.25	> 0.5	■	■						■													
Clindamycin	≤ 0.25	> 0.25											■										
	≤ 0.5	> 0.5													■	■	■	■					
Erythromycin	≤ 0.25	> 0.25													■	■	■	■					
	≤ 1	> 1											■										
	≤ 4	> 4									■[2]												
	≤ 8	> 8										■[2]											
Fluconazole	≤ 0.001	> 16																		■			
	≤ 2	> 4																	■		■	■	■
Fosfomycin	≤ 8	> 8	■																				
Fusidic acid	≤ 1	> 1											■										
Gentamicin	≤ 2	> 2	■	■							■[1]	■[1]	■										
	≤ 128	> 128												■									
Imipenem	≤ 0.001	> 4												■[5]									
Linezolid	≤ 4	> 4											■	■									
Mecillinam	≤ 8	> 8	■	■																			
Meropenem	≤ 2	> 2			■																		
	≤ 2	> 8	■	■				■[2]	■[2]	■[2]													
Micafungin	≤ 0.016	> 0.016																					
	≤ 0.03	> 0.03																	■	■			
	≤ 0.06	> 0.06																			■		■
	≤ 4	> 4																				■	
Mupirocin	≤ 1	> 256											■										
Nitrofurantoin	≤ 64	> 64	■																				
Pefloxacin	≥ 23 mm	< 23 mm						■[1]															
	≥ 24 mm	< 24 mm						■	■[2]														

Antimicrobials	MIC (mg/L) S	MIC (mg/L) R	*Escherichia coli*	*Klebsiella* spp.	*Haemophilus influenzae*	*Neisseria meningitidis*	*Neisseria gonorrhoeae*	*Salmonella* spp.	*Shigella* spp.	*Yersinia enterocolitica*	*Campylobacter jejuni*	*Campylobacter coli*	*Staphylococcus aureus*	*Enterococcus* spp.	*Streptococcus pneumoniae*	*Streptococcus pyogenes*	*Streptococcus agalactiae*	*Streptococcus dysgalactiae*	*Candida albicans*	*Candida glabrata*	*Candida tropicalis*	*Candida parapsilosis*	*Candida dubliniensis*
Penicillin G	≤ 0.03	> 0.03														■		■					
	≤ 0.06	> 1					■								■								
	≤ 0.125	> 0.125															■						
	≤ 0.25	> 0.25				■																	
Pip-Tazo**	≤ 8	> 8	■	■																			
Rifampicin	≤ 0.06	> 0.06											■										
	≤ 0.25	> 0.25				■																	
Spectinomycin	≤ 64	> 64					■																
Tetracycline	≤ 0.5	> 0.5					■																
	≤ 1	> 1											■		■	■	■	■					
	≤ 2	> 2			■	■					■[2]	■[2]											
	≤ 4	> 4								■[1]													
	≤ 8	> 8						■[1]															
	≥ 17 mm	< 17 mm						■[3]	■[3]	■[3]													
Tigecycline	≤ 0.5	> 0.5	■										■	■									
Trimethoprim	≤ 4	> 4	■	■																			
TMS***	≤ 0.5	> 1			■																		
	≤ 1	> 2													■	■		■					
	≤ 2	> 4	■	■									■										
Vancomycin	≤ 2	> 2											■				■						
	≤ 4	> 4												■									
Voriconazole	≤ 0.06	> 0.25																	■				■
	≤ 0.125	> 0.25																			■	■	

*Amoxi-Clav=Amoxicillin-clavulanic acid. **Pip-Tazo=Piperacillin-Tazobactam. ***TMS Trimethoprim-sulfamethoxazole. Breakpoints for the combination are given for the trimethoprim component only. [1]Epidemiological cut-off value (ECOFF) based on wild type distribution by EUCAST applied to separate between wild type and non-wild type populations. [2]EUCAST clinical breakpoints or screening cut-off values applied to separate between wild type and non-wild type populations. [3]There are no clinical breakpoints for tetracycline for *Salmonella*, *Shigella* and *Yersinia*. A clinical breakpoint of R < 17 mm based on national data was applied for all three species, and also as screening breakpoint for *Shigella*. [4]*Klebsiella* spp. breakpoints for amoxicillin-clavulanic acid do not apply to *K. aerogenes*. [5]*Enterococcus* spp. breakpoints for imipenem do not apply to species other than *E. faecalis*.

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